Effect of oral nutritional supplements with or without nutritional counselling on mortality, treatment tolerance, and quality of life in head and neck cancer patients receiving (chemo)radiotherapy: a systematic review and meta-analysis

Mello et al. (2020)

Supporting information

Table S1. Search strategies

Nº	Search terms
Medline (PubMed)	
#1	"Head and Neck Neoplasms"[mh]
#2	"Otorhinolaryngologic Neoplasms"[mh]
#3	head[tiab] OR neck[tiab] OR face[tiab] OR facial[tiab] OR thyroid[tiab] OR parathyroid[tiab] OR salivary[tiab] OR paranasal[tiab] OR "aero digestive"[tiab] OR aerodigestive[tiab] OR aero-digestive[tiab] OR UADT[tiab] OR otorhinolaryngologic[tiab] OR tracheal[tiab] OR larynx[tiab] OR laryngeal[tiab] OR glottis[tiab] OR glottic[tiab] OR "oral cavity"[tiab] OR nasopharynx[tiab] OR nasopharyngeal[tiab] OR hypopharynx[tiab] OR hypopharyngeal[tiab] OR pharynx[tiab] OR pharyngeal[tiab] OR para-pharyngeal[tiab] OR mouth[tiab] OR oral[tiab] OR gingival[tiab] OR gingiva[tiab] OR lip[tiab] OR palatal[tiab] OR palate[tiab] OR tongue[tiab]
#4	"Neoplasms"[mh]
#5	cancer*[tiab] OR carcinoma*[tiab] OR neoplasm*[tiab] OR tumor*[tiab] OR tumour*[tiab] OR metastas*[tiab] OR neoplasia*[tiab] OR malignan*[tiab]
#6	#4 OR #5
#7	#3 AND #6
#8	#1 OR #2 OR #7
#9	"Antineoplastic Protocols"[mh]
#10	"Antineoplastic Agents"[mh]
#11	"Radiotherapy"[mh]
#12	"Chemoradiotherapy"[mh]
#13	"Molecular Targeted Therapy"[mh]
#14	cetuximab[tiab] OR erlotinib[tiab] OR bevacuzimab[tiab] OR bevacizumab[tiab] OR panitumumab[tiab] OR trastuzumab[tiab] OR chemotherap*[tiab] OR chemoradiotherap*[tiab] OR chemo-radiotherap*[tiab] OR radiotherap*[tiab] OR radiochemotherap*[tiab] OR radio-chemotherap*[tiab] OR "molecular targeted therapy"[tiab] OR "molecular targeted therapies"[tiab] OR antineoplastic*[tiab] OR antitumor[tiab] OR antitumour[tiab] OR anticancer[tiab]
#15	#9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	"Nutrition Therapy"[mh]
#17	"Nutritional Support"[Mesh:NoExp]
#18	"Enteral Nutrition"[mh]
#19	"Dietary Supplements"[mh]
#20	"Food, Formulated"[mh]

#21	"Diet Therapy"[mh]
#22	"Food, Fortified"[mh]
#23	#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24	formulat*[tiab] OR supplement*[tiab] OR enriched[tiab] OR sip[tiab] OR oral[tiab] OR enteral[tiab] OR therap*[tiab] OR support[tiab]
#25	diet*[tiab] OR feed*[tiab] OR food*[tiab] OR nutrit*[tiab]
#26	#24 AND #25
#27	#23 OR #26
#28	randomized controlled trial [pt]
#29	controlled clinical trial [pt]
#30	randomized [tiab]
#31	placebo [tiab]
#32	drug therapy [sh]
#33	randomly [tiab]
#34	trial [tiab]
#35	groups [tiab]
#36	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35
#37	animals [mh] NOT humans [mh]
#38	#36 NOT #37
#39	#8 AND #15 AND #27 AND #38

Embase

#1	'head and neck tumor"/exp
#2	'head and neck cancer'/exp
#3	head:ab,ti OR neck:ab,ti OR face:ab,ti OR facial:ab,ti OR thyroid:ab,ti OR parathyroid:ab,ti OR salivary:ab,ti OR paranasal:ab,ti OR aerodigestive:ab,ti OR 'aero digestive':ab,ti OR uadt:ab,ti OR otorhinolaryngologic:ab,ti OR tracheal:ab,ti OR larynx:ab,ti OR laryngeal:ab,ti OR glottis:ab,ti OR glottic:ab,ti OR 'oral cavity':ab,ti OR nasopharynx:ab,ti OR nasopharyngeal:ab,ti OR hypopharynx:ab,ti OR hypopharyngeal:ab,ti OR pharynx:ab,ti OR pharyngeal:ab,ti OR 'para pharyngeal':ab,ti OR mouth:ab,ti OR oral:ab,ti OR gingival:ab,ti OR gingiva:ab,ti OR lip:ab,ti OR palatal:ab,ti OR palate:ab,ti OR tongue:ab,ti
#4	'neoplasm'/exp
#5	cancer*:ab,ti OR carcinoma*:ab,ti OR neoplasm*:ab,ti OR tumor*:ab,ti OR tumour*:ab,ti OR metastas*:ab,ti OR neoplasia*:ab,ti OR malignan*:ab,ti
#6	#4 OR #5
#7	#3 AND #6

#8	#1 OR #2 OR #7
#9	'chemotherapy'/exp
#10	'antineoplastic agent'/exp
#11	'radiotherapy'/exp
#12	'chemoradiotherapy'/exp
#13	'molecularly targeted therapy'/exp
#14	cetuximab:ab,ti OR erlotinib:ab,ti OR bevacuzimab:ab,ti OR bevacizumab:ab,ti OR panitumumab:ab,ti OR trastuzumab:ab,ti OR chemotherap*:ab,ti OR chemoradiotherap*:ab,ti OR 'chemo radiotherap*':ab,ti OR radiotherap*:ab,ti OR radiochemotherap*:ab,ti OR 'radio chemotherap*':ab,ti OR 'molecular targeted therapy':ab,ti OR 'molecular targeted therapies':ab,ti OR antineoplastic*:ab,ti OR antitumor:ab,ti OR antitumour:ab,ti OR anticancer:ab,ti
#15	#9 OR #10 OR #11 OR #12 OR #13 OR #14
#16	'diet therapy'/exp
#17	'nutritional support'/exp
#18	'enteric feeding'/exp
#19	'dietary supplement'/exp
#20	'nutrition supplement'/exp
#21	'oral nutritional supplement'/exp
#22	'fortified food'/exp
#23	#16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24	formulat*:ab,ti OR supplement*:ab,ti OR enriched:ab,ti OR sip:ab,ti OR oral:ab,ti OR enteral:ab,ti OR therap*:ab,ti OR support:ab,ti
#25	diet*:ab,ti OR feed*:ab,ti OR food*:ab,ti OR nutrit*:ab,ti
#26	#24 AND #25
#27	#23 OR #26
#28	'randomized controlled trial'/exp
#29	'controlled clinical trial'/exp
#30	random*:ab,ti
#31	'randomization'/exp
#32	'intermethod comparison'/exp
#33	placebo:ab,ti
#34	compare:ti OR compared:ti OR comparison:ti
#35	(evaluated:ab OR evaluate:ab OR evaluating:ab OR assessed:ab OR assess:ab) AND (compare:ab OR compared:ab OR comparing:ab OR comparison:ab)
#36	(open NEXT/1 label):ab,ti
#37	((double OR single OR doubly OR singly) NEXT/1 (blind OR blinded OR blindly)):ab,ti

#38	'double blind procedure'/exp
#39	(crossover:ab,ti OR cross:ab,ti) AND over:ab,ti
#40	((assign* OR match OR matched OR allocation) NEXT/5 (alternate OR group? OR intervention? OR patient? OR subject? OR participant?)):ab,ti
#41	parallel AND group?:ab,ti
#42	assigned:ab,ti OR allocated:ab,ti
#43	(controlled NEXT/7 (study OR design OR trial)):ab,ti
#44	volunteer:ab,ti OR volunteers:ab,ti
#45	'human experiment'/exp
#46	trial:ti
#47	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46
#48	(random* NEXT/1 sampl* NEXT/7 ('cross section*' OR questionnaire? OR survey* OR database?)):ab,ti
#49	((comparative AND 'study'/exp OR controlled) AND 'study'/exp OR randomi?ed) AND controlled:ab,ti OR 'randomly assigned':ab,ti
#50	#48 NOT #49
#51	'cross-sectional study'/exp NOT (((('randomized controlled trial'/exp OR 'controlled clinical study'/exp OR 'controlled study'/exp OR randomi?ed) AND controlled:ab,ti OR control) AND group?:ab,ti)
#52	((case NEXT/1 control*):ab,ti) AND random*:ab,ti NOT randomi?ed:ab,ti AND controlled:ab,ti
#53	systematic AND review:ti NOT (trial:ti OR study:ti)
#54	nonrandom*:ab,ti NOT random*:ab,ti
#55	'random field*':ab,ti
#56	random:ab,ti AND ((cluster NEXT/3 sampl*):ab,ti)
#57	review:ab AND review/it NOT trial:ti
#58	'we searched':ab AND (review:ti OR review/it)
#59	'update review':ab
#60	(databases NEXT/4 searched):ab
#61	(rat:ti OR rats:ti OR mouse:ti OR mice:ti OR swine:ti OR porcine:ti OR murine:ti OR sheep:ti OR lambs:ti OR pigs:ti OR piglets:ti OR rabbit:ti OR rabbits:ti OR cat:ti OR cats:ti OR dog:ti OR dogs:ti OR cattle:ti OR bovine:ti OR monkey:ti OR monkeys:ti OR trout:ti OR marmoset?:ti) AND 'animal experiment'/exp
#62	'animal experiment'/exp NOT ('human experiment'/exp OR 'human'/exp)
#63	#50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62

#64	#47 NOT #63
#65	#8 AND #15 AND #27 AND #64

CENTRAL

#1	[mh “Head and Neck Neoplasms”]
#2	[mh “Otorhinolaryngologic Neoplasms”]
#3	(head OR neck OR face OR facial OR thyroid OR parathyroid OR salivary OR paranasal OR "aero digestive" OR aerodigestive OR aero-digestive OR UADT OR otorhinolaryngologic OR tracheal OR larynx OR laryngeal OR glottis OR glottic OR "oral cavity" OR nasopharynx OR nasopharyngeal OR hypopharynx OR hypopharyngeal OR pharynx OR pharyngeal OR para-pharyngeal OR mouth OR oral OR gingival OR gingiva OR lip OR palatal OR palate OR tongue):ti,ab,kw
#4	[mh neoplasms]
#5	(cancer* or carcinoma* or neoplasm* or tumor* or tumour* or metastas* or neoplasia*):ti,ab,kw
#6	#4 OR #5
#7	#3 AND #6
#8	#1 OR #2 OR #7
#9	[mh "Antineoplastic Protocols"]
#10	[mh "Antineoplastic Agents"]
#11	[mh Radiotherapy]
#12	[mh "Chemoradiotherapy"]
#13	[mh "Molecular Targeted Therapy"]
#14	(cetuximab OR erlotinib OR bevacuzimab OR bevacizumab OR panitumumab OR trastuzumab OR chemotherap* OR chemoradiotherap* OR chemo-radiotherap* OR radiotherap* OR radiochemotherap* OR radio-chemotherap* OR "molecular targeted therapy" OR "molecular targeted therapies" OR antineoplastic* OR antitumor OR antitumour OR anticancer):ti,ab,kw
#15	{OR #9-#14}
#16	[mh “Nutrition Therapy”]
#17	[mh ^“Nutritional Support”]
#18	[mh “Enteral Nutrition”]
#19	[mh “Dietary Supplements”]
#20	[mh “Food, Formulated”]
#21	[mh "Diet Therapy"]
#22	[mh "Food, Fortified"]
#23	{OR #16-#22}
#24	(formulat* OR supplement* OR enriched OR sip OR oral OR enteral OR therap* OR support):ti,ab,kw
#25	(diet* OR feed* OR food* OR nutrit*):ti,ab,kw
#26	#24 AND #25
#27	#23 OR #26
#28	#8 AND #15 AND #27

CINAHL	
S1	(MH "Head and Neck Neoplasms+")
S2	(MH "Otorhinolaryngologic Neoplasms+")
S3	head OR neck OR face OR facial OR thyroid OR parathyroid OR salivary OR paranasal OR "aero digestive" OR aerodigestive OR aero-digestive OR UADT OR otorhinolaryngologic OR tracheal OR larynx OR laryngeal OR glottis OR glottic OR "oral cavity" OR nasopharynx OR nasopharyngeal OR hypopharynx OR hypopharyngeal OR pharynx OR pharyngeal OR para-pharyngeal OR mouth OR oral OR gingival OR gingiva OR lip OR palatal OR palate OR tongue
S4	(MH "Neoplasms+")
S5	cancer* OR carcinoma* OR neoplasm* OR tumor* OR tumour* OR metastas* OR neoplasia* OR malignan*
S6	S4 OR S5
S7	S3 AND S6
S8	S1 OR S2 OR S7
S9	(MH "Antineoplastic Protocols+")
S10	(MH "Antineoplastic Agents+")
S11	(MH "Radiotherapy+")
S12	(MH "Chemoradiotherapy+")
S13	(MH "Molecular Targeted Therapy+")
S14	cetuximab OR erlotinib OR bevacuzimab OR bevacizumab OR panitumumab OR trastuzumab OR chemotherap* OR chemoradiotherap* OR chemo-radiotherap* OR radiotherap* OR radiochemotherap* OR radio-chemotherap* OR "molecular targeted therapy" OR "molecular targeted therapies" OR antineoplastic* OR antitumor OR antitumour OR anticancer
S15	S9 OR S10 OR S11 OR S12 OR S13 OR S14
S16	(MW "Nutrition Therapy+")
S17	(MH "Nutritional Support")
S18	(MH "Enteral Nutrition+")
S19	(MH "Dietary Supplements+")
S20	(MH "Food, Formulated+")
S21	(MH "Diet Therapy+")
S22	(MH "Food, Fortified+")
S23	S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22
S24	formulat* OR supplement* OR enriched OR sip OR oral OR enteral OR therap* OR support
S25	diet* OR feed* OR food* OR nutrit*
S26	S24 AND S25
S27	S23 OR S26
S28	(MH "Clinical Trials+")
S29	PT Clinical trial

S30	TX clinic* n1 trial*
S31	TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S32	TX randomi* control* trial*
S33	(MH "Random Assignment")
S34	TX random* allocat*
S35	TX placebo*
S36	(MH "Placebos")
S37	(MH "Quantitative Studies")
S38	TX allocat* random*
S39	S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38
S40	S8 AND S15 AND S27 AND S39

Web of Science

#1	TS=(((formulat* OR supplement* OR enriched OR sip OR oral OR enteral OR therap* OR support) AND (diet* OR feed* OR food* OR nutrit*)) AND (cetuximab OR erlotinib OR bevacuzimab OR bevacizumab OR panitumumab OR trastuzumab OR chemotherap* OR chemoradiotherap* OR chemo-radiotherap* OR radiotherap* OR radiochemotherap* OR radio-chemotherap* OR "molecular targeted therapy" OR "molecular targeted therapies" OR antineoplastic* OR antitumor OR antitumour OR anticancer) AND ((head OR neck OR face OR facial OR thyroid OR parathyroid OR salivary OR paranasal OR "aero digestive" OR aerodigestive OR aero-digestive OR UADT OR otorhinolaryngologic OR tracheal OR larynx OR laryngeal OR glottis OR glottic OR "oral cavity" OR nasopharynx OR nasopharyngeal OR hypopharynx OR hypopharyngeal OR pharynx OR pharyngeal OR para-pharyngeal OR mouth OR oral OR gingival OR gingiva OR lip OR palatal OR palate OR tongue) AND (cancer* OR carcinoma* OR neoplasm* OR tumor* OR tumour* OR metastas* OR neoplasia* OR malignan*)))

Lilacs (BVS)

#1	(tw:(mh:("Head and Neck Neoplasms") OR mh:("Otorhinolaryngologic Neoplasms") OR ((head OR neck OR cabeça OR pescoço OR cabeza OR cuello OR tracheal OR traqueal OR traqueia OR tráquea OR larynx OR laryngeal OR laringe OR laríngeo OR glottis OR glotis OR glote OR glottic OR glótic* OR "oral cavity" OR "cavidade oral" OR "cavidade bucal" OR "cavidad bucal" OR "cavidad oral" OR nasopharynx OR nasofaringe OR rinofaringe OR cóana* OR cóano* OR coana* OR nasopharyngeal OR nasofaríngе* OR hypopharynx OR hipofaringe OR laringofaringe OR hypopharyngeal OR hipofaríngе* OR pharynx OR faringe OR garganta OR pharyngeal OR faríngе* OR para-pharyngeal OR parafaríngе* OR mouth OR boca OR oral OR bucal* OR gingiva OR gengiva OR encía OR gingival OR gengival OR gingival OR lip OR lábio OR labio OR or OR palate OR palato OR paladar OR palatal OR palatinos OR palato OR tongue OR língua OR lengua OR face OR cara OR facial OR thyroid OR tireoide OR tiroides OR parathyroid OR paratireoides OR paratiroides OR salivary OR salivares OR salivales OR paranasal OR paranasais OR paranasales OR “aero digestive” OR aerodigestive OR aero-digestive OR uadt OR aerodigestório OR aerodigestivo OR otorhinolaryngologic OR otorrinolaringológic*) AND

	((mh:(neoplasms) OR cancer* OR carcinoma* OR neoplasm* OR tumor* OR tumour* OR metastas* OR neoplasia* OR câncer* OR cáncer* OR cancro* OR neoplasma* OR tumor* OR malignan* OR malignidad*))))) AND (tw:(mh:("Antineoplastic Protocols") OR mh:("Antineoplastic Agents") OR mh:(radiotherapy) OR mh:(chemoradiotherapy) OR mh:("Molecular Targeted Therapy") OR (cetuximab OR erlotinib OR bevacuzimab OR bevacizumab OR panitumumab OR trastuzumab OR chemotherap* OR quimiotratamento* OR farmacotratamento* OR quimioterapia* OR quimiotratamiento* OR chemoradiotherap* OR quimioradioterapia* OR quimiorradioterapia* OR chemo-radiotherap* OR radiotherap* OR radioterapia OR radiación OR radiochemotherap* OR radio-chemotherap* OR "molecular targeted therapy" OR "molecular targeted therapies" OR "terapia molecular dirigida" OR "terapia de alvo molecular" OR "tratamiento molecular dirigido" OR "tratamiento molecular selectivo" OR "terapia alvo molecular" OR "terapia alvo-molecular" OR "terapia molecular alvo-dirigida" OR "terapia molecular dirigida" OR "tratamento molecular dirigido" OR "tratamento molecular seletivo" OR antineoplastic* OR antineoplásico* OR antitumor OR antitumour OR anticancer))) AND (tw:(mh:("Nutrition Therapy") OR (mh:("Nutritional Support") NOT mh:("Parenteral Nutrition")) OR mh:("Dietary Supplements") OR mh:("Food, Formulated") OR mh:("Diet Therapy") OR mh:("Food, Fortified") OR ((formulat* OR formulad* OR artificial* OR sintétic* OR fórmula* OR supplement* OR suplement* OR enriched OR fortificad* OR enriquecid* OR sip OR oral OR therap* OR terapia* OR support OR suporte OR apoio OR apoyo OR enteral) AND (diet* OR dieta OR feed* OR alimentação OR alimentación OR food* OR alimento* OR nutri*)))) AND (instance:"regional") AND (db:("LILACS"))

Open Grey

#1	(((formulat* OR supplement* OR enriched OR sip OR oral OR enteral OR therap* OR support) AND (diet* OR feed* OR food* OR nutrit*)) AND (cetuximab OR erlotinib OR bevacuzimab OR bevacizumab OR panitumumab OR trastuzumab OR chemotherap* OR chemoradiotherap* OR chemo-radiotherap* OR radiotherap* OR radiochemotherap* OR radio-chemotherap* OR "molecular targeted therapy" OR "molecular targeted therapies" OR antineoplastic* OR antitumor OR antitumour OR anticancer) AND ((head OR neck OR face OR facial OR thyroid OR parathyroid OR salivary OR paranasal OR "aero digestive" OR aerodigestive OR aero-digestive OR UADT OR otorhinolaryngologic OR tracheal OR larynx OR laryngeal OR glottis OR glottic OR "oral cavity" OR nasopharynx OR nasopharyngeal OR hypopharynx OR hypopharyngeal OR pharynx OR pharyngeal OR para-pharyngeal OR mouth OR oral OR gingival OR gingiva OR lip OR palatal OR palate OR tongue) AND (cancer* OR carcinoma* OR neoplasm* OR tumor* OR tumour* OR metastas* OR neoplasia* OR malignan*)))

ProQuest

#1	((MESH("Head and Neck Neoplasms") OR MESH("Otorhinolaryngologic Neoplasms") OR (NOFT(head OR neck OR tracheal OR larynx OR laryngeal OR glottis OR glottic OR "oral cavity" OR nasopharynx OR nasopharyngeal OR hypopharynx OR hypopharyngeal OR pharynx OR pharyngeal OR para-pharyngeal OR mouth OR oral OR gingiva OR gingival OR lip OR palate OR palatal OR tongue OR face

	OR facial OR thyroid OR parathyroid OR salivary OR paranasal OR "aero digestive" OR aerodigestive OR aero-digestive OR uadt OR otorhinolaryngologic) AND ((MESH(neoplasms) OR NOFT(cancer* OR carcinoma* OR neoplasm* OR tumor* OR tumour* OR metastas* OR neoplasia*))))) AND ((MESH("Antineoplastic Protocols") OR MESH("Antineoplastic Agents") OR MESH(radiotherapy) OR MESH(chemoradiotherapy) OR MESH("Molecular Targeted Therapy") OR NOFT(cetuximab OR erlotinib OR bevacuzimab OR bevacizumab OR panitumumab OR trastuzumab OR chemotherap* OR chemo-radiotherap* OR radiotherap* OR radiochemotherap* OR radio-chemotherap* OR "molecular targeted therapy" OR "molecular targeted therapies" OR antineoplastic* OR antitumor OR antitumour OR anticancer))) AND ((MESH("Nutrition Therapy") OR (MESH("Nutritional Support") NOT MESH("Parenteral Nutrition")) OR MESH("Dietary Supplements") OR MESH("Food, Formulated") OR MESH("Diet Therapy") OR MESH("Food, Fortified") OR (NOFT(formulat* OR formulad* OR fórmula* OR supplement* OR enriched OR sip OR oral OR therap* OR support OR enteral) AND NOFT(diet* OR feed* OR food* OR nutri*)))))
Google Scholar	
#1	oral nutritional supplements head and neck cancer
ClinicalTrials.gov	
-	((formulation OR supplement OR enriched OR sip OR oral OR enteral OR therapy OR support) AND (diet OR feed OR food OR nutrition))
-	Condition: head and neck
WHO International Clinical Trials Registry Platform (ICTRP)	
-	Intervention: ((formulation OR supplement OR enriched OR sip OR oral OR enteral OR therapy OR support) AND (diet OR feed OR food OR nutrition)) Condition: ((head OR neck OR face OR facial OR thyroid OR parathyroid OR salivary OR paranasal OR aero digestive OR aerodigestive OR aero-digestive OR UADT OR otorhinolaryngologic OR tracheal OR larynx OR laryngeal OR glottis OR glottic OR oral cavity OR nasopharynx OR nasopharyngeal OR hypopharynx OR hypopharyngeal OR pharynx OR pharyngeal OR para-pharyngeal OR mouth OR oral OR gingival OR gingiva OR lip OR palatal OR palate OR tongue) AND (cancer* OR carcinoma OR neoplasm OR tumor OR tumour OR metastas OR neoplasia OR malignan))

Table S2. Characteristics of ongoing or unpublished studies

Trial identifier	Participants	Interventions	Comparator	Outcomes of interest	Starting date	Contact information
UMIN000010370 [1]	Head and neck cancer patients undergoing chemoradiotherapy	Oral nutritional supplements	No administration of oral nutritional supplements	• CTCAE score for inflammation of oral/pharyngeal mucosa. • Rate of chemoradiotherapy completion • Body weight	March 31, 2013 (Registration date)	matsuhiroshi@med.niigata-u.ac.jp
NCT00296452 [2]	Head and neck cancer patients undergoing radiotherapy	Nutritional counseling plus oral nutritional supplements	Nutritional counseling alone	• Severity of mucositis • Weight loss • Quality of life	February 2006	Sharon.Foley@med.va.gov
NCT02776124 [3]	Nasopharyngeal cancer patients undergoing chemoradiotherapy	Nutritional counseling plus oral nutritional supplements	Nutritional counseling alone	• Body weight (kg) • Treatment-related adverse events • Quality of Life	June 2014	Guopei Zhu, Shanghai Ninth People's Hospital Affiliated to Shanghai Jiao Tong University
NCT03344068 [4]	Nasopharyngeal cancer patients undergoing radiotherapy with or without chemotherapy	Oral nutritional supplements	Nutritional counseling alone	• Body weight • Quality of life • Severe oral mucositis • Interruption rate of radiotherapy and/or chemotherapy caused by intolerance	January 1, 2018 (Estimated)	xiayf@sysucc.org.cn
ACTRN12617001248358p [5]	Head and neck cancer patients undergoing chemoradiotherapy	Oral nutritional supplements	Standard of care nutritional group (unclear if includes nutritional counseling)	• Body weight • Quality of life	August 28, 2017 (Registration date)	a.braakhuis@auckland.ac.nz

Table S3. Detailed information of the nutritional counseling interventions in the included trials

Study ID	Description	Goal	Content	Delivery	Frequency
Comparison one					
Arnold et al. (1989)[6]	Intensive nutritional counseling	NR	Recommendations of full liquid, pureed, or soft diets when appropriate, using common household foods.	Unclear	All patients were seen on a weekly basis.
Cereda et al. (2018)[7]	Individualized diet prescription	To achieve estimated protein-calorie requirements (HB x 1.5; protein 1.2 g/kg) and to take into account chewing and swallowing abilities.	Including sample meal plans and recipe suggestions; Prescription tailored on personal eating patterns and preferences.	Dietitian	Regular consultation by a registered dietitian (face-to-face interviews: weekly during treatment, at 1 month and at 3 months after the end of treatment; telephone interviews: during the 3 months after the end of treatment)
Chitapanarux et al. (2016)[8]	Individualized nutritional counseling	NR	NR	Dietitian	Weekly
Jiang et al. (2019)[9]	General dietary advice	NR	NR	NR	NR
Nayel et al. (1992)[10]	General dietary advice	NR	Quote: "All patients were encouraged to choose soft nonirritant foods of high calorie nutritional value"	NR	NR

Study ID	Description	Goal	Content	Delivery	Frequency
Comparison two					
Ding et al. (2018)[11]	Individualized nutritional counseling	NR	NR	Dietitian	Once before the start of treatment, then weekly after the start of treatment
Moriarty et al. (1981)[12]	Individualized nutritional advice	Increasing calorie and protein content of the diet	NR	Dietitian	Twice a week monitoring by a dietitian
Comparison four					
Ravasco et al. (2005)[13]	Individualized diet prescription	Adequate intake to provide requirements and alleviation or arrest of local symptoms, psychological factors, and digestive and absorptive capacity	Type, amount, and frequency of feeding, specific caloric/protein level to attain, indication of any restrictions and limited or increased individual dietary components; Prescription using regular foods, adjusted to personal eating patterns and preferences.	Individualized diet prescription	Adequate intake to provide requirements and alleviation or arrest of local symptoms, psychological factors, and digestive and absorptive capacity

Table S4. Complete risk of bias assessments including answers to signaling questions

Outcome	Mortality (3 months after the end of treatment)	**Study ID**	Arnold 1989	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	Quote: "Patients were randomized to supplemented or non-supplemented groups."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PY	Comment: baseline imbalances in number of participants in each group and some characteristics such as sex and disease stage (even though participants had been previously stratified according to tumor site and disease stage)
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			PY	Comment: During the first 10 weeks, 1 patient in the comparator group took oral supplements, and the reason was not stated in the study report.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			N	Comment: Participants in the intervention group apparently did not present any deviation from intended interventions related to experimental context in this period.
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			Y	Comment: Considering that oral nutritional supplements are the intervention of interest.
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Comment: Even though it is not clearly described, outcome data was available for all patients.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**High**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			Y	Comment: Outcome data for all participants is reported.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	
	Risk of bias judgement			**Low**	

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			PN	Comment: Even though it was not described, we assumed this outcome was probably measured appropriately.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "Nutritional assessment was performed at pre-treatment, 3, 5, 7, IO-week and 6-month intervals. Body weight, serum albumin, transferrin and 24 hour dietary recalls were recorded at this time." Comment: Apparently the opportunities for data collection were the same for both groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?			PY	Comment: no information about blinding of outcome assessor for this specific outcome, but since it was a non-blinded study with unclear allocation concealment, we made a judgement.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: This is an objective outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: Protocol is not available.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: Unlikely because of the nature of the outcome.
	5.3 ... multiple analyses of the data?			PN	Comment: Unlikely because of the nature of the outcome.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Body weight (at week 10 - after the end of treatment 5-8)	**Study ID**	Arnold 1989	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	Quote: “Patients were randomized to supplemented or non-supplemented groups.”
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PY	Comment: baseline imbalances in number of participants in each group and some characteristics such as sex and disease stage (even though participants had been previously stratified according to tumor site and disease stage)
	Risk of bias judgement			**High**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PY	Comment: During the first 10 weeks, 1 patient in the comparator group took oral supplements, and the reason was not stated in the study report.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	N	Comment: Participants in the intervention group apparently did not present any deviation from intended interventions related to experimental context in this period.
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	Y	Comment: Considering that oral nutritional supplements are the intervention of interest.
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Comment: Even though it is not clearly described, it could be assumed that at least a modified intention to treat analysis was performed. At 3 months, data for all patients were available, except for 3 patients that died in the period (unclear when).
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**High**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Comment: Initially it was unclear, but at the longest follow-up, the outcome of all patients is reported.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	Comment: No information reported.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "Nutritional assessment was performed at pre-treatment, 3, 5, 7, IO-week and 6-month intervals. Body weight, serum albumin, transferrin and 24 hour dietary recalls were recorded at this time." Comment: Apparently the opportunities for data collection were the same for both groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: no information about blinding of outcome assessor for this specific outcome, but since it was a non-blinded study with unclear allocation concealment, we made a judgement.

	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: Even though no method was reported for the assessment of body weight, this is an objective outcome commonly measured using a scale.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: Protocol is not available.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: Unlikely because of the nature of the outcome.
	5.3 ... multiple analyses of the data?			NI	Comment: analysis intentions is not available. Results are presented in a graph with percentage change from original weight.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Adverse effects	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes)." Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: no apparent imbalances
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS).

			Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 86% available in the intervention group; 85% available in the comparator group. The ratio of participants with missing data to participants with events was 23/9 (2.55) for gastrointestinal tolerance.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: "Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random."
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Quote: "Patients were actively monitored for the occurrence of gastrointestinal disorders (common adverse events). No serious adverse event associated with the consumption of ONS was expected." Quote: "Gastro-intestinal intolerance to ONS, particularly feeling of full-ness, was recorded in 9 patients; of these, 3 stopped their consumption. As reported above, 8 patients died during the study, but no death was related to the study intervention. No other intervention-related adverse events occurred." Comment: Even though the method

					of active monitoring was not fully described, we judged it to be probably adequate.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "Patients were actively monitored for the occurrence of gastrointestinal disorders (...)" Comment: Assessment opportunities were apparently the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: This is a participant-reported outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			Y	Comment: This is a participant-reported outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	Comment: Participants knew they were receiving the ONS and probably had been informed that adverse event might occur.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			N	Comment: The outcome was not pre-registered.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	Comment: The only issue raised was the definition of gastro-intestinal intolerance and how this information was reported by the participants. Was it an open question? A form with options? This could lead to different outcomes being reported.
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Handgrip strength (at end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes)." Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	

	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Comment: no apparent imbalances
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: “The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed.”
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 86% available in the intervention group; 85% available in the comparator group
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: “Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random.”
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			N	Quote: “Functional status was assessed by digital hand dynamometry (handgrip strength [HG]; DynEx TM , Akern/MD Systems)." [27] World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995;854:1–452.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Comment: assessment opportunities was the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?			PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			N	Comment: This is an objective outcome and was measured in a standardized way.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			Y	Quote in protocol: “Trends in handgrip strength during the study (assessment: at the end of radiotherapy; at 1 month and at 3 months since the end of radiotherapy”
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			N	Comment: The result is unlikely to have been chosen on the basis of its results.
	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, because of the uncertainty on the word “trend” used in the study protocol.
	Risk of bias judgement			**Low**	
Overall bias	**Risk of bias judgement**			**Low**	
Outcome	Temporary interruption of RT (at end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes).” Quote: “The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes.”
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	

	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Comment: no apparent imbalances
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: “The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed.”
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Comment: 86% available in the intervention group; 85% available in the comparator group. The ratio of participants with missing data to participants with events was 23/64 (0.36).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
	4.1 Was the method of measuring the outcome inappropriate?	NI	

Bias in measurement of the outcome	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "(...) tolerance to anti-cancer treatments was continuously monitored." Comment: Assessment opportunities were apparently the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?			PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			N	Comment: This is an objective outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			N	Quote in protocol: "Feasibility of radiotherapy: number of interruptions >5 days; total duration (days); dose reduction" Comment: The way this outcome was reported is not in accordance to the study protocol.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: Only temporary interruption >=5 days was stated in the protocol. The outcome domain "feasibility of radiotherapy" included other measurements that were not reported, but this result does not seem to have been selected on the basis of a "positive" result.
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**Some concerns**	
Outcome	Temporary interruption of RT >= 5 days (at end of treatment), CT dose reduction, RT dose reduction	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes).” Quote: “The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	

			was achieved by using sealed envelopes."
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Comment: no apparent imbalances
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Comment: 86% available in the intervention group; 85% available in the comparator group. The ratio of participants with missing data to participants with events was 23/44 (0.52) for RT interruption > 5 days; 23/7 (3.28) for RT dose reduction; 23/20 (1.15) for CT dose reduction.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	

	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "(...) tolerance to anti-cancer treatments was continuously monitored." Comment: Assessment opportunities were apparently the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?			PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			N	Comment: This is an objective outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			Y	Quote in protocol: "Feasibility of radiotherapy: number of interruptions >5 days; total duration (days); dose reduction"
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: The outcome domain "feasibility of radiotherapy" included other measurements that were not reported, but this result does not seem to have been selected on the basis of a "positive" result.
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Low**	
Overall bias	**Risk of bias judgement**			**Low**	
Outcome	Mortality (3 months after the end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes).” Quote: “The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes.”
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: no apparent imbalances
	Risk of bias judgement			**Low**	
Bias due to deviations	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention

from intended interventions	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 15.4% of patients in the intervention group, 18.5% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 78.2% available in the intervention group; 72.8% available in the comparator group
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: "Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random."
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Comment: Judgement based on the nature of the outcome.

	4.3 Were outcome assessors aware of the intervention received by study participants?			PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			N	Comment: Judgement based on the nature of the outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			N	Comment: The outcome was not pre-registered and was not directly reported, but as reasons for missing participants.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			N	Comment: The result is unlikely to have been chosen on the basis of its results.
	5.3 ... multiple analyses of the data?			N	Comment: The result is unlikely to have been chosen on the basis of its results.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**Some concerns**	
Outcome	Quality of life (at end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes)." Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: no apparent imbalances
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	

	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 86% available in the intervention group; 85% available in the comparator group
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: "Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random."
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "Quality of life was assessed using the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)"
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Comment: assessment opportunities was the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: quality of life is a participant-reported outcome.

	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			Y	Comment: quality of life is a participant-reported outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			Y	The patient may hold a strong belief that the supplement might help, depending on how the supplement was described to him and what was written on the package. In addition, they now they are receiving something "extra", beyond nutritional counseling that the control group is also receiving.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			Y	Quote in protocol: "Trends in quality of life during the study (assessment: at the end of radiotherapy; at 1 month and at 3 months since the end of radiotherapy)" Comment: The use of the word "trends" is not very specific, but because in the protocol it is also used the word "change" for other outcomes, it is assumed to be adequate; i.e. the measurement presented was probably not chosen based on results, and trend might mean "post-intervention score".
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			N	Comment: The result is unlikely to have been chosen on the basis of its results.
	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, because of the uncertainty on the word "trend" used in the study protocol.
	Risk of bias judgement			**Low**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Mucositis and severe mucositis (at end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes)." Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: no apparent imbalances
	Risk of bias judgement			**Low**	
Bias due to deviations	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention

from intended interventions	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: “The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed.”
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Comment: 86% available in the intervention group; 85% available in the comparator group. The ratio of participants with missing data to participants with events was 23/149 (0.1) for mucositis and 23/49 (0.47) for severe mucositis.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	Verify inconsistency of data.
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "(...) patients were regularly examined by the same radiotherapist (blinded to treatment allocation) to assess the presence and the severity of mucositis (score ranges 0–5) according to the National Cancer Institute Common Toxicology Criteria"

	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "(...) tolerance to anti-cancer treatments was continuously monitored." Comment: Assessment opportunities were apparently the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?			N	Quote: "(...) patients were regularly examined by the same radiotherapist (blinded to treatment allocation) to assess the presence and the severity of mucositis (score ranges 0–5) according to the National Cancer Institute Common Toxicology Criteria"
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			NA	
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			N	Comment: The outcome was not pre-registered.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PY	Comment: Considering that mucositis was part of the outcome domain "feasibility of radiotherapy", which included other measurements that were not reported. This outcome favored the intervention group.
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**High**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	RT dose reduction or complete suspension; ST dose reduction or complete suspension; composite RT and/or ST dose reduction or complete suspension (end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes).” Quote: “The randomization list was prepared by a local statistician, who
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	

			was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Comment: no apparent imbalances
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 86% available in the intervention group; 85% available in the comparator group. The ratio of participants with missing data to participants with events was 23/7 (3.29) for RT dose reduction or complete suspension, 23/20 (1.15) for ST dose reduction or complete suspension, and 23/25 (0.92) for composite RT and/or ST dose reduction or complete suspension.

	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: “Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random.”
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "(...) tolerance to anti-cancer treatments was continuously monitored." Comment: Assessment opportunities were apparently the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: This is an objective outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Quote in protocol: "Feasibility of radiotherapy: number of interruptions >5 days; total duration (days); dose reduction" Comment: The way that it was pre-registered, it is hard to compare the intended analysis to the reported results.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PY	Comment: Considering that these outcomes were part of the outcome domain "feasibility of radiotherapy", which included other measurements that were not reported. These outcomes favored the intervention group. It is unclear how the results would look like if on dose reduction was considered, not together with complete suspension. Also, the composite outcome of RT and/or ST reduction/complete suspension was the only statistically significant result.
	5.3 ... multiple analyses of the data?	NI	
	Risk of bias judgement	**High**	
Overall bias	**Risk of bias judgement**	**High**	

Outcome	Body weight (at end of treatment)	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes)." Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: no apparent imbalances
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			Y	Quote: "The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 86% available in the intervention group; 85% available in the comparator group
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: "Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random."
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "Body weight and height were measured using a calibrated scale with a stadiometer according to standard procedures and BMI was calculated [27]. Specifically, at all time points (baseline, end of RT, 1 month and 3 months after the end of RT), body weight was measured (to the nearest 0.1 kg) in subjects wearing only undergarments using the same calibrated scale (Wunder Sa.bi. S.r.l., Milano, Italy)." [27] World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995;854:1–452.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Comment: assessment opportunities was the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: This is an objective outcome and was measured in a standardized way.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	Quote in protocol: "Change in body weight at the end of radiotherapy (after 6 weeks)"
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	Comment: The result is unlikely to have been chosen on the basis of its results.

	5.3 ... multiple analyses of the data?			N	Comment: The presented result corresponds to what was intended in the study protocol.
	Risk of bias judgement			**Low**	
Overall bias	**Risk of bias judgement**			**Low**	
Outcome	Adverse events of ONS	**Study ID**	Chitapana rux 2016	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “randomly assigned in a 1:1 ratio by a computer program” Personal communication: Has any method been implemented to achieve allocation concealment in the study? If yes, would you be able to describe it? Personal communication quote: "YES". "Sealed envelope".
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PN	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: there was a strong similarity between group in regard to sex, but this could be due to chance.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: 7 patients withdrew from the study because of the taste of the supplements, so this was not judged to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			Y	Quote: "All randomized patients are included in the final intent to treat analysis." Comment: It is described as intention-to-treat, but the result in the table is presented alongside a sample size. Still, it would have been a modified intention to treat.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			PN	Comment: 65% available in the intervention group; 95% available in the comparator group.

	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			N	Comment: none found
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			Y	Comment: 6 participants in the intervention group were lost to follow-up because of the taste of the supplement. This characteristic is important to evaluate the supplement effectiveness.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			Y	Comment: Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value (taste of the supplement). Differences between intervention groups were also identified.
	Risk of bias judgement			**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			PN	CTCAE
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			PN	Comment: CTCAE at specific timepoints for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: Non-blinded study.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			Y	Comment: Non-blinded study.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	Comment: Participants knew they were receiving the ONS and probably had been informed that adverse event might occur.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: Protocol or analysis plan unavailable.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Completion of CCRT	**Study ID**	Chitapana rux 2016	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "randomly assigned in a 1:1 ratio by a computer program" Personal communication: Has any method been implemented to achieve allocation concealment in the study? If yes, would you be able to describe it?
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PN	

			Personal communication quote: "YES". "Sealed envelope".
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Comment: there was a strong similarity between group in regard to sex, but this could be due to chance.
	Risk of bias judgement	**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: 7 patients withdrew from the study because of the taste of the supplements, so this was not judged to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "All randomized patients are included in the final intent to treat analysis." Comment: It is described as intention-to-treat, but the result in the table is presented alongside a sample size. Still, it would have been a modified intention to treat.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PN	Comment: 30% available in the intervention group; 65% available in the comparator group. Unable to calculate the ratio of participants with missing data to participants with events because the number of events was not reported.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: none found
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Y	Comment: 6 participants in the intervention group were lost to follow-up because of the taste of the supplement. This characteristic is important to evaluate the supplement effectiveness.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	Y	Comment: Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value (taste of the supplement). Differences between intervention groups were also identified.

	Risk of bias judgement			**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			PN	Comment: Even though it was not adequately described, we judged it to be unlikely that the ascertainment of the outcomes has differed between groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?			PY	Comment: It is unclear who measured this outcome, but since this is a non-blinded study, the assessor might be aware of intervention status.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: This is an objective outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: Protocol or analysis plan unavailable.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Quality of life (at end of treatment)	**Study ID**	Chitapanarux 2016	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “randomly assigned in a 1:1 ratio by a computer program” Personal communication: Has any method been implemented to achieve allocation concealment in the study? If yes, would you be able to describe it? Personal communication quote: "YES". "Sealed envelope".
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PN	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: there was a strong similarity between group in regard to sex, but this could be due to chance.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended			N	Comment: 7 patients withdrew from the study because of the taste of the supplements, so this was not judged

	intervention that arose because of the experimental context?		to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	NI	Comment: For this specific outcome it is unclear if the results presented were obtained from intention-to-treat analysis or per-protocol (excluding participants that did not adhere to the intervention). In the full study both are presented, but this outcome is only available in a conference abstract.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	Y	Quote: "One patient in group A withdrew consent, whereas 7 patients (35%) in group B withdrew from the study (due to intolerable of the taste of immune-enhanced nutrition in 6 patients, and due to the toxicity of CCRT in 1 patient)"
	Risk of bias judgement	**High**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 65% available in the intervention group; 95% available in the comparator group
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: none found
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Y	Comment: 6 participants in the intervention group were lost to follow-up because of the taste of the supplement. This characteristic is important to evaluate the supplement effectiveness.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	Y	Comment: Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value (taste of the supplement). Differences between intervention groups were also identified.
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "European Organization for Research and Treatment of Cancer (EORTC) QoL questionnaire (QLQ-C30 version 3.0)."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "All patients in this study answered the questionnaire on the first day and the last day of CCRT."
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: quality of life is a participant-reported outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Comment: quality of life is a participant-reported outcome.

	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			Y	The patient may hold a strong belief that the supplement might help, depending on how the supplement was described to him and what was written on the package. In addition, they now they are receiving something "extra", beyond nutritional counseling that the control group is also receiving.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: Protocol or analysis plan unavailable.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: The result is unlikely to have been chosen on the basis of its results, even though no analysis plan was available.
	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, even though no analysis plan was available.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	High risk of bias because of missing outcomes and measurement of the outcome.
Outcome	Grade 3 mucositis, Dermatitis (at end of treatment)	**Study ID**	Chitapana rux 2016	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "randomly assigned in a 1:1 ratio by a computer program" Personal communication: Has any method been implemented to achieve allocation concealment in the study? If yes, would you be able to describe it? Personal communication quote: "YES". "Sealed envelope".
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PN	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: there was a strong similarity between group in regard to sex, but this could be due to chance.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: 7 patients withdrew from the study because of the taste of the supplements, so this was not judged to be related to the experimental context.

	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "All randomized patients are included in the final intent to treat analysis." Comment: It is described as intention-to-treat, but the result in the table is presented alongside a sample size. Still, it would have been a modified intention to treat.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 30% available in the intervention group; 65% available in the comparator group. The ratio of participants with missing data to participants with events was 8/5 (1.6) for grade 3 mucositis, 8/1 (8.0) for dermatitis
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: none found
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Y	Comment: 6 participants in the intervention group were lost to follow-up because of the taste of the supplement. This characteristic is important to evaluate the supplement effectiveness.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	Y	Comment: Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value (taste of the supplement). Differences between intervention groups were also identified.
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "Common Terminology Criteria for Adverse Events (CTCAE), version 4.03"
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: “(...) side effect of CCRT were recorded weekly.”
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: It is unclear who measured this outcome, but since this is a non-blinded study, the assessor might be aware of intervention status.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Comment: Even though the outcomes are measured according to a standard, it involves a judgement
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was	PY	Comment: It involves judgement.

	influenced by knowledge of intervention received?				
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: Protocol or analysis plan unavailable.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PY	Comment: The outcome domain was acute toxicities of CCRT and according to the method used, there were several grades for each outcome. Each outcome was presented in a different way either only grade 3, grade 4, or grades 3 and 4, or general occurrence.
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**High**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Body weight (at end of treatment)	**Study ID**	Chitapana rux 2016	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “randomly assigned in a 1:1 ratio by a computer program” Personal communication: Has any method been implemented to achieve allocation concealment in the study? If yes, would you be able to describe it? Personal communication quote: "YES". "Sealed envelope".
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PN	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: there was a strong similarity between group in regard to sex, but this could be due to chance.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: 7 patients withdrew from the study because of the taste of the supplements, so this was not judged to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			Y	Quote: "All randomized patients are included in the final intent to treat analysis." Comment: It is described as intention-to-treat, but the result in the table is

			presented alongside a sample size. Still, it would have been a modified intention to treat.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Comment: 30% available in the intervention group; 65% available in the comparator group
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: none found
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	Y	Comment: 6 participants in the intervention group were lost to follow-up because of the taste of the supplement. This characteristic is important to evaluate the supplement effectiveness.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	Y	Comment: Reported reasons for missing outcome data provide evidence that missingness in the outcome depends on its true value (taste of the supplement). Differences between intervention groups were also identified.
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: “Body weight and side effect of CCRT were recorded weekly.”
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: It is unclear who measured this outcome, but since this is a non-blinded study, the assessor might be aware of intervention status.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	Comment: This is an objective outcome, probably measured in a standardized way using a scale.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Comment: Protocol or analysis plan unavailable.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Comment: The result is unlikely to have been chosen on the basis of its results, even though no analysis plan was available.

	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, even though no analysis plan was available.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	High risk of bias because of missing outcomes.
Outcome	Quality of life (end of treatment)	**Study ID**	Ding 2018	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	Quote: "A prospective, randomized and comparative study was performed"
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			NI	Comment: Baseline characteristics are available only for participants included in the final analysis.
	Risk of bias judgement			**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Comment: Even though it is not clearly described, it could be assumed that at least a modified intention to treat analysis was performed.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			N	Quote: "A total of 64 patients were enrolled, and 42 patients completed nutritional assessment as required. Among them, 23 were in the experimental group and 19 in the control group." Comment: 66% overall
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			N	Comment: None reported.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NI	

	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NI	
	Risk of bias judgement			**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			N	Quote: “The quality of life of patients was assessed using the European Cancer Research and Treatment Organization Quality of Life Core Scale QLQ-C30 and the Head and Neck Cancer Module Scale QLQ-H&N35.”
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "The patient will be surveyed before treatment, every 2 weeks after the concurrent chemotherapy, and 3 months after the end of treatment."
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: quality of life is a participant-reported outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			Y	Comment: quality of life is a participant-reported outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	Comment: Patients probably knew they were receiving an extra (supplement + counselling) beyond the usual care that the other group was also receiving.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Body weight (end of treatment)	**Study ID**	Ding 2018	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	Quote: "A prospective, randomized and comparative study was performed"
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			NI	Comment: Baseline characteristics are available only for participants included in the final analysis.
	Risk of bias judgement			**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	

	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Comment: Even though it is not clearly described, it could be assumed that at least a modified intention to treat analysis was performed.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	Quote: "A total of 64 patients were enrolled, and 42 patients completed nutritional assessment as required. Among them, 23 were in the experimental group and 19 in the control group." Comment: 66% overall
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: None reported.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NI	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NI	
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Quote: “Body composition detection was performed using a Korean Biospace InbodyS10 body composition analyzer. Measurements include fat mass (FM), free fat mass (FFM), body cell mass (BCM), skeletal muscle mass (SM), and phase angle. , PA) and so on. All subjects were fasted 2 h before the measurement, and started to measure for 5 min. (...) The measurement of body composition instruments in this study was performed by a special person after unified training.”
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "The patient was measured 1 time before treatment, 1 time per week after the start of concurrent chemoradiotherapy, and 1 time after 3 months after the end of treatment."
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: Since this is a non-blinded study, the assessor might be aware of intervention status.

	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: This is an objective outcome, apparently measured in a standardized way.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Completion of regimen (end of treatment)	**Study ID**	Harada 2019	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Personal communication quote: "We made a list of patients and numbered them, & they were chosen by Random allocation; which means the patients for any particular treatment group or control group were chosen entirely by chance with no regard to the will of researchers or patients' condition and preference. This study is a randomized open study (no one was blinded)." Personal communication quote: "Unfortunately, in that study we didn't use any method to achieve allocation concealment."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			N	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Apparently no.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Quote: "This study was a randomized open study (no one was blinded)."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	

	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Comment: Probably yes because apparently there were no drop-outs.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Comment: Apparently there were no drop-outs, even though there is no CONSORT flowchart.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "(...) completion rates of scheduled (chemo) radiation treatments (...)" Quote: "Treatment completion included patients who underwent all scheduled chemotherapy and >60 Gy of radiation without interruption."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: Timepoints not clearly described, but supposedly at end the end of treatment. We judged this outcome unlikely to have been measured in a different way for one of the groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Quote: “This study was a randomized open study (no one was blinded).”
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: The outcome is objective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Comment: protocol not available.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Comment: The result is unlikely to have been chosen on the basis of its results, even though no analysis plan was available.
	5.3 ... multiple analyses of the data?	PN	Comment: Probably no, even though no analysis plan was available.

	Risk of bias judgement			Some concerns	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Interruption of regimen (end of treatment)	**Study ID**	Harada 2019	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Personal communication quote: "We made a list of patients and numbered them, & they were chosen by Random allocation; which means the patients for any particular treatment group or control group were chosen entirely by chance with no regard to the will of researchers or patients' condition and preference. This study is a randomized open study (no one was blinded)." Personal communication quote: "Unfortunately, in that study we didn't use any method to achieve allocation concealment."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			N	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Apparently no.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Quote: "This study was a randomized open study (no one was blinded)."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Comment: Probably yes because apparently there were no drop-outs.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			PY	Comment: Apparently there were no drop-outs, even though there is no CONSORT flowchart.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	

	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	
	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			N	Quote: "(...) completion rates of scheduled (chemo) radiation treatments (...)" Quote: "Treatment completion included patients who underwent all scheduled chemotherapy and >60 Gy of radiation without interruption." Comment: Not exactly describing what interruption meant, but supposedly any interruption.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			PN	Comment: Timepoints not clearly described, but supposedly at end the end of treatment. We judged this outcome unlikely to have been measured in a different way for one of the groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Quote: “This study was a randomized open study (no one was blinded).”
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			N	Comment: The outcome is objective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?				
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: protocol not available.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: The result is unlikely to have been chosen on the basis of its results, even though no analysis plan was available.
	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, even though no analysis plan was available.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Oral mucositis grades 1 or 2, grades 3 or 4 (end of treatment)	**Study ID**	Harada 2019	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the	1.1 Was the allocation sequence random?			Y	Personal communication quote: "We made a list of patients and numbered

randomization process	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	N	them, & they were chosen by Random allocation; which means the patients for any particular treatment group or control group were chosen entirely by chance with no regard to the will of researchers or patients' condition and preference. This study is a randomized open study (no one was blinded)." Personal communication quote: "Unfortunately, in that study we didn't use any method to achieve allocation concealment."
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Comment: Apparently no.
	Risk of bias judgement	**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Quote: "This study was a randomized open study (no one was blinded)."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Comment: Probably yes because apparently there were no drop-outs.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Comment: Apparently there were no drop-outs, even though there is no CONSORT flowchart.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	

Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Quote: "Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 (National Cancer Institute CTCAE v4.0)." Quote: "Resident physicians and radiologists collected and documented various data of patients including the severity of mucositis, nutritional status, and efficacy of RT/CRT treatment. Oral mucositis grade was assessed by independent physicians who compared their findings with patients' personal assessment of the mouth and throat soreness, pain level, and the activity score recorded by the patients on a daily basis."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "Resident physicians and radiologists collected and documented various data of patients including the severity of mucositis, nutritional status, and efficacy of RT/CRT treatment. Oral mucositis grade was assessed by independent physicians who compared their findings with patients' personal assessment of the mouth and throat soreness, pain level, and the activity score recorded by the patients on a daily basis."
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Quote: “This study was a randomized open study (no one was blinded).”
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Quote: "Oral mucositis grade was assessed by independent physicians who compared their findings with patients' personal assessment of the mouth and throat soreness, pain level, and the activity score recorded by the patients on a daily basis." Comment: The assessment involves a judgement and was done by independent physicians taking into consideration the patients perception of symptoms.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	Comment: Participants and physicians knew that the intervention group were receiving an extra besides usual care.
	Risk of bias judgement	**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Comment: protocol not available.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Comment: The result is unlikely to have been chosen on the basis of its results, even though no analysis plan was available.

	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, even though no analysis plan was available.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Body weight	**Study ID**	Harada 2019	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Personal communication quote: "We made a list of patients and numbered them, & they were chosen by Random allocation; which means the patients for any particular treatment group or control group were chosen entirely by chance with no regard to the will of researchers or patients' condition and preference. This study is a randomized open study (no one was blinded)." Personal communication quote: "Unfortunately, in that study we didn't use any method to achieve allocation concealment."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			N	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Apparently no.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Quote: "This study was a randomized open study (no one was blinded)."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Comment: Probably yes because apparently there were no drop-outs.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			PY	Comment: Apparently there were no drop-outs, even though there is no CONSORT flowchart.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	

	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	
	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "nutritional status before and after (chemo) radiation was investigated in terms of body weight and levels of total protein and C-reactive protein (CRP) in blood serum"
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Quote: “This study was a randomized open study (no one was blinded).”
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: even though the method of assessment is unclear, this outcome is objective and usually measured in a standardized way.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: protocol not available.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: The result is unlikely to have been chosen on the basis of its results, even though no analysis plan was available.
	5.3 ... multiple analyses of the data?			PN	Comment: Probably no, even though no analysis plan was available.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Adverse effects of ONS	**Study ID**	Jiang 2019	**Source**	Journal article(s) with results of the trial; Trial protocol
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “(…) patients were assigned to the ONS group (n = 50) and control group (n = 50) according to a computer-generated randomization sequence” Quote: “The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients.”
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: Apparently no.
	Risk of bias judgement			**Low**	

Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Quote: “Blind method was not used in this study.”
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Quote: “Parenteral nutritional support with glucose was provided for patients whose oral consumption was severely compromised due to CRT-induced toxicity, in order to help them continue therapy.” Comment: We considered this to reflect usual practice and not to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: “All patients were included in the intention- to-treat (ITT) analysis, and 95 patients were included in the efficacy analysis.”
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PN	95% overall (94% in the intervention group and 96% in the comparator group). The ratio of participants with missing data to participants with events was 2/3 (0.66) for severe nausea. Actually 5 participants withdrawn from the study, but since 3 of them were the ones experiencing adverse events, we did not count them in the ratio.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: None reported.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PY	Comment: Reasons for drop-outs were only reported for the intervention group. Since it was related to adverse events of the supplement, we judged it to be influenced by its true value.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	Comment: Proportion of missing data is similar between groups, but reasons in the intervention group are related to adverse events related to the supplement.
	Risk of bias judgement	**High**	
	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "All the adverse events were evaluated according to CTCAE 4.0."

Bias in measurement of the outcome	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "Patients were examined once a week to assess the severity of mucositis by the same radiation oncologist who was blinded to the intervention allocation. Other adverse events were monitored and recorded during the CRT."
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: non-blinded trial of nutritional intervention
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			Y	Comment: This is a participant-reported outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	Comment: Participants knew they were receiving the ONS and probably had been informed that adverse event might occur.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: The protocol is available, but no further detail about the outcomes other than their names is provided.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	Comment: No information about time points in the protocol.
	5.3 ... multiple analyses of the data?			NI	Comment: No information about the analysis in the protocol.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	CT incomplete (end of treatment)	**Study ID**	Jiang 2019	**Source**	Journal article(s) with results of the trial; Trial protocol
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "(…) patients were assigned to the ONS group (n = 50) and control group (n = 50) according to a computer-generated randomization sequence" Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: Apparently no.
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Quote: "Blind method was not used in this study."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	

	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Quote: "Parenteral nutritional support with glucose was provided for patients whose oral consumption was severely compromised due to CRT-induced toxicity, in order to help them continue therapy." Comment: We considered this to reflect usual practice and not to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "All patients were included in the intention- to-treat (ITT) analysis, and 95 patients were included in the efficacy analysis."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	95% overall (94% in the intervention group and 96% in the comparator group). The ratio of participants with missing data to participants with events was 5/21 (0.24).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Comment: No detail is given, but given the nature of the outcome it could be assumed that it was adequate.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: No detail is given, but given the nature of the outcome it could be assumed that it did not differed between groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Quote: "Blind method was not used in this study."
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: The outcome is objective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		
	Risk of bias judgement	**Low**	

Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: The protocol is available, but no further detail about the outcomes other than their names is provided.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	Comment: No information about time points in the protocol.
	5.3 ... multiple analyses of the data?			NI	Comment: No information about the analysis in the protocol.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**Some concerns**	
Outcome	RT interruption (end of treatment)	**Study ID**	Jiang 2019	**Source**	Journal article(s) with results of the trial; Trial protocol
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "(…) patients were assigned to the ONS group (n = 50) and control group (n = 50) according to a computer-generated randomization sequence" Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: Apparently no.
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Quote: "Blind method was not used in this study."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Quote: "Parenteral nutritional support with glucose was provided for patients whose oral consumption was severely compromised due to CRT-induced toxicity, in order to help them continue therapy." Comment: We considered this to reflect usual practice and not to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			Y	Quote: "All patients were included in the intention- to-treat (ITT) analysis, and 95 patients were included in the efficacy analysis."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the			NA	

	result) of the failure to analyze participants in the group to which they were randomized?		
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	N	95% overall (94% in the intervention group and 96% in the comparator group). The ratio of participants with missing data to participants with events was 5/4 (1.25).
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: None reported.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PY	Comment: Reasons for drop-outs were only reported for the intervention group. Since it was related to adverse events of the supplement, we judged it to be influenced by its true value.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	Comment: Proportion of missing data is similar between groups, but reasons in the intervention group are related to adverse events related to the supplement.
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	PN	Comment: No detail is given, but given the nature of the outcome it could be assumed that it was adequate.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: No detail is given, but given the nature of the outcome it could be assumed that it did not differed between groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Quote: “Blind method was not used in this study.”
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: The outcome is objective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	Comment: The protocol is available, but no further detail about the outcomes other than their names is provided.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	Comment: No information about time points in the protocol.
	5.3 ... multiple analyses of the data?	NI	Comment: No information about the analysis in the protocol.
	Risk of bias judgement	**Some concerns**	
Overall bias	**Risk of bias judgement**	**High**	

Outcome	Quality of life (end of treatment)	**Study ID**	Jiang 2019	**Source**	Journal article(s) with results of the trial; Trial protocol
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "(…) patients were assigned to the ONS group (n = 50) and control group (n = 50) according to a computer-generated randomization sequence" Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PY	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: Apparently no.
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Quote: "Blind method was not used in this study."
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Quote: "Parenteral nutritional support with glucose was provided for patients whose oral consumption was severely compromised due to CRT-induced toxicity, in order to help them continue therapy." Comment: We considered this to reflect usual practice and not to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			Y	Quote: "All patients were included in the intention- to-treat (ITT) analysis, and 95 patients were included in the efficacy analysis."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			Y	95% overall (94% in the intervention group and 96% in the comparator group)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	

	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			N	Quote: "QOL was assessed by the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the EORTC Head and Neck module (EORTC QLQ-H&N35). Raw scores obtained from the EORTC questionnaires were transformed into scores ranging from 0 to 100 according to the scoring procedures"
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "Data including weight, BMI, body composition, laboratory parameters, nutritional status and QOL were measured and collected at the end of CRT and 3 months after the end of CRT."
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Quote: “Blind method was not used in this study.”
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PY	Comment: The outcome is subjective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	Comment: Patients probably knew they were receiving an extra beyond the general advice that the other group was also receiving.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: The protocol is available, but no further detail about the outcomes other than their names is provided.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	Comment: No information about time points in the protocol.
	5.3 ... multiple analyses of the data?			NI	Comment: No information about the analysis in the protocol. The outcome could have been analyzed in many ways.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Body weight (whithin 3 days before the end of treatment)	**Study ID**	Jiang 2019	**Source**	Journal article(s) with results of the trial; Trial protocol
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: “(…) patients were assigned to the ONS group (n = 50) and control group (n = 50) according to a computer-generated randomization sequence” Quote: “The randomization list was prepared by a local statistician, who was not involved in the selection and
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			PY	

			enrollment of patients.”
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	Comment: Apparently no.
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Quote: “Blind method was not used in this study.”
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Quote: “Parenteral nutritional support with glucose was provided for patients whose oral consumption was severely compromised due to CRT-induced toxicity, in order to help them continue therapy.” Comment: We considered this to reflect usual practice and not to be related to the experimental context.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: “All patients were included in the intention- to-treat (ITT) analysis, and 95 patients were included in the efficacy analysis.”
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	95% overall (94% in the intervention group and 96% in the comparator group)
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "Body weight and height were measured using the same electric scale. Patients were asked to remove their outwears and shoes."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "Data including weight, BMI, body composition, laboratory parameters, nutritional status and QOL were measured and collected at the end of CRT and 3 months after the end of CRT."

	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Quote: "Blind method was not used in this study."
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: even though the method of assessment is unclear, this outcome is objective and usually measured in a standardized way.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	Comment: The protocol is available, but no further detail about the outcomes other than their names is provided.
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	Comment: No information about time points in the protocol.
	5.3 ... multiple analyses of the data?			NI	Comment: No information about the analysis in the protocol. The outcome could have been analyzed in many ways.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**Some concerns**	It does not seem that there was bias in the selection of reported results, but this cannot be proven with the information provided. We attempted to contact study authors.
Outcome	Mortality (longest follow-up: 6 months)	**Study ID**	Moriarty 1989	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			Y	Comment: The absence of key baseline characteristics (only sex, tumor site, age and height are reported) provide reasons to suspect that the randomization process was problematic.
	Risk of bias judgement			**High**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			NI	

	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Comment: Even though it is not clearly described, it could be assumed that an intention to treat analysis was performed. At the end of treatment, apparently data for all patients were available.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Some concerns**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PY	Comment: Apparently data for all participants was available, but it was not adequately and explicitly reported.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: We judged this to be unlikely based on the nature of the outcome.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Non-blinded study.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: The outcome is objective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	
	5.3 ... multiple analyses of the data?	NI	

	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Adverse effects	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)
	Risk of bias judgement			**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Unblinded trial of nutritional intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Apparently all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	

	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	
	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			PN	Quote: "Patients were asked to record any side effects that may be attributed to the oral nutritional supplementation, e.g., diarrhea or flatulence."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			PN	Comment: We answered "probably not" because of the nature of the outcome.
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: Unblinded trial of nutritional intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PY	Comment: This is a participant-reported outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	Comment: Participants knew they were receiving the ONS and probably had been informed that adverse event might occur.
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: We answered "probably no" because of the nature of the outcome.
	5.3 ... multiple analyses of the data?			PN	Comment: We answered "probably no" because of the nature of the outcome.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Dry mouth	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)
	Risk of bias judgement			**Some concerns**	
Bias due to deviations	2.1.Were participants aware of their assigned intervention during the trial?			Y	Unblinded trial of nutritional intervention.

from intended interventions	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Apparently, all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	Comment: The questionnaire used is not adequately described, and its validity to measure the outcome remains uncertain.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: Patients filled a questionnaire, which was probably standardized.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Unblinded trial of nutritional intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Comment: subjective measure plus patient expectation of benefit.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	
	Risk of bias judgement	**High**	
Bias in selection of	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized	NI	

the reported result	before unblinded outcome data were available for analysis?				
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PY	Comment: The outcome was measured weekly for 6 weeks, but the last timepoint in the graph corresponds to the 5th week.
	5.3 ... multiple analyses of the data?			PN	
	Risk of bias judgement			**High**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Interruption of regimen	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)
	Risk of bias judgement			**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Unblinded trial of nutritional intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Apparently, all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.

	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	
	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			PN	Comment: Treatment appeared to have been measured without any specific time cut-off.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			PN	Comment: We answered "probably not" because of the nature of the outcome.
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: Unblinded trial of nutritional intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PN	Comment: We answered "probably not" because of the nature of the outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			NA	
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: We answered "probably no" because of the nature of the outcome.
	5.3 ... multiple analyses of the data?			PN	Comment: We answered "probably no" because of the nature of the outcome.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**Some concerns**	
Outcome	Objective mucosal reaction	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)

	Risk of bias judgement	Some concerns	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Unblinded trial of nutritional intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Apparently, all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	Comment: The validity of the scale used to measure the outcome remains uncertain. How patients were assessed is unclear.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	NI	Comment: There is no information about how the patients were assessed.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Unblinded trial of nutritional intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PY	Comment: subjective measure plus assessor expectation of benefit.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	

	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PN	Comment: We answered "probably no" because of the nature of the outcome.
	5.3 ... multiple analyses of the data?			PN	Comment: We answered "probably no" because of the nature of the outcome.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Swallowing difficulty	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)
	Risk of bias judgement			**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Unblinded trial of nutritional intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Apparently, all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NA	
	Risk of bias judgement			**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			NI	Comment: The questionnaire used is not adequately described, and its validity to measure the outcome remains uncertain.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			PN	Comment: Patients filled a questionnaire, which was probably standardized.
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: Unblinded trial of nutritional intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PY	Comment: subjective measure plus patient expectation of benefit.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PY	Comment: The outcome was measured weekly for 6 weeks, but the last timepoint in the graph corresponds to the 5th week.
	5.3 ... multiple analyses of the data?			PN	
	Risk of bias judgement			**High**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Changes in taste and appetite loss	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	

	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)
	Risk of bias judgement	**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Unblinded trial of nutritional intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	PY	Apparently, all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	Comment: The questionnaire used is not adequately described, and its validity to measure the outcome remains uncertain.
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: Patients filled a questionnaire, which was probably standardized.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Unblinded trial of nutritional intervention.

	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			PY	Comment: subjective measure plus patient expectation of benefit.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?			PY	
	Risk of bias judgement			**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			PY	Comment: The outcome was measured weekly for 6 weeks, but the last timepoint in the graph corresponds to the 5th week.
	5.3 ... multiple analyses of the data?			PN	
	Risk of bias judgement			**High**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Body weight	**Study ID**	Nayel 1992	**Source**	Journal article(s) with results of the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			NI	
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			NI	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			PN	Comment: Even though many important variables were not reported at baseline, we answered this question as "probably not", because those variables were also not reported in the other timepoints (e.g. body weight was only presented as % change)
	Risk of bias judgement			**Some concerns**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Unblinded trial of nutritional intervention.
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			PY	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			PN	None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			PY	Apparently, all participants completed the study and were included in the analysis.
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the			NA	

	result) of the failure to analyze participants in the group to which they were randomized?		
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Quote: "were randomly allocated (...) to receive either radiotherapy alone (12 patients) or radiotherapy plus oral nutritional oral supplementation (11 patients)" Comment: Data for all randomized patients are presented.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	Quote: "Anthropometric evaluation consisted of weight (kg), (...)" "Quote: "Percentage weight loss was derived from the highest previous weight, and percentage weight gain was derived from the lowest weight (at onset of treatment)."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	PN	Comment: Although not properly described, the measurement of body weight is commonly standardized.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Unblinded trial of nutritional intervention.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	PN	Comment: Objective measure.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	
	5.3 ... multiple analyses of the data?	PY	Comment: Body weight was presented only as % change from the highest or lowest previous weight. Actual measurements of body weight are not presented in the study.
	Risk of bias judgement	**High**	
Overall bias	**Risk of bias judgement**	**High**	

Outcome	Quality of life (end of treatment)	**Study ID**	Ravasco 2005	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Patients stratified by cancer stage were randomly assigned at enrollment in permutation blocks of three, using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "(…) using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "A copy of the randomization sequence was kept separately from the study personnel. Randomization envelopes were opened before the first patient appointment by a person blind to the study procedures."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			Y	Quote: "All analyses were conducted on an intention-to-treat basis, and, therefore, available data from all study patients were used. If any missing data were observed, the missing value(s) would be replaced by the average of the study group, which would have no effect on the estimators."
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			NA	
	Risk of bias judgement			**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			Y	Comment: Data was available for all randomized participants.

	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "QOL was assessed (...), always using the EORTC Quality of Life Questionnaire version 3.0 (EORTC QLQ-C30). (...) Original scores were linearly transformed to obtain quantified scores within the range of 0 to 100; in addition, and for better validation in the clinical context, overall scores derived from function scales, symptom scales, and single items were calculated on the basis of the very high statistical significance of the interscale correlations, which were calculated according to EORTC's guidelines."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "Randomly assigned patients had scheduled visits and identical contact time with the research dietician (PR)." Quote: "QOL was assessed at the three time points"
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: quality of life is a participant-reported outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Comment: quality of life is a participant-reported outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	Comment: The patient may hold a strong belief that the supplement might help, depending on how the supplement was described to him and what was written on the package. Another possible interpretation in the context of this trial, is that the patient may think that he might be receiving less than the group receiving dietary counseling. Even though they had identical time with the dietitian, dietary counselling clearly was more intensive, since it was based on patients personal eating patterns and preferences. This makes it difficult to judge the direction of a possible bias.
	Risk of bias judgement	**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	

	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Survival (at the longest follow-up)	**Study ID**	Ravasco 2005	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Patients stratified by cancer stage were randomly assigned at enrollment in permutation blocks of three, using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "(…) using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "A copy of the randomization sequence was kept separately from the study personnel. Randomization envelopes were opened before the first patient appointment by a person blind to the study procedures."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			NI	
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?			PY	Comment: This judgement was made based on the number of missing outcome data.
	Risk of bias judgement			**High**	

Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?			PN	Comment: We attempted to clarify information on missing outcomes, but we did not receive any information. We made a judgement.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?			N	Comment: None reported.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?			NI	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?			NI	
	Risk of bias judgement			**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?			PN	Quote: "Some data was collected from patients' records at follow-up appointments every 3–6 months;"
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?			N	Quote: "(...)in addition, validated questionnaires to assess symptoms were used at programmed interviews after a median follow-up of 3.8 (range 2.0–6.3) yrs (PR)."
	4.3 Were outcome assessors aware of the intervention received by study participants?			Y	Comment: Non-blinded trial.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?			N	Comment: The outcome is objective.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?				
	Risk of bias judgement			**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?			NI	
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Anorexia Grade 1, Anorexia Grade 2, Nausea/vomiting Grade 1, Nausea/vomiting Grade 2, Xerostomia Grade 1, Xerostomia Grade 2, Odynophagia/dysphagia Grade 1,	**Study ID**	Ravasco 2005	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial

	Odynophagia/dysphagia Grade 2, Dysgueusia Grade 1, Dysgueusia Grade 2 (end of treatment)				

Domain	Signaling question	Response	Description
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	Quote: "Patients stratified by cancer stage were randomly assigned at enrollment in permutation blocks of three, using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "(…) using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "A copy of the randomization sequence was kept separately from the study personnel. Randomization envelopes were opened before the first patient appointment by a person blind to the study procedures."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	N	
	Risk of bias judgement	**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?	Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?	N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?	NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?	NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: "All analyses were conducted on an intention-to-treat basis, and, therefore, available data from all study patients were used. If any missing data were observed, the missing value(s) would be replaced by the average of the study group, which would have no effect on the estimators."

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y	Comment: Data was available for all randomized participants.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	NA	
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "acute RT-induced morbidity was scored from 0 to 4 in accordance with the European Organization for the Research and Treatment of Cancer/Radiation Therapy Oncology Group (EORTC/RTOG) criteria, in which higher scores indicate increased symptom severity."
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "Throughout RT, all medication and concurrent chemotherapy was registered, and acute RT-induced morbidity was scored (...)" Comment: It is not fully described, but we judged it unlikely to have differed between groups.
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Non-blinded trial.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Comment: The outcomes require a subjective judgement.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	Comment: The patient may hold a strong belief that the supplement might help, depending on how the supplement was described to him and what was written on the package. Another possible interpretation in the context of this trial, is that the patient may think that he might be receiving less than the group receiving dietary counseling. Even though they had identical time with the dietitian, dietary counselling clearly was more intensive, since it was based on patients personal eating patterns and preferences. This makes it difficult to judge the direction of a possible bias.
	Risk of bias judgement	**High**	
Bias in selection of	5.1 Were the data that produced this result analyzed in accordance with a pre-	NI	

the reported result	specified analysis plan that was finalized before unblinded outcome data were available for analysis?				
	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	Permanent xerostomia and/or taste alterations (at the longest follow-up)	**Study ID**	Ravasco 2005	**Source**	Journal article(s) with results of the trial; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Patients stratified by cancer stage were randomly assigned at enrollment in permutation blocks of three, using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "(…) using a sequential series of numbered opaque sealed envelopes containing computer-generated random assignments." Quote: "A copy of the randomization sequence was kept separately from the study personnel. Randomization envelopes were opened before the first patient appointment by a person blind to the study procedures."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: None reported.
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	
	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?			NI	

	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	PY	Comment: This judgement was made based on the number of missing outcome data.
	Risk of bias judgement	**High**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PN	Comment: We attempted to clarify information on missing outcomes, but we did not receive any information. We made a judgement.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	N	Comment: None reported.
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	PY	Comment: Apparently the reasons were mostly related to mortality.
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	PY	Comment: The participants that stayed in the trial were probably different from those that died.
	Risk of bias judgement	**High**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	N	Quote: "(...) in addition, validated questionnaires to assess symptoms were used at programmed interviews after a median follow-up of 3.8 (range 2.0–6.3) yrs (PR)"
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "(...)in addition, validated questionnaires to assess symptoms were used at programmed interviews after a median follow-up of 3.8 (range 2.0–6.3) yrs (PR)."
	4.3 Were outcome assessors aware of the intervention received by study participants?	Y	Comment: Non-blinded trial.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	Y	Comment: The outcomes require a subjective judgement.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	PY	Comment: The patient may hold a strong belief that the supplement might help, depending on how the supplement was described to him and what was written on the package. Another possible interpretation in the context of this trial, is that the patient may think that he might be receiving less than the group receiving dietary counseling. Even though they had identical time with the dietitian, dietary counselling clearly was more intensive, since it was based on patients personal eating patterns and preferences. This makes it difficult to judge the direction of a possible bias.
	Risk of bias judgement	**High**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	NI	

	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?			NI	
	5.3 ... multiple analyses of the data?			NI	Comment: One concern could be raised that xerostomia and taste alterations were evaluated in a composite outcome, instead of as independent outcomes.
	Risk of bias judgement			**Some concerns**	
Overall bias	**Risk of bias judgement**			**High**	
Outcome	CT dose reduction, RT dose reduction	**Study ID**	Cereda 2018	**Source**	Journal article(s) with results of the trial; Trial protocol; Conference abstract(s) about the trial
Domain	**Signaling question**			**Response**	**Description**
Bias arising from the randomization process	1.1 Was the allocation sequence random?			Y	Quote: "Allocation to the two intervention groups was performed according to a computer-generated random blocks randomization list (varying block sizes)." Quote: "The randomization list was prepared by a local statistician, who was not involved in the selection and enrollment of patients. Concealment was achieved by using sealed envelopes."
	1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?			Y	
	1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?			N	Comment: no apparent imbalances
	Risk of bias judgement			**Low**	
Bias due to deviations from intended interventions	2.1.Were participants aware of their assigned intervention during the trial?			Y	Comment: non-blinded trial of nutritional intervention
	2.2.Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?			Y	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the experimental context?			N	Comment: Artificial enteral nutrition was started in 9% of patients in the intervention group, 9.9% in the comparator group. Reason: treatment-related toxicity and its sequelae (<60% of estimated requirements for two consecutive weeks despite the use of ONS). Oral nutritional supplements were prescribed to 9.9% of patients in the comparator group. Reason: ethical reasons, to improve their protein-calorie intakes (food intake < 60% of estimated requirements for two consecutive weeks)
	2.4. If Y/PY to 2.3: Were these deviations from intended intervention balanced between groups?			NA	
	2.5 If N/PN/NI to 2.4: Were these deviations likely to have affected the outcome?			NA	

	2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?	Y	Quote: “The analysis compared patients, following a modified intention-to-treat principle. Then a series of supportive analyses of the primary endpoint were performed.”
	2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyze participants in the group to which they were randomized?	NA	
	Risk of bias judgement	**Low**	
Bias due to missing outcome data	3.1 Were data for this outcome available for all, or nearly all, participants randomized?	PN	Comment: 86% available in the intervention group; 85% available in the comparator group. The ratio of participants with missing data to participants with events was 23/7 (3.28) for RT dose reduction; 23/20 (1.15) for CT dose reduction.
	3.2 If N/PN/NI to 3.1: Is there evidence that result was not biased by missing outcome data?	PY	Quote: “Dropouts were not clinically and statistically different from patients remaining in the study, neither at baseline nor during follow-up (data not shown); thus we considered missingness to be at random.”
	3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA	
	3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA	
	Risk of bias judgement	**Low**	
Bias in measurement of the outcome	4.1 Was the method of measuring the outcome inappropriate?	NI	
	4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	N	Quote: "(...) tolerance to anti-cancer treatments was continuously monitored." Comment: Assessment opportunities were apparently the same for all participants.
	4.3 Were outcome assessors aware of the intervention received by study participants?	PY	Comment: It is unclear who measured this outcome, but the authors reported that outcome assessors of severity of mucositis were blinded and made no comment on this specific outcome.
	4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	N	Comment: This is an objective outcome.
	4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	**Low**	
Bias in selection of the reported result	5.1 Were the data that produced this result analyzed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?	Y	Quote in protocol: "Feasibility of radiotherapy: number of interruptions >5 days; total duration (days); dose reduction"

	5.2 ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Comment: The outcome domain "feasibility of radiotherapy" included other measurements that were not reported, but this result does not seem to have been selected on the basis of a "positive" result. Originally these outcomes were reported as composite outcomes including complete suspension. We contacted authors and they provided outcome data separately for these outcomes.
	5.3 ... multiple analyses of the data?	NI	
	Risk of bias judgement	**Low**	
Overall bias	**Risk of bias judgement**	**Low**	

Y: yes; **PY**: probably yes; **N**: no; **PN**: probably no; **NI**: no information; **ONS**: oral nutritional supplements; **RT**: radiotherapy; **CT**: chemo-therapy

Table S5. Assessments of missing results in the included studies for the main outcomes in each comparison

Study ID	Sample size	Mortality	Quality of life	Functional status	Treatment tolerance	Body weight	Adverse effects
Comparison one							
Arnold et al. (1989)[6]	50	A	?	?	?	A	?
Cereda et al. (2018)[7]	159	A	A	A	A	A	A
Chitapanarux et al. (2016)[8]	40	A	A	+	A	A	A
Jiang et al. (2019)[9]	100	A	A	+	A	A	A
Nayel et al. (1992)[10]	23	?	?	?	A	A	A
Comparison two							
Ding et al. (2018)[11]	64	?	A	?	?	A	?
Moriarty et al. (1981)[12]	97	A	?	?	?	-	?
Comparison three							
Calaguas et al. (2010)[14]	56	?	?	?	?	?	?
Harada et al. (2019)[15]	50	+	+	+	A	A	+

Study ID	Sample size	Mortality	Quality of life	Functional status	Treatment tolerance	Body weight	Adverse effects
Ravasco et al. (2005)[13]	50	A	A	?	?	?	?
Comparison four							
Ravasco et al. (2005)[13]	50	A	A	?	?	?	?

A : results available; **- :** result unavailable, (probably) because of the nature of the findings; **+ :** result unavailable, but (probably) not because of the nature of the findings; **?** : result unavailable, but unclear if outcome measured

Table S6. Funding and competing interests information in the included studies and assessments of the potential for concern about conflict of interest

Study ID	Funding	Declaration	Contribution	Judgement
Comparison one				
Arnold et al. (1989)[6]	The nutritional supplement, Sustacal™, was supplied by Mead Johnson. Inc., Evansville, Indiana.	Comment: no information.	N/A	No notable concern about conflict of interest
Cereda et al. (2018)[7]	Quote: "This work was supported by the Fondazione IRCCS Policlinico San Matteo, a grant from the Italian Ministry of Health (project code RF-2011-02351315), a grant from ESPEN (Research Fellowship 2013), and by Nestlé Health Science (provision of ONS)." Protocol: Akern Srl (among sponsors and collaborators)	Riccardo Caccialanza: Nutricia S.r.l, Akern S.r.l., Baxter S. p.a, Fresenius Kabi S.p.a, Eli Lilly S.p.a. (Consulting or Advisory Role); Nutricia S.r.l., Nestlè Health Science S.r.l, Baxter S.p.a. (Research Funding); Nutricia S.r.l., Nestlè Health Science S.r.l, Baxter S.p.a, Eli Lilly S.p.A. (Speaker's Honoraria) Emanuele Cereda: Nutricia S.r.l., Akern S.r.l., Wunder Sa.Bi. s.r.l., Fondazione Grigioni per il Morbo di Parkinson (Consulting or Advisory Role); Fondazione Grigioni per il Morbo di Parkin-son, ESPEN (Research Funding); Nutricia S.r.l., Nestlè Health Science S.r.l., Eli Lilly S.p.A. (Speaker's Honoraria) Paolo Pedrazzoli: Baxter S.p.a. (Speaker's Honoraria) Marco Benazzo, Silvia Cappello, Marilisa Caraccia, Sara Colombo, Franco Corbella, Catherine Klersy, Ilaria Imarisio, Teresa Monaco, Annalisa Turri: No relationship to disclose.	Quote: "The sponsors had no role in the study design and conduction, in the data collection, management, analysis, interpretation, or in the manuscript revision and approval."	Notable concern about conflict of interest

Study ID	Funding	Declaration	Contribution	Judgement
Chitapanarux et al. (2016)[8]	The immune enhanced nutrition in this study was supported by Thai Otsuka Pharmaceutical Company, Bangkok, Thailand.	The authors declare that they have no competing interests.	N/A	No notable concern about conflict of interest
Jiang et al. (2019)[9]	Quote: "The authors thank the EnterNutr China for providing the oral nutritional supplements."	Quote: "No potential conflict of interest was reported by the authors."	N/A	No notable concern about conflict of interest
Nayel et al. (1992)[10]	Comment: no information.	Comment: no information.	N/A	No notable concern about conflict of interest
Comparison two				
Ding et al. (2018)[11]	Comment: no information.	Comment: no information.	N/A	No notable concern about conflict of interest
Moriarty et al. (1981)[12]	Saint Luke's Cancer Research Fund and Mead Johnson	Comment: no information.	N/A	No notable concern about conflict of interest
Comparison three				
Calaguas et al. (2010)[14]	Comment: no information.	Comment: no information.	N/A	No notable concern about conflict of interest

Study ID	Funding	Declaration	Contribution	Judgement
Harada et al. (2019)[15]	Quote: “This study was supported in part by a Grant-in-Aid from the Japanese Ministry of Education, Science, and Culture (grant no. 15K11292). This study was also supported by EA Pharma Co., Ltd., Tokyo, Japan.”	Quote: “The authors declare that they have no competing interests.”	N/A	No notable concern about conflict of interest
Ravasco et al. (2005)[13]	Contract grant sponsor: Núcleo Regional do Sul da Liga Portuguesa contra o Cancro; Terry Fox Foundation	Quote: "No significant financial relationships to disclose."	N/A	No notable concern about conflict of interest
Comparison four				
Ravasco et al. (2005)[13]	Contract grant sponsor: Núcleo Regional do Sul da Liga Portuguesa contra o Cancro; Terry Fox Foundation	Quote: "No significant financial relationships to disclose."	N/A	No notable concern about conflict of interest

N/A: not applicable

Table S7. Summary of non-hematological toxicity outcomes for each comparison

Outcome	Number of participants (studies)	RR (95% CI)	Heterogeneity*	Risk of bias
Comparison one				
Dry mouth	123 (2)	1.00 (0.48 to 2.10)	$I^2 = 0\%$, $\tau^2 = 0$, P = 0.52	High
Mucositis	222 (3)	0.90 (0.58 to 1.39)	$I^2 = 37\%$, $\tau^2 = 0.01$, P = 0.21	High
Mucositis (grades 3-4)	322 (4)	0.72 (0.44 to 1.19)	$I^2 = 0\%$, $\tau^2 = 0$, P = 0.53	High - Some concerns
Mucositis (grades 3-4)	100 (1)	0.77 (0.37 to 1.59)	N/A	Some concerns
Nausea	100 (1)	0.76 (0.42 to 1.40)	N/A	High
Radiation dermatitis	140 (2)	1.04 (0.50 to 2.17)	$I^2 = 0\%$, $\tau^2 = 0$, P = 0.45	High
Swallowing difficulty	23 (1)	0.79 (0.53 to 1.18)	N/A	High
Taste and appetite changes	23 (1)	0.99 (0.77 to 1.28)	N/A	High
Comparison three				
Anorexia (grade 1)	50 (1)	1.00 (0.48 to 2.09)	N/A	High
Anorexia (grade 2)	50 (1)	0.71 (0.26 to 1.95)	N/A	High
Dysgeusia (grade 1)	50 (1)	0.91 (0.47 to 1.75)	N/A	High
Dysgeusia (grade 2)	50 (1)	0.92 (0.50 to 1.67)	N/A	High
Mucositis (grades 1-2)	50 (1)	2.44 (1.42 to 4.20)	N/A	High
Mucositis (grades 3-4)	50 (1)	0.19 (0.06 to 0.56)	N/A	High
Nausea/vomiting (grade 1)	50 (1)	1.00 (0.22 to 4.49)	N/A	High
Nausea/vomiting (grade 2)	50 (1)	1.00 (0.15 to 6.55)	N/A	High
Odynophagia/ dysphagia (grade 1)	50 (1)	1.00 (0.56 to 1.78)	N/A	High

Outcome	Number of participants (studies)	RR (95% CI)	Heterogeneity*	Risk of bias
Odynophagia/ dysphagia (grade 2)	50 (1)	0.83 (0.44 to 1.56)	N/A	High
Permanent xerostomia and/or taste alterations	30 (1)	0.92 (0.60 to 1.41)	N/A	High
Xerostomia (grade 1)	50 (1)	1.00 (0.51 to 1.97)	N/A	High
Xerostomia (grade 2)	50 (1)	0.86 (0.34 to 2.19)	N/A	High
Comparison four				
Anorexia (grade 1)	50 (1)	0.90 (0.44 to 1.83)	N/A	High
Anorexia (grade 2)	50 (1)	2.50 (0.53 to 11.70)	N/A	High
Dysgeusia (grade 1)	50 (1)	1.00 (0.51 to 1.97)	N/A	High
Dysgeusia (grade 2)	50 (1)	1.57 (0.73 to 3.39)	N/A	High
Nausea/vomiting (grade 1)	50 (1)	0.75 (0.19 to 3.01)	N/A	High
Nausea/vomiting (grade 2)	50 (1)	2.00 (0.19 to 20.67)	N/A	High
Odynophagia/ dysphagia (grade 1)	50 (1)	0.86 (0.50 to 1.46)	N/A	High
Odynophagia/ dysphagia (grade 2)	50 (1)	1.25 (0.59 to 2.64)	N/A	High
Permanent xerostomia and/or taste alterations	30 (1)	1.34 (0.79 to 2.27)	N/A	High
Xerostomia (grade 1)	50 (1)	0.83 (0.44 to 1.56)	N/A	High
Xerostomia (grade 2)	50 (1)	2.00 (0.56 to 7.12)	N/A	High

Outcome	Number of participants (studies)	RR (95% CI)	Heterogeneity*	Risk of bias

RR: risk ratio; **CI**: confidence interval; **N/A**: not applicable; * P value for Cochran's Q test

Table S8. Summary of quality of life domains scores for each comparison

Quality of life domain	Number of participants (studies)	SMD (95% CI)	Heterogeneity*	Minimal important difference [16]	Risk of bias
Comparison one					
Appetite loss †					
Cereda et al. (2018)[7]	136 (1)	-0.1 (-0.4 to 0.2)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	-1.3 (-1.9 to -0.6)	N/A	N/A	High
Cognitive functioning ‡				N/A	High
Cereda et al. (2018)[7]	136 (1)	0.1 (-0.3 to 0.4)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	1.7 (0.9 to 2.4)	N/A	N/A	High
Constipation †	136 (1)	0.1 (-0.2 to 0.5)	N/A	N/A	High
Diarrhoea †					
Cereda et al. (2018)[7]	136 (1)	0.1 (-0.2 to 0.4)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	-1.0 (-1.6 to -0.3)	N/A	N/A	High
Dyspnoea †					
Cereda et al. (2018)[7]	136 (1)	0.2 (-0.2 to 0.5)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	-1.0 (-1.6 to -0.3)	N/A	N/A	High
Emotional functioning ‡	176 (2)	-0.1 (-1.9 to 1.8)	$I^2 = 0\%$, $\tau^2 = 0$, P = 0.35	N/A	High
Fatigue †					
Cereda et al. (2018)[7]	136 (1)	2.4 (-7.0 to 11.8)	N/A	12 ¶	High
Chitapanarux et al. (2016)[8]	40 (1)	-5.0 (-7.1 to -2.9)	N/A	12 ¶	High
Financial †	176 (2)	0.1 (-1.6 to 1.9)	$I^2 = 0\%$, $\tau^2 = 0$, P = 0.36	N/A	High

Quality of life domain	Number of participants (studies)	SMD (95% CI)	Heterogeneity*	Minimal important difference [16]	Risk of bias
Insomnia †					
Cereda et al. (2018)[7]	136 (1)	0.3 (0.0 to 0.6)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	1.4 (0.7 to 2.1)	N/A	N/A	High
Nausea †					
Cereda et al. (2018)[7]	136 (1)	0.1 (-0.3 to 0.4)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	0.9 (0.2 to 1.5)	N/A	N/A	High
Pain †					
Cereda et al. (2018)[7]	136 (1)	0.0 (-0.4 to 0.3)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	-1.0 (-1.7 to -0.4)	N/A	N/A	High
Physical functioning ‡					
Cereda et al. (2018)[7]	136 (1)	-4.0 (-12.8 to 4.8)	N/A	-7.3 ¶	High
Chitapanarux et al. (2016)[8]	40 (1)	4.0 (1.3 to 6.7)	N/A	-7.3 ¶	High
Role functioning ‡					
Cereda et al. (2018)[7]	136 (1)	0.0 (-0.3 to 0.3)	N/A	N/A	High
Chitapanarux et al. (2016)[8]	40 (1)	0.7 (0.1 to 1.4)	N/A	N/A	High
Social functioning ‡	176 (2)	-8.6 (-22.5 to 5.2)	$I^2 = 0\%$, $\tau^2 = 0$, P = 0.32	6.1 #; -7.3 ¶	High
Comparison two					
Appetite loss †	42 (1)	0.1 (-0.5 to 0.7)	N/A	N/A	High
Constipation †	42 (1)	0.1 (-0.5 to 0.7)	N/A	N/A	High
Diarrhoea †	42 (1)	-0.3 (-0.9 to 0.3)	N/A	N/A	High

Quality of life domain	Number of participants (studies)	SMD (95% CI)	Heterogeneity*	Minimal important difference [16]	Risk of bias
Nausea †	42 (1)	1.2 (0.5 to 1.9)	N/A	N/A	High
Pain †	42 (1)	-1.0 (-1.7 to -0.4)	N/A	N/A	High
Comparison three					
Appetite loss †	50 (1)	59 / 65 ‖	N/A	N/A	High
Cognitive functioning ‡	50 (1)	51 / 20 ‖	N/A	N/A	High
Constipation †	50 (1)	9 / 8 ‖	N/A	N/A	High
Diarrhoea †	50 (1)	6 / 7 ‖	N/A	N/A	High
Dyspnoea †	50 (1)	40 / 38 ‖	N/A	N/A	High
Emotional functioning ‡	50 (1)	66 / 28 ‖	N/A	N/A	High
Fatigue †	50 (1)	75 / 78 ‖	N/A	N/A	High
Financial †	50 (1)	37 / 40 ‖	N/A	N/A	High
Insomnia †	50 (1)	55 / 60 ‖	N/A	N/A	High
Nausea †	50 (1)	71 / 72 ‖	N/A	N/A	High
Pain †	50 (1)	74 / 78 ‖	N/A	N/A	High
Physical functioning ‡	50 (1)	69 / 21 ‖	N/A	N/A	High
Role functioning ‡	50 (1)	68 / 20 ‖	N/A	N/A	High
Social functioning ‡	50 (1)	66 / 61 ‖	N/A	N/A	High
Comparison four					
Appetite loss †	50 (1)	59 / 68 ‖	N/A	N/A	High
Cognitive functioning ‡	50 (1)	51 / 58 ‖	N/A	N/A	High
Constipation †	50 (1)	9 / 10 ‖	N/A	N/A	High
Diarrhoea †	50 (1)	6 / 7 ‖	N/A	N/A	High
Dyspnoea †	50 (1)	40 / 39 ‖	N/A	N/A	High

Quality of life domain	Number of participants (studies)	SMD (95% CI)	Heterogeneity*	Minimal important difference [16]	Risk of bias
Emotional functioning ‡	50 (1)	66 / 79 ||	N/A	N/A	High
Fatigue †	50 (1)	75 / 55 ||	N/A	N/A	High
Financial †	50 (1)	37 / 38 ||	N/A	N/A	High
Insomnia †	50 (1)	55 / 55 ||	N/A	N/A	High
Nausea †	50 (1)	71 / 50 ||	N/A	N/A	High
Pain †	50 (1)	74 / 63 ||	N/A	N/A	High
Physical functioning ‡	50 (1)	69 / 74 ||	N/A	N/A	High
Role functioning ‡	50 (1)	68 / 78 ||	N/A	N/A	High
Social functioning ‡	50 (1)	66 / 82 ||	N/A	N/A	High

SMD: Standardized mean difference; **CI**: Confidence interval; **N/A**: Not applicable
* P value for Cochran's Q test;
† Higher score indicates increased symptoms or worse impairment;
‡ Higher score indicates better functioning;
§ Mean difference;
|| Median score in oral nutritional supplements group / comparator group;
¶ Minimal important difference for deterioration;
# Minimal important difference for improvement

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