Support Care Cancer (2016) 24:469–480
DOI 10.1007/s00520-015-2958-4

REVIEW ARTICLE

Nutrition intervention approaches to reduce malnutrition in oncology patients: a systematic review

Jia Li Charmaine Lee[1] · **Lai Peng Leong**[1] · **Su Lin Lim**[2,3]

Received: 30 June 2015 / Accepted: 14 September 2015 / Published online: 24 September 2015

Abstract
Purpose Malnutrition is a very common problem in oncology patients and is associated with many negative consequences including poorer prognosis, quality of life and survival. However, malnutrition in oncology patients is often overlooked although there is growing evidence showing that it can be prevented or reduced through nutrition intervention. This paper aims to provide an updated review on the effectiveness of different nutrition intervention approaches on nutrition status outcomes in oncology patients.
Methods Randomised controlled trials (RCTs) published between 1994 and 2014 which examined the effects of nutrition intervention approaches—in particular, nutrition counselling (NC), oral nutrition supplements (ONS) and tube feeding (TF)—on nutrition status outcomes of oncology patients were identified and reviewed.
Results Thirteen papers from 11 RCTs with a total of 1077 participants were included. The intervention approaches included NC (four studies), NC+ONS (five studies), ONS (three studies) and TF (three studies). The various results suggest that NC with or without ONS was associated with consistent improvements in several nutrition status outcomes. On the other hand, ONS and TF were associated with inconsistent improvements in few aspects of nutrition status outcomes.
Conclusions The referral of oncology patients for NC is recommended given the strong evidence of its beneficial effects on the prevention and reduction of malnutrition. Other forms of nutrition support including ONS and TF may then be included if deemed suitable and necessary for the individual.

Keywords Nutrition intervention · Nutrition status · Nutrition counselling · Oral nutrition supplements · Tube feeding · Cancer

Abbreviations

ADA-MNT	American Dietetic Association Medical Nutrition Therapy
BMI	Body mass index
CRT	Chemoradiotherapy
CT	Chemotherapy
EPA	Eicosapentaenoic acid
FFM	Fat-free mass
GR	Group rehabilitation
IS	Individual support
ISGR	Individual support and group rehabilitation
NC	Nutrition counselling
NGT	Nasogastric tube feeding
NI	No intervention
ONS	Oral nutrition supplements
PEG	Percutaneous endoscopic gastrostomy feeding
PG-SGA	Patient-generated subjective global assessment

✉ Su Lin Lim
su_lin_lim@nuhs.edu.sg

Jia Li Charmaine Lee
charmaine_lee@u.nus.edu

Lai Peng Leong
laipeng@nus.edu.sg

[1] Food Science and Technology Programme, Department of Chemistry, National University of Singapore, Singapore 117543, Singapore

[2] Dietetics Department, National University Hospital, 5 Lower Kent Ridge Road, Main Building, Singapore 119074, Singapore

[3] School of Exercise and Nutrition Sciences, Queensland University of Technology, Brisbane, Australia

PPDI	Patient participation-based dietary intervention
QoL	Quality of life
RCT	Randomised controlled trial
RT	Radiotherapy
TF	Tube feeding
UC	Usual care

Introduction

Malnutrition is prevalent in oncology patients with incidence ranging from 40 to 80 % [1–3]. Malnutrition in cancer patients may be caused by multiple factors, including response to the tumour and cancer treatments [4–6] as well as emotional and psychological changes in the patient [7]. Food aversion may also result from altered taste perception following cancer treatments such as chemotherapy and radiotherapy [8, 9]. Furthermore, individuals with cancers affecting the head, neck and gastrointestinal system may experience pain and discomfort during food consumption, resulting in reduced food intake [10] as well as poorer nutrient uptake and utilisation caused by decline in digestive organ function. Consequently, patients with these types of cancers are at the greatest risk of malnutrition [11].

Malnutrition leads to adverse consequences such as poorer prognosis and treatment outcome [11, 12], reduced functional status [13, 14], reduced quality of life (QoL)[1] [10, 14], increased risk of chemotherapy-induced toxicity [11] and postoperative complications [16]. These malnutrition-associated consequences of cancer in turn lead to poorer survival [17]. Furthermore, malnutrition was also associated with longer duration of hospital stays, poorer hospitalisation outcomes and higher healthcare costs [2].

Malnutrition in oncology patients often involves cancer cachexia, which is characterised by progressive muscle wasting that cannot be completely reversed by conventional nutrition support [18]. This condition is often accompanied by anorexia, reduced food intake, metabolic abnormalities, fatigue as well as impaired immune and physical function [18, 19] which exacerbates the condition of the patient.

Despite its high incidence and adverse effects, malnutrition in oncology patients is an often overlooked condition that should be addressed with early and systematic nutrition support [3, 14, 17]. Early and sustained nutrition intervention has been shown to be effective in reducing weight loss [15, 20, 21] and alleviating malnutrition-associated effects including improving tolerance to cancer treatment, reducing incidence of hospital admission [20] and improving QoL [15, 22]. At present, the main nutrition intervention approaches used for oncology patients include nutrition counselling (NC) by a dietitian or other healthcare professionals [21], prescription of oral nutrition supplements (ONS) [5, 23] as well as tube feeding (TF). These interventional approaches may be used alone or in combination. This review will critically evaluate the effectiveness of the different methods of nutrition intervention on nutrition status outcomes based on existing literature.

Materials and methods

Database search

Original research articles published from 1994 to 2014 which studied the effects of nutrition intervention approaches (i.e. NC, ONS and TF) on outcomes of oncology patients were sourced from electronic databases including PubMed (MEDLINE), the Cochrane Central Register of Controlled Trials (CENTRAL), the American Society for Parenteral and Enteral Nutrition (ASPEN) and the Academy of Nutrition and Dietetics (AND) Evidence Analysis Library. The primary outcomes analysed in this review are nutrition status outcomes (e.g. weight, patient-generated subjective global assessment (PG-SGA),[2] body mass index (BMI) and muscle mass) though other outcomes (e.g. mortality, infection and QoL) were also explored. The exposure search terms used were 'nutrition intervention', 'oral nutrition supplementation', 'nutrition therapy', 'enteral nutrition', 'tube feeding', 'gastrostomy feeding', 'jejunostomy feeding', 'nutrition counselling', 'dietary counselling' and 'dietitian counselling' and the outcome search terms used were 'malnutrition', 'nutrition status', 'weight', 'BMI' and 'SGA'. Studies on parenteral nutrition were excluded as practice guidelines recommend parenteral nutrition to be used only when the gastrointestinal tract is unable to function [24].

Selection of studies

The inclusion and exclusion criteria are listed in Table 1. Only randomised controlled trials (RCTs) and pseudo-randomised trials (trials which used quasi-random allocation methods such as assignment by postal code) were included. The studies had to involve adult oncology patients (>19 years). Patients of all types and stages of cancer, as well as receiving all types of oncology treatments (e.g. radiotherapy (RT), chemotherapy

[1] Quality of life (QoL) of patients is assessed using questionnaires with different items such as physical, emotional and social function as well as patient symptoms [15].

[2] Patient-generated subjective global assessment (PG-SGA) is a nutrition status assessment tool based on the dietary intake, weight change, functional capacity, symptoms and physical examination that has been validated for use on cancer patients. After the assessment, patients are classified as well-nourished (A), moderately malnourished (B) and severely malnourished (C) [20]. A numerical PG-SGA score is also given, with higher scores indicating poorer nutrition status [12].

Table 1 Inclusion and exclusion criteria of papers included in review

Selection criteria	Inclusion criteria	Exclusion criteria
Type of studies	RCTs and pseudo-randomised trials	Non-randomised trials, non-controlled trials, animal trials, in vitro studies, etc.
Patient characteristics	Adults (>19 years) All types and stages of cancer Receiving all types of oncology treatments (e.g. RT, CT, surgery) All types of settings (e.g. outpatient and hospitals)	Infants and children (≤19 years)
Type of nutrition intervention	NC and/or ONS (to increase energy and protein intake but not to modulate the immune function) and TF	ONS (to modulate the immune function), parenteral nutrition, drug interventions, etc.
Outcomes studied	Nutrition status (e.g. weight, BMI, PG-SGA score) and others, if any	

BMI body mass index, *CT* chemotherapy, *NC* nutrition counselling, *ONS* oral nutrition supplements, *PG-SGA* patient-generated subjective global assessment, *RCTs* randomised controlled trials, *RT* radiotherapy *TF* tube feeding

(CT), surgery), were included. The selection criteria for papers included in the systematic review are summarised in Fig. 1. We did not perform a meta-analysis due to the high degree of heterogeneity between the studies.

Results

Literature search

Thirteen papers with a total of 1077 participants were included. Four papers originated from two trials [25–28], with a short-term [26] and long-term study [25] of colorectal cancer patients as well as a single study on gastrointestinal tract as well as head and neck cancer patients which reported on different nutrition status outcomes in two papers [27, 28]. As such, there were 11 RCTs that were included in the review. The intervention approaches included NC (four studies; five papers) [25, 26, 29–31], NC+ONS (five studies; six papers) [21, 23, 27–29, 32], ONS (three studies; four papers) [25, 26, 29, 31] and TF (three studies; three papers) [15, 33, 34]. All the papers reviewed are summarised in Table 2.

Nutrition counselling

The first approach commonly used to prevent or manage malnutrition is NC, which is the provision of individualised advice to patients to modify or enhance their diet. Dietitians and other healthcare professionals may provide patients and their caregivers advice on ways to increase the

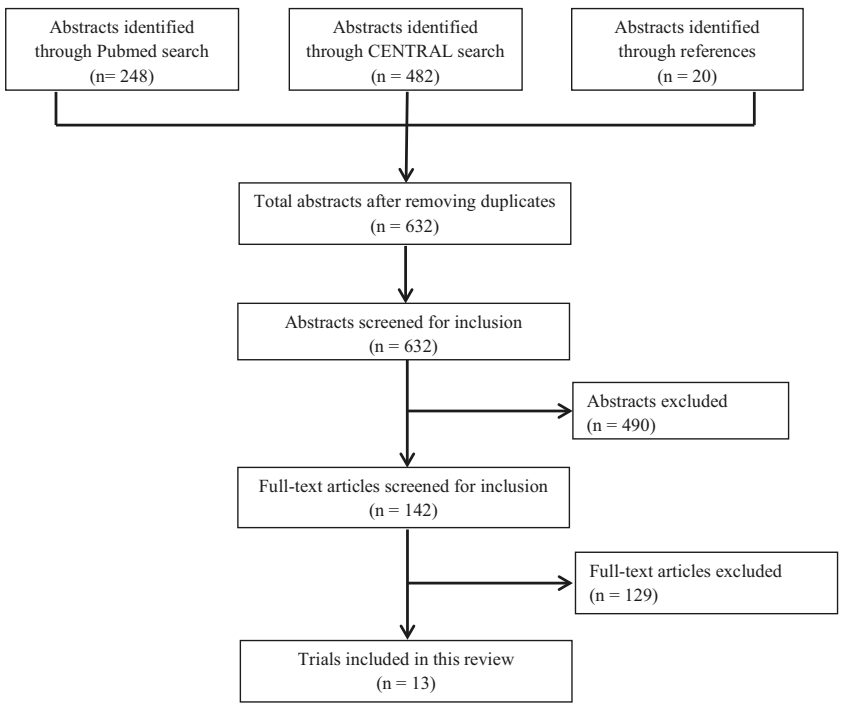

Fig. 1 Flow diagram for selection of studies

patient's calorie and protein intake through regular foods as well as encourage certain modifications to the patient's current diet. Furthermore, NC allows for nutrition advice based on each patient's health condition and lifestyle [29]. Here, we first review the effectiveness of NC with no prescription of ONS by the dietitian.

All the four studies that investigated the effect of NC (with no ONS prescription) on nutrition status [25, 26, 29–31] reported positive effects of NC on different aspects of nutrition status including weight gain [29], PG-SGA scores [25, 26, 30, 31] and BMI [25]. However, no significant difference in weight, BMI as well as triceps and scapular muscle mass change over 12 weeks was found between the NC and control groups although improvements in PG-SGA was reported following intervention in one study [30]. In another study which also reported improvements in PG-SGA, no significant difference in the number of patients who showed improvements in BMI between the NC and control groups was found [26].

A significant improvement in energy and protein intake was noted among NC patients as compared to control patients in all four papers that included nutrition intake as an outcome [25, 26, 30, 31]. Nutrition intake was also correlated with nutrition status [31]. Four of the five papers that included QoL as an outcome found improvements in QoL function scores [25, 26, 30, 31], with only one paper reporting no significant difference between groups for QoL change from baseline to week 6 and week 26 [29]. Furthermore, QoL change was also correlated with nutrition intake or status change in three papers [25, 26, 31]. NC was consistently associated with patients experiencing fewer [25, 26, 31] and less severe RT toxicity symptoms [25, 31]. In one paper, survival in colorectal cancer patients who received NC improved [25] while in another paper, no significant difference between both groups of patients was found [29].

Nutrition counselling with oral nutrition supplements

While there is evidence that NC alone improves nutrition status outcomes and other clinical outcomes of patients, the combined use of NC with ONS is usually recommended for oncology patients. This is especially for patients who have difficulties meeting the recommended nutrition intake through consumption of regular foods. In this section, we review the effectiveness of NC with ONS as recommended by the dietitian on the nutrition status of oncology patients.

Five studies (six papers) investigated the effect of NC+ONS on nutrition status outcomes [21, 23, 27–29, 32]. In one paper [29], although there was a group of patients who received NC+ONS, there was no specific comparison of this group of patients against those who received no form of intervention. It was only reported that the patients who received NC showed greater weight gain compared to those who did not [29]. The other five papers showed that the intervention approach (NC+ONS) was associated with improvements in nutrition status outcomes including weight gain [32], weight maintenance [21, 23, 28], BMI gain [32], PG-SGA improvement [27, 28] and fat-free mass (FFM) maintenance [23]. However, in three of the papers [21, 23, 28], no significant differences in BMI [21], FFM loss [28] and fat mass loss [23] were observed between the control and intervention groups.

The only paper which reported on nutrition intake as an outcome found that NC+ONS was associated with an increase in energy and protein intake [27]. As for QoL, one paper found that the intervention approach was associated with improvements in the maintenance of global QoL and physical function [28] while two other papers found no significant improvements in QoL [29, 32]. Survival was not significantly different between patients who received NC+ONS compared to those who did not in both papers which reported on survival as an outcome [29, 32].

Oral nutrition supplements

Oral nutrition supplementation without NC may also be used to increase caloric and protein intake of patients [26, 29, 31, 35]. ONS is usually used to supplement the regular diet, although they may act as a meal replacement for patients who are unable to consume regular foods.

Three studies (four papers) investigated the effect of ONS on the nutrition status of oncology patients in terms of weight, BMI and PG-SGA scores [25, 26, 29, 31]. In all four papers, ONS was associated with improvements in nutrition status outcomes compared to the control group though these improvements were mostly not statistically significant [25, 26, 29, 31].

Only one paper found statistically significant improvements in BMI and PG-SGA scores in patients who received ONS compared to control patients [26], while two other studies found no significant improvements in weight gain [29] and PG-SGA scores [31]. Another long-term follow-up study did not report clearly whether ONS was associated with any improvements in nutrition status [25].

Only one of three papers reporting on nutrition intake found significant improvements in patients using ONS [26]. However, the long-term follow-up [25] of that study and another short-term study [31] found no significant difference in nutrition intake in both groups. The paper that reported positive results also found that the intake eventually decreased to baseline or below baseline for both the ONS and control groups after 3 months [26]. Caloric and protein intake was positively correlated with nutrition status in both groups in one of the papers [31]. Two studies found short-term improvements in some QoL scores in the ONS group when compared to the control group which showed deterioration in all QoL scores [26, 31]. Two other studies [25, 29] found no

Table 2 Summary of RCTs studying the effect of nutrition intervention approaches on nutrition status outcomes of oncology patients

Author, year	No. of participants	Main inclusion criteria	Intervention	Length of follow-up	Nutrition status outcomes	Other outcomes
Baldwin et al., 2011 [29]	358	Advanced gastrointestinal tract cancer, non-small cell lung cancer or mesothelioma; CT; weight loss in the last 3 months	(A) NI (B) NC (to increase food intake by 600 kcal/day) (C) ONS (powder mix providing 588 kcal/day in 240 mL of full-cream milk+multivitamin and mineral supplement) (D) NC and ONS Start: before start of CT Duration: 6 weeks	52 weeks	*Weight gain at 1 year*: greater in patients who received NC than those who did not on an as-treated basis (4.78 vs. 7.5 kg, $P=.04$); greater in patients who received ONS compared to those who did not though this difference was not statistically significant.	*1-year survival, QoL change from baseline to 6 and 26 weeks and hand grip strength*: no significant difference between groups.
Kim et al., 2014 [30]	56	Stomach cancer (stage I to III); gastrectomy	(A) PPDI (includes NC by nurses) (B) UC Start: 1 day before hospital discharge Duration: 6 weeks	3 months	*Change in PG-SGA*: greater decrease (improvement) in PPDI group than UC group (−5.73 vs. −3.91, $P=.003$); *Weight and BMI deterioration over 12 weeks*: no significant difference; *Triceps muscle mass*: no significant difference.	*Nutrition intake*: improved in the PPDI group; *Functional and performance status*: improved in the PPDI group; *Adverse dietary symptoms*: fewer in the PPDI group than the UC group ($P<.05$).
Ravasco et al., 2012 [25]	89	Colorectal cancer; neoadjuvant RT	(A) NC (B) ONS (400 mL/day of high-protein and energy-dense liquid formulation providing 400 kcal and 40 g protein) (C) NI Start: after starting RT Duration: 6 weeks (throughout RT)	6.5 years	*Deterioration in PG-SGA and BMI at ~6.5 years follow-up*: more prevalent in ONS and NI groups than NC group ($P<.002$); *Maintenance or improvement in PG-SGA and BMI at ~6.5 years follow-up*: more prevalent in the NC group than the ONS and NI groups ($P<.005$).	*Energy and protein intake at 3 months after RT*: greater in the NC group than the ONS and NI groups which were similar to each other ($P<.002$); *Change in energy and protein intake after ~6.5 years*: maintained in the NC group but decreased for the ONS and NI groups ($P<.06$); *QoL*: better in the NC group than the ONS and NI groups which were similar to each other ($P<.002$); better QoL was associated with maintenance of adequate intake and nutrition status ($P<.002$); *Disease-specific median survival*: longer in the NC group than the ONS group which was in turn longer than the NI group (7.3 vs. 6.5 vs. 4.9 years, $P<.05$); *Late RT toxicity*: less prevalent and severe in the NC group than the ONS and NI groups which were similar to each other ($P<.002$).
Ravasco et al., 2005 [31]	75	Head and neck cancer; RT	(A) NC (B) ONS (400 mL/day of high-protein and energy-dense liquid formulation providing 400 kcal and 40 g protein) (C) NI Start: after starting RT Duration: 6 weeks (throughout RT)	3 months	*Number of patients who showed further PG-SGA deterioration at the end of RT and 3 months*: fewer in the NC group than the ONS and NI groups ($P<.002$); *Number of patients who maintained or showed improvements in PG-SGA scores both at the end of RT and 3 months*: greater in the NC group than the ONS and NI groups ($P<.001$); *Proportion of malnourished patients at baseline who improved in nutrition status*: 50 % in the NC group at 3 months, with an average recovery of 4 kg; none in the ONS and NI groups.	*Energy and protein intake*: increased in the NC and ONS groups from baseline to end of RT ($P\leq.05$), with a larger increase in energy intake in the NC group ($P=.005$); decreased in the NI group ($P<.01$); intake at 3 months was maintained in the NC group ($P<.05$) but decreased to baseline or below baseline in the ONS and NI groups ($P=.005$); intake correlated with nutrition status ($P\leq.002$); *Proportion of patients who experienced fewer or less severe RT-induced morbidity*: greater in the NC group than the ONS or NI groups (90 vs. 67 vs. 51 %, $P<.0001$); *QoL after RT*: improved in the NC and ONS groups ($P<.003$) but deteriorated in the NI group ($P<.05$); changes in QoL scores proportional to nutrition intake and status in all groups ($P<.05$); *Change in overall QoL in 3 months after RT*: maintained or improved in NC patients but maintained or worsened in ONS and NI patients.

Table 2 (continued)

Author, year	No. of participants	Main inclusion criteria	Intervention	Length of follow-up	Nutrition status outcomes	Other outcomes
Ravasco et al., 2005 [26]	111	Colorectal cancer; neoadjuvant RT	(A) NC (B) ONS (400 mL/day of high-protein and energy-dense liquid formulation providing 400 kcal and 40 g protein) (C) NI Start: after start of RT Duration: 6 weeks (throughout RT)	3 months	*Number of patients who deteriorated in PG-SGA scores at the end of RT and 3 months*: smaller in the NC group than the ONS and NI groups ($P<.002$); *Number of patients who maintained or improved in PG-SGA scores at the end of RT and 3 months*: greater in the NC group than the ONS and NI groups ($P<.001$); a similar trend was observed for BMI though the difference was not statistically significant; *Number of malnourished patients (at baseline) who deteriorated in both PG-SGA and BMI at the end of RT and 3 months*: lower in the NC group than the ONS group ($P<.001$) which was in turn lower than the NI group ($P<.008$); *Number of malnourished patients (at baseline) who improved in PG-SGA scores at 3 months*: 9 out of 15 malnourished patients in the NC group; none in ONS and NI groups.	*Energy and protein intake at the end of RT*: increased for the NC and ONS groups ($P\leq.04$) with a greater increase in energy intake in the NC than ONS group (555 vs. 296 kcal/day, $P=.001$) but decreased for the NI group ($P<.01$); *Energy and protein intake at 3 months*: maintained in the NC group but decreased to baseline or below baseline in the ONS and NI groups ($P\leq.06$); *Incidence of RT toxicity at the end of RT and 3 months*: greater in the UC group than the NC and ONS groups ($P<.05$); *Change in QoL at the end of RT and 3 months*: improvements in all function scores in the NC group, some function scores in the ONS group and deterioration in all function scores in the NI group; improvement or deterioration in QoL scores were correlated with improved or poorer nutrition intake or status in the NC and ONS groups ($P<.003$).
Persson et al., 2002 [32]	137	Colorectal and stomach cancer	(A) IS (includes NC and ONS) (B) GR (C) ISGR (D) UC Start: after diagnosis (IS); ~4 months after diagnosis (GR) Duration: 2 years	2 years	*Weight gain at 12 and 24 months*: greater in those who received IS (IS and ISGR) than those who did not (GR and UC) ($P<.04$); greater in the IS+GR group than the GR group ($P<.02$); *Change in BMI from baseline to 6 months*: increased in the IS+ISGR group ($P=.003$); no significant difference in the GR+UC group.	*QoL and survival*: no significant difference between groups.
Isenring et al., 2003 [23]	36	Head and neck cancer; RT	(A) NC (following ADA-MNT protocol; ONS provided if req) (B) UC (general advice from nurse+information booklet+ONS if req) Start: after start of RT Duration: 3 months	3 months	*Weight loss*: smaller in the NC group than the UC group (−1.1 vs. −4.3 kg, $P=.019$); *FFM loss*: smaller in the NC group than the UC group (−0.3 vs. −2.2 kg, $P=.029$); *Fat mass loss*: no significant difference.	–
Isenring et al., 2004 [28]	60	Gastrointestinal tract, head and neck cancer; RT	(A) NC (following ADA-MNT protocol; ONS provided if req) (B) UC (general nutrition talk and booklet+samples of ONS) Start: ≤4 days after starting RT Duration: 12 weeks	12 weeks	*Weight loss*: smaller in the NC group than the UC group (0.4 vs. 4.7 kg, $P<.001$); *Proportion of patients who were weight stable*: greater in the NC group than the UC group (24 vs. 11 %, $P=.016$); *Change in FFM*: no significant difference; *Change in PG-SGA*: decreased (improvement) in the NC group but increased in the UC group (−1.6 vs. 3.1, $P=.02$).	*Global QoL and physical function*: less deterioration and more rapid recovery over time in the NC group than the UC group ($P<.012$).
Isenring et al., 2007 [27]	60	Gastrointestinal tract, head and neck cancer; RT	(A) NC (following ADA-MNT protocol; ONS provided if req) (B) UC (general nutrition talk and booklet+samples of ONS) Start: ≤4 days after starting RT Duration: 12 weeks	12 weeks	*Number of malnourished (assessed using PG-SGA global score) patients*: lower in the NC group than the UC group at 8 weeks (8 vs. 18, $P=.020$); no significant difference at 12 weeks.	*Energy and protein intake*: higher in the NC group than the UC group ($P<.029$).

Table 2 (continued)

Author, year	No. of participants	Main inclusion criteria	Intervention	Length of follow-up	Nutrition status outcomes	Other outcomes
van den Berg et al., 2010 [21]	38	Head and neck cancer (stage II to IV); RT	(A) NC+ONS (TF if req) (B) UC Start: after start of RT Duration: 16 weeks (till end of rehabilitation)	20 weeks	*Weight loss at 2 months after RT*: smaller in the NC group than the UC group (P=.03); *Number of malnourished patients (≥5 % weight loss within 1 month)*: decreased over time in the NC group but increased in the UC group (P=.02); lower in the NC group than the UC group 2 weeks after RT (0 vs. 5, P=.02); *BMI*: no significant difference.	–
Corry et al., 2008 [33]	33	Squamous cell head and neck cancer (stages III and IV); ≥10 % weight loss before RT; receiving RT or CRT	(A) PEG (B) NGT Start: not stated Duration: till nutrition supplementation was not needed	6 months	*Weight loss*: greater in the NGT group than the PEG group at 6 weeks posttreatment (3 vs. 1.25 kg, P=.001); no significant difference at 6 months posttreatment; *Lower triceps skinfold thickness*: lower in the NGT group than the PEG group at 6 weeks posttreatment (9.5 vs. 13.5 mm, P=.03).	*Complication rates and patient satisfaction*: no significant difference; *Duration of feeding*: longer in the PEG group than the NGT group (139 vs. 66 days, P=.0006).
Silander et al., 2012 [15]	134	Advanced head and neck cancer; treated with curative intent (palliative treatment patients excluded)	(A) PEG (fibre-containing liquid formulation providing 20 g of protein and 515 kcal per 500 mL) (B) UC (NC and TF if necessary) Start: not stated Duration: not stated	2 years	*Weight loss after 6 months*: smaller in the PEG group than the UC group among patients who lost weight (11.4 vs. 13.6 %, P=.03); *Number of malnourished patients (> 10 % unintended weight loss during the last 6 months)*: consistently ~10 % less in the PEG group than the UC group; *BMI*: no significant difference; *Number of patients with BMI <20*: slightly higher in the PEG group than the control group at diagnosis, 6 months and 2 years but lower at 1 year.	*Length of hospital stay*: no significant difference; *QoL*: several functions better in the PEG group than the UC group at 3, 6 and 12 months (P<.04).
Salas et al., 2009 [34]	39	Squamous cell head and neck cancer (stages III and IV); <10 % weight loss during last 6 months; receiving CRT	(A) Systematic PEG (used before beginning of CRT) (B) UC (PEG used only when necessary) Start: before start of CRT Duration: ~1.5 months	6 months	*Change in BMI*: no significant difference.	*QoL at 6 months*: greater in the PEG group than the UC group (P=.001); *Mortality at 6 months*: no significant difference.

ADA-MNT American Dietetic Association Medical Nutrition Therapy, *BMI* body mass index, *CRT* chemoradiotherapy, *CT* chemotherapy, *FFM* fat-free mass, *GR* group rehabilitation, *IS* individual support, *ISGR* individual support and group rehabilitation, *NC* nutrition counselling, *NGT* nasogastric tube feeding, *NI* no intervention, *ONS* oral nutrition supplements, *PEG* percutaneous endoscopic gastrostomy feeding, *PG-SGA* patient-generated subjective global assessment, *PPDI* patient participation-based dietary intervention, *QoL* quality of life, *RCTs* randomised controlled trials, *RT* radiotherapy, *TF* tube feeding, *UC* usual care

significant difference in QoL between both groups. In three [25, 26, 31] of four papers, QoL change was associated with nutrition intake or status change in ONS patients [26, 31]. One study found that ONS reduced the incidence of anorexia, nausea, vomiting and diarrhoea after RT and 3 months [26]. However, the long-term follow-up [25] of the same study and another short-term study [31] found no significant difference between the ONS and control groups. One paper reported better survival in ONS patients [25], while another found no significant difference between the ONS and control groups [29].

Tube feeding

Tube feeding (TF) is another nutrition intervention that is mostly used for oncology patients who have problems with oral consumption. This includes many head and neck cancer patients as the tumour may physically obstruct the passage of food or cause difficulties and pain during swallowing, resulting in reduced nutrition intake [15]. Liquid nutrition formulations are delivered to the patient's stomach or small intestine by means of a tube that is either placed through the nostril, with the most common being nasogastric tube feeding (NGT), or a tube that goes through the abdomen wall directly, with the most common being percutaneous endoscopic gastrostomy (PEG). However, there is also concern about the complications that are associated with tube feeding which include infections and tube dislodgement [33].

Three studies examined the effects of TF on nutrition status outcomes in oncology patients, in particular head and neck cancer patients [15, 33, 34]. Two studies compared patients who were randomised to either PEG or usual care [15, 34], while another study compared patients who were randomised to either PEG or NGT [33]. No RCTs on the comparison of NGT patients with control patients or on other forms of TF such as nasojejunal feeding and jejunostomy were found.

Mixed results were found in the two papers that compared patients who received PEG feeding to those who received usual care [15, 34]. Only one paper found positive results associated with PEG feeding in terms of weight maintenance [15], while both papers found no significant difference in BMI between PEG patients and control patients [15, 34]. In the paper comparing NGT and PEG on nutrition status outcomes [33], patients who received PEG feeding showed better weight maintenance and larger triceps skinfold thickness at 6 weeks posttreatment though there was no improvement in absolute weight or upper arm circumference at the same time point. The difference in weight maintenance also ceased to be significant at 6 months posttreatment [33].

The two papers comparing PEG with usual care reported on QoL as an outcome and found improvements in QoL in general at 6 months [34] and several QoL functions at 3, 6 and 12 months [15]. No significant differences in overall complication rates and chest infection rates were found between the PEG and NGT groups [33] though tube dislodgement occurred in 12 NGT patients and none of the PEG patients. Mortality was not found to be significantly different between the PEG and NGT patients [33].

Discussion

Summary of key findings

It has been demonstrated that different nutrition intervention approaches have differing degrees of effectiveness on nutrition status outcomes as well as other clinical outcomes. In particular, NC with or without ONS has been associated with consistent improvements in different aspects of nutrition status outcomes including weight gain and maintenance, BMI and PG-SGA change. On the other hand, ONS on its own was associated with slight but mostly insignificant improvements in aspects of nutrition status outcomes like weight gain, BMI and PG-SGA scores, with only one paper finding significant improvements in BMI and PG-SGA scores. PEG was associated with inconsistent improvements in nutrition status outcomes with one paper finding improvements in weight maintenance and both papers finding no improvements in BMI. In the single study that compared PEG with NGT, PEG patients showed better weight maintenance and greater triceps skinfold thickness at 6 weeks than NGT patients though the difference in weight maintenance ceased to be significant at 6 months. Furthermore, there were no significant differences in other nutrition status outcomes such as absolute weight and upper arm circumference between the PEG and NGT patients.

Analysis of results

Nutrition counselling (NC) with or without ONS was associated with much more consistent and significant improvements in nutrition status outcomes compared to other forms of nutrition intervention (e.g. TF or ONS alone) or no intervention. In advanced stage cancer patients, nutrition intervention is usually only able to reduce, rather than reverse, weight loss [36, 37]. Although all the studies on NC involved patients with advanced stage cancers [21, 23, 25–32], improvements in weight maintenance [23, 28], and even weight gain [29, 32], were observed, thus highlighting the efficacy of NC in improving nutrition status outcomes.

This could be because NC patients adhere more strictly to the recommended dietary changes due to regular appointments with dietitians or other healthcare professionals [38]. Other than providing dietary advice, these healthcare professionals are likely to also provide encouragement and positive reinforcement to patients which are important in supporting

the dietary change of the patient [39]. On the other hand, other forms of intervention such as ONS lack constant review and support, possibly contributing to the problem of non-compliance. Furthermore, unlike most other nutrition interventional approaches, dietary advice given during NC is individualised to suit the lifestyle and condition of patients and may alter based on changes in the patient's conditions [38].

ONS was only associated with significant improvements to nutrition status outcomes such as BMI and PG-SGA scores in a study on colorectal cancer patients [26]. However, another study on head and neck cancer patients conducted by the same group of researchers which was executed in a comparable manner (same prescription of ONS, duration of intervention, similar mean age of patients and proportion of stage I/II patients and stage III/IV patients) showed no significant improvements in weight gain [31]. This could suggest that at least in the short-term, colorectal cancer patients are receptive to this form of nutrition intervention approach, unlike head and neck cancer patients. However, there is also the possibility that head and neck cancer patients did not show positive changes in nutrition status outcomes upon ONS prescription as they were less compliant to the ONS prescription due to pain or discomfort during consumption of regular food and ONS [10].

Another study on patients with advanced gastrointestinal tract cancer, non-small cell lung cancers or mesothelioma also found no significant improvements in weight change at 6 weeks, 26 weeks and 1 year upon the prescription of ONS [29]. Overall, there is little evidence to show that ONS alone is effective in improving nutrition status outcomes in oncology patients. Furthermore, while ONS has the advantage of being one of the simplest methods to increase caloric intake [38], it may be financially unsustainable in the long-term for some patients and often has the problem of non-compliance [35].

There was also insufficient evidence to show that TF was effective in improving nutrition status outcomes in oncology patients. In both studies comparing PEG to usual care, no significant improvements in several nutrition status outcomes including BMI and number of malnourished patients were observed [15, 34]. The only positive outcome associated with PEG was significantly less weight loss at 6 months among patients who lost weight [15]. However, it is important to note that only advanced cancer patients were included in these two studies [15, 34]. Early stage cancer patients have been found to be more receptive to nutrition intervention approaches than advanced stage cancer patients [36]. As such, while TF may be ineffective in improving nutrition status outcomes for advanced stage cancer patients [15, 34], it is possible that TF may be effective for early stage cancer patients.

The only study that compared NGT feeding against PEG feeding [33] found that PEG patients showed better nutrition status outcomes including weight maintenance and triceps skinfold thickness than NGT patients though there were no significant differences in other nutrition status outcomes [33]. However, the small number of RCTs and sample size of the studies available contribute to the inconclusiveness of the actual efficacy of TF on nutrition status outcomes [15, 33, 34].

Comparison of main findings with other reviews

A comprehensive literature search yielded no reviews that focused on the effects of nutrition intervention approaches on nutrition status outcomes of oncology patients in general (i.e. not focused specifically on a type of cancer) which only used RCTs. However, there were two reviews which focused on head and neck cancer patients conducted by Langius et al. [40] (10 RCTs; n=536) and Garg et al. [41] (10 RCTs; n=585). Both reviews examined the efficacy of nutrition intervention approaches on nutrition status outcomes in head and neck cancer patients receiving RT [41] and RT or chemoradiotherapy (CRT) [40]. Similar to the present review, NC was associated with consistent improvements in nutrition status while ONS was associated with inconsistent effects on nutrition status outcomes [40]. The present review is also in agreement with the review by Langius et al. which found that PEG was not associated with consistent benefit to nutrition status when compared to control (received TF [15, 34] and NC [15] only when required) and was associated with some nutrition status improvements after RT when compared to NGT [40]. Evidence on the efficacy of TF on nutrition status outcomes was also very limited in the review by Garg et al. [41], with only one study comparing patients who received NGT against those who received optimal oral nutrition [42]. In that study, NGT patients showed significantly less weight loss. However, due to limited number of studies and sample size, no definite conclusion on the efficacy of TF on nutrition status could be drawn as well.

Limitations

The different studies that were included in the present review had a high degree of heterogeneity including variations in cancer type and staging, intervention duration, frequency and intensity as well as inclusion criteria for participants. In particular, the variability in cancer types and stages of the patients from the different studies is likely to account for a large part of the differences in results. The risk and severity of malnutrition differs with cancer type [11], with lung and upper gastrointestinal tract cancer patients showing a higher incidence of cachexia than lower gastrointestinal tract cancer patients [43]. In addition, patients with advanced stage cancers tend to show less improvement in nutrition status compared to patients with early stage cancers [36]. As such, patients of different types and stages of cancers are likely to show different extents of nutrition status improvement in response to the same nutrition intervention.

Furthermore, the definition of the control groups differed greatly, with some studies using no intervention [25, 26, 29, 31] and others using usual care [15, 21, 23, 27, 28, 30, 32, 34] as the control. This is because in most situations, it is unethical to completely deny patients of any form of nutrition intervention, especially when the patient is malnourished or at risk of malnutrition. In different studies, the protocol for usual care also varied greatly for different countries and hospitals. This high degree of heterogeneity among the studies may contribute to the differences in outcomes in different studies of the same intervention approach.

In particular, there is a high degree of heterogeneity in the execution of NC given its very nature of being individualised and dependent on individual judgement. The type of advice provided as well as the way the advice was delivered to the patient differs greatly depending on the experience, discernment [44] and even soft skills of the dietitian. These in turn are strongly influenced by the conventions of the region, hospital protocols, training received by the dietitian and the dietitian himself/herself. Furthermore, while the duration and frequency of NC are commonly reported in studies, it is difficult and almost impossible to document other aspects including the content and intensity of NC. Despite all these differences, the fact that consistent nutrition status improvements were observed in all NC studies is proof of its efficacy in reducing malnutrition.

The review also did not encompass certain aspects of nutrition intervention such as parenteral nutrition and some novel nutrition intervention methods. Parenteral nutrition was excluded as practice guidelines recommend parenteral nutrition to be used only when the gastrointestinal tract is unable to function [24]. Other novel nutrition intervention methods which involve the use of immune function modulating ONS such as eicosapentaenoic acid (EPA) as well as pharmacological drugs like megestrol acetate were also excluded from the study as these compounds affect the nutrition status and other outcomes of patients through mechanisms other than the increase in caloric or protein intake. In particular, there is some evidence that EPA can alter the metabolic pathways involved in cancer [45] while megestrol acetate helps to stimulate appetite and may also alter metabolism and catabolic cytokine production [46].

Future directions

The RCTs of nutrition intervention approaches, especially for TF, on nutrition status outcomes are still very limited. As such, more studies are required to provide more definitive evidence with regard to the efficacy of these approaches. The multiple factors present in the studies which may influence patient outcomes also make it difficult for comparison between different studies. Future research may take these factors into consideration by adjusting a single factor (e.g. duration or intensity of intervention) and studying whether it affects outcomes.

Conclusion

From this review, NC with or without ONS appeared to be the most effective nutrition intervention method, with significant and consistent improvements in several nutrition status outcomes. On the other hand, ONS and TF were associated with inconsistent results, with improvements in few aspects of nutrition status outcomes and no significant differences in others. More studies are, however, required to provide a more concrete conclusion. At present, it is recommended that a systematic protocol be in place for the early referral of oncology patients to dietitians for NC in order to reduce their risk and severity of malnutrition which could be detrimental to other clinical outcomes such as survival and QoL. Individualised advice on whether other nutrition intervention approaches such as ONS and TF are required can then be provided based on the condition of the patient.

Conflict of interest The authors declare that they have no competing interests.

References

1. Montoya J, Domingo F Jr, Luna C, Berroya R, Catli C, Ginete J, Sanchez O, Juat N, Tiangco B, Jamias J (2010) Nutritional status of cancer patients admitted for chemotherapy at the National Kidney and Transplant Institute. Singap Med J 51(11):860–864
2. Lim SL, Ong KC, Chan YH, Loke WC, Ferguson M, Daniels L (2012) Malnutrition and its impact on cost of hospitalization, length of stay, readmission and 3-year mortality. Clin Nutr 31(3):345–350. doi:10.1016/j.clnu.2011.11.001
3. Wie GA, Cho YA, Kim SY, Kim SM, Bae JM, Joung H (2010) Prevalence and risk factors of malnutrition among cancer patients according to tumor location and stage in the National Cancer Center in Korea. Nutrition 26(3):263–268. doi:10.1016/j.nut.2009.04.013
4. Martin L, Jia C, Rouvelas I, Lagergren P (2008) Risk factors for malnutrition after oesophageal and cardia cancer surgery. Br J Surg 95(11):1362–1368. doi:10.1002/bjs.6374
5. Garabige V, Giraud P, De Rycke Y, Girod A, Jouffroy T, Jaulerry C, Brunin F, Rodriguez J (2007) Impact of nutrition management in patients with head and neck cancers treated with irradiation: is the nutritional intervention useful? Cancer Radiother 11(3):111–116. doi:10.1016/j.canrad.2006.11.005
6. Bower MR, Martin RC 2nd (2009) Nutritional management during neoadjuvant therapy for esophageal cancer. J Surg Oncol 100(1):82–87. doi:10.1002/jso.21289
7. Britton B, Clover K, Bateman L, Odelli C, Wenham K, Zeman A, Carter GL (2012) Baseline depression predicts malnutrition in head and neck cancer patients undergoing radiotherapy. Support Care Cancer 20(2):335–342. doi:10.1007/s00520-011-1087-y
8. Hong JH, Omur-Ozbek P, Stanek BT, Dietrich AM, Duncan SE, Lee YW, Lesser G (2009) Taste and odor abnormalities in cancer patients. J Support Oncol 7(2):58–65
9. Steinbach S, Hummel T, Bohner C, Berktold S, Hundt W, Kriner M, Heinrich P, Sommer H, Hanusch C, Prechtl A, Schmidt B, Bauerfeind I, Seck K, Jacobs VR, Schmalfeldt B, Harbeck N (2009) Qualitative and quantitative assessment of taste and smell changes in patients undergoing chemotherapy for breast cancer or

gynecologic malignancies. J Clin Oncol 27(11):1899–1905. doi:10.1200/JCO.2008.19.2690
10. Jager-Wittenaar H, Dijkstra PU, Vissink A, van der Laan BF, van Oort RP, Roodenburg JL (2011) Malnutrition and quality of life in patients treated for oral or oropharyngeal cancer. Head Neck 33(4): 490–496. doi:10.1002/hed.21473
11. Van Cutsem E, Arends J (2005) The causes and consequences of cancer-associated malnutrition. Eur J Oncol Nurs 9(Suppl 2):S51–63. doi:10.1016/j.ejon.2005.09.007
12. Hill A, Kiss N, Hodgson B, Crowe TC, Walsh AD (2011) Associations between nutritional status, weight loss, radiotherapy treatment toxicity and treatment outcomes in gastrointestinal cancer patients. Clin Nutr 30(1):92–98. doi:10.1016/j.clnu.2010.07.015
13. Norman K, Stobaus N, Smoliner C, Zocher D, Scheufele R, Valentini L, Lochs H, Pirlich M (2010) Determinants of hand grip strength, knee extension strength and functional status in cancer patients. Clin Nutr 29(5):586–591. doi:10.1016/j.clnu.2010.02.007
14. Capuano G, Gentile PC, Bianciardi F, Tosti M, Palladino A, Di Palma M (2010) Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment. Support Care Cancer 18(4): 433–437. doi:10.1007/s00520-009-0681-8
15. Silander E, Nyman J, Bove M, Johansson L, Larsson S, Hammerlid E (2012) Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer: a randomized study. Head Neck 34(1):1–9. doi:10.1002/hed.21700
16. Kanda M, Fujii T, Kodera Y, Nagai S, Takeda S, Nakao A (2011) Nutritional predictors of postoperative outcome in pancreatic cancer. Br J Surg 98(2):268–274. doi:10.1002/bjs.7305
17. Datema FR, Ferrier MB, Baatenburg de Jong RJ (2011) Impact of severe malnutrition on short-term mortality and overall survival in head and neck cancer. Oral Oncol 47(9):910–914. doi:10.1016/j.oraloncology.2011.06.510
18. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, Jatoi A, Loprinzi C, MacDonald N, Mantovani G (2011) Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 12(5):489–495
19. Dodson S, Baracos VE, Jatoi A, Evans WJ, Cella D, Dalton JT, Steiner MS (2011) Muscle wasting in cancer cachexia: clinical implications, diagnosis, and emerging treatment strategies. Annu Rev Med 62:265–279. doi:10.1146/annurev-med-061509-131248
20. Paccagnella A, Morello M, Da Mosto MC, Baruffi C, Marcon ML, Gava A, Baggio V, Lamon S, Babare R, Rosti G, Giometto M, Boscolo-Rizzo P, Kiwanuka E, Tessarin M, Caregaro L, Marchiori C (2010) Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy. Support Care Cancer 18(7):837–845. doi:10.1007/s00520-009-0717-0
21. van den Berg MG, Rasmussen-Conrad EL, Wei KH, Lintz-Luidens H, Kaanders JH, Merkx MA (2010) Comparison of the effect of individual dietary counselling and of standard nutritional care on weight loss in patients with head and neck cancer undergoing radiotherapy. Br J Nutr 104(6):872–877. doi:10.1017/S0007114510001315
22. Lis CG, Gupta D, Lammersfeld CA, Markman M, Vashi PG (2012) Role of nutritional status in predicting quality of life outcomes in cancer—a systematic review of the epidemiological literature. Nutr J 11:27. doi:10.1186/1475-2891-11-27
23. Isenring E, Capra S, Bauer J, Davies PS (2003) The impact of nutrition support on body composition in cancer outpatients receiving radiotherapy. Acta Diabetol 40(Suppl 1):S162–164. doi:10.1007/s00592-003-0054-6
24. Simpson F, Doig GS (2005) Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intensive Care Med 31(1):12–23
25. Ravasco P, Monteiro-Grillo I, Camilo M (2012) Individualized nutrition intervention is of major benefit to colorectal cancer patients: long-term follow-up of a randomized controlled trial of nutritional therapy. Am J Clin Nutr 96(6):1346–1353. doi:10.3945/ajcn.111.018838
26. Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME (2005) Dietary counseling improves patient outcomes: a prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. J Clin Oncol 23(7):1431–1438. doi:10.1200/jco.2005.02.054
27. Isenring EA, Bauer JD, Capra S (2007) Nutrition support using the American Dietetic Association medical nutrition therapy protocol for radiation oncology patients improves dietary intake compared with standard practice. J Am Diet Assoc 107(3):404–412. doi:10.1016/j.jada.2006.12.007
28. Isenring EA, Capra S, Bauer JD (2004) Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. Br J Cancer 91(3):447–452. doi:10.1038/sj.bjc.6601962
29. Baldwin C, Spiro A, McGough C, Norman AR, Gillbanks A, Thomas K, Cunningham D, O'Brien M, Andreyev HJ (2011) Simple nutritional intervention in patients with advanced cancers of the gastrointestinal tract, non-small cell lung cancers or mesothelioma and weight loss receiving chemotherapy: a randomised controlled trial. J Hum Nutr Diet 24(5):431–440. doi:10.1111/j.1365-277X.2011.01189.x
30. Kim H, Suh EE, Lee HJ, Yang HK (2014) The effects of patient participation-based dietary intervention on nutritional and functional status for patients with gastrectomy: a randomized controlled trial. Cancer Nurs 37(2):E10–e20. doi:10.1097/NCC.0b013e31829193c8
31. Ravasco P, Monteiro-Grillo I, Marques Vidal P, Camilo ME (2005) Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. Head Neck 27(8):659–668. doi:10.1002/hed.20221
32. Persson CR, Johansson BB, Sjöden PO, Glimelius BL (2002) A randomized study of nutritional support in patients with colorectal and gastric cancer. Nutr Cancer 42(1):48–58. doi:10.1207/S15327914NC421_7
33. Corry J, Poon W, McPhee N, Milner AD, Cruickshank D, Porceddu SV, Rischin D, Peters LJ (2008) Randomized study of percutaneous endoscopic gastrostomy versus nasogastric tubes for enteral feeding in head and neck cancer patients treated with (chemo)radiation. J Med Imaging Radiat Oncol 52(5):503–510. doi:10.1111/j.1440-1673.2008.02003.x
34. Salas S, Baumstarck-Barrau K, Alfonsi M, Digue L, Bagarry D, Feham N, Bensadoun RJ, Pignon T, Loundon A, Deville JL, Zanaret M, Favre R, Duffaud F, Auquier P (2009) Impact of the prophylactic gastrostomy for unresectable squamous cell head and neck carcinomas treated with radio-chemotherapy on quality of life: prospective randomized trial. Radiother Oncol 93(3):503–509. doi:10.1016/j.radonc.2009.05.016
35. Baldwin C, Weekes CE (2012) Dietary counselling with or without oral nutritional supplements in the management of malnourished patients: a systematic review and meta-analysis of randomised controlled trials. J Hum Nutr Diet 25(5):411–426. doi:10.1111/j.1365-277X.2012.01264.x
36. Davies M (2005) Nutritional screening and assessment in cancer-associated malnutrition. Eur J Oncol Nurs 9:S64–S73
37. MacDonald N (2003) Is there evidence for earlier intervention in cancer-associated weight loss? J Support Oncol 1: 279–286
38. van Bokhorst-de van der Schueren MA (2005) Nutritional support strategies for malnourished cancer patients. Eur J Oncol Nurs 9: S74–S83

39. Caro MMM, Laviano A, Pichard C (2007) Nutritional intervention and quality of life in adult oncology patients. Clin Nutr 26(3):289–301
40. Langius JA, Zandbergen MC, Eerenstein SE, van Tulder MW, Leemans CR, Kramer MH, Weijs PJ (2013) Effect of nutritional interventions on nutritional status, quality of life and mortality in patients with head and neck cancer receiving (chemo)radiotherapy: a systematic review. Clin Nutr 32(5):671–678. doi:10.1016/j.clnu.2013.06.012
41. Garg S, Yoo J, Winquist E (2010) Nutritional support for head and neck cancer patients receiving radiotherapy: a systematic review. Support Care Cancer 18(6):667–677
42. Daly JM, Hearne B, Dunaj J, LePorte B, Vikram B, Strong E, Green M, Mugglo F, Groshen S, DeCosse JJ (1984) Nutritional rehabilitation in patients with advanced head and neck cancer receiving radiation therapy. Am J Surg 148(4):514–520
43. Tisdale MJ (2003) Pathogenesis of cancer cachexia. J Support Oncol 1(3):159–168
44. Elia M (2011) Oral nutritional support in patients with cancer of the gastrointestinal tract. J Hum Nutr Diet 24(5):417–420
45. Murphy RA, Yeung E, Mazurak VC, Mourtzakis M (2011) Influence of eicosapentaenoic acid supplementation on lean body mass in cancer cachexia. Br J Cancer 105(10):1469–1473
46. Kumar NB, Kazi A, Smith T, Crocker T, Yu D, Reich R, Bepler G (2010) Cancer cachexia: traditional therapies and novel molecular mechanism-based approaches to treatment. Curr Treat Options in Oncol 11(3–4):107–117