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MANAGEMENT AND TREATMENT OF TASTE AND SMELL ALTERATIONS IN ONCOLOGIC PATIENTS UNDERGOING ANTITUMORAL THERAPY AND RADIOTHERAPY

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Abstract – *Objective:* *The objective of this review is to investigate strategies to manage and treat taste and smell alterations in oncologic patients to minimize the effect these have on their quality of life and their nutritional model as well.*

Materials and Methods: *A scoping review was conducted, and the following international databases were consulted: PubMed, CINAHL, Cochrane, and Scopus. The scoping review process was conducted using Arksey & O'Malley's framework.*

Results: *A total of 18 studies were considered relevant and were divided into three macro areas: pharmacological interventions, aimed to manage and treat taste and smell alterations; non-pharmacological interventions and self-care strategies to adapt oneself as to not perceive the information provided by these senses and to accept the current situation as no reparatory interventions are available.*

Conclusions: *Both dysgeusia and dysosmia require complex evaluations, the etiopathogenesis mechanisms are not yet completely known and there are no universal evaluation instruments available. A precocious evaluation of these symptoms needs to include the physical, psychological, and social spheres of patients. Healthcare staff plays a key role as they link the primary care and home care of these symptoms. Taste and smell disturbances are underestimated and are not the focus of enough studies, and it is, therefore, desirable that the future holds an enlargement in the number of studies regarding aetiology, objective and subjective evaluation, and application of interventions to prevent, treat and manage these symptoms.*

KEYWORDS: *Cancer, Tumour, Chemotherapy, Radiotherapy, Cancer patients, Smell, Olfaction Disorders.*

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INTRODUCTION

Taste and smell disturbances are a common issue in oncologic patients[1-3]. Taste and smell receptors are destroyed by chemotherapy and radiotherapy and cause a partial loss of taste in 30% to 75% of patients[4,5]. Other causes of taste and smell disturbances include poor oral hygiene, gastrointestinal reflux, post-nasal drip, and oral mucositis[6]. Previous studies have shown that dysgeusia (taste disturbance), xerostomia (dryness of the mouth), and oral mucositis (inflammation and ulceration of the gastrointestinal mucous membrane) influence a patient's eating habits starting from their first dose of cumulative radiation of 30Gy and their effects increase at 50 Gy[7]. Taste and smell disturbances can manifest as loss of taste (ageusia), alteration of taste (dysgeusia), and increased sensibility in taste (hypogeusia)[8] and can lead to malnutrition, weight loss, and significant morbidity[9,10], compromising the assumption of proteins, electrolytes, and nutrients[11,12].

Patients with grave chemosensory disturbances demonstrated a lower amount of energy, increased weight loss, as far as anorexia[13] and lower quality of life than patients with moderate chemosensory disturbances[14]. Around 75% of patients that undergo their first round of chemotherapy experience an alteration to their sense of taste[15], which in most cases manifests as an unbearably strong metallic taste[16,17]. Taste disturbances and dryness of the mouth (xerostomia) can persist up to three years after treatment[18] and patients that experience these changes consume 20-25% fewer calories than patients that don't experience these changes[19]. It has been documented that during chemotherapy patients accepted umami tastes, somewhat accepted sweet, sour, and salty tastes but not bitter ones[17]. A reduction in the desire for food can determine an increase in the risk of infection and reduction in being able to receive an appropriate amount of medical care, this negatively influences the survival rates[17,20] and prognosis of these patients[21,22]. Managing supportive care for cancer patients means helping them face all issues associated with cancer and its treatment[23], and it is fundamental that the care received is of elevated quality and centered on the individual[24,25].

This review aimed to critically assess literature published between 2010 and 2020 to research interventions and strategies put in place to manage and treat taste and smell disturbances in adult cancer patients that are undergoing treatment with anti-neoplastic drugs and/or radiotherapy to minimize the impact taste and smell disturbances have on the quality of life and nutritional model of these patients.

MATERIALS AND METHODS

This scoping review was conducted using Arksey and O'Malley's framework, composed of five phases, and developed by Levac et al[27] and Grant et al[28].

The five phases of this framework are as follows: (1) identification of the research question, (2) identification of relevant studies, (3) selection of the studies to include, (4) charting the data, (5) collating, summarizing and reporting the results.

Identification of the research question

The objective of this review is to answer the following research questions:

- Which are the specific interventions to prevent, manage and treat taste and smell disturbances caused by chemotherapy and/or radiotherapy in oncologic patients?
- Did the interventions and strategies put in place have a positive impact on the quality of life and did they reduce the impact that taste and smell disturbances have on oncologic patient's health?
- Details regarding the construction of the research question and its relative aspects such as population, interventions, comparison, and outcomes are detailed in Table 1.

Identification of relevant studies

The following electronic databases were taken into consideration: MEDLINE (including PubMed), CINAHL, PsycINFO, and Web of Sci-

TABLE 1. PICOS Methodology to individuate the research question.

P	POPULATION	Adult patients (aged 18 or over) affected by tumours and undergoing chemotherapy and/or radiotherapy that have taste and smell disturbances.
I	INTERVENTION	Implementation of interventions to prevent, manage and treat taste and smell disturbances.
C	COMPARISION	No comparison.
O	OUTCOME	Improvement of the quality of life and impact that taste and smell disturbances have on the nutritional model.
S	SETTING	Oncology and/or haematology.

ence. Studies were reported following the Preferred Reporting Items extension for scoping reviews (PRISMA-ScR)[29] guidelines.

Studies published in the last 10 years were taken into consideration, from 1/01/2010 to 30/09/2020 that only concerned human beings, and an adult population (18 years or older), that had at least one intervention in place to prevent, manage and/or treat taste and smell disturbances in oncologic patients undergoing chemotherapy and/or radiotherapy treatment. All observational, experimental, quasi-experimental and systematic reviews in the English and Italian languages were included. Articles written in languages other than the English and Italian ones were excluded, as were articles that regarded the paediatric population.

Selection of the studies

Following the execution of the research strategy, the first phase of the selection process took place, titles and abstracts of articles were read independently by two members of the research team (AF, GA) and they assessed whether the inclusion and exclusion criteria were satisfied by these articles.

During the screening phase, the reference manager software Zotero® was utilized to indicate whether studies were to be considered relevant or not. Duplicates, studies considered irrelevant or not associated with the aim of this review, were removed in this phase. If the relevance of the study wasn't clear from the title and abstract, the revisors read the full-text article to determine its eligibility. Discrepancies were resolved by discussion. Full-text versions of the articles deemed relevant were obtained and evaluated according to their relevance to inclusion criteria by the research team. Any discord was resolved through discussion and consensus. When this wasn't reached, arbitration and the final decision came down to a third member of the team (FS). All studies which didn't have an accessible full text were excluded, as were those that didn't present specific interventions, treatments, and management of taste and smell disturbances. All included studies are pertinent to the inclusion criteria and objectives of the revision.

Charting data

A data extraction form was designed to chart the data; it included a table divided into predetermined categories that linked with the purpose and research questions of the scoping review. This table captured data from each article on the studies characteristics and the content concerning management and treatment of taste and smell alterations.

Collating, summarizing, and reporting the results

The data extraction information was collated and summarized, and the results were reported using the same framework we had established for the purpose and research questions and the data extraction form.

RESULTS

As shown in the PRISMA flow diagram (Figure 1), 544 records were retrieved from the database search. After duplicates were removed, 420 records were screened for their relevance by title and abstract. Among 26 full-text articles included for eligibility, 5 were removed because their relative full texts weren't available, 3 were removed because they didn't satisfy inclusion criteria. Finally, 18 articles were included in this review, as reported in Figure 1. The full texts were read and allowed for the classification and organization of the data in an extraction table thanks to Excel®. A summary of the results of the articles included in this systematic review is shown in Table 2.

General characteristics of the studies

A total of 18 articles were identified that corresponded to the research question. The full texts were scrupulously evaluated, and the information of interest was reported in specific tables, dividing records based on their common characteristics. Of these 18 articles, 10 were published between 2010 and 2015[11,12,19,30-36], and 8 were published between 2016 and 2020[37-44]. The main characteristics of the 18 included studies in this review are outlined and summarized in Table 2.

The interventions described in the 18 articles (Table 3) can be divided by type into three big macro-areas:

- Pharmacologic interventions (8 records);
- Non-pharmacologic interventions: education and nutritional counselling (7 records);
- Self-care strategies (3 records) .

Pharmacologic interventions

Eight of the included studies were focused on pharmacologic interventions aimed towards the prevention, management, and treatment of taste and smell alterations; of this 1 nonrandomized pilot study, 1 series of cases, 2 revisions, 3 systematic reviews, and 1 RCT. The interventions taken

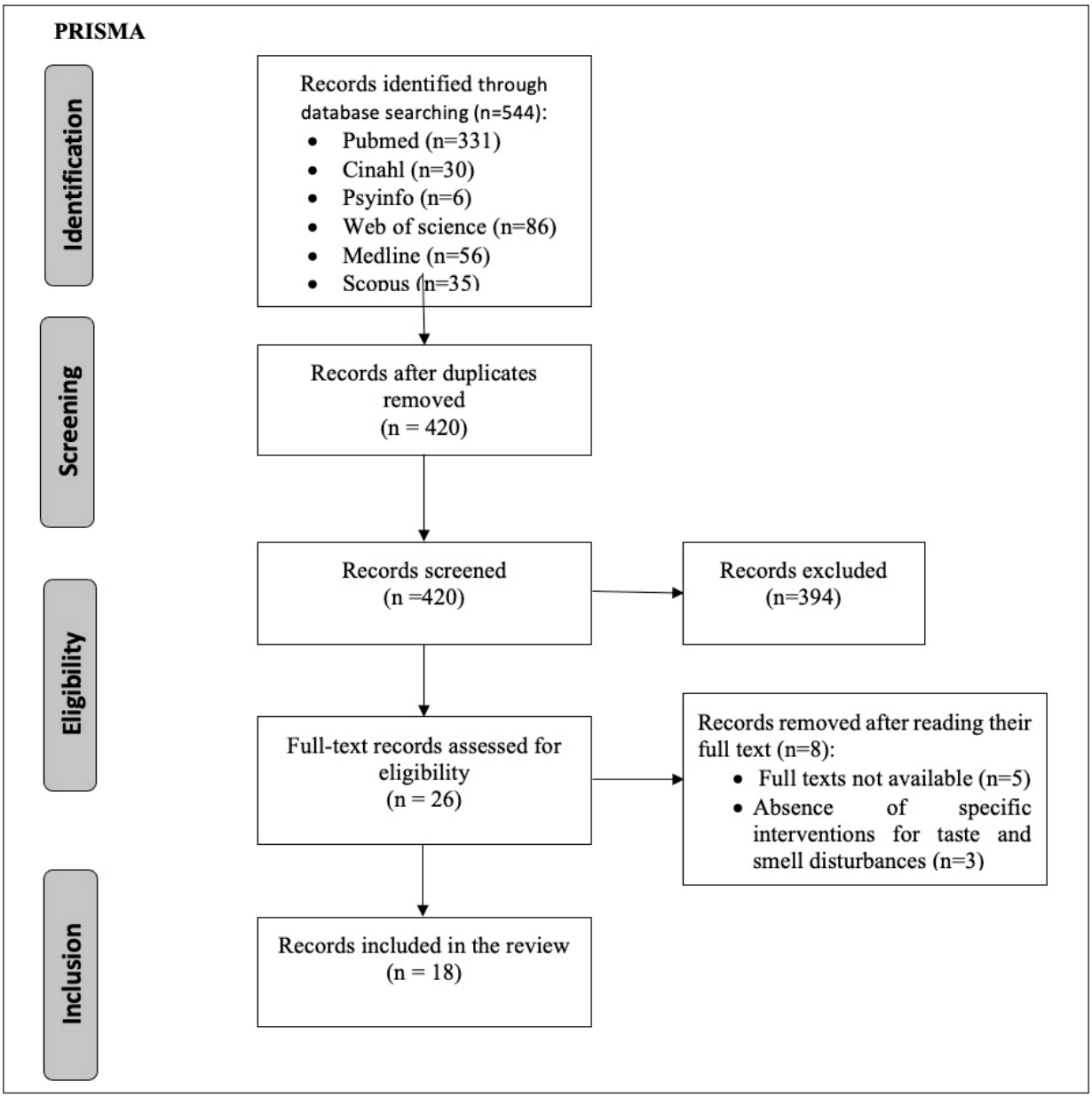

Fig. 1. PRISMA Flow chart.

into consideration are as follows:

- Photobiomodulation: 1 record
- THC or Marinol: 2 records
- Miracle fruit: 2 records
- Zinc: 4 records
- Megestrol acetate: 1 record
- Oral glutamine: 2 records
- Amifostine: 3 records
- Bethanechol: 2 records
- Marinol: 2 records
- Saliva substitutes: 1 record
- Local anaesthesia: 1 record
- Ginkgo biloba: 1 record
- Proton pump inhibitor H2 blockers: 1 record
- L-thyroxine: 1 record
- Lipoic acid: 1 record

The series of cases El Mobadder et al[41] observed have shown the efficacy of photobiomodulation for oral complications caused by cancer. In the third case, a 42-year-old man underwent intensive radiotherapy to the head-neck district which resulted in a loss in taste and a burning sensation in the mouth. The patient underwent a session of photobiomodulation every 24 hours for 5 consecutive days. After this therapy, the patient was assigned a taste alteration score of 5 out of 5 (the patient recognised all the tastes in the "sip and spit" test). After 10 sessions of treatment, a significant improvement of the perception of taste and the sensation of burning of the mouth were noticed, after 5 sessions a significant decrease in the patients' dysphagia and an increase in salivation were noticed[41].

TABLE 2. Extraction of the selected articles.

Title	*Authors*	*Objective*	*Sample*	*Results*
Characterization of chemosensory alterations in advanced cancer reveals specific chemosensory phenotypes impacting dietary intake and quality of life[19].	Brisbois et al[19]	Determine whether THC can improve the perception caloric intake, and quality of life (QOL) in cancer patients with chemosensory alterations.	46 patients, (n=24 intervention group; n=22 placebo group)	Chemosensory improvement was twice as frequent with THC treatment (36%) compared to placebo (15%), furthermore, the majority of the patients that received treatment with THC reported being able to better distinguish tastes and smells. Patients treated with THC reported an increased intake of proteins. THC can offer multiple clinical benefits for cancer patients and can alleviate taste and smell alterations, depression, anxiety, and insomnia.
Pilot study of "miracle fruit" to improve food palatability for patients receiving chemotherapy[30].	Wilken et al[30]	Determine whether the consumption of the Miracle Fruit™ supplement improves taste alterations associated with chemotherapy with consequent improvement in nutrition.	8 patients (n=4 intervention group; n= 4 placebo group)	Bad tastes improved in all 8 participants. The supplement improved taste in all the participants and increased appetite in some.
"Eat to Live"-Piloting a Culinary Medicine Program for Head & Neck Radiotherapy Patients[37].	Allen-Winters et al[37]	To study the feasibility of implementing intervention strategies based on cooking confidence and support in meal preparation for head and neck radiotherapy patients	7 participants (4 patients and 3 caregivers)	After participating in the cooking class, participants selected fruit, vegetables, grains, lean cuts of meat, and dairy products. Patients also changed their behaviour towards food, adopting healthier habits such as eating out less and grill cooking instead of frying food.
Taste disorders in cancer patients: Pathogenesis, and approach to assessment and management[11].	Epstein et al[11]	To study the importance of evaluation and management of taste and smell disturbances, and their relation to weight loss and quality of life in cancer patients.		The smell should be evaluated through smell tests that usually comprehend the identification of 10 smells. The taste should at least be evaluated through the use of impregnated strips to simulate the 5 fundamental tastes. Regarding prevention, it is important to eliminate extrinsic risk factors such as bad oral hygiene or the use of tobacco. The use of radioprotectors such as amifostine can contribute to taste maintenance thanks to its protective effect on taste buds. Zinc integrators can be taken into consideration for patients that report a persistent taste alteration.
Characterization of chemosensory alterations in advanced cancer reveals specific chemosensory phenotypes impacting dietary intake and quality of life[19].	Brisbois et al[19]	Determine whether THC can improve the perception caloric intake, and quality of life (QOL) in cancer patients with chemosensory alterations.	46 patients, (n=24 intervention group; n=22 placebo group)	Chemosensory improvement was twice as frequent with THC treatment (36%) compared to placebo (15%), furthermore, the majority of the patients that received treatment with THC reported being able to better distinguish tastes and smells. Patients treated with THC reported an increased intake of proteins. THC can offer multiple clinical benefits for cancer patients and can alleviate taste and smell alterations, depression, anxiety, and insomnia.

Continued

TABLE 2 *(CONTINUED)*. Extraction of the selected articles.

Title	*Authors*	*Objective*	*Sample*	*Results*
Pilot study of "miracle fruit" to improve food palatability for patients receiving chemotherapy[30].	Wilken et al[30]	Determine whether the consumption of the Miracle Fruit™ supplement improves taste alterations associated with chemotherapy with consequent improvement in nutrition.	8 patients (n=4 intervention group; n= 4 placebo group)	Bad tastes improved in all 8 participants. The supplement improved taste in all the participants and increased appetite in some.
"Eat to Live"-Piloting a Culinary Medicine Program for Head & Neck Radiotherapy Patients[37].	Allen-Winters et al[37]	To study the feasibility of implementing intervention strategies based on cooking confidence and support in meal preparation for head and neck radiotherapy patients	7 participants (4 patients and 3 caregivers)	After participating in the cooking class, participants selected fruit, vegetables, grains, lean cuts of meat, and dairy products. Patients also changed their behaviour towards food, adopting healthier habits such as eating out less and grill cooking instead of frying food.
Taste disorders in cancer patients: Pathogenesis, and approach to assessment and management[11].	Epstein et al[11]	To study the importance of evaluation and management of taste and smell disturbances, and their relation to weight loss and quality of life in cancer patients.		The smell should be evaluated through smell tests that usually comprehend the identification of 10 smells. The taste should at least be evaluated through the use of impregnated strips to simulate the 5 fundamental tastes. Regarding prevention, it is important to eliminate extrinsic risk factors such as bad oral hygiene or the use of tobacco. The use of radioprotectors such as amifostine can contribute to taste maintenance thanks to its protective effect on taste buds. Zinc integrators can be taken into consideration for patients that report a persistent taste alteration.
Food caregivers influence on nutritional intake among admitted haematological cancer patients - a prospective study[31].	Lindman et al[31]	This study examines how food caregivers can increase nutritional intake and knowledge in haematological cancer patients.	Comparison between two cross-sectional studies before (n=42) and after (n=45) The implementation of food caregivers.	Energy requirements were met with 76,2% and 93,3% of the calculated need in the before and after group. Two-thirds of the patients reported side effects such as fatigue, loss of appetite, vomiting, xerostomia, or taste disorders that impacted nutritional intake. Patients in the after group increased energy intake by 22%. After the implementation of food caregivers, a significant number of patients declared that they were informed about their nutritional needs, 41% in the before group and 67% in the after group.
A systematic review of dysgeusia induced by cancer therapies[12].	Hovan et al[12]	To revise existing literature from 1990 to 2008 that focuses on the prevalence and management of dysgeusia as a collateral effect of cancer treatment.	26 articles were included.	The prevalence of dysgeusia was identified with a weighted prevalence of 56-76%, depending on the type of cancer treatment. Attempts to prevent dysgeusia through the prophylactic use of zinc sulphate or amifostine have been of limited benefit. Nutritional counselling can be of use for some patients when it comes to reducing dysgeusia symptoms.
Exploring an Integrative Patient-Tailored Complementary Medicine Approach for Chemotherapy Induced Taste Disorders[38].	Ben-Arye et al[38]	Evaluate the impact of complementary and integrative medicine (CIM) based on taste disturbance severity.	34 patients	Most of the patients (29) treated with CIM reported a decrease in the severity of their symptoms, 3 reported no improvement was reported, 2 referred unclear results, and no patients reported an increase in the severity of their symptoms. Acupuncture and herbal remedies were the most used CIM interventions used. The evaluation was considered optimal in 18 of the 29 patients that reported an improvement in ESAS scores for fatigue, drowsiness, and depression.

Continued

TABLE 2 *(CONTINUED).* Extraction of the selected articles.

Title	*Authors*	*Objective*	*Sample*	*Results*
Impact of taste and smell training on taste disorders during chemotherapy - TASTE trial[39].	Grundherr et al[39]	Improve taste disorders through taste and smell training	N=25 intervention group; n=27 non-intervention group	92% (n=23 of 25) of the patients of the intervention group, whose taste significantly improved by at least two points on the taste strips test. Circa 64% (n=16 of 25) of the intervention group had an improvement of at least 3 points in the taste strip test. The study demonstrated a short-term improvement of taste disturbances, which could in turn reduce the deterioration of nutritional status in the long term.
Dysgeusia and weight loss under treatment with vismodegib: benefit of nutritional management[32].	Le Moigne et al[32]	The main objective of this study is that of monitoring the nutritional status of patients treated with vismodegib. The secondary objective of this study is that of assessing the incidence of dysgeusia and the benefits of early. nutritional management	45 patients (n=21 intervention group, Nutrition cohort; n=24 control group, historical cohort)	38% of patients undergoing preventive nutritional interventions reported a lower rate of weight loss compared to 54% of the patients of the control group that didn't receive any nutritional management intervention. Nutritional screening evaluates eating habits and the risks that derive from dysgeusia and allow for the creation of a management plan to avoid malnutrition that includes dietary advice, and monthly weight monitoring.
A state-of-the-art review of the management and treatment of taste and smell alterations in adult oncology patients[33].	Thorne et al[33]	The objective of this review is that of examining all interventions for preventing and managing taste and smell alterations in adult cancer patients	12 articles	Four articles examined zinc supplementation and reported its effectiveness, whilst two reported that it did not affect taste and smell disturbances. The remaining research groups examined eight interventions, with differing results. marinol, megestrol acetate, and Synsepalum dulcificum seem to be promising.
Taste alteration in breast cancer patients treated with taxane chemotherapy: experience, effect, and coping strategies[34].	Speck et al[34]	Examination of the experiences and coping strategies for female breast cancer patients treated with docetaxel or paclitaxel.	25 patients	Of all the side-effects reported, the most common was taste alteration (8 patients out of 10 treated with docetaxel, 3 patients out of 15 with paclitaxel). The women adopted a series of new behaviours to deal with taste alterations, such as trying new recipes, eating strongly flavoured foods, honouring specific food cravings, eating sweets before meals, cutting food with lemon, using plastic utensils, drinking sweetened drinks, drinking from a straw, brushing their teeth and tongue before a meal, docetaxel or paclitaxel.
The Effect of Special Diets on Weight and Nutritional Intake in Hematological Cancer Patients: A Randomized Study[40].	Bille et al[40]	Test food preferences in haematologic patients undergoing chemotherapy.	32 patients	Special diets have shown statistically significant benefits in the development of weight, with 1,2 ± 1,9 kg in the intervention period, and -2,8±5,2 kg (-4%) in the control period. Use of curry and preferring food with the umami taste showed a significant increase in weight, this proves the need to develop diets that consider taste alterations.
Polaprezinc prevents oral mucositis associated with radiochemotherapy in patients with head and neck cancer[35].	Watanabe et al[35]	To study the effect of polaprezinc (zinc L-carnosine), a gastric mucosa protective drug, on oral mucositis induced by radiotherapy or chemotherapy, pain, xerostomia, and taste disturbances in patients with head and neck cancer.	N=16 intervention group, (administration of polaprezinc) n=15 control group (azulene oral rinse)	Incidence rates of mucositis, pain, xerostomia and taste disturbances were significantly lower in the intervention group compared to the control group. Furthermore, the use of analgesics was significantly lower and the quantity of food was significantly higher in patients in the group taking polaprezinc compared to the control group.

Continued

TABLE 2 *(CONTINUED).* Extraction of the selected articles.

Title	*Authors*	*Objective*	*Sample*	*Results*
Photobiomodulation Therapy in the Treatment of Oral Mucositis, Dysphagia, Oral Dryness, Taste Alteration, and Burning Mouth Sensation Due to Cancer Therapy: A Case Series[41].	El Mobadder et al[41]	Verify the efficacy of photobiomodulation therapy (PBM) in the management of oral complications of cancer therapy.	3 case studies	Five sessions interleaved with 24 h breaks were conducted for the dysphagia and oral dryness; 10 sessions were conducted for taste alteration and mouth burning sensation. PBM can be considered safe, time-saving and a promising approach for the management of oral complications of cancer therapy. independently from the limitations of this series of cases.
Effects of a multi-disciplinary residential nutritional rehabilitation program in head and neck cancer survivors results from the Nutri-hab randomized controlled trial[42].	Kristensen et al[42]	The objective of the trial was that of testing the effect of a multidisciplinary residential nutritional rehabilitation programme addressing physical, psychological, and social aspects of eating problems after treatment for head and neck cancer	71 patients (n=36 intervention group; n=35 control group)	No significant differences were observed in the percentage change in body weight, but there was an overall trend towards an improvement in physical functionality and quality of life in the intervention group.
Taste disorder's management: a systematic review[43].	Braud and Boucher[43]	The aim of the systematic review was that of evaluating the effects of palliative and curative interventions on taste recovery in recent literature	28 articles	The interventions included zinc (sulphate, acetate, gluconate, aspartate, picolinate, and Polaprezinc®), omeprazole, L-thyroxin, bethanechol, oral glutamine, delta-9-tetrahydrocannabinol, alpha-lipoic acid, Ginkgo biloba, artificial saliva, pilocarpine, local anaesthesia, and better oral hygiene. The quality of the proof varied from low to high. The improvement of oral hygiene can promote taste. Zinc can prevent and alleviate and prevent taste disturbances in patients undergoing radiotherapy for head and neck cancer. This systematic review provided evidence on the clinical efficacy of the integration of zinc and palliative care in patients.
Coming to Your Senses: Detecting Taste and Smell Alterations in Chemotherapy Patients. A Systematic Review[36].	Gamper et al[36]	Provide a systematic assessment of the literature on taste and smell disturbances in chemo-therapy patients and highlight research questions that aren't the focus of studies.	22 studies	The methodologic quality of the included studies varied, especially concerning smell alterations, which were not coherent and difficult to interpret. Regarding taste alterations, it is clear that they are due to chemotherapy which alters the taste. Qualitative changes, such as metallic tastes, are frequent but cannot be attributed to specific chemotherapy regimens. Big gaps in the literature are present when it comes to taste and smell alterations in different patient populations and the impact of different chemotherapy regimens. Management strategies are rare. Only one RCT was conducted on the benefits of zinc, patients undergoing chemotherapy demonstrated low levels of serum zinc, receiving zinc sulphate infusions showed better taste perception than patients receiving placebo. Coping strategies, education strategies, and nutritional strategies (such as metallic tastes being associated with cold foods) lead to physical improvements in these patients and a higher nutritional intake. One study regarding THC showed how it increases chemosensorial perceptions but also appetite.
Dealing with taste and smell alterations- A qualitative interview study of people treated for lung cancer[44].	Belqaid et al[44]	Explore how people experiencing the taste and smell alterations caused by lung cancer, reason about resources and strategies offered and used to manage those symptoms	17 patients	Most of the strategies to tackle taste and smell alterations were actively implemented in patients' daily lives, individually and in the family context. The involvement of healthcare workers was described as limited but seem to satisfy the expectations of most of the participants. However, healthcare professionals have the potential to influence the strategies and resources used by these patients to deal with the taste and smell alterations.

TABLE 3. Main characteristics of the included studies in this systematic review.

Title	Authors	Types of Cancer	Study Design	Year	Journal	Language	City
1 Characterization of chemosensory alterations in advanced cancer reveals specific chemosensory phenotypes impacting dietary intake and quality of life[19].	Brisbois et al[19]	Advanced cancer (locally recurring, locally advanced, or metastatic: lung, breast, genitourinary, gastrointestinal, other)	Randomised pilot study, double-blind, placebo-controlled	2011	Journal Pain Symptom Manage	English	Montreal (Canada)
2 Pilot study of "miracle fruit" to improve food palatability for patients receiving chemotherapy[30].	Wilken et al[30]	Patients with cancer undergoing chemotherapy (breast, ovaries, pancreas, lymphoma, endometrium, carcinomatosis of unknown origin, thigh sarcoma)	Pilot study, placebo-controlled, non-randomised	2012	Clinical Journal of Oncology Nursing	Inglese	Omaha (USA)
3 "Eat to Live"-Piloting a Culinary Medicine Program for Head & Neck Radiotherapy Patients[37].	Allen-Winters et al[37]	Head and neck cancer	Pilot study	2019	Supportive Care in Cancer	English	USA
4 Taste disorders in cancer patients: Pathogenesis, and approach to assessment and management[11]	Epstein et al[11]	Patients with cancer	Review	2010	Oral oncology	English	USA
5 Food caregivers influence on nutritional intake among admitted haematological cancer patients - a prospective study[31].	Lindman et al[31]	Haematological cancer patients: acute leukaemia, lymphoproliferative disorders, multiple myeloma	Quasi-experimental study: comparison between two cross-sectional studies.	2013	European Journal of Oncology Nursing	English	Denmark
6 A systematic review of dysgeusia induced by cancer therapies[12].	Hovan et al[12]	Onomatological patients with head-neck cancer and cancer in other sites (breast, lung, prostate, etc)	Systematic review	2010	Support Care Cancer	English	Canada
7 Exploring an Integrative Patient-Tailored Complementary Medicine Approach for Chemotherapy-Induced Taste Disorders[38].	Ben-Arye et al[38]	Adult cancer patients with localised or metastatic cancer	Prospective study	2018	Explore	English	Israeli
8 Impact of taste and smell training on taste disorders during chemotherapy - TASTE trial[39].	Grundherr et al[39]	Patients undergoing chemo-therapy with localised cancer to lungs, breast, oesophagus, pancreas, stomach, and intestine	Phase II monocentre trial	2019	Cancer Management and Research	English	Hamburg (Germany)
9 Dysgeusia and weight loss under treatment with vismodegib: benefit of nutritional management[32]	Le Moigne et al[32]	Patients with basal cell carcinoma, locally advanced and metastatic	Prospective multicentric trial	2015	Support Care Cancer	English	Nantes (France)

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TABLE 3 *(CONTINUED)*. Main characteristics of the included studies in this systematic review.

Title	*Authors*	*Types of Cancer*	*Study Design*	*Year*	*Journal*	*Language*	*City*
10 A state-of-the-art review of the management and treatment of taste and smell alterations in adult oncology patients[33].	Thorne et al[33]	Adult patients with cancer	Review	2015	Support Care Cancer	English	Alberta (Canada)
11 Taste alteration in breast cancer patients treated with taxane chemotherapy: experience, effect, and coping strategies[34].	Speck et al[34]	Female patients with breast cancer undergoing treatment with the taxane (docetaxel or paclitaxel)	Descriptive study, with a qualitative approach	2012	Support Care Cancer	English (USA)	Philadelphia
12 The Effect of Special Diets on Weight and Nutritional Intake in Haematological Cancer Patients: A Randomized Study[40].	Bille et al[40]	Acute and chronic leukaemia, Hodgkin's lymphoma and non-Hodgkin's lymphoma, in chemotherapy treatment	2 pilot studies, single-blind	2018	Nutrition and Cancer,	English	Copenhagen (Denmark)
13 Polaprezinc prevents oral mucositis associated with radiochemotherapy in patients with head and neck cancer[35].	Watanabe et al[35]	Patients with head-neck cancer undergoing radiotherapy	Randomised controlled trial	2010	International Journal of Cancer	English	Japan
14 Photobiomodulation Therapy in the Treatment of Oral Mucositis, Dysphagia, Oral Dryness, Taste Alteration, and Burning Mouth Sensation Due to Cancer Therapy: A Case Series[41].	El Mobadder et al[41]	Head-neck cancer, breast cancer, and adenocarcinoma	Series of cases	2019	International Journal of Environmental Research and Public Health	English	Belgium
15 Effects of a multidisciplinary residential nutritional rehabilitation program in head and neck cancer survivors—results from the nutritional rehabilitation randomized controlled trial[42].	Kristensen et al[42]	Head-neck cancer	Randomised controlled trial	2020	Nutrients	English	Denmark
16 Taste disorder's management: a systematic review43.	Braud and Boucher[43]	Patients with cancer undergoing radio or chemotherapy	Systematic review	2020	Clinical Oral Investigations	English	Paris (France)
17 Coming to Your Senses: Detecting Taste and Smell Alterations in Chemotherapy Patients. A Systematic Review[36].	Gamper et al[36]	Oncologic patients undergoing chemotherapy	Systematic review	2012	Journal of Pain and Symptom Management	English	Kufstein (Austria)
18 Dealing with taste and smell alterations. A qualitative interview study of people treated for lung cancer[44].	Belqaid et al[44]	Lung cancer	Qualitative study	2018	Plosone	English	Stockholm (Sweden)

Continued

In Brisbois et al[19] study on the efficacy of THC was evaluated regarding the treatment of chemosensory alterations. In a sample of 13 patients, 8 received TCH treatment whilst 7 received placebo treatment, it was found that chemosensory alterations improved twice as much (36%) compared to placebo (15%); furthermore, most of the patients referred an increased ability in discerning tastes and smells. None of the patients receiving THC treatment manifested a loss of appetite, but rather showed an increase in the assumption of proteins. As well as having beneficial effects on taste and smell alterations, THC has been demonstrated to alleviate depression, anxiety, and insomnia[19]. Wilken et al[30] evaluated the efficacy of the integration of the Miracle Fruit™, containing synsepalum dulcificum, "miracle fruit", a fruit that thanks to a protein, miraculin, can transform a sweet taste into an acidic one. Of the 8 participants in the pilot study, 4 underwent treatment with Miracle Fruit™ and the other 4 were given a placebo; before treatment, the patients were weighed and questioned about their usual eating habits. For 28 days both groups had to keep a food diary in which they had to report the type of food and the quantity ingested immediately after haven taken the integrator or the placebo. The study showed not only an improvement in the nutritional intake but also that bad tastes were changed thanks to Miracle Fruit™[30]. Watanabe et al[35] tested the effect of polaprezinc on oncologic patients with tumours in the head-neck district that underwent chemotherapy. The main aim of the study was to prevent mucositis, whilst the secondary aim was to dimmish oral pain, xerostomia, and taste alterations. A total of 516 patients were administered polaprezinc and a control group made up of 515 patients was administered azulene for oral rinses. All patients in the control group experienced mucositis, pain, and xerostomia, and 87% of the patients reported taste alterations. Rinses with PZ reduced the risk of mucositis by 56.7% and reduced the use of oral analgesics by 73.9%, xerostomia by 83%, and taste alterations by 88.3%; furthermore, it also impeded the reduction of the quantity of food consumed indicating an improvement in the quality of life without influencing the response to radiochemotherapy[35].

The main interventions individuated in Thorne et al's review[33] included the integration of zinc, megestrol acetate, oral glutamine, amifostine, self-care interventions, diabetes counselling, bethanechol, use of Miracle Fruit™ and Marinol. The most promising treatments were Marinol, megestrol acetate, and Miracle Fruit™ [33]. Braud and Boucher[43] analysed preventive interventions, therapeutic interventions, and palliative interventions for tase alterations. Some of the preventive interventions analysed included oral hygiene, saliva substitutes, zinc, and Ginkgo Biloba; only oral hygiene demonstrated tangible benefits. Regarding therapeutic interventions, zinc and saliva substitutes were shown to have been effective in patients that underwent head-neck district chemotherapy; whilst proton pump inhibitors, L-thyroxine, glutamine, lipoic acid, and local anaesthesia were useful in the treatment of idiopathic or medication-induced dysgeusia, and taste disturbances in patients undergoing haemodialysis. Only one study reported the palliative effect of cannabis and cannabinoids on taste alterations[43]. The use of amifostine as a radioprotector has a protective effect on tastebuds and contributes to the preservation of a normal sense of taste[11]. Hovan et al[12] highlighted the use of zinc phosphate or amifostine had a limited capacity of preventing dysgeusia.

Nonpharmacological interventions: education and nutritional counselling

Seven records focus on nonpharmacological interventions for the treatment and management of taste and smell alterations; of these seven records 2 were pilot studies, 1 quasi-experimental study, 2 prospective studies, 1 2nd phase monocentric trial, and 1 RCT. Interventions taken into consideration were:

- Nutritional interventions and diet amendments: 4 records
- Integrative complementary medicine interventions: 1 record
- Culinary medicine: 1 record
- Multidisciplinary residential nutritional rehabilitation program: 1 record

It was demonstrated in Lindman et al's study[31] that involving kitchen staff, as culinary caregivers, in support of oncologic patients raised energy consumption from 76.2% to 93.3%. The results of this study indicate that an organization based on centralized food production, and the employment of trained personnel with qualified healthcare workers play a big role in nutritional management[31].

The study conducted by Bille et al[40] reported how the use of curry or the tendency to predilect food with an umami taste led to a significant increase in the weight of patients involved in the study, this suggests and demonstrates that it is necessary to develop diets that consider taste alterations. A prospective study that takes into consideration 45 patients undergoing treatment with vismodegib analyses the efficacy of early nutritional management[32]. Nutritional manage-

ment was composed of the following interventions malnutrition screening, calculation of BMI, evaluation of a dietician, providing of an informative note with diet suggestions, and monthly weight monitoring. 38% of the patients that underwent these early nutritional interventions lost less weight compared to 54% of patients of the control group that didn't undergo any nutritional management intervention. Nutritional screening, evaluation of eating habits, explaining risks that derive from dysgeusia, providing diet advice, and monitoring weight monthly contribute to avoiding the insurgence of malnutrition[32].

In Von Grundherr et al[39] monocentric trial, a nutritional consult and training to better taste and smell perceptions were proposed to oncologic patients undergoing chemotherapy. Patients were tested for taste alterations by using test strips, BMI was measured as well as the quality of life and malnutrition risk and based on the results the patients were divided into two groups, the intervention group (n:25) with taste and smell alterations that had received taste and smell training and a nutritional consult, and a control group (n:27) without taste and smell alterations who only received a generalized nutritional education. The intervention group underwent 15-minute training sessions during which certain drinks or objects to be smelled were given to the patients to strengthen their sense of taste and smell and received detailed instructions to ensure proper oral hygiene. 92% of the patients bettered their reactive strip score by 2 points, 64% had an increase of 3 points. The study demonstrated a short-term betterment of smell and taste alterations and could perhaps reduce nutritional status detriment in the long term[39]. Another study evaluated the efficacy of a program of culinary medicine "Eat to live", which consisted of cooking lessons for caregivers and patients intending to change cooking habits, dietary choices and improve taste alterations. The results of this study have shown that following these cooking lessons, participants were more likely to select fruit and vegetables, cereals, meat, and dairy products; furthermore, patients' tendency to have dinner at a restaurant decreased as did their use of ready-made meals as they found pleasure in cooking[37].

Ben-Arye et al[38] prospective study focused on the impact of complementary and integrative medicine (CIM) treatment programs specifically made for patients with taste disorders due to chemotherapy (CITD). Of the 626 patients that were directed to a CIM program, 43 were diagnosed with CITD, 29 of these referred an improvement following the program. This study also demonstrated that integrators, such as glutamine and zinc, had no impact on taste disorders but, other complementary medicine methods such as herbs, acupuncture, manual therapies reduced CITD's and improved quality of life[38].

In Kristensen et al's RCT[42] a residential multidisciplinary nutritional program's efficacy that tackles physical aspects, psychological aspects, and social aspects of alimentary problems was tested on patients that had recovered from cancer of the head-neck district. A total of 71 survivors were included, 36 of which underwent treatment, and the remaining 35 were part of the control group. The intervention was based on a 5-day stay, individual and group sessions with a dietitian, a cooking lesson, educational group sessions on oral hygiene and swallowing, physical activity sessions with a physiotherapist were also proposed to participants, as well as equilibrium or resistance exercises and group sessions with a psychologist or priest. The control group did not receive any intervention. The main aim was to evaluate variation in the percentage of body weight, whilst secondary objectives included evaluation of BMI, physical functionality, quality of life, anxiety, and depression. The study didn't show any effects regarding the primary outcome but showed a positive effect on physical functionality and quality of life[42].

Self-care strategies

Of the three articles taken into consideration, one was a qualitative study, one was a descriptive study with a qualitative approach, and one was a review.

Belqaid et al's qualitative study[44] highlighted that patients encountered two main difficulties when managing taste and smell disturbances: adapting to not being able to process the information these senses provide and accepting their new situation as no restorative interventions are available. All of the patients reported issues when consuming coffee, red meat, desserts, chemical odors, cooking odors, smoke, and body odor. Adaptation strategies were mainly those of avoiding the foods listed above by replacing them with other food or by adding spices and condiments to them. Furthermore, patients reported how being able to have a nurse they could contact in moments of need was of comfort to them. The results show that much of the management of these disorders were handled on an individual basis and with the support of family members, even though the support given by healthcare staff was described as limited but had the potential to influence some aspects of acceptance and adaptation of taste and smell disturbances[44].

TABLE 4. Main characteristics of the included studies in this systematic review.

Title	*Authors*	*Objective*	*Sample*	*Results*
Characterization of chemosensory alterations in advanced cancer reveals specific chemosensory phenotypes impacting dietary intake and quality of life[19].	Brisbois et al[19]	Determine whether THC can improve the perception of taste and smell, appetite, caloric intake, and quality of life (QOL) in cancer patients with chemosensory alterations.	46 patients, (n=24 intervention group; n=22 placebo group)	Chemosensory improvement was twice as frequent with THC treatment (36%) compared to placebo (15%), furthermore, the majority of the patients that received treatment with THC reported being able to better distinguish tastes and smells. Patients treated with THC reported an increased intake of proteins. THC can offer multiple clinical benefits for cancer patients and can alleviate taste and smell alterations, depression, anxiety, and insomnia.
Pilot study of "miracle fruit" to improve food palatability for patients receiving chemotherapy[30].	Wilken et al[30]	Determine whether the consumption of the Miracle Fruit™ supplement improves taste alterations associated with chemotherapy with consequent improvement in nutrition.	8 patients (n=4 intervention group; n= 4 placebo group)	Bad tastes improved in all 8 participants. The supplement improved taste in all the participants and increased appetite in some.
"Eat to Live"-Piloting a Culinary Medicine Program for Head & Neck Radiotherapy Patients[37].	Allen-Winters et al[37]	To study the feasibility of implementing intervention strategies based on cooking confidence and support in meal preparation for head and neck radiotherapy patients.	7 participants (4 patients and 3 caregivers)	After participating in the cooking class, participants selected fruit, vegetables, grains, lean cuts of meat, and dairy products. Patients also changed their behaviour towards food, adopting healthier habits such as eating out less and grill cooking instead of frying food.
Taste disorders in cancer patients: Pathogenesis, and approach to assessment and management[11].	Epstein et al[11]	To study the importance of evaluation and management of taste and smell disturbances, and their relation to weight loss and quality of life in cancer patients.		The smell should be evaluated through smell tests that usually comprehend the identification of 10 smells. The taste should at least be evaluated through the use of impregnated strips to simulate the 5 fundamental tastes. Regarding prevention, it is important to eliminate extrinsic risk factors such as bad oral hygiene or the use of tobacco. The use of radioprotectors such as amifostine can contribute to taste maintenance thanks to its protective effect on taste buds. Zinc integrators can be taken into consideration for patients that report a persistent taste alteration.
Food caregivers influence on nutritional intake among admitted haematological cancer patients - a prospective study[31].	Lindman et al[31]	This study examines how food caregivers can increase nutritional intake and knowledge in haematological cancer patients.	Comparison between two cross-sectional studies before (n=42) and after (n=45) The implementation of food caregivers.	Energy requirements were met with 76,2% and 93,3% of the calculated need in the before and after group. Two-thirds of the patients reported side effects such as fatigue, loss of appetite, vomiting, xerostomia, or taste disorders that impacted nutritional intake. Patients in the after group increased energy intake by 22%. After the implementation of food caregivers, a significant number of patients declared that they were informed about their nutritional needs, 41% in the before group and 67% in the after group.

Continued

TABLE 4 *(CONTINUED).* Main characteristics of the included studies in this systematic review.

Title	*Authors*	*Objective*	*Sample*	*Results*
A systematic review of dysgeusia induced by cancer therapies[12].	Hovan et al[12]	To revise existing literature from 1990 to 2008 that focuses on the prevalence and management of dysgeusia as a collateral effect of cancer treatment.	26 articles were included.	The prevalence of dysgeusia was identified with a weighted prevalence of 56-76%, depending on the type of cancer treatment. Attempts to prevent dysgeusia through the prophylactic use of zinc sulphate or amifostine have been of limited benefit. Nutritional counselling can be of use for some patients when it comes to reducing dysgeusia symptoms.
Exploring an Integrative Patient-Tailored Complementary Medicine Approach for Chemotherapy-Induced Taste Disorders[38].	Ben-Arye et al[38]	Evaluate the impact of complementary and integrative medicine (CIM) based on taste disturbance severity.	34 patients	Most of the patients (29) treated with CIM reported a decrease in the severity of their symptoms, 3 reported no improvement was reported, 2 referred unclear results, and no patients reported an increase in the severity of their symptoms. Acupuncture and herbal remedies were the most used CIM interventions used. The evaluation was considered optimal in 18 of the 29 patients that reported an improvement in ESAS scores for fatigue, drowsiness, and depression.
Impact of taste and smell training on taste disorders during chemotherapy - TASTE trial[39].	Grundherr et al[39]	Improve taste disorders through taste and smell training.	N=25 intervention group; n=27 non-intervention group.	92% (n=23 of 25) of the patients of the intervention group, whose taste significantly improved by at least two points on the taste strips test. Circa 64% (n=16 of 25) of the intervention group had an improvement of at least 3 points in the taste strip test. The study demonstrated a short-term improvement of taste disturbances, which could in turn reduce the deterioration of nutritional status in the long term.
Dysgeusia and weight loss under treatment with vismodegib: benefit of nutritional management[32].	Le Moigne et al[32]	The main objective of this study is that of monitoring the nutritional status of patients treated with vismodegib. The secondary objective of this study is that of assessing the incidence of dysgeusia and the benefits of early nutritional management.	45 patients (n=21 intervention group, Nutrition cohort; n=24 control group, historical cohort)	38% of patients undergoing preventive nutritional interventions reported a lower rate of weight loss compared to 54% of the patients of the control group that didn't receive any nutritional management intervention. Nutritional screening evaluates eating habits and the risks that derive from dysgeusia and allow for the creation of a management plan to avoid malnutrition that includes dietary advice, and monthly weight monitoring.
A state-of-the-art review of the management and treatment of taste and smell alterations in adult oncology patients[33].	Thorne et al[33]	The objective of this review is that of examining all interventions for preventing and managing taste and smell alterations in adult cancer patients.	12 articles	Four articles examined zinc supplementation and reported its effectiveness, whilst two reported that it did not affect taste and smell disturbances. The remaining research groups examined eight interventions, with differing results. marinol, megestrol acetate, and Synsepalum dulcificum seem to be promising.

Continued

TABLE 4 *(CONTINUED)*. Main characteristics of the included studies in this systematic review.

Title	*Authors*	*Objective*	*Sample*	*Results*
Taste alteration in breast cancer patients treated with taxane chemotherapy: experience, effect, and coping strategies[34].	Speck et al[34]	Examination of the experiences and coping strategies for female breast cancer patients treated with docetaxel or paclitaxel.	25 patients	Of all the side-effects reported, the most common was taste alteration (8 patients out of 10 treated with docetaxel, 3 patients out of 15 with paclitaxel). The women adopted a series of new behaviours to deal with taste alterations, such as trying new recipes, eating strongly flavoured foods, honouring specific food cravings, eating sweets before meals, cutting food with lemon, using plastic utensils, drinking sweetened drinks, drinking from a straw, brushing their teeth and tongue before a meal, docetaxel or paclitaxel.
The Effect of Special Diets on Weight and Nutritional Intake in Hematological Cancer Patients: A Randomized Study[40].	Bille et al[40]	Test food preferences in haematologic patients undergoing chemotherapy.	32 patients	Special diets have shown statistically significant benefits in the development of weight, with 1,2 ± 1,9 kg in the intervention period, and -2,8±5,2 kg (-4%) in the control period. Use of curry and preferring food with the umami taste showed a significant increase in weight, this proves the need to develop diets that consider taste alterations.
Polaprezinc prevents oral mucositis associated with radiochemotherapy in patients with head and neck cancer[35].	Watanabe et al[35]	To study the effect of polaprezinc (zinc L-carnosine), a gastric mucosa protective drug, on oral mucositis induced by radiotherapy or chemotherapy, pain, xerostomia, and taste disturbances in patients with head and neck cancer.	N=16 intervention group, (administration of polaprezinc) n=15 control group (azulene oral rinse)	Incidence rates of mucositis, pain, xerostomia and taste disturbances were significantly lower in the intervention group compared to the control group. Furthermore, the use of analgesics was significantly lower and the quantity of food was significantly higher in patients in the group taking polaprezinc compared to the control group.
Photobiomodulation Therapy in the Treatment of Oral Mucositis, Dysphagia, Oral Dryness, Taste Alteration, and Burning Mouth Sensation Due to Cancer Therapy: A Case Series[41].	El Mobadder et al[41]	Verify the efficacy of photobiomodulation therapy (PBM) in the management of oral complications of cancer therapy.	3 case studies	Five sessions interleaved with 24 h breaks were conducted for the dysphagia and oral dryness; 10 sessions were conducted for taste alteration and mouth burning sensation. PBM can be considered safe, time-saving and a promising approach for the management of oral complications of cancer therapy. independently from the limitations of this series of cases.
Effects of a multi-disciplinary residential nutritional rehabilitation program in head and neck cancer survivors–results from the Nutri-hab randomized controlled trial[42].	Kristensen et al[42]	The objective of the trial was that of testing the effect of a multidisciplinary residential nutritional rehabilitation programme addressing physical, psychological, and social aspects of eating problems after treatment for head and neck cancer.	71 patients (n=36 intervention group; n=35 control group)	No significant differences were observed in the percentage change in body weight, but there was an overall trend towards an improvement in physical functionality and quality of life in the intervention group.

Continued

TABLE 4 *(CONTINUED).* Main characteristics of the included studies in this systematic review.

Title	*Authors*	*Objective*	*Sample*	*Results*
Taste disorder's management: a systematic review[43].	Braud and Boucher[43]	The aim of the systematic review was that of evaluating the effects of palliative and curative interventions on taste recovery in recent literature.	28 articles	The interventions included zinc (sulphate, acetate, gluconate, aspartate, picolinate, and Polaprezinc®), omeprazole, L-thyroxin, bethanechol, oral glutamine, delta-9-tetrahydrocannabinol, alpha-lipoic acid, Ginkgo biloba, artificial saliva, pilocarpine, local anaesthesia, and better oral hygiene. The quality of the proof varied from low to high. The improvement of oral hygiene can promote taste. Zinc can prevent and alleviate and prevent taste disturbances in patients undergoing radiotherapy for head and neck cancer. This systematic review provided evidence on the clinical efficacy of the integration of zinc and palliative care in patients.
Coming to Your Senses: Detecting Taste and Smell Alterations in Chemotherapy Patients. A Systematic Review[36].	Gamper et al[36]	Provide a systematic assessment of the literature on taste and smell disturbances in chemotherapy patients and highlight research questions that aren't the focus of studies.	22 studies	The methodologic quality of the included studies varied, especially concerning smell alterations, which were not coherent and difficult to interpret. Regarding taste alterations, it is clear that they are due to chemotherapy which alters the taste. Qualitative changes, such as metallic tastes, are frequent but cannot be attributed to specific chemotherapy regimens. Big gaps in the literature are present when it comes to taste and smell alterations in different patient populations and the impact of different chemotherapy regimens. Management strategies are rare. Only one RCT was conducted on the benefits of zinc, patients undergoing chemotherapy demonstrated low levels of serum zinc, receiving zinc sulphate infusions showed better taste perception than patients receiving placebo. Coping strategies, education strategies, and nutritional strategies (such as metallic tastes being associated with cold foods) lead to physical improvements in these patients and a higher nutritional intake. One study regarding THC showed how it increases chemosensorial perceptions but also appetite.
Dealing with taste and smell alterations- A qualitative interview study of people treated for lung cancer[44].	Belqaid et al[44]	Explore how people experiencing the taste and smell alterations caused by lung cancer, reason about resources and strategies offered and used to manage those symptoms.	17 patients	Most of the strategies to tackle taste and smell alterations were actively implemented in patients' daily lives, individually and in the family context. The involvement of healthcare workers was described as limited but seem to satisfy the expectations of most of the participants. However, healthcare professionals have the potential to influence the strategies and resources used by these patients to deal with the taste and smell alterations.

A descriptive study[34] conducted on a sample of 25 patients, 11 of which reported taste alterations, showed patients' strategies to manage said alterations: consumption of seasoned food, compliance of cravings, eating sweets before meals, adding of lemon to food, drinking sweetened drinks, utilization of plastic cutlery, drinking from a straw, brushing teeth before meals using a mouthwash[34]. In Epstein et al's review[11], the most used interventions were chewing gum or sweets to stimulate salivation or adding seasoning to food and rotation of the type of meals eaten[11].

DISCUSSION

Even though the literature has highlighted how taste and smell disturbances are a common issue in oncologic patients undergoing radiotherapy and/or chemotherapy, it is still a topic that isn't studied much as evidenced by a lack of scientific evidence available. All the studies included in this review agreed that taste and smell disturbances strongly impacted the quality of life and nutritional model of patients, and that they are directly correlated to weight loss and risk of malnutrition[38,45-47]; despite the importance of this issue, patients often report not receiving appropriate support from healthcare professionals for these disturbances and not being sufficiently informed about the onset of these alterations as a direct consequence of the antitumoral treatments they were undergoing. From the results obtained, the importance of an early evaluation of these symptoms, by using appropriate scales and instruments, such as reactive strips and electrogustometry for taste and the sniffing test for smell[11,36], that cannot provide a multidimensional evaluation that these disturbances require. Evaluation of these disturbances is an obstacle by the heterogeneity of these symptoms and the difficulty patients have in describing them, as there isn't a standardized language to describe them[44]. The main objective of this review was to individuate known treatments that are put in place to prevent, treat or manage taste and smell disturbances, and reduce the effects that they have on the health and quality of life of patients. For convenience, interventions present in the literature were divided into three groups: pharmacologic treatments, non-pharmacologic treatments (education, counselling, and nutritional rehabilitation), and self-care interventions that patients implemented. Pharmacologic interventions mainly concerned the use of zinc[11,33,35,38,43], which didn't demonstrate its' efficacy in prevention but were shown to be useful in patients with head-neck tumours undergoing radiotherapy and patients with a zinc deficiency (anorexia, increased excretion of zinc etc); however, the various studies expressed contrasting opinions due to the different paths of administrations and dosages analysed[33,43]. According to scientific evidence, it isn't recommended to use zinc gluconate to prevent dysgeusia in patients with head-neck tumours, but it can be effective against idiopathic dysgeusia[38]. The use of Polaprezinc was effective in reducing the risk of mucositis, use of analgesics, pain, xerostomia, and taste alterations[35]. An intervention that proved particularly effective, especially if taken right before meals, is the use of Miracle Fruit™, which allows for the transformation of acidic tastes into sweet ones[30,33]. The use of THC is also a valid intervention that not only affects taste and smell disturbances but also has favorable effects on appetite, sleep disturbances, depression, and anxiety on patients that use said substance[19,43]. Photobiomodulation, utilized following protocols and clear schemes, proved its usefulness in the prevention of taste and smell disturbances, mucositis, dysphagia, xerostomia, and BMS[41]. Many studies proposed educational and rehabilitative interventions regarding nutritional models by varying these patients' diets using spices[40], or by teaching patients how to obtain specific nutritional competencies and meal preparation practices to increase their appeal and reduce aversion towards food[37]. The importance of this process was highlighted not only by the involvement of patients and caretakers, who often are the ones who prepare the meals and offer emotional support to the patients but also by the involvement of all the professionals that were involved in the management of the patients'[31]. Adequate nutritional screening is fundamental for these patients so that their diet can be adapted to their new perceptions and help them enjoy the taste of their meals. One study showed how nutritional counselling, paired with specific taste and smell training exercises (giving patients specific drinks ad objects to smell) could reduce nutritional status' deterioration in the long term[39]. Complementary integrative medicine[38] and nutritional rehabilitation programs[45] had good results by targeting not only the physical aspects but also psychological and social ones that these patients face. Oncologic patients are often malnourished, and these disturbances can significantly contribute to weight loss, development of food aversion, and loss of interest in anything regarding food[32,37,39,44,45,48,49]. Patients also often tend to avoid the most important elements of a balanced diet (red meat, pasta, vegetables, coffee, alcohol, sweets)[44,45,48] and they also tend to consume pre-packaged meals or unhealthy food that do not contribute to the nutritional needs of an oncolog-

ic patient. The impact of these alterations on patients' quality of life led to them finding strategies to manage the issues that stemmed from these alterations. The main strategies adopted included eating food with strong flavors, following cravings for specific foods, eating sweets before meals, use of lemon, drinking sugary drinks, using plastic cutlery, drinking from a straw, and brushing one's teeth before a meal[34]. These strategies were determined subconsciously rather than consciously, specifically the choice to avoid certain foods or increase the intake of sugar which are not beneficial and proves the need these patients have of receiving support from professionals[34,44]. Moreover, although Vitamin supplementation in the form of tablets, capsules or pastes have been tried with varying degree of success in both chemo/radiotherapy-induced mucositis[50], no study was considered pertinent with the aim of this review.

In only a few articles[41,48] the importance of the presence of healthcare professionals when managing these symptoms was taken into consideration, and patients often report a lack of information received and the divide present between hospital care and home care when it comes to these symptoms, which is often delegated to caregivers or the patients themselves who don't possess the skills needed to handle these symptoms[51]. Of all the articles included in the systematic review[12], only one contained prevention strategies for dysgeusia with levels of evidence, grades of recommendation, and classification of guidelines. The prevention strategies included the use of zinc gluconate, amifostine, nutritional counselling, and educational interventions.

Zinc gluconate: II level of evidence, grade of recommendation C, it is not suggested to use zinc gluconate to prevent dysgeusia in patients with head-neck district cancer, even though it has shown beneficial effects in a cohort with idiopathic dysgeusia not related to cancer.

Amifostine: II level of evidence, grade of recommendation B, it is recommended to not exclusively use amifostine for the prevention of dysgeusia in patients with head-neck district cancer.

Nutritional counselling and education: II level of evidence, recommendation grade B, it is suggested to employ counselling and education to prevent dysgeusia.

Interventions such as the normalization of routine evaluations of taste and smell disorders, the presence of a nurse, and counselling could be useful for clinical practice. Gamper et al's study[36] shows that the lack of randomized controlled trials highlights the few interventions available that are effective and how not much is known on the aetiology of these alterations, future research questions could be "which alterations are clinically significative?", "how do different chemotherapic regimes impact taste and smell perceptions?", "what possible interventions require further inquiries?"[36].

Our scoping review has a few limitations. First, it did not examine the risk of bias as assessed in systematic reviews. However, the aim was to find the current themes being studied on the topic, which this review successfully captured. Second, search abstracts published in a language other than English and Italian were excluded due to the cost and time involved in translating material. Third, grey literature was not searched. Further research is needed to examine nonpharmacological interventions and self-care strategies.

CONCLUSIONS

Taste and smell disturbances in oncologic patients undergoing chemotherapy and/or radiotherapy form a vast set of symptoms that are complex and difficult to completely assess. This difficulty is also due to the etiopathogenetic mechanisms of these alterations that are not yet completely known and thus there are no valid and univocal assessment instruments. It is clear from the literature that it is important to assess these symptoms early and that not only must the patients' physical sphere be taken into consideration, but the psychological and social ones as well. Disinformation and lack of a definitive treatment led these patients to feel a lack of confidence that leads to underreporting of symptoms, as they feel like there isn't a way to overcome these symptoms and consequently these patients face a loss of interest in food, social relations thus leading to malnutrition, non-adherence to therapeutic plans and a decrease in the quality of life. Healthcare professionals could play a key role as they could be the connecting point between primary care and home care for patients with these symptoms. Taste and smell disturbances in patients undergoing chemotherapy and/or radiotherapy are a relevant issue in the oncologic population, but they are underrated and not studied much, as is clear from the lack of literature concerning these disturbances and specifically from the lack of randomized controlled trials, and it is advisable to increase the number of studies that take aetiology, objective and subjective evaluation, application of interventions to prevent, treat and manage taste and smell alterations.

Conflict of Interest:
The authors declare that they have no conflict of interests and that the article has not been published previously and has not been forwarded to another journal.

Authors' contribution:
Concept/design: FS; AF; LC; Data collection: AF; GL; FS; Data analysis/interpretation: EDS; FS; Drafting article: GL; ADL; SD; Critical revision of article: EDS; SD; MDM; NG; Approval of article: NG, MDM; FS.

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