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Clinical and economic value of oral nutrition supplements in cancer patients: a position paper from the Survivorship Care and Nutritional Support Working Group of Alliance Against Cancer.

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Ministero della Salute

Research Article

Keywords: oral nutrition supplements, cancer patients, cancer treatment, nutritional support, malnutrition, cost-effectiveness

Posted Date: March 8th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1357518/v1

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Abstract

Malnutrition is a common clinical and public health problem that can frequently affect subjects in hospital and community settings. In particular, cancer-related malnutrition results from a combination of metabolic dysregulation and anorexia, caused both by the tumor itself and by its treatment. Patients with head-neck cancer, or with gastroesophageal, pancreatic, lung and colorectal cancer, are particularly at risk of developing malnutrition, with a prevalence varying between 30% and 50% since the early disease phases, according to the tumor location and anti-cancer treatment complications. Prevention and adequate management of malnutrition is now considered an essential key point of therapeutic pathways of cancer patients, with the aim to enhance their quality of life, reduce complications and improve clinical outcomes. Oral nutritional supplements (ONS) are part of the nutritional therapy and represent an effective tool to deal with cancer-related malnutrition, as supported by growing literature data. However, patients' access to ONS - which is regulated by different national and regional policies in terms of reimbursement - is quite heterogeneous.

This narrative review aims to summarize the current knowledge about the role of ONS in terms of cost-effectiveness in the management of actively treated cancer patients, following surgery and/or radiotherapy/chemotherapy treatment and to present the position on this issue of Alliance Against Cancer, the Italian National Oncology Network.

Introduction

The term malnutrition is commonly used to indicate a condition of under-nutrition, i. e. a condition resulting from inadequate nutrition - due to starvation, disease or advanced ageing, alone or in combination - that leads to alterations in body composition and body cell mass, with consequent reduced physical and mental function and impaired disease clinical outcomes (1).

Malnutrition is a common clinical and public health problem that affects subjects in hospital and community settings. In particular, malnutrition is a frequent comorbidity of cancer which results from a combination of changes associated with the tumor (e.g. malabsorption, obstruction, diarrhea, protein catabolism and vomiting), and the physical and psychological patient's reaction to the tumor, causing anorexia and impaired metabolism, and the side effects of anticancer treatments. Cancer-related malnutrition is considered a negative prognostic factor, as it may affect patients' survival, quality of life (QoL), functional status and tolerance to anticancer therapies (2, 3). Research data suggest that about 20–30% of cancer patients may die due to the consequences of malnutrition, rather than of cancer itself (4).

Several nutrition screening tools for the hospital setting have been developed so far to facilitate patients' nutritional status screening; however, there is currently no international consensus on a single optimal tool valid for all populations, ages and settings (5).

The Global Leadership Initiative on Malnutrition, endorsed by all major nutritional and medical societies worldwide, has recently developed a novel definition of malnutrition. Accordingly, the diagnosis of malnutrition should be based on a two-step procedure: in case of a positive nutritional screening, at least one phenotypic (weight loss, low body mass index [BMI], reduced muscle mass) and one etiological (reduced food intake or assimilation, inflammation/disease burden) criterion should be met (6).

The Alliance Against Cancer (ACC) is a National Oncology Network founded in 2002 by the Italian Ministry of Health, currently joined by 28 Italian Institutes, with the mission to bring technological and organizational innovation from basic research to clinical practice, raising and unifying the level of care, treatment, and rehabilitation of cancer patients throughout Italy. In this narrative review, the ACC Survivorship Care and Nutritional Support Working Group created in 2021 aims to summarize the state of the art concerning the use of nutritional support, and in particular of oral nutritional supplements (ONS) in actively treated cancer patients, with a focus on the most recent data highlighting their beneficial effects in terms of improvement of patients' clinical conditions and of cost-effectiveness for the healthcare system. Based on this framework, a literature search in PubMed was performed with particular reference the latest five years. The search used combinations of the following terms: cancer, head and neck cancer, pancreatic cancer, lung cancer, colorectal cancer, nutrition, oral nutritional supplements, malnutrition, cachexia, survival, nutrients, cost-effectiveness. Key words were linked using the "OR" Boolean function and the results of the single components were combined by using the "AND" Boolean function. Guidelines, clinical trials and observational studies written in English were selected.

Epidemiology Of Malnutrition In Cancer Patients

In the oncologic setting, the prospective, observational PreMiO study conducted at 22 medical oncology centers in Italy revealed that 51% of patients had a nutritional impairment, 9% were overtly malnourished, and 43% was at risk for malnutrition even at their first visit. The severity of malnutrition was positively correlated with cancer stage. Over 40% of patients were affected by anorexia, while 64% experienced weight loss during the prior six months (7). These data are consistent with findings of other studies, reporting malnutrition in a range from 15–80% of cancer patients (8–10). A prevalence of malnourishment was also found in 29.3% of pediatric cancer patients (11). Patients with head-neck cancer (HNC), including cancer of the oral cavity, pharynx, larynx, hypopharynx, paranasal sinus and esophageal cancer, or with gastroesophageal, pancreatic, lung and colorectal cancers, are particularly at risk of developing malnutrition, with a prevalence between 30% and 50% since the early disease phases, due to the tumor location and anticancer treatment (surgery, chemotherapy [CT], radiotherapy [RT] or concurrent chemoradiotherapy [CRT]) complications (10, 12). QoL-related scores have been found to be particularly low in HNC patients submitted to RT and are specifically susceptible to malnutrition during treatment, with no improvement in body weight or QoL (13). An aggregate burden of symptoms is a significant independent predictor of reduced food intake, weight loss and reduced survival in HNC patients before RT and/or chemotherapy, with the highest impact due to loss of appetite and difficulty chewing (14). These findings suggest that individual symptom profiles require a careful management to improve nutritional status. Also, McKenna *et al*. found that commonly available data, such as BMI and

percent weight loss, could be used to risk-stratify patients undergoing major surgical operations for different types of cancer. Moreover, the optimal definition of malnutrition used to assess the post-operative risk should be cancer-specific, introducing the concept of a tailored approach to malnutrition risk assessment (15). The prevalence of severe malnutrition in patients with gastrointestinal (GI) cancers ranges from 9–20%. Further studies estimated a 70% prevalence of malnutrition in upper GI cancers and pancreatic cancer, and 40% in colorectal cancer patients (7, 16). Guo *et al*. found 80.4% of hospitalized gastric cancer patients were malnourished and 45.1% needed an urgent nutritional support (17). Malnutrition and alteration in glucose homeostasis are common also in patients suffering from pancreatic cancer, considering the involvement of pancreas in food and nutrients metabolism through its secretion of enzymes and hormones. This may result in a catabolic state due to a combination of inadequate intake of nutrients and a pathological process of increased nutrient consumption because of tumor cytokine release. In 40.5% of patients affected by pancreatic cancer, cachexia is already present at the time of tumor surgical resection; moreover, the survival in presence of cachexia was significantly reduced in patients undergoing tumor resection as well as in palliative-treated patients (18). Others indicated that over 80% of pancreatic cancer patients report weight loss at the time of diagnosis and over a third of these patients lost more than 10% of their initial body weight (19). Furthermore, pancreatic cancer patients with malnutrition or cachexia experience a lower QoL, increased morbidity and mortality, longer hospital stays, and a reduced response to treatment (20).

Finally, malnutrition in lung cancer was found in 26–40% of patients before treatment and in 34.5–69% of cases considering all stages of the disease, as well (21–23). Moreover, a higher BMI has been associated with improved outcomes in patients who underwent surgical resection for lung cancer (including those with stage III + disease) (24).

Unmet nutritional needs in cancer patients: causes and potential remedies

Despite the clear indications emerging from the clinical practice that nutritional status deterioration negatively affects QoL, survival and tolerance to anticancer treatments (12, 25, 26) and the availability of national and international guidelines for nutritional care in oncology (27–29), many cancer patients still do not receive an early and adequate nutritional support before and/or during active anticancer treatment. As a matter of fact, nutritional support has been considered so far as part of palliative care for advanced cancer patients, aimed only at improving QoL, and clinical nutrition support is generally prescribed as an end-of-life intervention, overlooking its potential in enhancing active anticancer treatment efficacy and in improving disease outcomes (30).

A retrospective analysis of administrative data in the years 2013–2014 from Lausanne, Switzerland, revealed an improvement in screening of nutritionally ‘at-risk’ patients from 16.5% in 2013 to 41.9% in 2014. However, less than half of patients ‘at-risk’ received any nutritional care, and this value decreased between 2013 and 2014, with consequent higher in-hospital mortality and higher costs *vs.* ‘not at-risk’

patients (31). A retrospective analysis of data from three administrative healthcare datasets from France, Germany, and Italy on hospitalized GI cancer patients found that clinical nutrition is often not prescribed or prescribed as an end-of-life intervention only, indicating that in the real-world clinical practice, cancer-related malnutrition is underdiagnosed, under-reported and undertreated (32).

The guidelines issued by the Italian Ministry of Health in collaboration with the joint Working Group of the Italian Association of Medical Oncology (AIOM), the Italian Society of Artificial Nutrition and metabolism (SINPE), and the Italian Federation of Volunteer-based Cancer Organizations (FAVO) on nutritional pathways in cancer patients plead with Italian regions and healthcare companies to ensure that cancer patients receive an early nutritional assessment and a proper nutritional support to prevent or treat malnutrition (27). Unfortunately, no official data are currently available about the actual implementation of these guidelines (33), and recent surveys indicate that nutritional care practices still appear largely inappropriate (30). The lack of early and adequate nutritional support in actively treated cancer patients could be related mainly to the low awareness of nutritional issues among healthcare professionals, to low adherence to national and international guidelines and to the lack of a well-established collaboration between oncologists and clinical nutrition specialists (33–35). The European Society for Clinical Nutrition and Metabolism (ESPEN) launched a project to show the medical students the need of clinical nutrition (36). Other helpful initiatives to encourage the timely implementation of appropriate nutritional therapies for cancer patients have been described elsewhere (30).

Oral Nutritional Supplements

Foods for special medical purposes are defined by the European Commission Directive 609/2013/EC as a category of dietary foods which should be used under medical supervision and are specially processed or formulated for the dietary management of patients that are in the impossibility to take, digest, absorb, metabolize or excrete ordinary foodstuffs, or certain nutrients contained therein or metabolites, or that have specific medically-determined nutrient requirements that cannot be satisfied by modifying the normal diet (37, 38). This category is currently under the Regulation N. 2016/128 of the European Commission and includes ONS, as well as enteral tube feeding formulas.

ONS are commercially available medical nutrition products in the form of ready-to-drink liquids, semi-solids, powders (with proteins, maltodextrins or lipids) or creams (for patients with dysphagia) that provide macronutrients and micronutrients required when normal food is insufficient to maintain or increase energy and intake (28). They are usually nutritionally complete mixtures for oral consumption and are most often recommended to supplement volitional food intake. If nutrient intake remains inadequate, a medical nutrition therapy can be administered by oral, enteral or parenteral route, depending on the functionality of the GI tract. The criteria for the escalation of nutritional measures in cancer patients include: a) inadequate food intake anticipated for more than 10 days due to surgery, CT or RT; b) food intake < 50% of the requirements for more than 1–2 weeks; c) anticipation that patient will not be able to eat and/or absorb the adequate amount of nutrients for a long period time, due to

anticancer treatments; and d) the tumor itself impairs oral intake and food progression through the upper GI tract (39).

Various clinical trials are currently investigating the efficacy of perioperative enteral immunonutrition, i.e. ONS enriched in immunonutrients (arginine, glutamine, omega-3-fatty acids, ribonucleotides), and pre- and probiotics, with the aim of stimulating the host immune response, and improving control of the inflammatory response in cancer patients submitted to major surgery or CRT, as covered also by the most recent ESPEN guidelines (40, 41).

Advantages of medical nutrition intervention with ONS in cancer patients in the hemotherapy/radiotherapy/surgical setting

Literature data are increasingly supporting the effectiveness of nutritional therapy in cancer patients, with particular reference to hospital readmissions, hospital length of stay (LOS), response to anticancer treatments, and clinical outcomes. A retrospective cohort study recently analyzed the ONS utilization rate, hospital LOS and 30-day unscheduled hospital readmissions in an academic medical center hospital in United States and revealed that only 3.1% of malnourished patients received ONS, and that ONS users in oncology departments had 46.1% fewer readmissions than non-ONS counterparts; in addition, a shorter hospital LOS was observed when the interval between admission and ONS initiation was reduced (42).

A secondary analysis of the data from the Swiss prospective, randomized-controlled, multicenter trial EFFORT compared the outcomes of a protocol-guided individualized nutritional support (intervention group) to standard hospital food (control group) in 506 patients with a main admission diagnosis of cancer and characterized by a broad spectrum of cancer sites, treatment types and disease severities. Individualized nutritional support reduced the risk of mortality and improved functional and QoL outcomes in cancer patients with increased nutritional risk, further supporting the inclusion of nutritional care in cancer management guidelines (43). An improvement of nutritional status has been detected in pediatric cancer patients in the first 3 months of treatment, through the administration of ONS to subjects with a food intake < 75% of the recommended nutritional values for 3–5 consecutive days or through a nasoenteric tube when oral feeding was impossible, or when food intake was insufficient (oral intake < 60% of the recommendations) for 3–5 consecutive days (11). A double-blind, controlled trial evaluating the safety and tolerability of an oral targeted medical nutrition (TMN) supplement for the management of cachexia in patients with non-small-cell lung cancer revealed a trend for improved clinical outcomes and fewer adverse events with TMN vs. the comparator group (44).

In HNC, GI, and pancreatic cancer patients, the common anticancer treatments (i.e. surgery, RT, CT, or their combination) can often lead to consequences (e.g. dysphagia and xerostomia) that further complicate and challenge oral intake of food, with additional deleterious consequences on nutritional status (45).

However, a growing number of clinical studies is supporting ONS administration as an effective tool to limit cancer treatment consequences in those cancers. Preoperative nutrition intervention prior to upper GI cancer resection in 200 patients from Australia led to lower weight loss compared to those who did not follow the intervention and to lower hospital LOS in the group of patients who received ONS for > 2 weeks (46). A review of 29 trials, including studies on GI cancer patients, did not show a longer survival through the use of an adjuvant nutritional support, but revealed a significant benefit for a longer survival in a few selected subgroups of patients, depending on the tumor stage and compliance with nutritional support (47). Body weight loss was found lower in the ONS compared to the control group in a meta-analysis of randomized controlled trials involving GI cancer patients submitted to gastrectomy and/or chemotherapy. However, other anthropometric parameters did not differ significantly between the ONS and the control group (48). Kim et al. showed an increase in body weight, fat-free mass, skeletal muscle mass, body cell and fat mass in the ONS group vs. a decrease of those data in the control group in pancreatic and bile duct cancer patients receiving CT. Even the subjective global assessment and the fatigue scores were improved in the ONS group (49). A nutritional intervention in GI cancer patients undergoing perioperative CT should be aimed at preventing unintentional weight loss, thus reducing the risk of postoperative complications and sarcopenia, and improving the short-term survival (50). ONS administration for three months together with dietary advice in post-discharge patients at nutritional risk following colorectal cancer surgery reduced skeletal muscle loss and sarcopenia prevalence, as well as improved CT tolerance, compared to the group with dietary advice alone, thus underlying the importance of ONS treatment in post-discharge patients at nutritional risk (51). Despite these positive data, it should be noticed that the evidence for a positive influence of ONS on weight and nutritional status in patients undergoing surgery after CT for GI cancer should be supported by further research into optimal and customized nutrition support interventions and timing of interventions (52).

Nutritional counseling in combination with the administration of ONS from the start of RT in HNC patients and continuing for up to 3 months after its end showed better results *versus* nutritional counseling alone in terms of weight maintenance, with a smaller loss of body weight, increased protein-calorie intake, improved QoL and a better anticancer treatment tolerance. In addition, the use of ONS decreased the need for reduction or complete suspension of scheduled anticancer treatments (53). A cross-sectional study including 97 patients treated for oral and oropharyngeal cancer with a combination of surgery and CRT reported an immediate decrease of the QoL after the treatment and a 40.2% prevalence of malnutrition. However, malnutrition was prevented in a significant number of patients (72.5%) who were provided with ONS (54).

Also for lung cancer patients some studies have shown some improvements in weight maintenance, muscle function, and quality of life (22). ONS enriched with omega-3 fatty acids seemed to improve energy and protein intake, body composition and decreased fatigue, loss of appetite and neuropathy (55).

With reference to the immunonutrition described above, clinical data are increasingly emerging about its use in the oncologic setting and have shown that it is able to reduce overall infectious complications and hospital LOS in patients undergoing cancer surgery, but without affecting mortality (56). The meta-

analysis of six randomized clinical trials enrolling patients affected by pancreatic cancer and undergoing surgical intervention revealed that immunonutrition significantly decreased the rate of infectious complications and the LOS by modulating the immune system, especially in the preoperative period (57). A single armed study with a historical control group including consecutive patients undergoing salvage surgery for recurrent HNC showed that preoperative immunonutrition was associated with a significant reduction in overall complications (35% *vs.* 58% in control group) and in hospital LOS (6 days *vs.* 17 days in control group) (58). The effectiveness of immunonutrition in addition to nutritional counseling in increasing the tolerance to CRT is now being tested *vs.* standard ONS in a pragmatic, bicentric, randomized, parallel-group, open label, controlled, pilot clinical trial enrolling HNC patients (59).

Benefits and advantages of an early nutritional intervention for cancer patients

Early identification of cancer patients at risk of malnutrition or who are malnourished is crucial in order to start a timely and adequate nutritional therapy. A seminal study including data from hundreds of patients in various hospital types showed that an early nutritional intervention reduced the average hospital LOS of 3.0 days *versus* a late nutritional intervention (60). With particular reference to cancer patients, a bicentric single-arm clinical trial enrolling 131 hypophagic, hospitalized cancer patients at nutritional risk and with contraindications for enteral nutrition revealed that an early 7-day supplemental parenteral nutrition resulted in improved body composition, handgrip strength and serum prealbumin levels, in the absence of any relevant clinical complications (61).

Wei *et al.* analyzed retrospectively the effect of early nutritional intervention on RT-induced oral mucositis and nutritional status in patients with HNC *vs*. enteral nutrition after restricted feeding. The authors reported an incidence of high-grade oral mucositis significantly lower in the early group *vs.* the late group (17.9% *vs.* 50%). Also, nutritional status assessments showed significantly weight and BMI losses in the latter group than in the former group at weeks 4 and 7 after RT. Moreover, fewer patients were malnourished in the early nutrition intervention group compared to the late intervention group (62).

These results are consistent with findings of another retrospective, exploratory study analyzing the electronic medical record data of patients with HNC undergoing CRT or RT. The patients that received a nutritional intervention since admission by a nutritional support team experienced a median weight loss of 3.3% *vs.* 7.3% in nonintervention group. In addition, grade 3 mucositis was observed in 25.0% of patients in the early nutritional intervention group *vs.* 70.0% in the nonintervention group. Finally, patients in the early nutritional intervention group were discharged earlier than those in the nonintervention group, with a median hospital LOS from the end of treatment of 12 days *vs*. 18 days (63).

New opportunities in the field of nutritional support are emerging from the application of artificial intelligence (AI). Machine learning (ML) is currently being tested on large electronic data sets as a tool to identify and grade malnutrition using large-scale data from cancer patients and could be helpful to speed

up the diagnosis of malnutrition and implement a timely, individualized nutritional support in at-risk patients. In this setting, an observational, nationwide, multicenter cohort study that included 14134 cancer patients revealed the effectiveness of a ML-based algorithm to develop a fusion decision system that can be used to facilitate the identification and severity grading of malnutrition in patients with cancer (64). Research is also focusing on the application of AI in the imaging of sarcopenia, to improve its evaluation and prediction of outcomes (65). ML-based algorithms could represent a more flexible, automatic, and unified nutritional risk screening approach, with subsequent escalation of patients to nutrition groups as appropriate (66).

Cost-effectiveness Of Ons-based Malnutrition Treatment In Cancer Patients

In addition to adverse consequences on QoL and disease prognosis, malnutrition in cancer patients can result in higher overall treatment costs, with an estimated annual cost up to 120 billion euros in Europe, an additional cost of 1.640–5.829 euros per hospitalized patient and an overall cost ranging between 2.1 and 10% of the health expenditures of every single European Country (31).

ONS have been used in the clinical practice since two decades; however, only recently the number of studies assessing to which extent nutritional interventions in a hospital setting, and, in particular, in the treatment of cancer patients, can impact on the budget of healthcare systems, is increasing. Actually, nutrition has often been neglected as a potential cost containment measure because its benefits are not always immediate. Consequently, nutrition intervention has been long considered an added cost of questionable benefit. Data from studies in different healthcare settings worldwide are now overturning this concept. Among others, a systematic review of nine publications focusing on the cost and cost effectiveness of standard ONS in the hospital setting revealed a mean significant net cost saving of 12.2% with the use of ONS *vs.* no use of ONS (or routine care), with cost savings associated with significantly improved outcomes (reduced mortality, reduced complications, about 13.0% reduction in LOS) (67). An earlier study by Tucker et al. reported a saving of about 1.464 USD for each patient when considering a reduction of the average LOS of 2.1 days when early *vs.* late nutrition intervention is applied, as emerged from the Malnutrition Cost Survey, a tool designed to evaluate hospital malnutrition in terms of both patient outcome and total hospital costs in Georgia, USA (60). A nutrition-focused quality improvement program (QIP) applied on hospitalization rates and healthcare costs for a period of 90 days involving at risk/malnourished adult individuals in a home health setting in United States, led to a reduced relative risk of hospitalization post-enrollment to the QIP by 24.3%, 22.8%, and 18.3% at 30, 60, and 90 days, respectively, when compared with a control group, with a cost saving of 1.500 USD/patient derived from the reduced utilization of healthcare resources (68). The ASPEN Value Project Task Force reviewed the existing literature from 2013 to 2018 to evaluate the clinical and economic impact of nutrition intervention on patient outcomes across 13 therapeutic areas, including GI cancer using ad-hoc models. The study revealed annual cost savings of 18 million USD in the setting of GI cancer following the implementation of a nutrition support therapy (69).

With reference to the cost-effectiveness of nutritional support specifically in the oncological setting, data from the prospective, single-center randomized clinical trial on HNC patients undergoing RT on nutritional counseling with or without systematic use of ONS described above (53) have been subsequently used in a cost-effectiveness analysis of ONS use in cancer patients over a period of 5 months (70). The mean costs in the intervention group with ONS were about 987 euros, while the mean costs in the control group with nutritional counseling only were about 996 euros, returning a difference of -8.96 euros. Of note, the difference in mean costs was not significant from both a statistical and economic point of view, meaning that the additional costs of ONS were offset by the higher hospitalization and artificial nutrition costs in the control group. At a median 6-year follow up, the ONS treatment group had a significantly better survival rate when adjusting for late effect. Finally, ONS in addition to nutritional counseling proved to be less costly and more effective than nutritional counseling alone, with an incremental cost-effectiveness ratio of -3,277 euros per quality-adjusted life years.

A recent study analyzed the public policies that are assumed to affect patient access to ONS, using the Italian regionalized healthcare system as a case study and the centralized British National Health System (NHS) as a counter-factual example, providing important reflections on policy that could inform other countries (71). In more detail, the analysis by Cavazza *et al.* has shown that, on average, 32% (0.26 euros *per capita*) of the 49.5 euros million total market (0.82 euros *per capita*) for ONS in Italy in 2015 was covered by the national healthcare system, with a large regional variation in the proportion covered by public funds. However, no clear relationship between regional policies in terms of cost reimbursement to patients and access to ONS emerged, concluding that patient access to ONS could be enhanced by integrating heterogeneous regional policies with national and systematic measures aimed at increasing awareness of the role of healthcare providers in different therapeutic areas. These actions have been successfully implemented by the British NHS.

Interestingly, the use of ONS in the community significantly reduces hospital (re)admissions from 33.8–23.9%, particularly in older patient groups, with economic implications for healthcare, as revealed by a systematic review and meta-analysis of nine randomized clinical trials (72).

Of note, the current analysis of cost-effectiveness of immunonutrition in GI oncologic surgery is also leading to generally positive outcomes, with immunonutrition overcompensating costs for post-operative complications (e.g. infections) with a significant net saving, despite the generally higher cost of immunonutrition *vs*. standard ONS (73, 74).

Overall data on cost-effectiveness of ONS implementation in the clinical practice are positive and encouraging. The favorable cost-effectiveness outcomes associated with the use of ONS in a hospital setting was at least in part expected if considering their positive clinical effects described above and their small cost compared to total expenses of hospitalization. Nonetheless, additional studies, based on more homogeneous and stringent criteria, e.g. with reference to the type of intervention, healthcare setting, condition being treated, the patients' nutritional status and the type of nutritional support, ranging from specialized form of nutritional support, such as enteral tube feeding and parenteral nutrition, to oral

nutrition support, are warranted to confirm the results we summarized. These studies could represent a valuable tool for Institutions involved in healthcare planning and in policy making.

An emerging critical point is the key role played by the collaboration between specialists in clinical nutrition and primary care physicians in the implementation of ONS in therapeutic pathways. Such collaboration would be fundamental for the identification of target patients and their referral to the appropriate clinical nutrition specialists or dedicated centers/units. This requires organizational efforts, but, above all, corrective measures (e.g. at educational and organizational level).

Conclusions

A comprehensive care of cancer patients, and in particular those affected by HNC, GI, pancreatic and lung cancer, should include a careful evaluation of their nutritional status before initiating cancer treatment, as well as frequent re-evaluation during and after therapy administration.

A flexible, individualized and integrated approach seems to be favorable, and an early counselling by a multidisciplinary team, including nutritionists, dieticians, oncologists and nurses, who guides and evaluates nutritional management, is of fundamental importance.

The available cost-effectiveness data show that additional costs of ONS administration to malnourished or at-risk cancer patients are offset by the lower hospitalization and treatment costs.

Well-sized and well-designed clinical trials are needed to further confirm the role of ONS in different care settings for cancer patients. Moreover, national and international healthcare guidelines and public policies should be revised to take into greater account the importance of ONS in improving the cost-effectiveness balance in cancer care.

The final statements of the present position paper are summarized in **Table 1**.

Table 1

Final statements by the ACC Survivorship Care and Nutritional Support Working Group

- In addition to adverse consequences on anticancer treatments' tolerance, quality of life and prognosis, malnutrition in cancer patients can result in higher overall healthcare costs.

- The additional costs of ONS administration to malnourished or at-risk cancer patients are offset by the lower hospitalization and treatment costs.

- Nutritional assessment and support should be considered in all stages of cancer, with particular attention to the early stage of the disease, when advantages for patients in terms of disease outcomes and quality of life are particularly evident.

- Identification and setting up of a malnutrition multidimensional screening tool should be considered to help professionals to profile patients and build up a standard evaluation scale for their nutritional risk.

- Unique individual profiles should be assessed and managed to risk-stratify patients for the type of cancer, type of intervention and clinical data.

- Evidence for the use of specific ONS in cancer patients undergoing surgery or chemo/radio/immunotherapy should be sustained by further research into tailored optimal nutrition support interventions and timing of administration.

Declarations

Acknowledgments

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Funding:

This paper was partially funded by an unconditional grant from Unione Italiana Food.

Conflicts of interest/Competing interests:

All authors have no conflict of interest to declare.

Availability of data and material:

Not applicable.

Code availability:

Not applicable.

Authors' contributions:

All authors contributed to the article conception and design.Material preparation and literature collection were performed by all authors.The first draft of the manuscript was written by Riccardo Caccialanza, Alessandro Laviano and Paolo Pedrazzoli. All authors commented on previous versions of the manuscript.All authors and the ACC Survivorship Care and Nutritional Support Working Group (Nutrional Support Commission) read and approved the final version of the manuscript.

Ethics approval:

Not applicable.

Consent to participate:

Not applicable.

Consent for publication:

Not applicable.

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