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MEDICAL NUTRITION IN ONCOLOGY: POTENTIAL SOLUTION FOR MANAGING MALNUTRITION IN CANCER PATIENTS IN SWITZERLAND

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Medical Nutrition in Oncology: Potential solution for managing malnutrition in cancer patients in Switzerland

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ABBREVIATIONS

WHO – World Health Organization

QoL – Quality of Life

EN – Enteral Nutrition

TPN – Total Parenteral Nutrition

REE – Resting Energy Expenditures

TEE – Total Energy Expenditures

TNF-α – Tumor Necrosis Factor alpha

IL-1 – Interleukine 1

IL-6 – Interleukine 6

IFN-γ – Interferon gamma

LIF - Leukemia inhibitory factor

PIF - Proteolysis-inducing factor

LMF – Lipid mobilizing factor

IL-1β - Interleukin 1 -beta

LBM – Lean Body Mass

EORTC QLQ-C30 –European Organization for Research and Treatment of Cancer questionnary

FACT-G – Functional Assessment of Cancer Therapy General Scale

SF-36 – Short Form health survey

FSMP – Food for Special Medical Purpose

ONS – Oral Nutritional Supplements

EPA – Eicosapentaenoic acid

BMT – Bone Marrow Transplantation

HPN – Home Parenteral Nutrition

BMI – Body Mass Index

ESPEN – European Society for Parenteral and Enteral Nutrition

MUST – Malnutrition Universal Screening Tool

BAPEN – British Association for Parenteral and Enteral Nutrition

NRS – 2002 – Nutritional Risk Screening

MNA – Mini Nutritional Assessment

1. INTRODUCTION

The term “cancer” describes a wide range of malignant tumours, which may affect almost every organ and tissue of the body. It is essentially a consequence of genetic mutations within a cell, which result in the proliferation of abnormal cells.

In majority of patients, the cause of cancer is unknown. About 5% of all cases result from inherited genetic mutations and 95% of cases are defined as sporadic, which means that they are unpredictable consequence of a combination of genetic, environmental and chance factors.

Cancer is a leading cause of death worldwide. According to World Health Organization (WHO), the disease accounted for 7.4 million deaths (or around 13% of all deaths worldwide) in 2004. The main types of cancer leading to overall cancer mortality each year are:

- lung (1.3 million deaths)
- stomach (803 000 deaths)
- colorectal (639 000 deaths)
- liver (610 000 deaths)
- breast (519 000 deaths).

Deaths from cancer worldwide are projected to continue rising, with an estimated 12 million deaths in 2030.

Cancer rates could as well further increase by 50% to 15 million new cases in the year 2020, according to the World Cancer Report, the most comprehensive global examination of the disease to date.

The predicted sharp increase in new cases, from 10 million new cases globally in 2000, to 15 million in 2020, will mainly be due to steadily ageing populations in both developed and developing countries and also to current trends in smoking prevalence and the growing adoption of unhealthy lifestyles.

Patients with cancer may develop a wide range of symptoms and side effects due to the oncology treatment. Nutrition related symptoms, such as weight loss and malnutrition, reflect impaired nutritional status, which is often associated with reduced quality of life and response or tolerance to cancer treatment. In addition, it is well known that anticancer therapies may produce significant side effects, such as altered perception of taste and smell, food aversions, nausea and vomiting, mucositis, bowel change and early satiety (Figure 1) (Benjamin HL et al. 2008). Depending on the type of cancer treatment (either curative or palliative) and on patients’ clinical conditions and nutritional status, adequate and patient-tailored nutritional intervention should be prescribed (nutritional counselling, oral supplementation, enteral or total parantral nutrition). Such an approach, which should be started as early as possible, can reduce or even reverse the patients’ poor nutritional status, improve their performance status and consequently their quality of life (QoL).

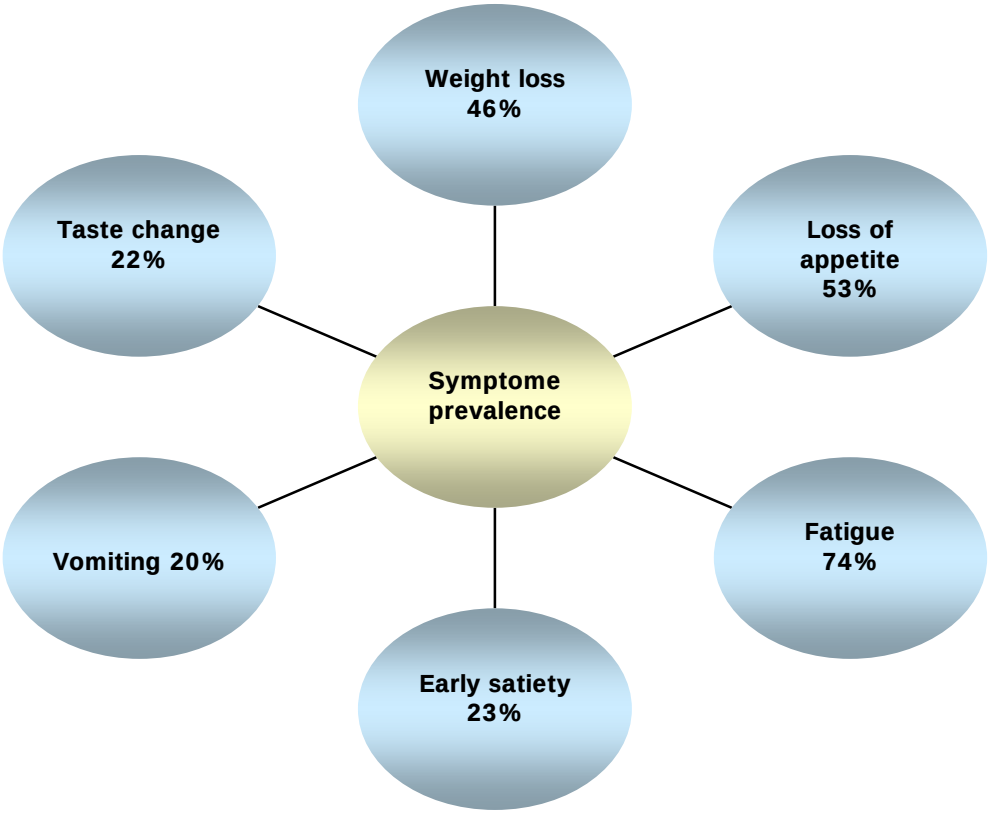

Figure 1: Prevalence of cancer-related symptoms and side-effects (Benjamin HL et al. 2008)

Despite growing evidence that nutritional support improves patients' clinical outcome, its use is not widely considered as a routine by most healthcare professionals. Many factors, depending on physicians, patients and institutions, could explain such a resistance to implement nutritional therapy in routine care. One of these factors is as well the lack of indisputable evidence that nutritional intervention improves patients' quality of life and it is cost-effective.

2. OBJECTIVE OF THE STUDY

The increasing prevalence of cancer and its related complications requires that personalized and specific nutritional intervention should be delivered concomitant with oncology treatment in order to improve performance status, quality of life and health care cost.

The nutritional needs of patients with cancer may differ from those of the healthy population due to hypermetabolism, impaired organ function, increased nutrient losses and therapy-related malnutrition.

In order to ensure sufficient nutritional care it is mandatory to identify the effect of malnutrition and nutritional care on direct cost and reimbursement.

The objective of this study is to:

- Describe the cancer related complications, prevalence and economic burden of cancer
- Provide the review of the studies that have been done until now proving that specialized nutrition can improve QoL, shorten the length of hospital stay and reduce overall cost of patients care
- Describe different types of specialized nutritional support and tools/guidelines used for nutritional screening
- Justify the use of specialized nutrition as an integral part of cancer treatment

Specialized nutrition should help in controlling cancer-related symptoms, reduces postoperative complications and infection rate, shortens length of the hospital stay, improves tolerance to treatment, and enhances immunometabolic host response. By decreasing the length of the hospital stay, reducing the utilization of medical services for cancer related problems and by improving the nutritional status of the cancer patients, specialized nutrition should show the advantages by controlling and reducing the overall cost of patients care for hospitals and health insurances.

3. PART 1: GENERAL OVERVIEW OF CANCER

3.1 CLASSIFICATION OF CANCER

Classification of cancer determines appropriate treatment and helps determine the prognosis. Cancer develops progressively from an alteration in a cell's genetic structure due to mutations, to cells with uncontrolled growth patterns. Classification is made according to the **site of origin**, histology (or cell analysis; called **grading**), and the extent of the disease (called **staging**).

Site of Origin

This classification describes the type of tissue in which the cancer cells begin to develop.

Here are some common examples of site of origin classification:

- Adenocarcinoma - originates in glandular tissue
- Blastoma–originates in embryonic tissue of organs
- Carcinoma–originates in epithelial tissue (i.e., tissue that lines organs and tubes)
- Leukaemia–originates in tissues that form blood cells
- Lymphoma–originates in lymphatic tissue
- Myeloma–originates in bone marrow
- Sarcoma–originates in connective or supportive tissue (e.g., bone, cartilage, muscle)

Grading

Grading involves examining tumour cells that have been obtained through biopsy under a microscope. The abnormality of the cells determines the grade of the cancer. Increasing abnormality increases the grade, from 1 - 4. Cells that are well differentiated closely resemble mature, specialized cells. Cells that are undifferentiated are highly abnormal, that is, immature and primitive.

Grade 1	Cells slightly abnormal and well differentiated
Grade 2	Cells more abnormal and moderately differentiated
Grade 3	Cells very abnormal and poorly differentiated
Grade 4	Cells immature and undifferentiated

Staging

Staging is the classification of the extent of the disease. A numerical system is most frequently used to classify the extent of disease.

Stage 0	Cancer in situ (limited to surface cells)
Stage 1	Cancer limited to the tissue of origin, evidence of tumour growth, no remote metastases
Stage 2	Locally limited extension with/without minimal node satellite extension and with no remote metastases
Stage 3	Extensive local and regional spread with/without major node satellite extension and with no remote metastases
Stage 4	Locally advanced tumour and/or distant metastases

3.2 PATHOPHYSIOLOGIE AND CLINICAL COMPLICATIONS

Weight loss, malnutrition, anorexia and cachexia are common in cancer patients, negatively affecting their quality of life and treatment outcomes.

3.2.1 Weight loss

Weight loss is one of the factors that define malnutrition in patients with cancer and is a major cause of morbidity and mortality. Patients with pancreatic or gastric cancer appear to have the highest prevalence of weight loss; also, patients with head and neck, oesophageal or lung cancer often lose weight. It has been reported that 54% of patients had experienced weight loss prior to treatment: less than 5% of weight had been lost in 22% of patients, 5-10% in 17% and 15% of patients had lost over 10% of their normal body weight, suggesting cancer-associated nutritional decline occurs before clinical symptoms arise (Argilés, 2005). The extent of weight loss varies, with up to 45% of cancer patients experiencing severe weight loss, losing more than 10% of their pre-treatment body mass during the course of the disease.

Weight loss depends as well of the stage of the disease; it is greater in patients with stage III/IV disease than in those with stage I/II (Figure 2) (Ravasco et al. 2004).

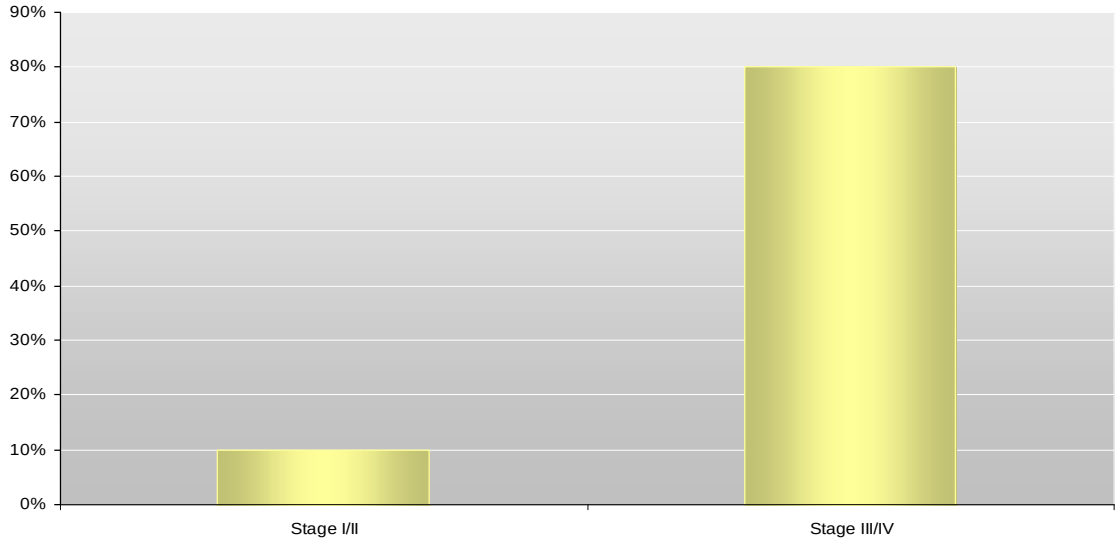

Figure 2: Percent of patients experiencing weight loss (>10%) based on stage of cancer (Ravasco et al. 2004)

The prognostic effect of weight loss prior to chemotherapy was analysed in 3047 patients enrolled in 12 different studies. (DeWys et al. 1980) Patients with breast, colon, prostate, lung or gastric cancer who had experienced no weight loss lived longer (Figure 3).

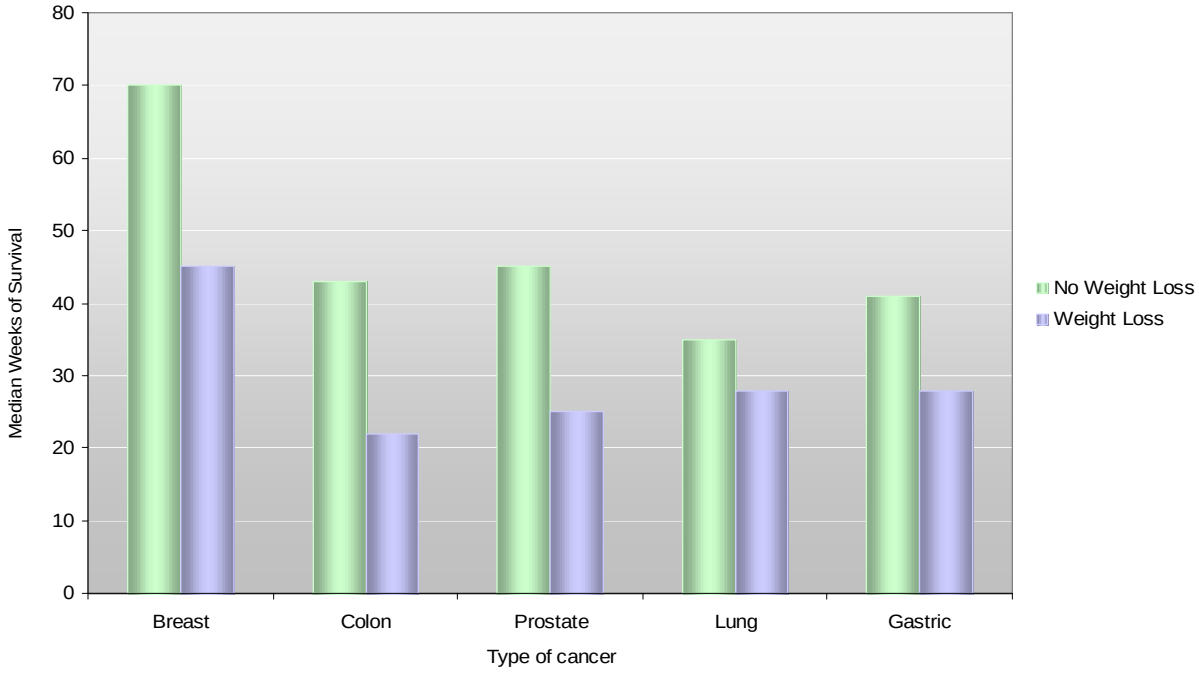

Figure 3: Effect of weight loss on survival (DeWys et al. 1980)

Chemotherapy response rates were lower in the patients with weight loss, but only in patients with breast cancer this difference was significant. Decreasing weight was correlated with decreasing performance status except for patients with pancreatic and gastric cancer. Within performance status categories, weight loss was associated with decreased median survival. The frequency of weight loss increased with increasing number of anatomic sites involved with metastases, but within categories of anatomic involvement, weight loss was associated with decreased median survival.

3.2.2 Malnutrition

The global incidence of malnutrition in cancer patients ranges from 30% to 85% being most prevalent in patients with gastric, pancreatic, lung, prostate and colon cancer (Argiles, 2005). In addition to the type, location, grade and stage of cancer, the incidence of malnutrition is also affected by anticancer treatments and patient characteristics including age, gender and individual susceptibilities. Cancer-associated malnutrition occurs when the nutritional needs of the patient are not met due to poor food intake, absorption and/or assimilation, and increased nutrient losses due to the tumour metabolism. At the time of diagnosis, approximately 75% of cancer patients are malnourished (Argiles, 2005).

The prevalence of malnutrition for different type of cancer is expressed in table 1.

Table 1: Prevalence of malnutrition for different type of cancer (von Meyenfeldt, 2005)

Tumour site	Prevalence of malnutrition (%)
Pancreas	80 – 85
Stomach	65 – 85
Head and neck	65 – 75
Oesophagus	60 – 80
Lung	45 – 60
Colon/Rectum	30 – 60
Urogical	10
Gynaecological	15

Competition for nutrients between the tumour and the host can result in an accelerated starvation state which further promotes metabolic disturbances, including increased metabolic rate, and hence resting energy expenditure (REE) and energy inefficiency (Moses et al., 2004) Metabolic changes associated with cancer affect the metabolism of protein, fat and carbohydrate (Tisdale, 2001).

Hypermetabolism is common and abnormal plasma amino acid profile, increased gluconeogenesis and changes in liver and muscle protein turnover are present in patients with cancer. In healthy subjects, muscle amino acids and some visceral proteins are used as precursors for neoglucogenesis. Protein catabolism decreases slowly and functional lean body mass is more or less preserved. This adaptive mechanism seems to be absent in cancer, leading to noticeable protein depletion and muscle atrophy. The metabolic alteration associated with this process includes an increase in protein turnover, reduction in muscle protein synthesis and an increase in hepatic protein synthesis. Hepatic production of glucose is also increased in patients with cancer. However, due to insulin resistance and glucose intolerance, this is poorly used by peripheral tissues. Additionally, some tumours consume large amounts of glucose, suggesting that these tumours can act as “metabolic traps” (Martignoni et al. 2003). Increase mobilisation of peripheral fat and excessive oxidation of fatty acids are the most consistent metabolic abnormalities observed. Derangement in lipid metabolism can lead to increased lipolysis and lipid oxidation and decreased lipogenesis and thus to weight loss.

Nutritional status and food intake are also influenced by disease stage and treatment associated side effects. The ten most common symptoms which are pain, fatigue, weakness, anorexia, weight loss, lack of energy, dry mouth, constipation, dyspnea and early satiety can have a significantly negative impact on nutritional status.

The consequences of cancer-associated malnutrition are presented in the figure 4.

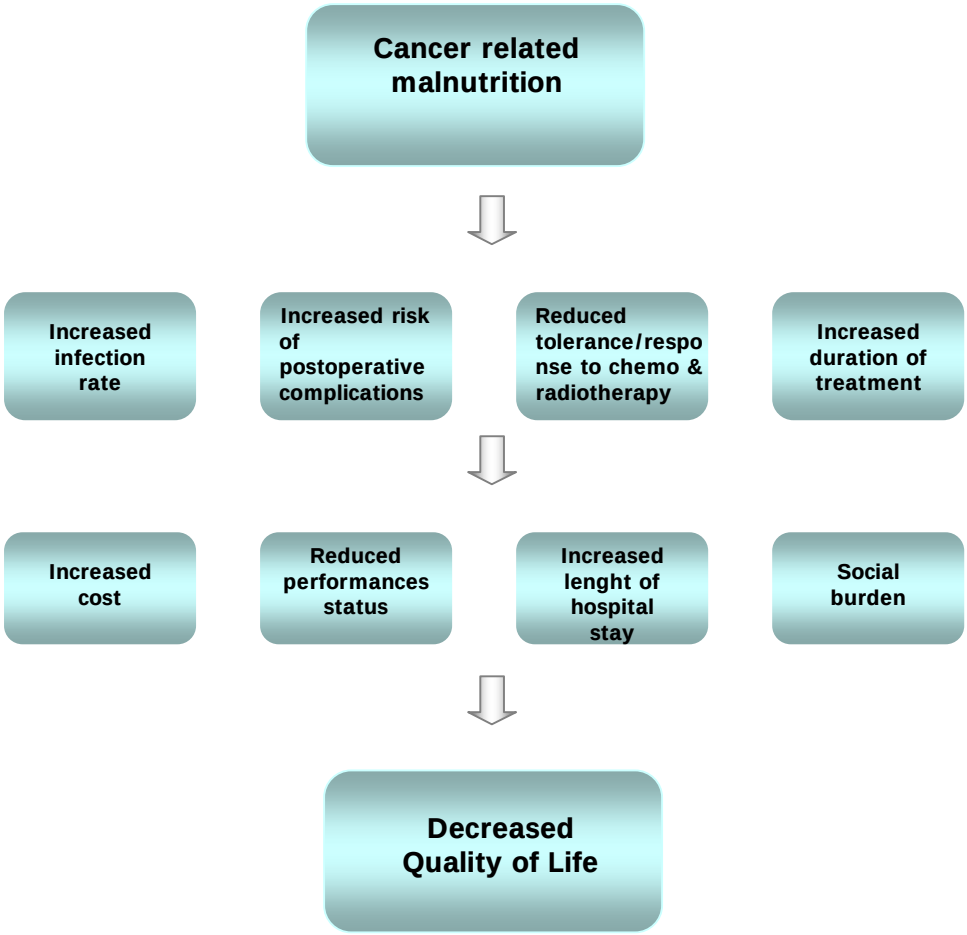

Figure 4: Consequences of cancer-associated malnutrition (Caro MM et al., 2006)

Prolonged malnutrition can result in cachexia.

3.2.3 Cachexia

Cancer cahexia is a specific form of cancer associated malnutrition, often occurring in patients with advanced disease. The condition is characterised by progressive, involuntary weight loss with depletion of lean body mass and muscle wasting. Additional features associated with cachexia include anorexia, chronic nausea and weakness, fatigue, depression and overall reduction in quality of life (Bruera, 1997). The pathogenesis of cachexia is complex, involving at least two major processes: malnutrition due to anorexia and major alterations in host metabolism causing tumor-induced weight loss, or cachexia (Sharma and Anker, 2002). Poor food intake and anorexia affect approximately 60 to 70% of patients with cancer (Tchekmedyian, 1995). Segura et al. (2005) noted that serious eating problems were encountered in 68% of advanced cancer patients, with the main problem being anorexia (42.2%). Although anorexia contributes to malnutrition and cachexia in cancer patients, many of the changes in body composition and the severe weight loss of cancer cachexia are thought to be the result of tumor-induced pathophysiological changes in normal metabolism (Tisdale, 2001a and b).

Cachexia is a significant cause of morbidity and mortality, occurring in 50 to 80% of cancer patients (Gordon, 2005).

Different tumors display varying propensities to induce cachexia, with it most commonly seen in subjects with gastrointestinal, lung and prostate cancers, in contrast to haematological and breast malignancies where it is rare. With the exception of breast cancer, patients with

solid tumors are at greater risk of developing cachexia.

In cachexia patients may first notice simple weight loss and then progress through degrees of severity to the point where they are depleted of energy reserves, have gross muscle wasting, are immunocompromised, and will die primarily as a result of these issues. The initial phase (precachexia) may have little impact, whereas the advanced phase (cachexia syndrome) will impact on both quality and quantity of life. Three key features of cachexia that impact on patients are weight loss (>10%), systemic inflammation (C-reactive protein >10mg/l), and reduced food intake (< 1500 kcal per day) (Benjamin HL et al. 2008).

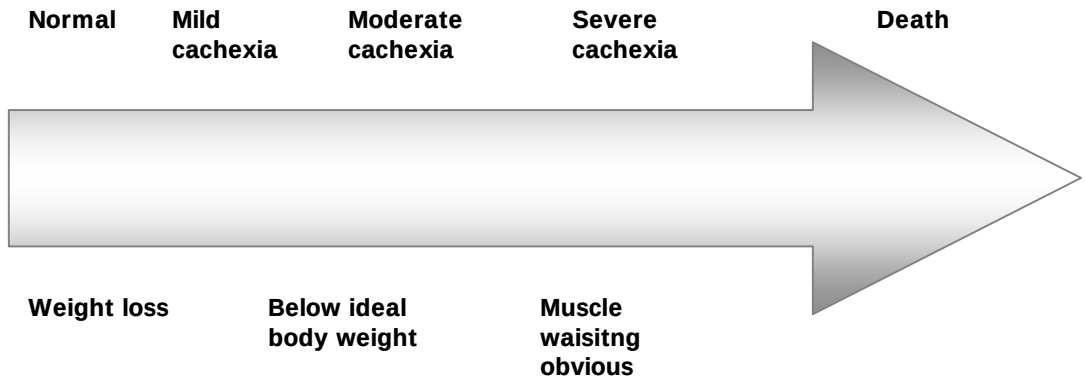

Figure 5: The cachexia journey (Benjamin HL et al. 2008)

Cancer cachexia syndrome includes loss of body fat, predominantly muscle mass and visceral protein, which are used to meet the energy demands of the body. Muscle wasting in the presence of significant weight loss is a hallmark of cachexia. Lung cancer patients, who lost 30% of their pre-illness body weight, experienced an 85% reduction in total body fat and a 75% reduction in skeletal muscle protein (Tisdale, 2002). This loss of lean tissue leads to reduced organ functional capacity and weakness, resulting in immobility and death due to loss of respiratory muscle function. Typically, a weight loss of greater than 15% in cancer patients, results in impaired physiological function, with death commonly occurring in approximately 30% of patients (Tisdale, 2002).

Major metabolic changes occur in the patient with cancer (Argiles et al., 2005; Tisdale, 2001 a, b; Tisdale, 1999). As already mentioned some patients with advanced cancer become hypermetabolic. This abnormality leads to increased energy requirements and impaired response to starvation, including altered insulin sensitivity, protein use and increased cytokine synthesis. The increased metabolic rate and reduced food intake contribute to an overall negative energy balance and accelerated weight loss in the cancer patient.

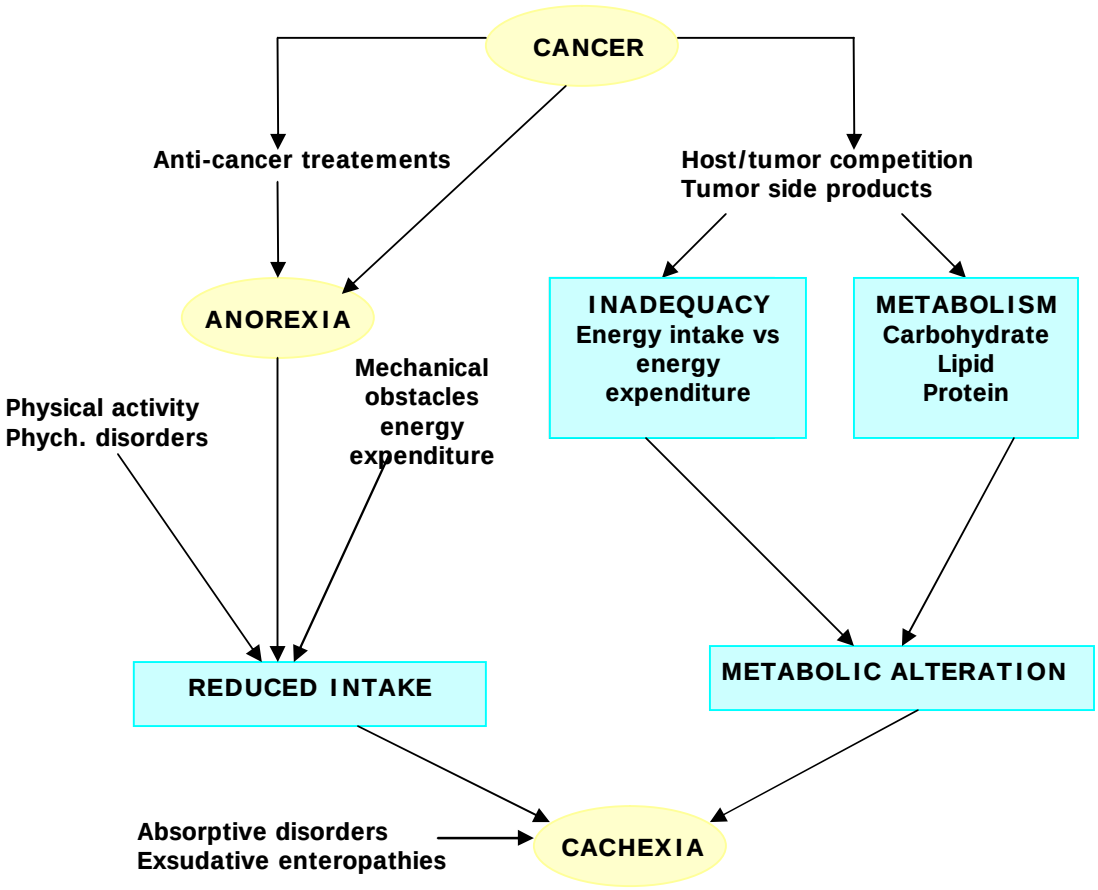

Figure 6: Multifactorial causes of cancer cachexia (Van Cutsem E, Arends J, 2005)

§ Mediators of Cancer Cachexia

The growth of the tumor is accompanied by the production and release of a number of tumor-derived factors which together with host factors such as hormones and cytokines contribute to a cascading pattern of altered metabolism, muscle wasting and poor appetite (Tisdale, 1999; **Table 2**).

Table 2: Mediators of cancer cachexia

Pro-Inflammatory and Procachectic Cytokines	Hormones	Tumor-derived Factors
TNF-α	Cortisol	PIF
IL-1	Hyperglucagonemia	LMF
IL-6	Increased insulin resistance	
IFN-γ		
LIF		

In the fight against cancer, the body's immune system produces a number of pro-inflammatory and pro-cachectic cytokines such as tumor necrosis factor-alpha (TNF-α),

interleukin-1 (IL-1), interleukin-6 (IL-6), interferon-gamma (IFN-γ) and leukemia inhibitory factor (LIF). Experimental studies suggest that these cytokines are involved in the pathogenesis of weight loss by increasing metabolism, promoting muscle protein breakdown, depletion of adipose tissue, and causing insulin resistance (Tisdale, 1999; Barber et al., 2001; Argilés et al., 2003). In addition, hormones such as cortisol, glucagon and insulin, are affected by cancer, disrupting normal metabolism. In cancer cachexia, cortisol is increased, as is glucagon production. Patients with cancer cachexia often have peripheral insulin resistance with apparent hypoinsulinemia (Barrera, 2002).

The tumor itself produces 'factors' that disrupt normal host metabolism. One of these is increasingly recognized as important in weight loss and malnutrition in cancer patients, proteolysis-inducing factor (PIF), which has been coined "the cancer cachectic factor" (Tisdale, 2001a and b; Tisdale, 2003). PIF is a glycoprotein produced by human tumors which has been shown to initiate muscle protein degradation directly through activation of the proteasome pathway and expression of ATP-ubiquitin-dependent proteolytic pathway (Tisdale, 2001a and b; Argilés et al., 2003).

Patients with cachexia may also have high levels of tumor-produced lipid mobilizing factor (LMF) and PIF which stimulate metabolic changes that have a major impact on body composition (Tisdale, 1999; Tisdale, 2001). Tumor-produced LMF causes breakdown of lipids and affects protein synthesis and catabolism, while PIF appears to cause changes in the way that fatty acids and amino acids are handled by adipose tissue and skeletal muscle, respectively.

Massive loss of skeletal muscle mass is the hallmark of cancer cachexia and may be a result of increased levels of tumor-derived factors, cytokines and hormones that cause decreased muscle protein synthesis, and increased muscle protein degradation, all of which can lead to negative protein (nitrogen) balance. In addition to muscle protein loss, cancer cachexia is also associated with increased programmed cell death in the muscle, most probably through PIF and TNF-α (Argilés et al., 2003).

Tumor-induced pathological changes in metabolism are thus associated with cancer cachexia (Tisdale, 2002). Table 3 summarizes events working together that promote cachexia in patients having cancer.

Table 3: Factors contributing to cachexia in patients with solid tumor cancer

Tumor			
↓		↓	
Produces tumor derived factors		Causes inflammatory response, which causes	
↓	↓	↓	↓
Lipid Mobilizing Factor	Proteolysis Inducing Factor	Change in hormones regulation	Synthesis of inflammatory cytokines
↓	↓	↓	↓
Promotes breakdown of fats	Promotes muscle breakdown/increases metabolism	Alters glucose metabolism/increases metabolism	Decreases appetite
↓	↓	↓	↓
Loss of fat tissue	Loss of muscle tissue	Decreases muscle glucose utilization	Decreases food intake
↓	↓	↓	↓
Cachexia (Weight Loss/Muscle Wasting)			

§ Metabolic Alterations in Cachexia

Protein Metabolism

Cancer patients experience an increased rate of body protein breakdown (by 50 to 70%) while protein synthesis fails to keep up. Although the protein-synthetic rate is substantially reduced in cachexia, net loss of protein appears to be related to increase breakdown rather than decreased synthesis of muscle protein. The patient suffering from cachexia are unable to conserve body protein stores and are breaking down muscle protein to provide energy for use in glucose synthesis (Tisdale, 2003). This results in an accelerated rate of skeletal muscle protein breakdown and reduced rate of protein synthesis, causing an elevated state of protein catabolism (Kotler, 2000). Stimulation of protein synthesis requires an optimal plasma profile of amino acids, particularly the branched chain amino acids. It is thus especially important to encourage the consumption of calorically dense, high protein nutritional supplements that can promote muscle protein synthesis (Ravasco et al., 2003, 2004).

Lipid Metabolism

Cachexia results in increased llipolysis, decreased lipogenesis, hyperlipidaemia, raised circulated levels of free fatty acids and glycerol, and ultimately the loss of large amount (up to 85%) of adipose tissue. Some of these changes may be mediated by pro-inflammatory cytokines, such as tumor-necrosis factor α (TNFα), interferon γ (INFγ) and interleukin 1β (IL-1β), all of which can inhibit lipoprotein lipase, preventing adipocytes from extracting fatty acids from plasma lipoproteins for storage. More recently, patients with cachexia have been found to excrete a lipid-mobilizing factor (LMF) in their urine. This factor acts directly on adipocytes to stimulate lipolysis (Younes, 2000).

Carbohydrate Metabolism

Carbohydrate metabolism is also altered in cancer patients. Glucose breakdown is increased in association with increased energy demands and tumor burden (Albrecht and Canada, 1996; Kotler, 2000). Glucose intolerance, hyperglycemia and delayed glucose clearance are frequently observed in cancer patients. Insulin resistance has been observed in gastrointestinal cancer patients. Table 4 summarizes the alterations in macronutrient metabolism associated with cachexia.

Table 4: Metabolic alterations in cachexia

Protein	Lipid	Carbohydrate
↑ protein breakdown	↑ fat breakdown	↑ glucose utilization
↑ skeletal muscle protein breakdown	↓ fat synthesis	↑ glucose synthesis
↓ synthesis of skeletal muscle protein	↓ serum lipoprotein lipase activity	Glucose intolerance
↑ synthesis of acute phase proteins	↑ blood lipids	Insulin resistance
↑ urinary nitrogen loss		Hyperinsulinemia

The mechanisms beyond the classical host-tumour interaction that may also contribute to the deterioration of nutritional status of cachectic cancer patients are explained below:

§ Age

Most patients with cancer are aged over 70 years (Skipworth et al., 2007). Moreover, the main reason for a persistent rise in the incidence of cancer in Western society is the increasing

age of the population in general. From the age of 50 years onwards, aging is associated with the degenerative loss of skeletal muscle, a condition known as sarcopenia. Furthermore, sarcopenia is exacerbated by chronic illness inadequate diet and inactivity. However, one of the predominant mechanisms appears to be the anabolic resistance of elderly muscles to post-prandial amino acid loading (Skipworth et al., 2007). Normally, in the physiological post-absorptive state there is a negative balance between whole-body protein synthesis and degradation. Any protein loss is immediately made-up in the post-prandial state by protein gain stimulated by nutrient intake. Sarcopenia appears to be, at least partially, the result of deficit in intracellular anabolic signalling pathways normally involved in these processes. Although the basal (post-absorptive) rates of muscle protein synthesis are similar between elderly and young human muscle, elderly muscle demonstrates less anabolic sensitivity and responsiveness of protein synthesis to essential amino acids (Skipworth et al., 2007).

- **Physical activity**

Cancer patients may lose weight despite a normal food intake, implying that resting energy requirements are increased. However, in practice, measured resting energy expenditure (REE) levels have been variable. Indeed increased, normal and reduced REE have all been described in cancer patients. One possible answer is that the different histological tumour types (and stage of disease) may have different effects on REE (e.g. lung and pancreatic cancer may induce and increased REE, while gastric and colorectal cancer have little impact). Although REE may be increased in some hypermetabolic, wasted cancer patients, total energy expenditure (TEE) may actually fall due to a reduction in physical activity. It has been proven that the physical activity level, in cancer patients, was much lower than the one recorded in healthy adults of similar age. It is well known that low level of activity can exacerbate sarcopenia and cause deconditioning and deterioration in skeletal muscle mass (Skipworth et al., 2007). The reduction in whole-body protein with physical inactivity is a result of the loss of the stimulatory effect of physical activity on amino-acid mediated promotion of muscle protein synthesis. The loss of anabolic stimulation by physical activity only tends to affect bed-rested individuals during the fed state; their protein balance is similar to that observed in healthy controls during the fasted state. These facts suggest that a supra-normal protein intake is required to achieve the same post-prandial anabolic effect during muscle inactivity and cachexia. It also points to the importance of maintaining even modest levels of physical activity.

In relation to the approval of novel therapeutics for cachexia, regulatory authorities suggest that it is important not only to show efficacy for improved nutritional status such as lean body mass (LBM) but also functional status such as performance status. Ongoing weight loss has been the main criteria used to enter patients into either mechanistic studies or therapeutic trials. However it is not clear to what extent weight loss alone is associated with adverse functional status. Poor physical function in cachexia may relate to many factors, including loss of body mass, reduced substrate supply (food intake), or fatigue or depression; all of which have been related at least in a part, to the systemic inflammation (Skipworth et al., 2007).

3.3 TREATMENT OF CANCER

Choice of cancer treatment is influenced by several factors, including the specific characteristics and type of cancer; the patient's overall condition; and whether the goal of treatment is to cure the cancer, keep the cancer from spreading, or to relieve the symptoms caused by cancer. Depending on these factors, the patient may receive one or more of the following treatments:

- **Chemotherapy**
- **Radiation therapy**
- **Surgery**
- **Immunotherapy**
- **Hormone therapy**
- **Other treatment methods (gene therapy, bone marrow transplantation, angiogenesis inhibition therapy, etc.)**

3.4 SIDE EFFECTS OF CANCER TREATEMENT

3.4.1 Nausea and Vomiting

Nausea and vomiting are the two most common side effects of cancer treatment, occurring in 21 to 68% of advanced cancer patients (Bruera and Sweeney, 2002). Nausea and vomiting can affect the amount and types of food eaten during treatment and nausea may be even more distressing for patients than vomiting. It is thus very important to prevent and control nausea and vomiting in patients with cancer. Uncontrolled nausea and vomiting can interfere with the patient's ability to receive cancer treatment and care for himself or herself by causing chemical changes in the body, loss of appetite, physical and mental difficulties and the reopening of surgical wounds. Patients who have advanced cancer commonly experience chronic nausea and vomiting, which can significantly impair quality of life. Radiation therapy may also cause nausea and vomiting, especially in patients who are undergoing radiation to the GI tract (particularly the small intestine and stomach) or brain. The risk for nausea and vomiting increases as the dose of radiation and area being irradiated increases.

3.4.2 Gastrointestinal complications

Gastrointestinal complications (constipation, bowel obstruction, and diarrhea) are common problems in oncology patients. The growth and spread of cancer, as well as its treatment, contribute to these conditions. **Constipation** is the slow movement of feces through the large intestine that results in the passage of dry, hard stool, and can result in discomfort or pain. The longer the transit time of stool in the large intestine, the greater the fluid absorption and the drier and harder the stool becomes. Functional disorders such as inactivity, immobility, or physical and social impediments (particularly inconvenient bathroom availability) can contribute to constipation. Depression and anxiety caused by cancer treatment or cancer pain can lead to constipation, either alone or with other functional and physiologic disorders.

The most common causes of constipation are inadequate fluid intake and pain medications; however, these causes are manageable. **Fecal impaction** can be life-threatening. Impaction refers to the accumulation of dry, hardened feces in the rectum or colon. The patient with a fecal impaction may present with circulatory, cardiac, or respiratory symptoms rather than with gastrointestinal symptoms. If the fecal impaction is not recognized, the signs and symptoms may progress and result in death. **Diarrhea** can occur throughout the continuum of cancer care, and the effects can be physically and emotionally devastating. Although less prevalent than constipation, diarrhea remains a significant symptom burden for people with cancer. Diarrhea can alter dietary patterns, trigger dehydration, create electrolyte imbalance, impair function, cause fatigue, impair skin integrity, limit activity, and in some cases, be life threatening. Furthermore, diarrhea can lead to increased caregiver burden.

Specific definitions of diarrhea vary a lot. Acute diarrhea is generally considered to be an abnormal increase in stool liquid that lasts more than 4 days but less than 2 weeks. Another definition suggests that diarrhea is an increase in stool liquidity (more than 300 mL of stool) and frequency (the passage of more than 3 unformed stools) during a 24-hour period. Diarrhea is considered chronic when it persists longer than 2 months.

3.4.3 Oral and Intestinal Mucositis

Cancer patients who develop treatment induced oral or intestinal mucositis have higher hospital costs and longer hospital stays (Elting et al., 2003). Mucositis, an inflammation of lining of the mouth and gastrointestinal tract, is a common side-effect of cancer chemotherapy and/or radiation therapy. Severe inflammation, lesions, ulceration and bleeding can occur in the mouth, esophagus and intestine (Duncan and Grant, 2003). Patients can experience severe pain, cramping, nausea, and gastroenteritis. The severity and nature of the mucositis varies based on the patient's treatment regimen (type, dosage, duration, and sequence; Duncan and Grant, 2003). Among patients with mucositis, food and fluid intake may be drastically limited, and nutrient absorption may be reduced.

Oral mucositis related pain affects a patient's ability to eat, drink, speak, and sleep, thus negatively influencing their nutritional status, quality of life and interrupting their treatment regimen (Goldberg et al., 2004). Oral mucositis is observed in 100% of head-neck cancer patients undergoing radiation therapy, 70-80% of hematopoietic stem cell transplant recipients, 40% of patients receiving primary chemotherapy and 10% of patients receiving adjunctive chemotherapy (Goldberg et al., 2004).

In a retrospective study of 599 patients who developed chemotherapy-induced reduction in bone marrow activity, Elting et al. (2003) noted that intestinal mucositis developed during 37% of 1,236 cycles of chemotherapy. Episodes of bleeding were significantly more common during treatment cycles with gastrointestinal mucositis than during cycles without mucositis (13 versus 8%). Episodes of infection were significantly more common during cycles with mucositis than during treatment cycles without mucositis (73 versus 36%). Gastrointestinal mucositis was associated with both bleeding and infections whereas oral mucositis was associated with infection only. Patients with mucositis require more health resources (Figure 7).

Reasons for increased health resources for patients with mucositis are:

- Increased risk of infection
- Increased risk of infectious complications
- Use of antibiotics
- Increased length of hospital stay

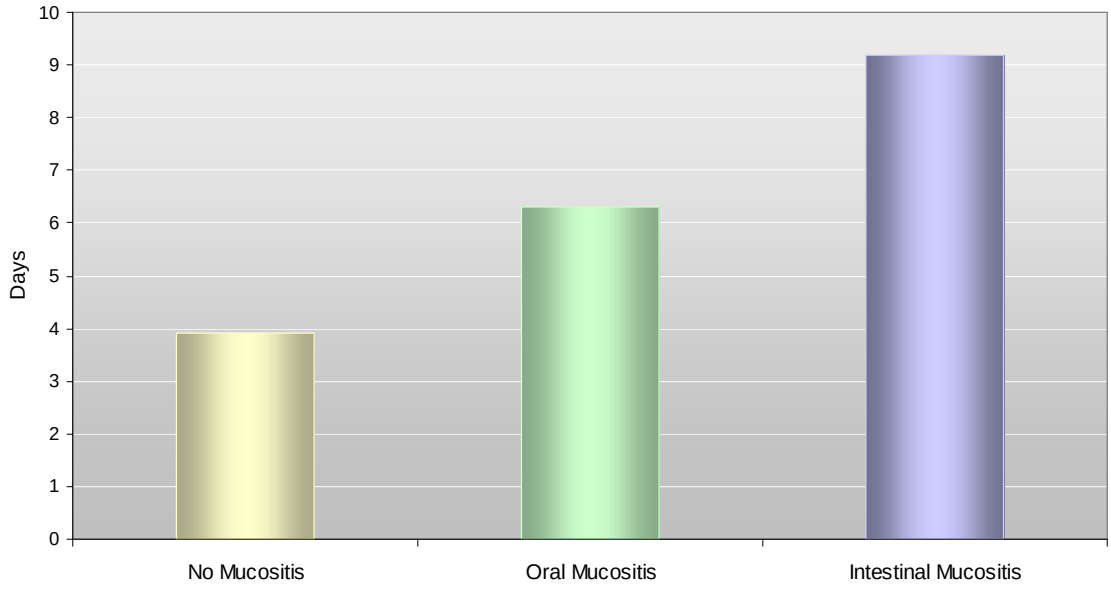

Figure 7: Hospital length of stay (days) for patients with mucositis (Elting et al. (2003))

Worthington et al. (2004) observed the time to heal for oral mucositis ranged from 2.8 to 70.8 days, which can substantially increase health care costs.

Elting et al. (2003) investigated hospital costs of mucositis among bone marrow suppressed patients with solid tumors or lymphoma. Using an average estimated cost per hospital day of $1,000, these investigators estimated an increase in cost per treatment cycle of $2,725 with grade 1-2 mucositis and $5,565 with grade 3-4 mucositis.

Peterman et al. (2001) estimated the mean increase in cost for the treatment of mucositis in head-neck cancer patients ranged from $2,949 to $4,037. This included hospitalization costs for managing pain, nutrition and hydration status. Heath care costs were higher for those with severe mucositis (grades 2-4) than for those with less severe mucositis (grades 0-1).

3.4.4 Stomatitis

Stomatitis, similar to mucositis, is an inflammation of the soft tissues in the mouth resulting in mouth sores. It is also a common side effect of chemotherapy and radiation therapy. Jones et al. (2004) observed the average increase in length of stay in the hospital for breast cancer patients with stomatitis to be 10-14 days, with an average cost per hospital stay increased from £3340 to £4676, further suggesting that the side-effects of cancer therapy are costly to treat.

Mucositis and stomatitis are thus painful side-effects of cancer therapy, which can negatively influence nutritional status, extend healing time, increase both the length of hospitalization and cost of treatment. Nutrition interventions that address these conditions can help improve patient outcomes.

3.5 Cancer Incidence and mortality

In this chapter a number of new cases and number of deaths due to different types of cancer are represented for Europe and Switzerland. It is important to notice that number of new cases is very high as well as the mortality. For some type of cancers, like lung cancer and oesophagus cancer the mortality is close to 100% since the number of new cases and number of deaths for these two types of cancer is almost equal.

3.5.1 Cancer incidence and mortality in Europe

Cancer represents a major global public health problem. Worldwide, it accounts for 7.4 million deaths annually; it is the second most frequent cause of death in Europe, and is becoming the leading cause of death in old age, with more than 70% of cancers occurring in those aged over 65 years. Cancer will affect one in three in the population at some time in their life. In Europe each year there are 2.9 million new cases and 1.7 million deaths from the disease. The prevalence of cancer will continue to increase as a result of the increasing elderly population. Estimates predict that, by 2020, there will be 15 million new cancer cases every year (Boyle, 2005).

In a recent survey of cancer incidence and mortality in Europe, lung cancer accounted for 13.2% (or 381 500 cases) of cases during 2004. Colorectal and breast cancer represented 13% (or 376 400 cases) and 12.8% (370 100) of cases, respectively (Figure 8). Lung cancer was the largest cause of death (341 800 deaths or 20% of all deaths), followed by colorectal (203 700 deaths or 11.9%), stomach (137 900 deaths or 8.1%) and breast cancer (129 900 deaths or 7.6%) (Figure 9) (Boyle, 2005).

In men, lung cancer was most common (19.4%), followed by prostate cancer (15.5%). In women, breast cancer was by far the most common form; with 27.4% new cases diagnosed each year.

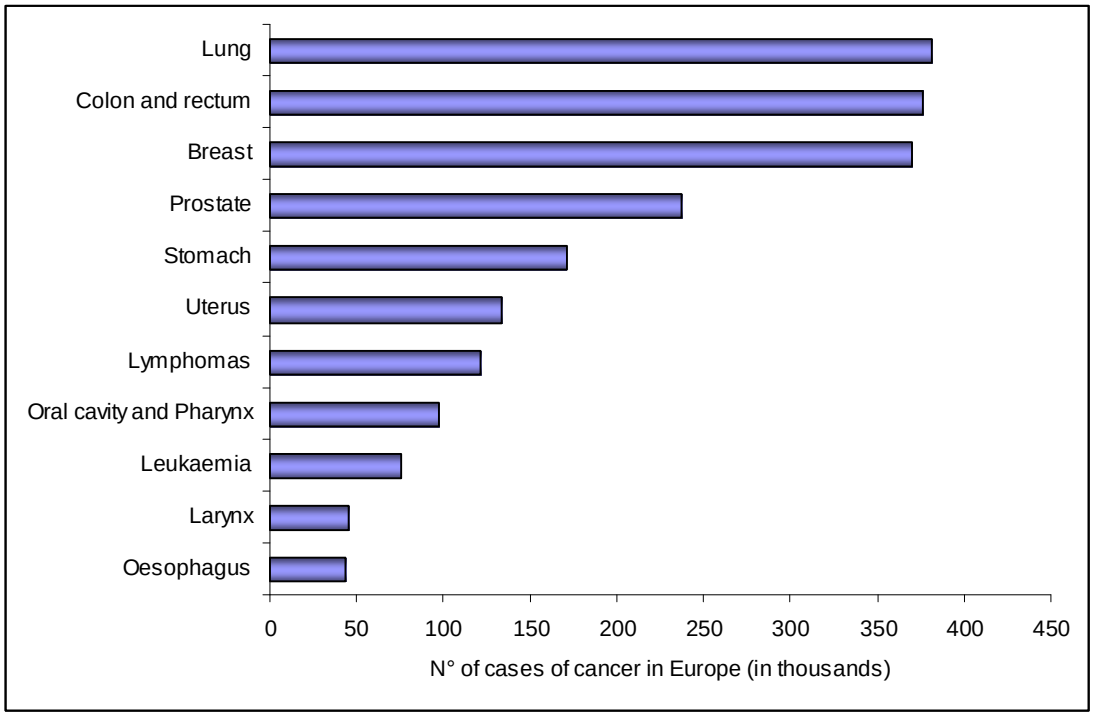

Figure 8: Estimates of numbers of cases of cancer in Europe (both sexes combined) in 2004 (Boyle, 2005)

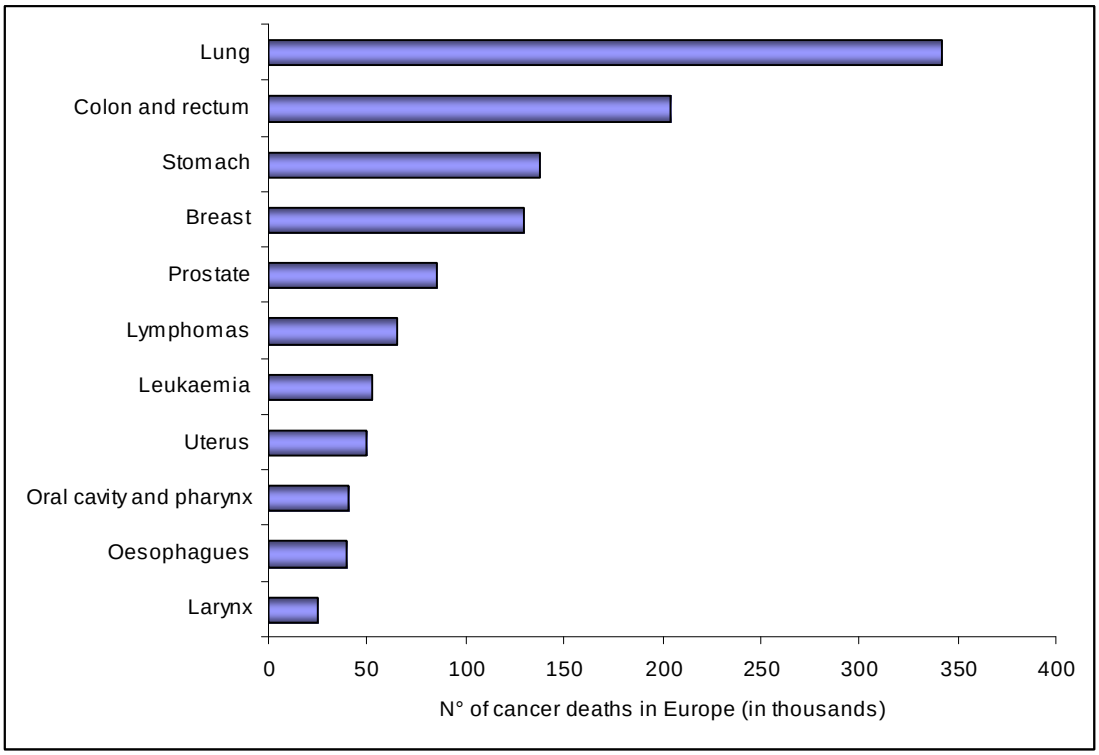

Figure 9: Estimates of number of cancer deaths in Europe (both sexes combined) in 2004 (Boyle, 2005)

3.5.2 Cancer incidence and mortality in Switzerland

According to medical statistics of Swiss hospitals from 2005, hospitalizations due to the cancer are on the fifth place. 54% of patients hospitalized for the cancer treatment are in the age group from 40 to 69 years while 35% are above 70 years old (www.swisscancer.ch).

Table 5: Cause of hospitalization in Switzerland in 2005

Diagnostic group	Number of cases
Osteo-articular system	155 589
Traumatic lesion	148 593
Appareil circulatoire	137 725
Digestive Tract	111 564
Cancer	**94 807**
Pregnancy, Delivery	94 760
Genito-urinary tract	83 585
Mental troubles	77 801
Respiratory tract	69 454
Eyes	44 516

The most prevalent forms of cancer in Switzerland are prostate, breast, colon and rectum and lung cancer (Figure 10).

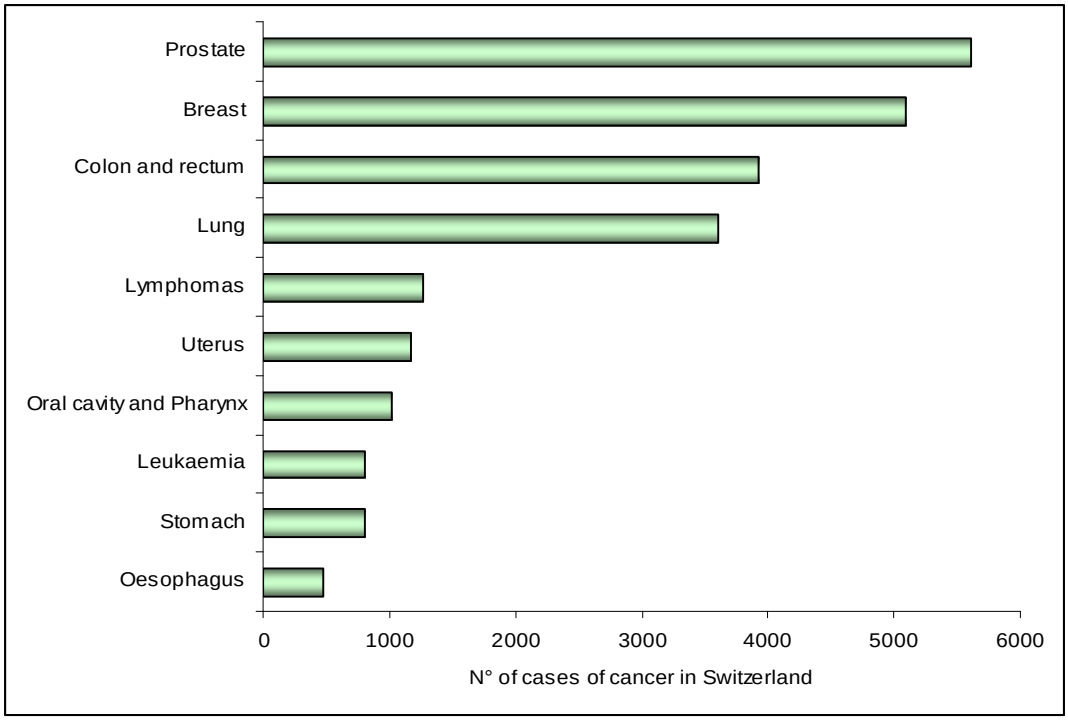

Figure 10: Estimates of number of cancers in Switzerland (both sexes combined) (www.swisscancer.ch)

The incidence of cancer is much higher in population over 50 years old (87%)

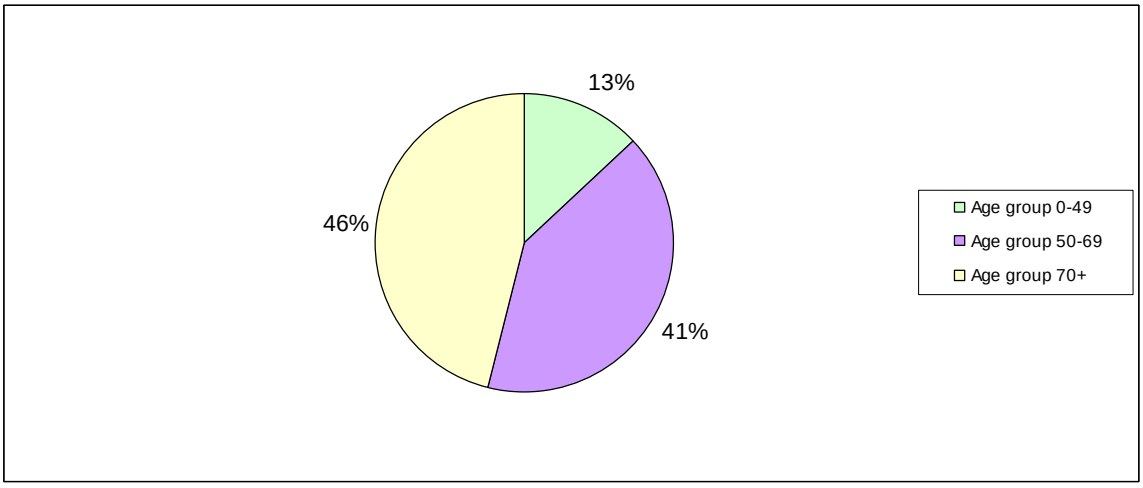

Figure 11: Percentage of new cases of cancer per age group in Switzerland (www.swisscancer.ch)

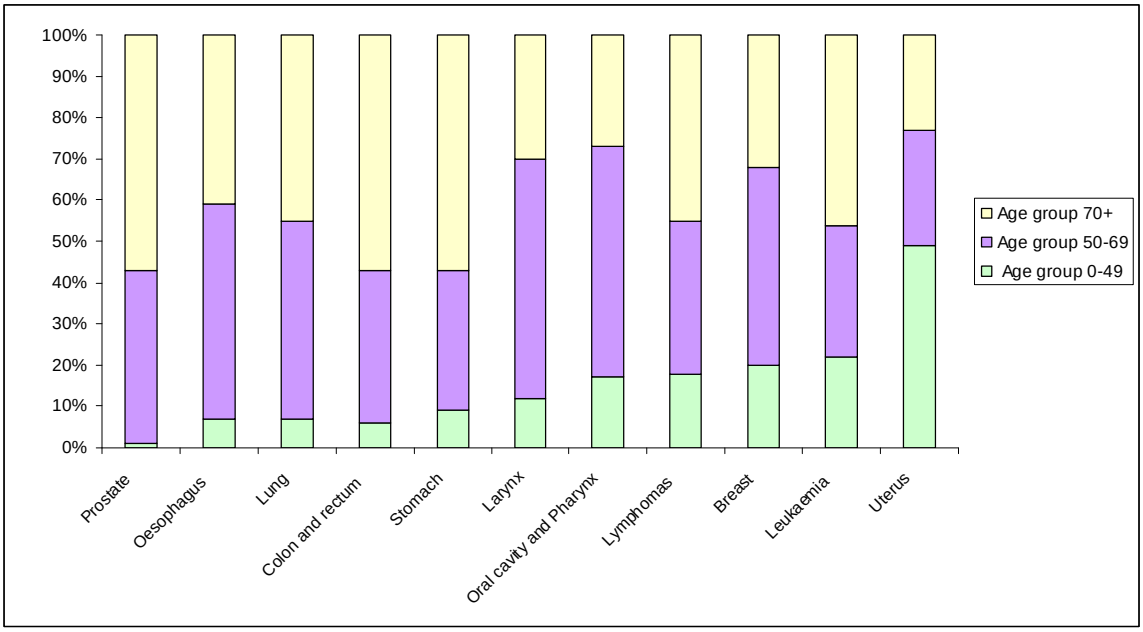

Figure 12: Number of new cases of cancer per cancer type and per age group in Switzerland (www.swisscancer.ch)

Cancer is responsible for 25% of deaths in Switzerland.

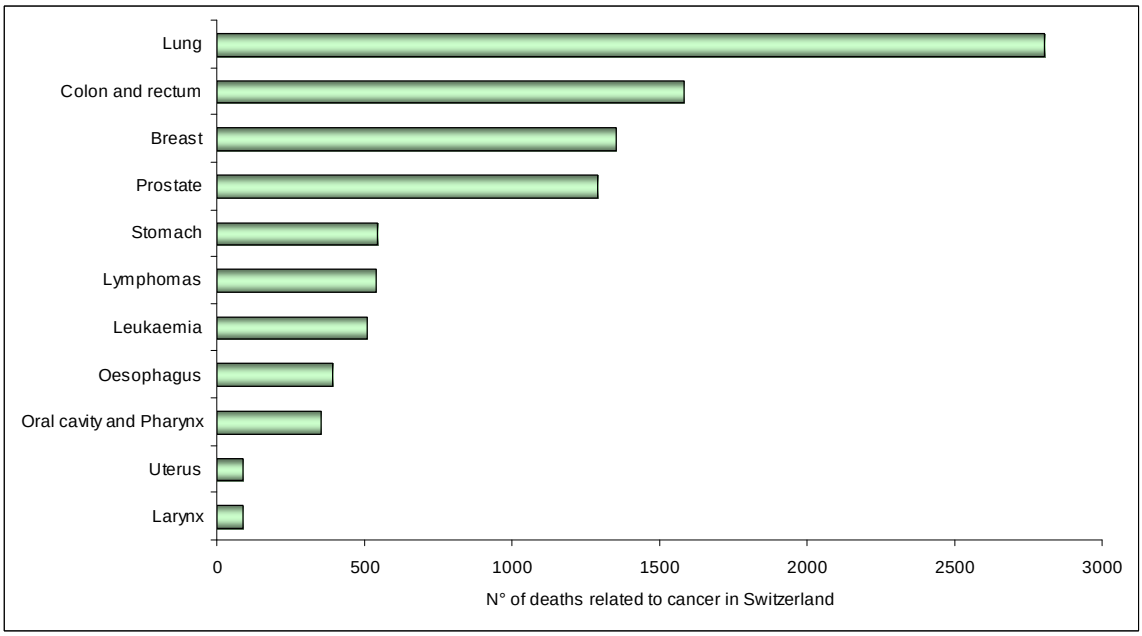

Figure 13: Estimates of number of cancer deaths in Switzerland (both sexes combined) (www.swisscancer.ch)

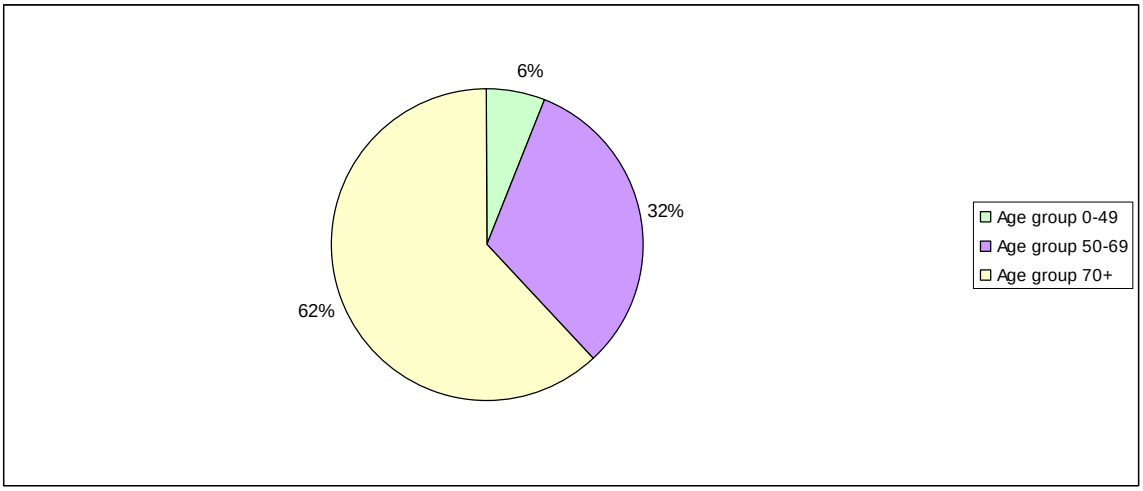

Figure 14: Percentage of cancer related deaths per age group in Switzerland (www.swisscancer.ch)

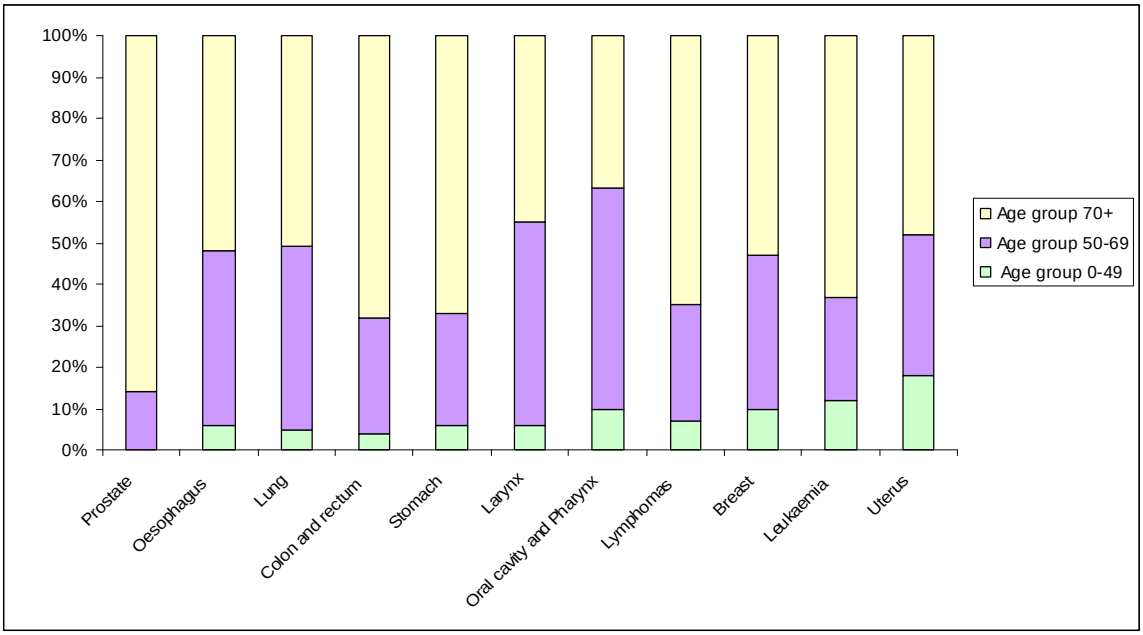

Figure 15: Number of deaths due to the cancer per cancer type and per age group in Switzerland (www.swisscancer.ch)

3.6 ECONOMIC BURDEN OF CANCER

Cost can be broadly categorized into direct and indirect cost. Direct costs quantify resources consumed (medical and nonmedical) that are directly related to the medical interventions, whereas indirect cost (also known as productivity loss) quantify the time consumed or saved by patients and their caregivers as a result of the interventions. Indirect costs are sometimes extended to measure the long term labour market consequences of illnesses or interventions; under these circumstances, indirect costs are further divided into morbidity cost (i.e. productivity loss due to the illness) and mortality costs (i.e. productivity loss due to premature death).

In this sense the economic cost for cachexia extends much further than the cost of

therapeutic diets, nutritional supplements, medication, laboratory tests and supplies. Staff salaries, service costs and other indirect medical costs related to the provision of medical care must also be included. Unfortunately it is difficult to asses accurately the financial cost of cachexia due to the missing data.

Less apparent are the costs associated with managing the consequences of involuntary weight loss. Involuntary weight loss is associated with anaemia, postural hypotension, cognitive dysfunction, falls and hip fractures. Pressure ulcers are another frequent complication seen in patients near the end of the ataxia journey.

Compared to well nourish individuals, malnourished pancreatic cancer patients experience higher risk of infections, slower postoperative wound healing and more than twice the hospital length of stay (Otter, 1996). Twenty (20%) to 40% of mortality among pancreatic cancer patients is attributed to malnutrition and its associated complications (Ottery, 1996).

Average hospital length of stay for a malnourished cancer patient is twice as long as for a well nourished patient with the same diagnosis (Table 6); (Ottery, 1996; Haydock and Hill, 1986).

Table 6: Average hospital length of stay based on nutritional status

Nutritional status	Length of stay (days)
Well-nourished	5.8
Malnourished	13.4

Treatment of the malnourished patient (general medicine and surgery patients) with complications results in higher hospital costs and charges to the patient compared to patients without complications (Reilly et al., 1988) (Figure 16).

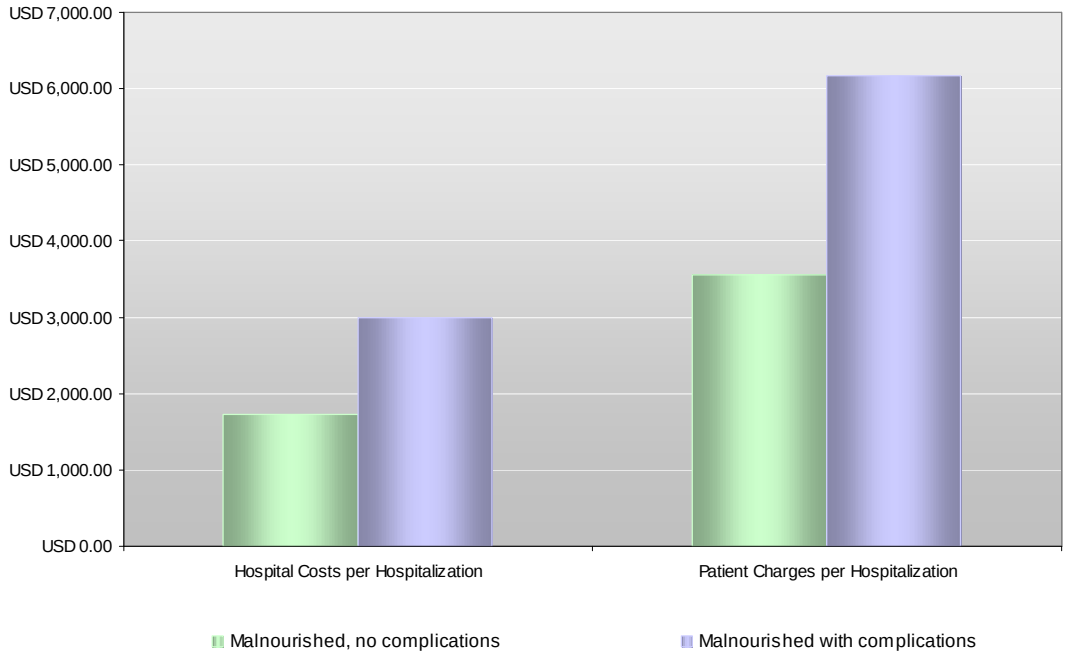

Figure 16: Malnutrition contributes to increases in hospital costs and patient charges compared to patients without complications (Reilly et al., 1988)

Results of a prospective audit of 100 admissions to a general U.S. medical unit by Robinson et al. (1987) showed that hospital charges were significantly higher for both malnourished and borderline malnourished patients compared with the well-nourished group (Figure 17).

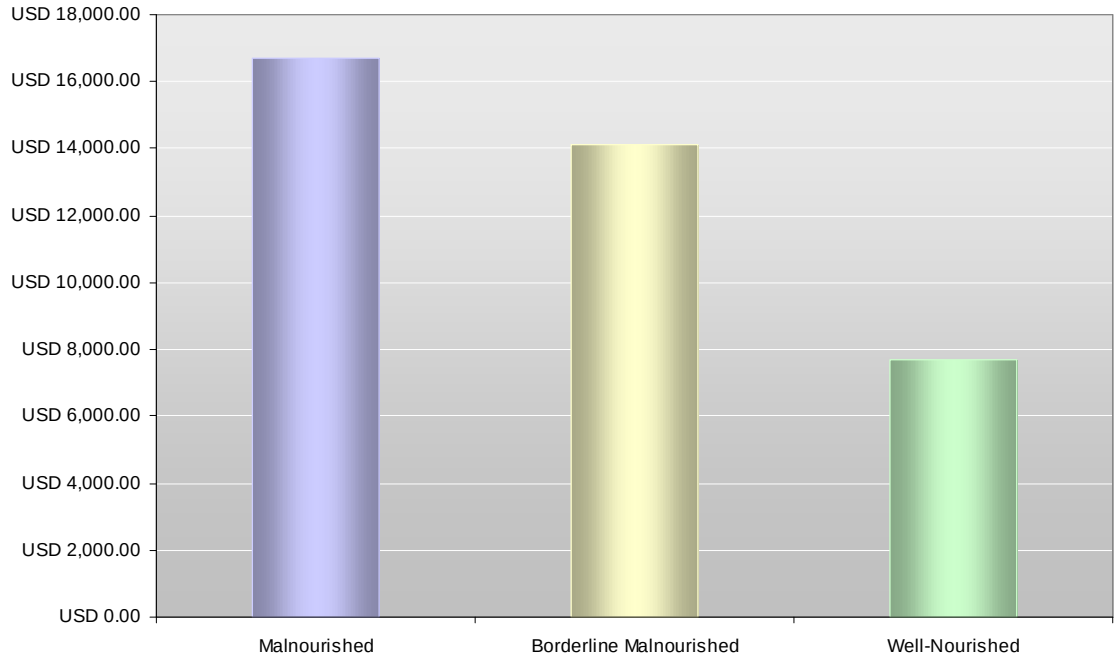

Figure 17: Hospital charges (per hospitalization) of general medicine patients based on nutritional status of patients (Robinson et al. (1987))

Robinson et al. (1987) also observed a significantly longer average length of stay in the malnourished group (15.6 days) compared to the well-nourished group (8.2 days). Forty-five percent (45%) of the malnourished patients were hospitalized longer than allowed under DRG (diagnosis-related groups) rules, compared to 37% of patients in the borderline malnourished group and 30% of well-nourished patients, thus contributing to higher hospital charges.

Figure 18 represents the summary of events all that lead to the higher cost for the health care system in malnourished patients.

Figure 18: Events that lead to the higher cost for health care system in malnourished patients

3.7 QUALITY OF LIFE

In oncology patients, quality of life (QoL) is becoming a critical issue because more and more patients can now be treated, but not necessarily cured. Therefore, the expected survival of these patients is longer now than it was a few years ago, and so there is a consequent need to satisfy patients' needs and expectations regarding their every day life. In this respect, it is important to note that cancer patients often prefer to trade off months of survival if this is associated with a better QoL. The World Health Organization in 1948 defined "health as being not only the absence of disease and infirmity but also the presence of physical, mental and social well-being". Health related QoL is a multidimensional concept which quantifies the psychological, physical and social effects of an illness and its therapy. It is assessed with questionnaires being generally answered by the patient. A large number of generic or disease specific QoL questionnaires have been developed. Some of them were extensively validated such as the EORTC QLQ-C30, the FACT-G or the SF-36 (Ravasco, 2007). Although apparently similar, the different questionnaires vary in their main focus (physical ability, symptoms, etc.).

It must be acknowledged that each cancer patient has different health and performance expectations, hence QoL is highly individualized. It must not be forgotten that when measuring QoL in cancer patient, individuals may be at different time points of their illness and expectations are likely to change over time (Ravasco, 2007).

The majority of studies that have been performed in cancer patients indicate that personalized and specific nutritional intervention should be delivered concomitant with oncology treatment in order to improve performance status and ultimately QoL. Although nutritional intervention is not primary part of specific treatment, it is necessary at all stages of the disease and of the therapeutic strategy. It helps controlling cancer-related symptoms, reduces postoperative complications and infection rate, shortens length of the hospital stay, improves tolerance to treatment, and enhances immunometabolic host response. In the curative phase, nutritional care is aimed primarily at increasing patient tolerance and response to oncology treatment, reducing the rate of complications and morbidity, and increasing QoL (Caro MM et al., 2007). Curative oncology treatment is very intensive and promotes vulnerability to develop malnutrition, which may be further exacerbated if therapy is prolonged for months based on the patient's response. However, the risk of impairment of patient's nutritional status strongly depends on tumour site and on the nutritional risk inherent to the type of treatment. Clinical conditions in which the nutritional risk is particularly elevated are the concomitant use of radiotherapy and chemotherapy in patients with head and neck cancer, the administration of high doses of antineoplastic agents or large resections of the digestive tract. The ideal nutritional intervention starts with the evaluation of the patient's nutritional status, and based on this preliminary assessment, it may include dietary counselling, oral nutritional supplementation, enteral nutrition (EN) or total parental nutrition (TPN) (Caro MM et al., 2007). Regularly scheduled nutritional re-evaluations are necessary to monitor the efficacy or reconsider the type of intervention, until a normal nutritional status is restored. By definition, palliative oncology treatment is chosen for patients whose disease is not responsive to curative treatment. If the life expectancy is less than 1 month, patients are considered to be in the terminal phase. The aim of palliative treatment is the achievement of the best QoL for patients and their families, by maintaining or restoring the patients "well-being" and their performance in every day life. Nutritional intervention in palliative care focuses primarily on controlling symptoms. Maintaining an adequate hydration status and preserving as far as possible body weight and composition (fat and lean tissues vs. oedema and ascites). It also focuses on the wishes of patient and the family, and takes into account the risks and benefits related to EN and TPN. As previously mentioned, nutritional intervention should not be considered only when cancer patients are in the palliative phase of their disease, but in any phase of the clinical course of the disease (Caro MM et al., 2007). Early customized and intensive nutritional treatment ameliorates QoL.

O'Gorman et al. (1998) conducted a study in outpatients diagnosed with gastrointestinal cancer (n=119) to determine the relationship between weight loss and performance status and quality of life. Over a 3-month period preceding the study, 22 (18%) of the patients were weight-stable, while a weight loss of >5% was documented for the remaining 97 (82%) patients. Quality of life scores were significantly lower (i.e., worse) in the weight loss group compared with the weight stable group (0.52 vs. 0.85, respectively). The results for several of the subscales of the quality of life questionnaire were also lower in the weight loss group (Figure 19).

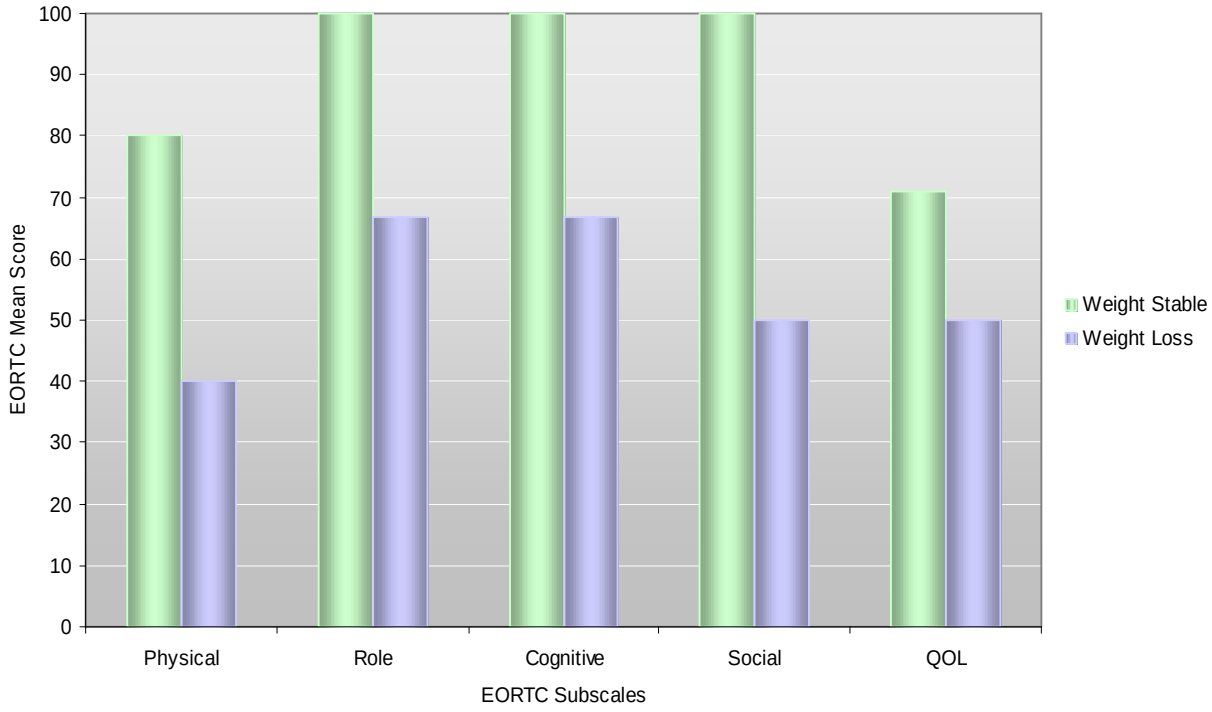

Figure 19: Quality of life of patients with gastrointestinal cancer (O'Gorman et al. (1998))

Andreyev et al. (1998) also showed that weight loss significantly predicted quality of life and performance status in cancer patients presenting for initial chemotherapy. Patients with gastric, pancreatic, or colorectal cancers who had experienced weight loss had significantly lower (i.e., worse) mean scores on the quality of life questionnaire compared with patients who had no weight loss (Figure 20). Patients were also significantly more likely to have a worse performance status if they had lost weight and had gastric, pancreatic, or colorectal cancer.

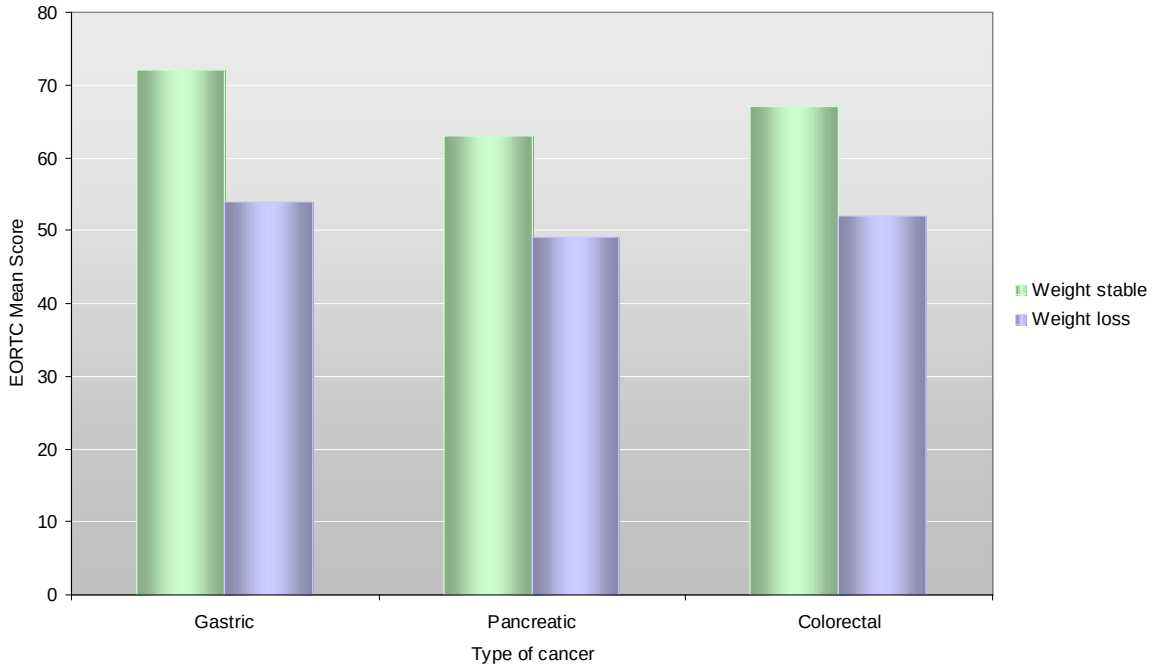

Figure 20: Weight loss and quality-of-life scores (Andreyev et al. (1998))

As already mentioned, fatigue, anorexia and emotional stress, common in cancer patients, may be further aggravated and/or worsened by poor nutritional status which in turn, can negatively impact functional status and quality of life (Andreyev et al., 1998; Ravasco et al., 2003).

Ravasco et al. (2003) observed better quality of life in the low-risk, i.e., well-nourished, cancer patients, compared to the high-risk, i.e., malnourished, cancer patients. At the end of radiation therapy, increased nutritional intake was associated with improvement in quality of life among the high-risk cancer patients. Poor nutritional intake and nutritional status are significantly associated with poor quality of life. This suggests that early and individualized nutritional intervention can potentially help improve quality of life in high-risk cancer patients.

Table 7 summarizes the associations between nutritional intake and nutritional status and the various factors influencing quality of life in cancer patients (Ravasco et al., 2003).

Table 7: Influence of nutritional intake and nutritional status on indicators of quality of life in cancer patients

	Increase in energy and protein intake by cancer patients is associated with	Malnutrition among cancer patients is associated with
Global quality of life	↑	↓
Physical functional capacity	↑	↓
Emotional well-being	↑	↓
Cognitive capacity	↑	↓
Social functioning	↑	↓
Anorexia	↓	↑
Diarrhea	↓	↑
Dyspnea	↓	↑
Fatigue	↓	↑
Insomnia	↓	↑
Nausea and vomiting	↓	↑
Pain	↓	↑

In addition to the studies that have already been mentioned, the following studies, resumed in the table 8, have been performed in order to confirm that different types of nutritional intervention have a positive impact on quality of life in cancer patients (Caro MM et al, 2006).

Table 8: Effects of nutritional intervention on quality of life (QoL) in cancer patients

Type of study	Type of nutritional support	Type of oncology treatment*	Subjects (number / type of patients)	Comments
Ravasco et al. Prospective descriptive	Nutritional counselling	RT	125 high risk: head-neck, GI tract; low risk: prostate, breast, lung, brain, uterus	Nutritional counselling contributes to an increase of patients' QoL because of improvement of their nutritional intake
Ravasco et al. Prospective cross-sectional	Evaluation of usual diet	RT	271 head-neck, oesophagus, stomach and colorectal	In some diagnoses the influence of nutritional status on QoL was higher than the influence of the illness itself
Tian and Chen	Evaluation of usual diet	S	285 stomach	A correlation between a deficiency of food intake and QoL has been found
Ravasco et al. Prospective randomized controlled	Nutritional counselling, oral nutritional supplementation	RT	75 head-neck	QoL function scores improved proportionally to improved nutritional intake and status. Counselling had a significant impact on outcomes
Ravasco et al. Prospective randomized controlled	Nutritional counselling, oral nutritional supplementation	RT	111 colorectal	Nutritional counselling performed better. During 3 months after RT it was the only method to sustain a significant impact on patients' outcome. Improvement of QoL function scores in association with adequate dietary intake and nutritional status.
Bauer and Capra Pilot study	Nutritional counselling and oral nutritional supplementation with eicosapentaenoic acid	CH	7 pancreatic and non-small-cell lung cancer (with cachexia)	The intervention leads to an improvement of the patients' QoL. Nutritional intervention and chemotherapy improved outcomes over the 8 weeks of study duration.
Isenring et al. Prospective randomized	Nutritional counselling, oral nutritional supplementation	RT	60 head-neck, gastro-intestinal tract	The nutritional intervention which was applied early and intensively, improved the patients' global QoL.
Davidson et al. Multicenter	Oral nutritional supplementation (enriched n-3 fatty acids)	None	107 unresectable pancreatic cancer	It was possible to attenuate the weight loss after 8 weeks of intensive nutritional intervention. The patients' QoL was improved.

Fearon et al. Multicenter randomized double blind	Oral nutritional supplementation (enriched n-3 fatty acids)	None	200 advanced pancreatic cancer	QoL improved, the patients lean-body mass and weight has been increased
Moses et al. Multicenter randomized double blind	Oral nutritional supplementation (enriched n-3 fatty acids)	None	24 unresectable pancreatic cancer	n-3 fatty acids might be related to an improvement of QoL. This has been extrapolated from the increase of the patients' physical activity
Jatoi et al. Multicenter randomized	Oral nutritional supplementation (enriched n-3 fatty acids and megestrol acetate)	CH or RT	421 patients with cancer-associated wasting	No weight, appetite and QoL improvements could be achieved by applying EPA supplements compared to megestrol acetate alone or in combination with EPA.
Fearon et al. Multicenter randomized-double blind placebo controlled	EPA diethyl ester	None	518 advanced gastrointestinal or lung cancer	No indication of improvements on weight and lean body mass with single agent EPA in cancer cachexia was found.
Van bokhorst-de van der Schuer et al. Randomized clinical trial (perioperative administration)	Enteral Nutrition	S	49 severly malnourished head and neck cancer	In the period preceding the surgery QoL could be improved by enteral nutrition.
Shang et al. Prospective randomized	Intensified oral enteral nutrition with or without supplementation with parenteral nutrition	Palliative CH or combined RT and CH	152 rectum, oesophagus, gastric, pancreatic, ovarian, breast carcinoma	The additional supplementation with PN could reduce progressive weight loss, improve body composition, ameliorate the appetite and improve QoL.
Bozzeti et al. Multicenter	Home parenteral nutrition	CH is some cases	69 advanced cancer, severly malnourished	QoL could be stabilized until about 2 to 3 months before death.
Orreval et al. Semi-structured interviews	Home parenteral nutrition	6 patients were on palliative CH	13 advanced cancer	Positive impact on body weight, energy level, strength and activity has been detected, which was also reflected on the patients QoL.
Gramignano et al.	Administration of L-carnitine	CH	12 advanced cancer	Increase of lean body mass and improvement of QoL

*CH - chemotherapy; RT – radiotherapy; S - surgery

As already described, global quality of life is decreased in patients experiencing weight loss, pain and fatigue. Figure 21 summarizes the various factors affecting the quality of life of cancer patients.

Figure 21: Factors influencing the quality of life of cancer patients

4. PART 2: SPECIALIZED NUTRITIONAL SUPPORT AND NUTRITIONAL SCREENING

The products that are intended to improve nutritional status of patients that might be compromised due to the specific disease, inadequate intake of regular food or simply the weight loss despite the correct nutritional intake are considered as nutritional support. In Europe these product fall under the regulation for Food for Special Medical Purpose (FSMP). The nutritional support products are not considered as a drug since they are not intended to diagnose, treat or cure any disease but to prevent deterioration of patients' nutritional status or to improve their nutritional status.

4.1 ROLE AND AIM OF NUTRITIONAL SUPPORT IN CANCER PATIENTS

Nutrition can play an important role in the management of cancer patients, from the initial phases of treatment and recovery through the long-term continuum of care (Rock, 2005). Maintenance of good nutritional status during cancer treatment is essential to increase the probability of successful completion of prescribed cancer therapies and to promote improved quality of life during and after treatments. Adequate and appropriate dietary intake can help to:

- Slow or minimize reduction in body weight
- Reduce incidence and severity of cachexia and anorexia
- Reduce cancer treatment associated side-effects
- Improve treatment efficacy
- Reduce risk of other comorbid disease
- Increase likelihood of survival
- Support adequate calorie and nutrient intake
- Prevent weight loss, malnutrition, anorexia and cachexia
- Reverse malnutrition and weight loss that have already occurred
- Improve body composition
- Enhance immune function
- Improve functional or performance status
- Reduce fatigue
- Improve physical functioning and quality of life

Nutritional support is given in addition to the patient's normal diet.

4.2 NUTRITIONAL REQUIREMENTS OF CANCER PATIENTS

Nutritional status has an important effect on a patient's quality of life and sense of wellbeing, as well as affecting the patient's ability to fight disease and to withstand the rigors of

anticancer treatments. Early and sustained nutritional support is one of the most valuable adjuncts to optimal management of cancer and should aim for the reduction of weight loss by helping to reduce muscle wasting and prevent nutrient deficiencies.

As a first step, sufficient calories and protein should be provided to meet the complete nutritional and energy needs of each patient and to minimize protein catabolism and the use of stored energy reserves. In order to support protein synthesis and minimize the magnitude of nitrogen deficit, sufficient protein should be provided. Requirements for protein in most patients range from 1 to 1.5 g/kg per day. Carbohydrates should provide the primary source of energy and fat should represent 25-30% of calories to provide essential fatty acids and meet energy demands, while providing adequate protein, vitamins, minerals and trace elements (Barrera, 2002). Additionally, to address treatment induced side-effects such as constipation and diarrhea, adequate dietary fiber and fluid intake should be ensured. Since patients may frequently experience a feeling of early satiety a high-energy, high-protein nutritional supplement may be preferable.

Appropriate nutrition can also play a role in controlling nausea and vomiting, thus reducing the need for drugs. There are several ways to control or relieve nausea such as consuming clear or ice-cold drinks, eating slowly and smaller more frequent meals, drinking beverages slowly. Persistent vomiting combined with diarrhea can result in dehydration. Ways to relieve vomiting includes: gradually drinking larger amounts of clear liquids; avoiding solid food until the vomiting episode has passed; resting; and temporarily discontinuing all oral medications, which can irritate the stomach and make the vomiting worse. If vomiting and diarrhea last more than 24 hours, an oral rehydrating solution can be used to avoid dehydration.

Consumption of adequate fluids, replacement of fluid losses with sodium and potassium containing fluids, and consumption of clear liquids are critical to avoid dehydration associated with diarrhea. Additionally, consumption of soluble fiber can help control frequency of diarrhea. Thus, ensuring adequate fiber intake is crucial for patients suffering from either constipation or diarrhea. Fiber plays a crucial role in general intestinal health and has an overall normalizing effect on digestive function. Intake of fiber can help prevent or ameliorate constipation by softening, adding bulk to, and speeding the passage of contents through the colon. Fiber's physical and biomolecular properties act to bind water and promote a normal pattern of sodium transport and water absorption.

4.3 DIFFERENT TYPES OF NUTRITIONAL INTERVENTION

Different type of nutritional intervention can be considered depending on patients' level of malnutrition. The choice can range from nutritional counselling in the preventive early stages of diagnosis to complete enteral nutritional support in patients that are unable to meet their nutrient requirements orally. In current clinical practice, it is uncommon to advocate parental nutritional support, although there may be rare instances when it is indicated for patients with cancer.

- **Nutritional counselling**

Nutritional counselling consists of giving the patient general or specific dietary recommendations. Illness and therapy in oncology patients are usually accompanied by qualitatively and quantitatively insufficient dietary intake. The majority of patients could benefit from nutritional counselling to optimize their eating behaviour; this frequently results in better control of symptoms, preservation of nutritional status and prevention of malnutrition. Bearing in mind that reduced food intake and weight loss negatively affect QoL, it is conceivable that nutritional counselling may positively influence QoL beyond its impact on nutritional status. It has been proven that QoL of patients receiving nutritional counselling is improved compared with the QoL of those not receiving any nutritional intervention.

(Ravasco, 2005). The efficacy of nutritional counselling in stabilizing or improving nutritional status and QoL depends on the ability to tailor the intervention to the patient's specific needs and expectations. As a consequence, nutritional counselling to oncology patients is a time-consuming effort which should be delivered by dedicated teams.

§ Oral nutritional supplementation

Oral nutritional supplements (ONS) are effective when patients are unable to meet requirements with normal food alone, despite nutritional counselling. This is the simplest, most natural and least invasive method of increasing nutrient intake in all patients. In the multistep nutritional approach to oncology patients, ONS should always be considered before enteral and parenteral nutrition are started. Specific supplements include in their composition a number of nutrients with immunomodulating or anti-inflammatory properties. Among these nutrients, an important role is played by polyunsaturated fatty acids (eicosapentaenoic acid and docosahexaenoic acid), and arginine or nucleotides (RNA and DNA). Their administration reduces inflammatory responses and therefore improves immune function, gut function, oxygen metabolism and nutritional status. Clinical trials testing the efficacy of ONS containing n-3 fatty acids provided encouraging results in cachectic pancreatic cancer patients, in whom body weight stabilized or even increased (Moses, 2004) in the short term, and a significant gain in lean body mass accounted for most of the body weight gain. This suggests that supplementation with n-3 fatty acids might be associated with improved QoL, as inferred from increased physical activity and extended survival. The reasons for those findings are probably attenuation of the acute phase response associated with tumour growth and modulation of the expression of proinflammatory mediators, including cytokines, prostaglandins and leucotriens, by n-3 fatty acids. These effects may explain the inhibitory effects of EPA on the ubiquitin-proteasome system, the main catabolic pathway involved in cancer cachexia. In addition to its effect on inflammatory response, EPA also appears to have an immune enhancing effect. It has been suggested that EPA influences neutrophil and monocyte function, T- and B-lymphocyte function and proliferation, and eicosanoid production (van Bokhorst-de van der Schueren, 2005). A limitation of nutritional intervention based on n-3 fatty acids is that ONS containing these nutrients requires approximately 2-3 weeks of administration to achieve sufficient circulating and intramembrane levels to influence cellular molecular biochemistry and so improve nutritional status. Nutritional supplementation may improve malnutrition and alleviate cachexia, but it appears to play minimal role in prevention of cachexia. Nevertheless, further studies on role of n-3 fatty acids and other nutrients (e.g. vitamin E), separately or in combination are necessary.

§ Enteral nutrition

Patients in whom nutritional needs cannot be met orally must be fed by gastrically or intestinally placed feeding tubes. This may be due to an incapacity or limited ability to eat, as a result of dysphagia, upper gastro-intestinal obstruction or central nervous system pathology. Enteral tube feeding may also be indicated in cases where nutritional needs cannot be met due to other side effects, for exemple when patient suffer from increased nutritional losses due to impaired digestion or absorption. Enteral nutrition has the advantages over parental nutrition of being more physiological, because it makes use of gastrointestinal tract. This approach enhances immune competences and reduces risk for infection, as compared with parenteral nutrition, and by these means it results in reduced length of hospital stay and significant cost saving.

Enteral nutrition is associated with several beneficial effects on clinical condition; including improved nutritional status and reduced postoperative respiratory complications. In malnourished gastrointestinal cancer patients and candidates to major surgery, the complication rate and the duration of postoperative hospital stay was significantly reduced by early postoperative enteral nutrition compared to paranteral nutrition. (Bozzeti, 2007) In oesophageal cancer patients eligible to curative surgery, enteral nutrition is associated to improved nutritional status and reduced postoperative respiratory complications. (Kruizenga

et al., 2005)

However, the presence of a feeding tube is a marker of reduced QoL. This negative relationship appears to be due to inadequate nutritional status or complications resulting form the illness and oncology treatment, which are ultimately indication for use of enteral nutrition. In other words, a feeding tube is a marker of decreased QoL not because enteral nutrition negatively influences QoL but rather because it is placed in patients whose clinical and nutritional conditions impinge on QoL (Ravasco, 2005).

Although preliminary results are promising, there are not enough data to conclude that enteral nutrition enriched with immunomodulatory components should be routinely prescribed to all cancer patients; this is particularly the case in nonsurgical cancer patients.

§ Parenteral nutrition

Patients who cannot tolerate enteral nutrition because of the occurrence of severe gastrointestinal symptoms or whose gastrointestinal tract is not accessible must be fed via total parenteral nutrition (TPN). Although effective, this type of nutritional intervention is associated with well recognized risks, including infection rates and hyperglycaemia among others and higher cost. For example, in patients with solid tumours or haematological malignancies receiving bone marrow transplantation (BMT), TPN is frequently the only possibility to nutritionally support the patient. Because of the toxicity of BMT-related therapies, which includes potentially severe mucositis, EN is usually poorly tolerated (Caro MM et al., 2007).

When it is used based on clear indications TPN and in particular home parenteral nutrition (HPN) – have positive effects in patients suffering from advanced cancer. Interviews with patients with advanced cancer and their families concerning their experience with HPN suggest that HPN is related to greater energy, strength, activity levels and body weight gain. Also, HPN conferred upon patients a feeling of improved security about having their nutritional needs met. It is likely that these improvements can be associated with improved QoL.

An interesting aspect of nutritional support of oncology patients is whether parenteral nutrition may enhance the positive effects on nutritional status and QoL of enteral nutrition or ONS. In clinical trials, malnourished patients with advanced incurable cancer receiving ONS were compared with patients receiving the same ONS and additional parenteral nutrition. In the parenteral nutrition group, improved body composition, increased appetite, reduced anorexia and decreased progressive weight loss were observed, which were associated with improved survival and QoL.

Despite growing evidence that nutritional support improves patients' clinical outcome, its use is not widely considered as a routine by most healthcare professionals. Many, factors, depending on physicians, patients and institutions, could explain such a resistance to implement nutritional therapy in routine care. One of these factors is the lack of indisputable evidence that nutritional intervention improves patients' quality of life and is cost-effective.

§ Impact of different nutritional interventions on patients' health

Evans et al. (1987) observed that nutritional counseling resulted in significant increase in caloric intake (89 kcal with counseling vs. 68 kcal in usual care group) and a non-significant reduction in weight loss (-0.6 kg with counseling vs. -2.1 kg in usual care group) in the first cycle of chemotherapy in a group of non-small cell lung cancer patients. Increased percent of weight loss, serum albumin concentrations and presence of liver metastases were significant predictors of reduced survival in this group of patients.

Ovesen et al. (1993) observed an increase in weight among cancer patients receiving nutritional counseling and oral energy-protein supplementation (1 kg increase). The dietary counseling and oral supplementation resulted in significantly increased energy (239 kcal) and protein intake (10 g/day). After 5 months, counseling led to a significant increase in triceps

skinfold measurement. At 5 months, the response to chemotherapy was 63% in the counseled group and 46% in the control group, while the 2 year survival rate was 39% in counseled patients vs. 32% in control patients.

In colorectal cancer patients undergoing radiation therapy, an increase in energy (555 and 296 kcal/day) intake was observed with dietary counseling and oral protein supplements (Ravasco et al., 2005). A decline in energy intake (-285 kcal/day) was observed in the ad lib group of patients. Similar increases were observed in protein intake (20 to 35 g/day) with dietary counseling and oral protein supplements, whereas it decreased in the ad lib group (-10 g/day). Marked reduction in the incidence and severity of anorexia and diarrhea and improvement in quality of life was observed. Significant improvements in nutritional status and reductions in the use of anti-emetic and anti-diarrhea medications were observed with nutritional intervention. Ravasco et al. (2005) concluded that **"**the impairment in structure, function and well-being that form malnutrition, are nutritionally responsive" in malnourished cancer patients undergoing radiation therapy.

Nayel et al. (1992) observed a significant reduction in radiation toxicity and treatment interruptions with oral high-protein nutritional supplementation. Patients who received nutrition support experienced an increase in body weight and triceps skinfold thickness, whereas 58% of the radiation only group (no nutritional supplement) experienced weight loss. No patients treated with radiotherapy plus nutritional supplementation experienced grade III mucosal reaction, whereas 33 and 25% of patients in the radiotherapy only group had grade III functional and mucosal reactions, respectively. Irradiation had to be suspended in 5 out of the 12 patients (42%) who received no nutritional support because of severe mucosal reaction and/or poor performance status, whereas all patients who received nutrient supplementation completed their course of irradiation without interruption.

A systematic literature review of 36 papers with respect to pelvic malignancy, that included 2,646 patients, suggests that low-fat diets, probiotic supplementation and elemental diets may be beneficial in preventing acute gastrointestinal symptoms associated with radiation therapy (McGough et al., 2004).

Bauer and Capra (2004) observed that among pancreatic and non-small cell lung cancer patients receiving nutritional counseling plus oral supplementation with an energy-dense oral nutritional supplementation containing eicosapentaenoic acid for 8 weeks resulted in a significant increase in:

- Total energy intake (36 KJ/kg/day)
- Total protein intake (0.3 g/kg/day)
- Total fiber intake (6.3 g/day)
- Improved quality of life
- Clinically significant increase in body weight (2.3 kg) and lean body mass (4.4 kg) in the supplementation group.

Supplementation did not appear to inhibit meal intake.

Isenring et al. (2004) observed that intensive, individualized nutrition counseling along with oral supplements resulted in minimum reductions in body weight, nutritional status and global quality of life scores compared to patients receiving usual care. In patients receiving radiotherapy, early and aggressive nutritional intervention was beneficial in minimizing weight loss and deterioration in nutritional status and improving overall quality of life and physical functioning.

In patients with cancer cachexia, it may not be enough to replace the missing protein and calories with standard nutritional formulas since protein requirements are estimated to range from 1.5 to 2.5 g/kg per day in depleted cancer patients due to negative nitrogen balance

(Martin, 2000). Cancer cachexia is expressed on the basis of protein-energy malnutrition but defined by complex metabolic, immunological and tumor-associated pathologies that combine to deplete body mass and accelerate muscle wasting, resulting in severe malnutrition. Replacement of lost calories and protein alone is therefore not sufficient to help reverse the changes or help modify the pathology of cancer cachexia (Argiles et al., 2005; Tisdale, 2001a, b).

Standard nutritional supplements will not be effective enough to help counteract the process of muscle wasting, as this arises from activation of the proteasome proteolytic pathway by PIF and is independent of nutrient intake or calories alone (Tisdale, 2003). The use of standard nutritional supplements does not deliver enough protein or essential amino acids to minimize or help reverse the prevailing nitrogen deficit and indeed standard nutrition cannot help reduce protein degradation rates. Thus, standard nutritional support cannot help stop or restore weight loss or help compensate for the changes in body composition (i.e., loss of muscle mass) that occur in cancer cachexia as standard nutritional supplements are not formulated to address the specific metabolic imbalances unique to cancer cachexia (Argilés et al., 2001).

Fish oil, which contains the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosohexaenoic acid (DHA), has been used to reduce the risk and in the management of coronary artery disease, hypertension, diabetes mellitus, arthritis, and other inflammatory and autoimmune diseases. EPA has been observed to reduce weight loss in cachectic cancer patients (Wigmore et al., 2000).

EPA along with a high-protein, energy-dense supplement, was observed to promote weight gain. Barber et al. (1999) conducted a study in 20 patients with pancreatic cancer who were experiencing ongoing weight loss. All patients consumed two cans of a nutritional supplement containing EPA (2.1 g/day) in addition to their normal daily food intake for 7 weeks. As early as 3 weeks after consuming the supplement, patients gained weight and experienced an increase in lean body mass.

4.4 EUROPEAN GUIDELINES FOR NUTRITIONAL SCREENING

The purpose of nutritional screening is to predict the probability of a better or worse outcome due to nutritional factors, and whether nutritional treatment is likely to influence this. Outcome from treatment may be assessed in a number of ways:

- Improvement or at least prevention of deterioration in mental and physical function
- Reduced number or severity of complications of disease or its treatment.
- Accelerated recovery from disease and shortened convalescence.
- Reduced consumption of resources, e.g. length of hospital stay and other prescriptions.

The nutritional impairment identified by screening should therefore be relevant to these aims and outcomes and may vary according to circumstances, e.g. age or type of illness. In hospitals, other aspects of disease need to be considered in combination with purely nutritional measurements in order to determine whether nutritional support is likely to be beneficial. Randomized controlled trials of nutritional support in particular disease groups may therefore provide important evidence on which to base our criteria of nutritional risk.

Nutritional screening tool should be linked to specific protocols for action. Hospital and healthcare organizations should have a policy and a specific set of protocols for identifying patients at nutritional risk, leading to appropriate nutritional care plans: an estimate of energy and protein requirements including possible allowance for weight gain, followed by prescription of food, oral supplements, tube feeding or parenteral nutrition, or a combination

of these (Kondrup et al., 2003). It is suggested that the following course of action be adopted:

1. Screening: This is a rapid and simple process conducted by admitting staff or community healthcare teams. All patients should be screened on admission to hospital or other institutions. The outcome of screening must be linked to defined courses of action:

a. The patient is not at risk, but may need to be re-screened at specified intervals, e.g. weekly during hospital stay.

b. The patient is at risk and a nutrition plan is worked out by the staff.

c. The patient is at risk, but metabolic or functional problems prevent a standard plan being carried out.

d. There is doubt as whether the patient is at risk.

In the two latter cases, referral should be made to an expert for more detailed assessment.

2. Assessment: This is a detailed examination of metabolic, nutritional or functional variables by an expert clinician, dietician or nutrition nurse. It is a longer process than screening which leads to an appropriate care plan considering indications, possible side-effects, and, in some cases, special feeding techniques. It is based, like all diagnosis, upon a full history, examination and, where appropriate, laboratory investigations. It will include the evaluation or measurement of the functional consequences of undernutrition, such as muscle weakness, fatigue and depression. It involves consideration of drugs that the patient is taking and which may be contributing to the symptoms, and of personal habits such as eating patterns and alcohol intake. It includes gastrointestinal assessment, including dentition, swallowing, bowel function, etc. It necessitates an understanding of the interpretation of laboratory tests, e.g. plasma albumin which is more likely to be a measure of disease severity than of malnutrition per se. Calcium, magnesium and zinc levels may be important, and in some cases laboratory measurement of micronutrient levels may be appropriate.

3. Monitoring and outcome: A process of monitoring and defining outcome should be in place. The effectiveness of the care plan should be monitored by defined measurements and observations, such as recording of dietary intake, body weight and function, and a schedule for detecting possible side effects. This may lead to alterations in treatment during the natural history of the patient's condition.

4. Communication: Results of screening, assessment and nutrition care plans should be communicated to other healthcare professionals when the patient is transferred, either back into the community or to another institution. When patients are transferred from the community to hospital or vice versa, it is important that the nutritional data and future care plans be communicated.

5. Audit: If this process is carried out in a systematic way, it will allow audit of outcomes which may inform future policy decisions. Although this document will focus mainly on the process of screening, this cannot be considered in isolation and must be linked to the pathway of care described above.

§ **Components of nutritional screening** (Kondrup et al. 2003)

Screening tools are designed to detect protein and energy undernutrition, and/or to predict whether undernutrition is likely to develop/worsen under the present and future conditions of the patient. Therefore, screening tools embody the following four main principles:

1. What is the condition now? Height and weight allow calculation of body mass index (BMI). Normal range 20–25, obesity >30, borderline underweight 18.5–20, undernutrition <18.5. In cases where it is not possible to obtain height and weight, e.g. in severely ill patients, a useful surrogate may be mid-arm circumference, measured with a tape around the upper arm midway between the acromion and the olecranon. This can be related to centiles of tables for that particular population, age and sex. BMI may be less useful in growing children and

adolescents, and in the very elderly. Nevertheless, the BMI provides the best generally accepted measure of weight for height.

2. Is the condition stable? Recent weight loss is obtained from the patient's history, or, even better, from previous measurements in medical records. More than 5% involuntary weight loss over 3 months is usually regarded as significant. This may reveal undernutrition which was not discovered by 1., e.g. weight loss in obesity, and may also predict further nutritional deterioration depending on 3 and 4.

3. Will the condition get worse? This question may be answered by asking whether food intake has been decreased up to the time of screening, and if so by approximately how much and for how long. Confirmatory measurements can be made of the patient's food intake in hospital or by food diary. If these are found to be less than the patient's requirements with normal intake, then further weight loss is likely.

4. Will the disease process accelerate nutritional deterioration? In addition to decreasing appetite, the disease process may increase nutritional requirements due to the stress metabolism associated with severe disease (e.g. major surgery, sepsis, multitrauma), causing nutritional status to worsen more rapidly, or to develop rapidly from fairly normal states of (1–3) above.

Variables 1–3 should be included in all screening tools, while 4 is relevant mainly to hospitals. In screening tools, each variable should be given a score, thereby quantifying the degree of risk and allowing a direct link to a defined course of action.

§ **Screening tools recommended by European Society for Parenteral and Enteral Nutrition (ESPEN)** (Kondrup et al, 2003; Anthony, 2008)

Malnutrition Universal Screening Tool (MUST)

The MUST was developed by the Malnutrition Advisory Group, a standing committee of the British Association for parenteral and enteral Nutrition (BAPEN) in 2003. It is validated, evidence-based tool designed to identify adults who are malnourished or at risk of malnutrition. In hospitals, MUST predicts length of hospital stay, discharge destination and mortality after controlling for age. In community care, it predicts rate of hospital admissions and general practitioner visits, and shows that appropriate nutritional intervention improves outcome. The tool is internally consistent and reliable, with good reproducibility between healthcare providers. Three criteria are used by MUST to determine the overall risk of malnutrition: body mass index (BMI), unintentional weight loss and acute disease effect.

The MUST is recommended by ESPEN as the preferred screening tool for patients in the community but as stated above, is used in all care settings, especially in U.K.

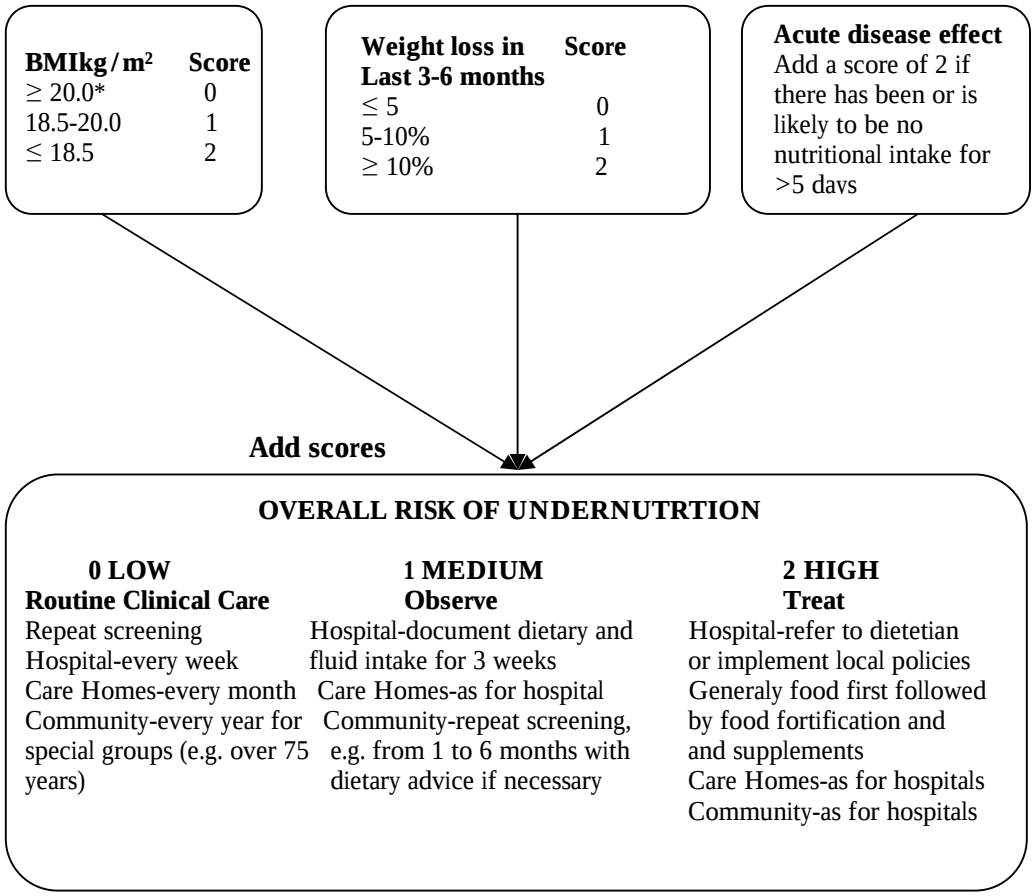

Figure 22: The Malnutrition Universal Screening Tool

* BMI>30 - obesity

Nutritional Risk Screening (NRS-2002)

The purpose of the NRS-2002 system is to detect the presence of undernutrition and the risk of developing undernutrition in the hospital setting. It contains the nutritional components of MUST, and in addition, a grading of severity of disease as a reflection of increased nutritional requirements. It includes four questions as a pre-screening for departments with few at risk patients. The NRS 2002 is recommended by ESPEN as the preferred screening tool for hospitalized patients. It has well been accepted within Europe, although no data are available as to how extensively it is used. One positive aspect of the toll is that it is not essential to calculate BMI; weight change alone can be used. The tool does require subjective assessment of severity of illness, which could impact the total score, but its reliability has been validated between a nurse, a dietetician and a physician with substantial reliability. NRS 2002 has been validated to identify those patients who will benefit from nutritional intervention – it does not categorize the risk of malnutrition.

Table 1 Initial screening		Yes	No
1	Is BMI<20.5?		
2	Has the patient lost weight in last 3 months		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill? (e.g. in intensive therapy)		

Yes: If the answer is 'Yes' to any question, the screening in Table 2 is performed.

No: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan considered to avoid the associated risk status.

Table 2 Final screening			
Impaired nutritional status		Severity of disease (≈ increase in requirements)	
Absent Score 0	Normal nutritional status	Absent Score 0	Normal nutritional requirements
Mild Score 1	Weight loss >5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild Score 1	Hip fracture, Chronic patients, in particular with acute complications: Cirrhosis, COPD. Chronic hemodialysis, diabetes, oncology
Moderate Score 2	Weight loss >5% in 2 mths or BMI 18.5-20.5 + impaired general condition or food intake 25–60% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery, Stroke Severe pneumonia, hematologic malignancy
Severe Score 3	Wight loss >5% in 1 mth (>15% in 3 mths) or BMI <18.5+impaired general condition or Food intake 0-25% of normal requirement in preceding week	Severe Score 3	Head injury, Bone marrow Transplantation, Intensive care patients
Score:	+	Score:	=Total Score
Age if ≥70 years: add 1 to total score above =age-adjusted total score			
Score ≥3: the patient is nutritionally at-risk and a nutritional care plan is initiated Score <3: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status			

Mini Nutritional Assessment (MNA)

The purpose of MNA is to detect the presence of undernutrition and the risk of developing undernutrition among the elderly in home-care programmes, nursing homes and hospitals. The prevalence of undernutrition among the elderly may reach significant levels (15–60%) under these circumstances. The screening methods mentioned above will detect undernutrition among many elderly patients, but for the frail elderly the MNA screening is more likely to identify risk of developing undernutrition, and undernutrition at an early stage, since it also includes physical and mental aspects that frequently affect the nutritional status of the elderly, as well as a dietary questionnaire. The full MNA has 4 sections: anthropometrics (BMI, weight loss, arm and calf circumference), general assessment (lifestyle, medication, mobility, presence of depression or dementia), dietary assessment (number of meals, food and fluid intake, autonomy of feeding), and subjective assessment (self-perception of health and nutrition). The full MNA takes less than 15 minutes to complete. The maximum score is 30, with ≥24 being well nourished, 17-23.5 indicating risk of malnutrition, and <17 indicating malnutrition.

5. PART 3: IMPLEMENTATION OF NUTRITIONAL SUPPORT IN SWISS HOSPITALS AS AN INTEGRAL PART OF ONCOLOGY TREATEMENT

5.1 NUTRITIONAL GUIDELINES USED IN SWITZERLAND

Switzerland is referring to ESPEN guidelines for nutritional screening, nevertheless their usage depend on the hospital. In Switzerland there are no national guidelines or program to manage malnutrition in hospitals. The situation is the same concerning nutritional screening since there is no national directive that covers screening, evaluation of the chosen nutritional intervention and surveillance of the patients. Very frequently malnutrition is not treated at all. Less than one third of Swiss hospitals have Commission for Nutrition and only 14 hospitals out of this one third (which represents only 2.5% of Swiss hospitals) have a specialized team in this area.

University Hospital in Lausanne has introduced the NRS-2002 questionnaire in order to evaluate the nutritional status of the patients. Unfortunately none of the methods available today, if it is used alone, doesn't permit to have the correct evaluation of nutritional status. This is why the triceps skinfold thickness, mid arm circumference and mid arm muscle circumference are as well used in order to determine the nutritional status. Evaluation of body composition, dosage of biological markers and energy balance can help as well the nutritionist to have a correct nutritional evaluation.

5.2 STATUS OF PREVENTION OF MALNUTRITION IN CANCER PATIENTS IN SWISS HOSPITALS

Malnutrition in Switzerland becomes more and more recognized as a health problem but the current procedures and structures in Swiss hospitals do not permit to prevent it or treat it efficiently. Due to the problem of resources and time, the actions that tend to prevent or overcome the malnutrition are very limited. The data concerning malnutrition and hospital cost due to the malnutrition in Switzerland are not very well known even if there has been a lot of research in this area.

The study done in University hospital in Geneva shows that 43% of patients that are malnourished consume the quantities inferior to the recommended daily intake in calories despite the sufficient quantity of food that they receive. If we enlarge this to other nutrients than protein, fat and carbohydrates, 70% of patients do not have the sufficient intake of mineral and vitamins.

Since May 2003, department of medicine of seven swiss hospitals participate in project "Malnutrition" lead by Cantonal Hospital in Winterthur. The nutritional status of all patients admitted to the department of medicine is measured by using the questionnary "Nutrition Risk Score -2002" elaborated by ESPEN. Based on the information given by Dr Imoberdorf from the Cantonal hospital of Winterthur, out of 22 233 patients that have participated in this study, 4057 (18.2%) were malnourished. Only 66% of these malnourished patients have received the nutritional supplements (Keller, 2005).

5.3 MALNUTRITION IN SWISS HOSPITALS – MEDICAL COSTS AND POTENTIAL ECONOMIES

The objective of this chapter is to evaluate the cost of medical treatments provoqued by malnutrition in Swiss hospitals and to evaluate the potential economies in this area.

The prevalence of malnutrition in Switzerland in 2004 represented around 20% (minimum 15% - maximum 30%). Based on the health insurance statistics for 2004, there was 787 000 hospitalisation. This means that around 157 400 hospitalized patients are malnourished (118 000 – 236 000) (Frei, 2006).

Infectious rate and non infectious complication rate is around 40%, so almost double in malnourished patients. Malnourished patients have an increased consumption of drugs and they are less autonomous once they leave the hospital, than well nourished patients.

All these factors contribute to the extension of hospital length of stay in malnourished patients by 4.9 days compared to the well nourished patients. If we compare this to the average cost per day of hospitalization, we can estimate the cost due to the malnutrition. Since all the difference in duration of hospital stay cannot be attributed only to malnutrition; it has been assumed that the half (2.45 days) is related to malnutrition (minimum 1/3 or 1.63 days, maximum 2/3 or 3.27 days) (Frei, 2006).

The cost of hospitalization in 2004, if we exclude the ambulatory treatment, elevates to 8499 millions of Swiss francs. If we divide this by number of days of hospitalization, we obtain the cost per day of 1365 Swiss francs (www.bag.admin.ch)

The yearly cost of malnutrition for Switzerland has been calculated by multiplying the number of patients suffering from malnutrition by the cost per patient per day. The additional cost per patient is around 3344 CHF (minimum 2229, maximum 4459). If these figures are combined with the prevalence rate the hospital cost are estimated to 526 millions of francs. This estimation variates from 263 millions of Swiss francs if we use the minimum value for the prevalence rate (15%) and duration of hospital stay (1.63 days) up to 1053 millions of Swiss francs if we take into account the maximum values for these two parameters.

The numerous interventions that tend to treat and prevent malnutrition exist already.

Based on the informations received from the Centre Hospitalier Universitaire Vaudois, the cost of oral nutritional supplements in swiss hospitals goes from 4 to 5 Swiss francs per unit. The recommended daily intake is usually one serving (around 240 ml) twice per day, this means that the cost of oral nutritional supplements per day variates from 4 to 10 Swiss francs. Today none of oral nutritional supplements is reimbursed by the basic health insurance LAMal in Switzerland. The price of enteral nutrition variates from 40 up to 65 Swiss francs per day, while the cost of parenteral nutrition goes from 200 to 300 Swiss francs per day. As already explained in the previous chapter, the enteral and parenteral nutrition should only be prescribed if the nutritional needs can not be met orally or if it is impossible to administrate the nutritional support orally. It is important to mention that the cost of hospital staff and service cost has to be added on the price of different nutritional support in order to evaluate the price of nutritional intervention.

The potential savings from 1400 to 2800 Swiss francs, which are basically one to two days of hospital stay, for the investment of only few hundred Swiss francs per patient and per hospital stay, are realistic (Frei, 2006).

5.4 RECOMMENDATIONS FOR IMPLEMENTATION OF NUTRITIONAL GUIDELINES AND NUTRITIONAL SUPPORT IN SWISS HOSPITALS

As it has been already explained in previous chapters malnutrition is strongly associated with numerous medical problems that lead to prolonged recovery time and increased cost of both hospital and nursing home care. Investing in specialized nutrition products for prevention and treatment of malnutrition provides an optimal solution for improvement in patients' health and the control/reduction of treatment cost.

Today in Switzerland there is no national standards or recommendations for nutritional screening, evaluation and monitoring of nutritional status of malnourished patients. The situation is the same concerning prevention and treatment of malnutrition.

Taking into account all these facts it is imperative to create the national standards and recommendations for nutritional screening of patients that have risk of developing malnutrition, the guidelines for the evaluation and the surveillance of their nutritional status after the nutritional intervention has been put in place should be the part of this national standard. Different aspects related to treatment of malnutrition and nutrition in hospital should be the part of this document as well.

The following recommendations should be taken into account when creating the national standards for management of malnutrition in hospitals (Keller, 2005):

- In order to identify the patients at risk of developing the malnutrition, le physician has to perform the standard tests used for detection of malnutrition. The age, the gender, the stage of cancer, the psychological condition and medical treatment have to be taken into account.
- The medical file and the transfer documents have to contain the informations related to nutritional status of the patient and have to mention malnutrition if present
- Once the nutritional status of the patient has been defined an action plan with clear objectives has to be created in order to prevent or treat the malnutrition
- Healthcare professionals should look to evidence based guidelines to assist them in selecting the most appropriate method of nutritional support for their patient taking account of the patient's likes and dislikes, nutritional needs, diagnosis and prognosis and ability to adhere to the intervention. It is essential that healthcare professionals combine their clinical experience with a sound knowledge of the evidence base and practical common sense in the provision of nutrition support e.g. a patient with a poor appetite may not be able or willing to consume extra food as snacks or may lack the energy or ability to prepare them.
- The nutrient intake has to be permanently evaluated during the hospitalization
- It is important to avoid the prescription, if possible, of drugs that have an indesirable effect on the appetite, provoque nausea and vomiting or have an impact on taste. If this is not possible the physician has to survey the nutritional status of the patient frequently
- The guidelines for administration of nutritional support, possible modifications or interruption of nutritional supplements have to be put in place
- Enteral or parenteral nutrition should only be prescribed if oral administration of nutritional supplements is not possible. The choice between enteral and parenteral nutrition has to be discussed with patient
- The standards concerning the meals in the hospital have to be put in place
- The quality and the quantity of the meal have to be discussed with the patient

- It is necessary to promote the training in field of nutrition for doctors and hospital staff in order to constantly expand their knowledge in field of clinical nutrition. The possibility is as well to integrate clinical nutrition and the treatment of malnutrition in the current program of studies of medicine.
- The subject of malnutrition has to be the part of training for nutritionist and dieteticians

It has been noticed that the gaps in diagnosis and treatment of malnutrition are due to the insufficient collaboration and communication between physicians, nutritionist, dieteticians and pharmacist. There is no rule concerning the attribution of responsibilities and competences to the different departments. The lack of consistent criteria to identify the malnutrition or risk of malnutrition is one of the important problems as well.

The collaboration and the communication between different departments can be optimised by creating organizational structures like Commission for Nutrition and Multidisciplinary Group for Nutrition that have clearly defined responsibilities (Keller, 2005).

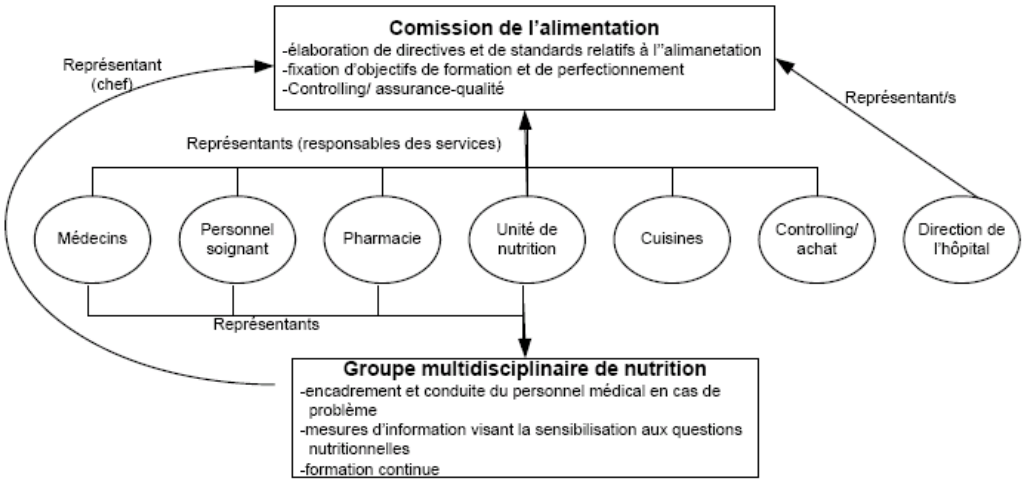

Figure 23: Composition and tasks of Commission for nutrition and Multidisciplinary group for nutrition

The Commission for nutrition depends directly from hospital direction. It is composed from representatives of each service. This department should have the same status as other specialised commissions like commission for hygiene. The responsibilities of this commission should be the part of the national standard. Commission for nutrition has as a task to develop directives for management of nutrition and malnutrition in hospital. This commission is responsible for usage of different recommendations and their efficiency as well as the training of hospital staff in field of nutrition.

Multidisciplinary group for nutrition gives the support and the advice to the physicians in case of problem by organizing the regular patients' visit with the physicians. They are responsible for the content of the training proposed to the hospital staff in field of nutrition.

6. CONCLUSION

Cancer became a major global public health problem and leading cause of death worldwide. According to WHO, the disease accounted for 7.4 million deaths (or around 13% of all deaths worldwide) in 2004.

In Europe, cancer is second most frequent cause of death and is becoming the leading cause of death in old age with more than 70% of cancer occurring in those aged over 65 years.

In Switzerland, cancer is fifth cause of hospitalization and it is responsible for 25% of deaths. Percentage of cancer related deaths per age group shows that 62% of patients are over 70 years old, while 32% of patients are in the age group between 50 and 69 years.

Patients with cancer may develop a wide range of symptoms and side effects due to the oncology treatment. Nutrition related symptoms, such as weight loss and malnutrition, reflect impaired nutritional status, which is often associated with reduced quality of life and response or tolerance to cancer treatment. In addition, it is well known that anticancer therapies may produce significant side effects, such as altered perception of taste and smell, food aversions, nausea and vomiting, oral and intestinal mucositis, stomatitis, bowel change and early satiety.

Depending on the type of cancer treatment (either curative or palliative) and on patients' clinical conditions and nutritional status, adequate and patient-tailored nutritional intervention should be prescribed (nutritional counselling, oral supplementation, enteral or total parantral nutrition). Such an approach, which should be started as early as possible, can reduce or even reverse the patients' poor nutritional status, improve their performance status and consequently their quality of life (QoL).

Average hospital length of stay for malnourished cancer patients is twice longer than for a well nourished patient with the same diagnosis.

In Switzerland the prevalence of malnutrition is around 20%. The extension of hospital length of stay in malnourished patients ranges from 1.63 up to 3.27 days compared to the well nourished patients. This leads to the cost related to management of malnutrition which ranges from 263 millions up to 1053 millions of Swiss francs. Malnutrition is a universal and costly public health problem in Switzerland, but is still largely unrecognised by individuals, by health and social care systems and by governments. This problem needs to be tackled at every level; by governments, by health and social care providers, by professionals and by individuals themselves.

Therefore, in addition of offering different type of nutritional supports for management of malnutrition, national guidelines for prevention and management of malnutrition have to be put in place together with government, physicians and health insurance companies. The prevention has to focus on two points: prevention of weight loss and weight maintenance in patients that are at risk of developing malnutrition.

Continued effort is needed to ensure guidelines are updated to reflect the evidence base; to integrate good nutritional care into guidelines for specific diseases (e.g. nutritional support as part of cancer care guidelines); and to ensure that these guidelines are recognised and established as a credible and essential basis for good patient care. Translation of "academic guidelines" into practical advice for healthcare professionals is needed to achieve both improved patient outcomes and to ensure appropriate use of resources. Sustained effort is needed as well to implement guidelines in practice; the link between guidelines, practical advice and individual care plans is critical and should be regularly audited and evaluated to identify challenges and successes which should be acted upon.

Specialized nutrition should help in controlling cancer-related symptoms, reduces postoperative complications and infection rate, shortens length of the hospital stay, improves tolerance to treatment, and enhances immunometabolic host response. By decreasing the length of the hospital stay, reducing the utilization of medical services for cancer related problems and by improving the nutritional status of the cancer patients, specialized nutrition should show the advantages by controlling and reducing the overall cost of patients care for hospitals and health insurances.

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