



Metallic taste prevalence in patients treated for cancer: a systematic literature review and meta-analysis

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Abstract

Background Metallic taste (MT) is a taste abnormality often reported by cancer patients. The aim of this systematic review was to exhaustively report MT incidences in cancer patients and to evaluate the risk of bias in the pertinent studies in accordance with a meta-analysis approach.

Methods The research objective was to determine the prevalence of MT in patients treated for cancer. A literature search was conducted using PubMed, Web of Science, and Embase. The authors each screened articles and evaluated the eligibility and individual risk of bias for each article. Then, all of the results were compared. A meta-analysis was conducted on studies that specifically focused on MT evaluation.

Results Very few articles have been published on the incidence of MT among taste and smell abnormalities in cancerology (22 of 1674, 1.3%), and the quality of the reports on MT was often low. The most common bias was the methodology used for MT evaluation. Pooling the results of the 22 studies led to an estimated MT incidence in the cancer patient population of 29% (95% CI [0.21; 0.39]) with high and significant heterogeneity observed among the studies. A heterogeneity analysis was performed to identify the causal factors of this heterogeneity. The specific impact of MT on nutritional status (two) and quality of life (five) studies were reported, respectively, and without a specific evaluation of MT. There was no mention of oral health in any of the studies.

Conclusion Although in clinical practice cancer patients often report MT, its incidence has only been reported in 22 studies, most of which have a moderate to severe risk of bias. Considering the rather high prevalence of MT, more research should be conducted in this field to better identify its causes and mechanisms.

Keywords Metallic taste · Incidence · Cancer · Treatment · Meta-analysis

Introduction

Taste and smell abnormalities (TSAs) are frequent in oncology regardless of the type of cancer (any solid or hematological type [1, 2, 3, 4, 5]) and are often considered caused by the treatments administered. For instance, dysgeusia affects 50 to 75% of patients depending on the administered treatment(s) (chemotherapy, radiotherapy, or

radiochemotherapy) [2, 6]. Perception thresholds can be modified (increased or decreased), perceptions can be distorted (parageusia or parosmia), and/or patients may have perceptions of flavors that do not exist (phantogeusia or phantosmia). TSAs can also impact nutritional status by limiting oral intake [7, 8] and subsequently decreasing quality of life [2, 9, 10].

Metallic taste (MT) is an unusual form of parageusia. Patients describe MT as a spontaneous, unpleasant, persistent metallic sensation in the mouth. Very little is known about the trigger mechanisms for this sensation, possibly due to oncologists' inconsistent reporting of this symptom, one illustration of which being the large difference in MT incidence reported by patients and their oncologists [11] in which oncologists believed that only 9.9% of their patients suffered from MT, whereas 32.2% of patients reported MT. A few conditions associated with MT are well known, such

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as oral candidiasis and/or dry mouth [12, 13]. However, the specific mechanisms underlying MT sensation are poorly understood, although several hypotheses have been suggested. The origin of MT may be (i) biochemical, through oxidation between Fe^{2+} and oral lipids in the mouth [14]; (ii) electrical, induced by local hydrolysis and a spontaneous electrical current between dental amalgams [15]; (iii) neurological, due to the removal of inhibition of the facial nerve on the glossopharyngeal nerve [16, 17, 18]; and/or (iv) proteomic in origin linked to the overexpression of bitter receptors on the tongue [19, 20].

Little is known about the impact of TSAs on cancer patients' food behavior and nutritional status. However, several studies have reported correlations between chemical sensory alterations and the food behavior of patients while receiving chemotherapy. A recent review [21] noted that the occurrence of chemosensory disorders was associated with a decrease in the oral intake of patients diagnosed with cancer and the evolution of patients' food preferences and food behavior while receiving chemotherapy. Moreover, among TSAs, the sensation of MT is likely one of the most negatively influential factors on food behavior [22].

To gain further insights into the impact of MT, we performed a systematic review and meta-analysis of the literature to delineate the prevalence of MT in cancer patients.

Methods

The research objective was to determine the prevalence of metallic taste in patients treated for cancer.

PICO question

Population: patients treated for cancer.

Intervention: chemotherapy, radiotherapy, surgery, other (target and hormonal therapies)

Comparison: N/A

Outcomes: the prevalence of MT

Data sources and search strategy

An initial search was performed in September 2019 in PubMed, Web of Science (WoS), and Embase. Two updates were performed in January 2020 and November 2020. The search terms used are given below.

- EMBASE: 'neoplasm'/exp AND ('taste disorder' OR 'metallic taste')
- PubMed: "neoplasms"[MeSH] AND ("taste disorders"[MeSH] OR ("metallic"[All Fields] AND "taste"[All Fields]) OR "metallic taste"[All Fields])

- Web of Science: ALL=(neoplasm* OR tumor* OR cancer*) AND (ALL=(taste* OR ageusia OR hypogeusia* OR gustat*)) AND (ALL=(disorder* OR alteration* OR metal*))

This systematic review was conducted following the PRISMA 2020 guidelines [23], which are described in the supplementary material (Tables S1 and S2). The study protocol was registered in November 2019 on PROSPERO (an international database of prospectively registered systematic reviews) under the number CRD42020157450. Several changes to the initial protocol were made: (i) nutritional and quality of life aspects could not be assessed because very few articles have been published on MT and nutritional and/or quality-of-life issues and (ii) a meta-analysis on MT prevalence was performed that was not part of the initial plan.

Study selection

Screening step

The screening was conducted by the three investigators (GB, GF, and TTD). GB and GF screened all of the identified titles and abstracts, and discrepancies were resolved by the third investigator (TTD). The inclusion criteria for the screening steps were (a) title or abstract describing any taste disorder in cancer patients, not necessarily MT, or (b) full papers mentioning MT and its prevalence. When only the title (without an abstract) was accessible in the first step and there was doubt concerning eligibility, the corresponding record was considered for the second step. No restrictions were placed on language or publication dates. Abstracts and full papers were included. Case reports, reviews, meta-analyses, commentaries, and editorials were excluded.

Determination of eligibility

Eligibility was assessed by all three investigators. GB and GF screened all the retrieved articles. Discrepancies were resolved by the third investigator (TTD). The eligibility criteria consisted of a specific description of metallic taste (MT), including data on the prevalence (number and/or % of patients).

The screening and eligibility steps were performed using the Rayyan web app for systematic reviews [24].

Data extraction

The three investigators extracted the following data for each study: author names, year, title, journal, study design, sample size, sex, age (mean, SD, and range), country, type of cancer, type of treatment, prevalence of MT (n/N and/or %), date of measurement (in months), and methodology for MT

evaluation. When detailed data on MT prevalence were not provided in a paper, the respective authors were contacted.

Individual risk of bias

A bias analysis was performed for each study using the ROBIN-I tool following the Cochrane guidelines for non-randomized studies and the RoB2 tool for randomized studies [25, 26].

The main confounding domain was used to evaluate MT based on three criteria, namely, the date of MT measurement after treatment, MT awareness of participant, and specificity of MT evaluation. Other identified confounding variables were age, sex, toxicity factors (smoking and alcohol consumption), and oral health.

Outcome

The outcome was the prevalence of MT in cancer patients.

Data analysis

Prevalence was expressed as the number of patients reporting MT divided by the total number of patients. MT prevalence was estimated using a random-effects meta-analysis model. The random-effects model was chosen assuming that clinical and methodological heterogeneity were likely

to exist and affect the results. The DerSimonian and Laird method was used to pool the studies [27]. The Clopper-Pearson interval, also called the “exact” binomial interval, was used to calculate confidence intervals [28, 29].

Heterogeneity was assessed by the I^2 statistic [30]. Contour-enhanced funnel plots were used to investigate small study effects [31]. Funnel plot asymmetry was tested using the weighted linear regression method [32]. Leave-one-out analysis was performed on the included studies. The analyses were conducted with R software (v3.5.3) using the package Meta and the function Metaprop for meta-analysis of single proportions (the R code is provided in Doc S1).

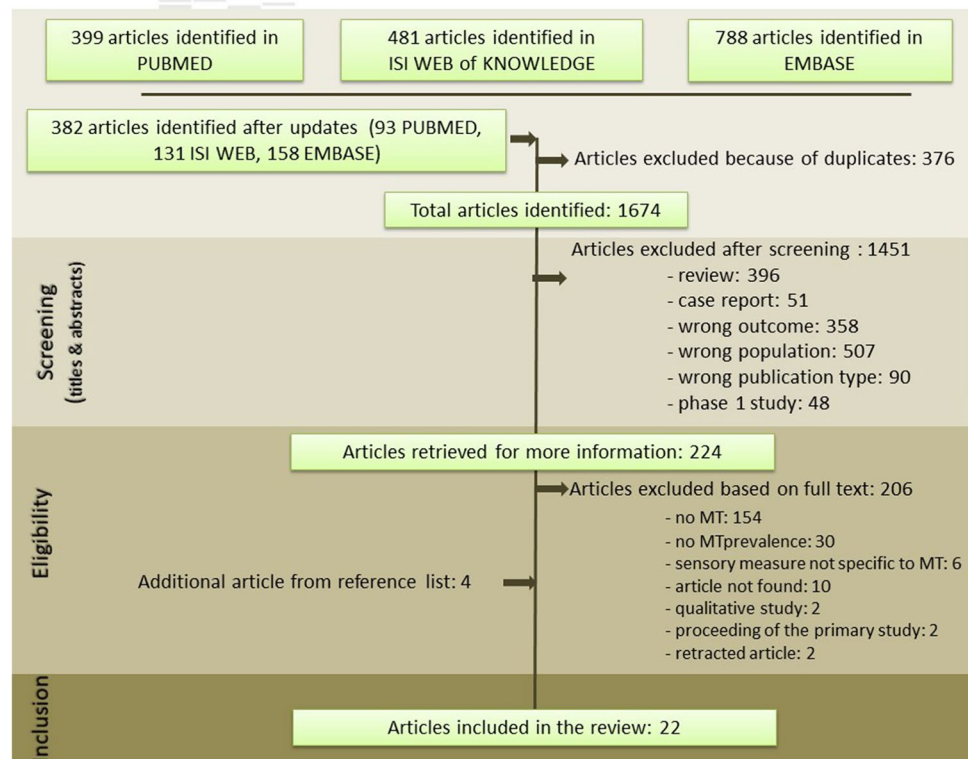
Registration of the review This review was not previously registered.

Results

Search results

The PRISMA flowchart for article selection is presented in Fig. 1. The search of the three databases identified 2050 records in the cancer area mentioning dysgeusia; 1678 articles remained after removing duplicates. A further 1451 articles were excluded through title and abstract screening because the selection criteria were not met. Specifically, 507

Fig. 1 PRISMA flowchart



articles dealt with an irrelevant population, 358 articles dealt with an unrelated outcome, and 396 articles were reviewed. Of the 224 remaining articles, 206 were excluded after full-text review principally because the text did not mention MT ($n = 154$) or MT prevalence ($n = 30$). Despite our efforts to access all the references, including contacting the authors directly, 10 articles remained inaccessible. Of these 10 articles, seven were published before 2000, only titles were available for six, and six were in a language other than English and published in local journals. Finally, 22 articles were included in the meta-analysis [8, 11, 33–52].

Characteristics of included studies

The characteristics of the included studies are presented in Table 1. Among the 22 included articles, there were 11 cross-sectional studies, three randomized controlled trials (RCTs), four cohort studies, one observational retrospective study, one study in which variables were controlled before and after the study was performed, one case–control study, and one quasi-randomized control study. The studies were categorized in terms of the type of cancer as follows: 13 dealt with any solid or hematological cancer, three with head and neck cancer, one with breast cancer, two with lung cancer, one with colorectal cancer, one with testicular cancer, and in one study the cancer location was not specified. In this last study, the treatments were chemotherapy (platinum based, taxan based, and others), hormonal therapies, target therapies (tyrosine-kinase inhibitors, others), and concomitant radiochemotherapy [42].

Assessment of MT

Most of the studies used a questionnaire to evaluate MT in cancer patients. However, there were significant variations regarding questionnaire implementation. Only 6 studies reported the time at which MT was evaluated after treatment; 8 studies explicitly included training patients for MT recognition; and 4 studies used an evaluation methodology specific to MT. These variations led to a significant risk of bias for MT evaluation, as presented below and in Figures S1A and S1B of the supplementary material.

Risk of bias

The risk of bias analyses for the 3 RCTs and the 19 non-RCTs are presented in the supplementary material (Table S3). The distribution of the risk of bias for the 3 RCTs and 19 non-RCTs is presented in Fig. 2A and B, respectively.

None of the included non-RCTs had a low risk of bias regarding MT evaluation. The risk of bias in the non-RCT studies was moderate for four (21%), serious for 13 (68%), and critical for 2 (11%) of the studies. The 3 available RCTs

were judged to have a high risk of bias (100%) for MT evaluation.

The main issue encountered was a risk of bias for the MT evaluation confounding domain, especially the absence of precision in assessing oral health status (mucositis, candidiasis, and dry mouth) or tobacco consumption. Twelve studies showed a high risk of bias; we had concerns regarding 6 studies; and only two studies were evaluated as having a low risk of bias (see Figs. S1A and S1B in the supplementary material).

MT incidence

A forest plot is presented in Fig. 3. The incidence of MT (with random effects) was estimated at 29% in the general cancer population (95% CI [0.21; 0.39]).

The heterogeneity among studies was high and significant ($I^2 = 97%$, $\tau = 0.85$, $p < 0.01$) which prompted us to perform subgroup analyses in an attempt to explain this heterogeneity, and the test results are presented in the supplementary material. Many factors were considered to account for the heterogeneity: the cancer type (Fig. S2), treatment type (Figure S3), overall risk of bias (Figure S4), and risk of bias of the sensory evaluation method (Figure S5). The heterogeneity remained close to 1 and significant for every factor considered, except lung cancer. However, only two studies [43, 46] on lung cancer were included, making it difficult to draw sound conclusions. Finally, leave-one-out analysis (Figure S6) confirmed that no single study substantially influenced the MT prevalence estimation. The funnel plot analysis (Figure S7) showed that several of the studies ($n = 16$) lay outside the 95% confidence interval, which confirmed the heterogeneity among the studies. However, the funnel plot did not provide any evidence indicating that the results of studies with few patients were systematically different from those with a larger number of patients (test of funnel asymmetry: $t = 0.87$, p value = 0.40).

Discussion

We carried out a systematic literature review and meta-analysis of the prevalence of MT in cancer patients. Five main results can be highlighted. First, very few articles reported MT incidence among TSAs in oncology (22 out of 1678 (1.3%)). Then, the pooled results led to an estimated MT incidence of 29% in the general cancer population (95% CI [0.21; 0.39]). The specific impact of MT on nutritional status and quality of life has rarely been evaluated. Only five studies reported MT and nutritional status, and only two studies mentioned MT and the quality of life of patients, but without specific evaluation. Furthermore, the quality of the reports concerning MT was often low (Figs. 2, 3, and 4) and we did

Table 1 List of the 22 selected articles

Reference	Study design	Sample size (women, men)	Mean age \pm SD [range] (years)	Country	Type of cancer	Type of treatment	Prevalence of MT (specified the dates in months) <i>n/N</i> (%)	Methodology for measurement
Al-Taie et al. [33]	Cross-sectional	80 (25, 55)	58.4 \pm 14.8 [60–92]	Turkey	Any type (lung, breast, brain, skin, colorectal, prostate, pelvis)	RT	40/80 (50%)	Not specified
Alvarez-Camacho et al. [34]	Cross-sectional	19 (2, 17)	Less physical symptom burden group: 58 [56–65]; greater physical symptom burden group: 57 [50–58]	Canada	Head & neck	RT, CT + RT, surgery + RT, surgery + CT + RT, RT + target therapy	1/19 (5.2%)	Questionnaire TSS [53]
Amezaga et al. [35]	Cross-sectional	151 (96, 55)	60.3 \pm 11.3 (28–87)	Spain	Any type (breast, colon, lung, prostate, ovarian, lymphoma, others)	CT	59/151 (39.1%)	Questionnaire
Bernhardson et al. [36]	Cross-sectional	518 (398, 120)	58.71 \pm 10.77 [24; 85]	Sweden	Any type of solid cancers (breast, GI, gynecological, others)	CT	50/518 (9.7%)	Questionnaire
Coa et al. [8]	Cross-sectional	1199 (717, 450)	Not specified	USA	Any type (breast, gastro-intestinal, lung cancer, other solid cancers, hematologic, or unknown malignancies)	CT, RT, surgery, hormone therapy, transplant	223/1199 (18.6%)	Questionnaire
Cusmir et al. [37]	RCT with crossover	47 (25, 22)	61	USA	Any type (gastro-intestinal, breast, other)	CT	38/47 (80%) at baseline	Questionnaire Wickham [49]
Derksen et al. [38]	Cohort (prospective)	87 (26, 61)	64 \pm 7.6	Netherlands	Colon	Adjuvant CT	8/45 (18%)	Questionnaire
Genyresse et al. [39]	Observational retrospective	63 (34, 29)	Group 1: median age = 75.5 [70–87]; group 2: median age = 64 [42–69]	Germany	Any type (non-Hodgkin's lymphoma, pancreatic, breast, esophageal, lung)	CT	12/63 (19%)	Not described
Halyard et al. [40]	RCT	169 (51, 118)	median 59 [31–88] for treatment; 58 [38–95] for placebo	USA	Head & neck	RT	10%	Questionnaire

Table 1 (continued)

Reference	Study design	Sample size (women, men)	Mean age \pm SD [range] (years)	Country	Type of cancer	Type of treatment	Prevalence of MT (specified the dates in months) <i>n/N</i> (%)	Methodology for measurement
I Jipma et al. [41]	Cohort (prospective)	21 (0, 21)	Median 32 [27–36]	Netherlands	Testicular	CT	5/21 (24%) at baseline, 3/21 (14%) at 14 days, 2/21 (9.5%) at 1 month after CT	Questionnaire
I Jipma et al. [42]	Cross-sectional	127 (73, 54)	56.8 \pm 13.7	Netherlands	Any type (not precised)	CT, CT + RT, hormonal therapy, target therapies	20/127 (15.7%)	Questionnaire
Lindsey et al. [43]	Cohort (prospective)	10 (0, 10)	55.5 (43–67)	USA	Small cell lung carcinoma	CT + prophylactic cranial RT	1/10 (10%) at 3 months	Questionnaire
Logan et al. [44]	Case-control	100 (28, 72) in case and 101 (29, 79) in control	64.9 \pm 10.9 in case and 64.1 \pm 10.7 in control; [32–90]	USA	Head & neck	RT, CT + RT, RT & surgery, RT + CT + surgery	Patients: 29/98 (29%) responding (100 in total); Controls: 8/100 (8%) responding (101 in total)	Questionnaire
McDaniel et al. [45]	Cross-sectional	40 (40, 0)	[18–68]	USA	Breast	CT	20/40 (50%)	Interview
McGreevy et al. [46]	Cross-sectional	89 (49, 40)	67 \pm 9	Sweden	Lung	Surgery, CT, RT, target therapies, alone, or in combination	9/89 (10.1%)	Questionnaire TSS [53]
Newell et al. [11]	Cross-sectional	204 (126, 78)	57 [20; 86]	Australia	Any type (colorectal, breast, head & neck, stomach, lung, others)	CT	121 (59.3%); 32.2% declared by patients and 9.9% by oncologists	Questionnaire
Ponticelli et al. [47]	Cross-sectional	289 (154, 155)	61 \pm 13.07	Italy	Any type (lymphoma, myeloma, leukemia, breast, colorectal, lung, stomach, head & neck, other)	CT in combination with RT or target therapies	61/289 (21%)	Questionnaire
Rehwaldt et al. [48]	Before & after (uncontrolled)	42 (35, 7)	56 \pm 14.7	USA	Any type (lymphoma, breast, lung, ovarian)	CT	33 (78%)	Questionnaire TSS [53]
Soares et al. [49]	RCT with crossover	23 (11, 12)	63	USA	Any types (gastrointestinal, breast, other)	CT	20/23 (87%)	Questionnaire Wickham [49]
Uj Dhuibhir et al. [50]	Cross-sectional	30 (26, 4)	53.7 \pm 13.6	Ireland	Any type (gynecological, breast, colorectal)	Surgery, CT, RT	2/30 (6.7%)	Questionnaire

Table 1 (continued)

Reference	Study design	Sample size (women, men)	Mean age \pm SD [range] (years)	Country	Type of cancer	Type of treatment	Prevalence of MT (specified the dates in months) n/N (%)	Methodology for measurement
Wickham et al. [51]	Cross-sectional	284 (179, 105)	58 \pm 15	USA	Any type (colon/rectum, breast, lung, lymphoma, ovarian, other)	CT	89/284 (41%)	Questionnaire
Wilken et al. [52]	Quasi-randomized (cross-over, non-randomized order)	8 (6,1,1 not specified)	60.8 \pm 8.9	USA	Any type (breast, ovarian, pancreatic, endometrial, carcinomatosis of unknown origin, lymphoma, sarcoma of the thigh)	CT	5/8 (62%)	Questionnaire/interview

CT, chemotherapy; RCT, randomized controlled trials; RT, radiotherapy; TSS, taste and smell survey

not identify any studies with a low risk of bias; only 18% of the studies had a moderate risk of bias. Finally, there was no mention of oral health in any study.

Most of the included studies were observational cross-sectional studies. Three RCTs and three longitudinal cohort studies were included. The primary outcome of the latter was the incidence of TSAs, but not MT specifically.

Exploration of heterogeneity

A heterogeneity test assesses whether the results of studies can be considered to be similar (homogeneity hypothesis); if all the results are similar, the studies can be considered together. If the heterogeneity is significant, then there is at least one study for which the results cannot be considered identical to those of the others, making it inappropriate to pool the studies. Significant heterogeneity can usually be resolved by subgroup analyses [53]. Considering the significant and high heterogeneity (0.97, $p < 0.01$) encountered in our meta-analysis, several subgroup analyses were carried out (see the [supplementary material](#)). However, the heterogeneity remained high and significant according to the cancer type (except for the two studies on lung cancer [43, 46]), the treatment type, the global risk of bias, and the risk of bias for sensory evaluation. Several hypotheses can be proposed as a possible explanation of this heterogeneity. First, the treatments in the 22 included articles were mainly chemotherapies using many different drugs and administration schemes (depending on the cancer type). A subgroup analysis by drug type could not be performed because individual data was not available. Second, a large variability in the time of MT measurement was observed (e.g., immediately after chemotherapy or many months after the end of the treatment), which might account for a large part of the observed heterogeneity. Third, several confounding variables, such as tobacco use, alcohol consumption, or oral health status were not controlled. Indeed, it has been shown that chemotherapy can cause oral mucosal lesions, oral candidiasis, and an increased abundance of acidophilic oral microflora, which may induce the measured taste disturbances [13, 54].

Two studies [37, 49] reported a high MT incidence but were based on the same cohort; only the population size varied between these two studies. None of the included studies reported MT incidence in the noncancer population, and we found no corresponding data in the literature. However, one of the coauthors of Logan's paper [44] (Prof. L. Bartoshuk) shared data for the control group with us, in which the MT incidence was 8%. Many factors were considered in the analysis of MT sensation for the general population [15, 42, 44, 55]: high intense sweetener consumption, anodic stimulation of the tongue, chorda tympani damage or direct stimulation, pregnancy, burning mouth syndrome, the presence of metals (iron, copper, zinc, platinum) or salts (calcium, magnesium)

Fig. 2 Review authors’ judgments of the risk of bias for each item, presented as percentages across all included studies. **A** Nonrandomized controlled studies and **B** randomized controlled studies

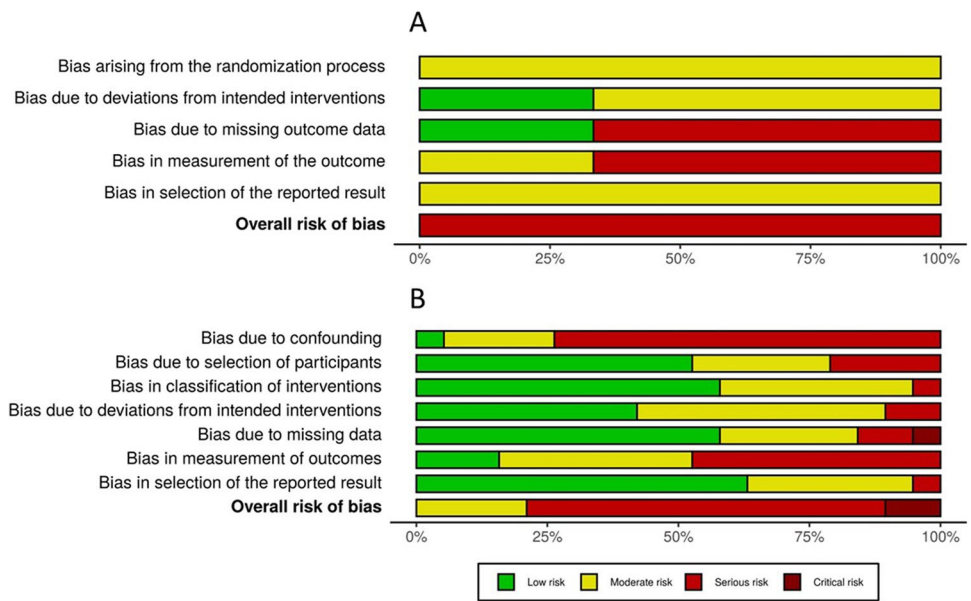
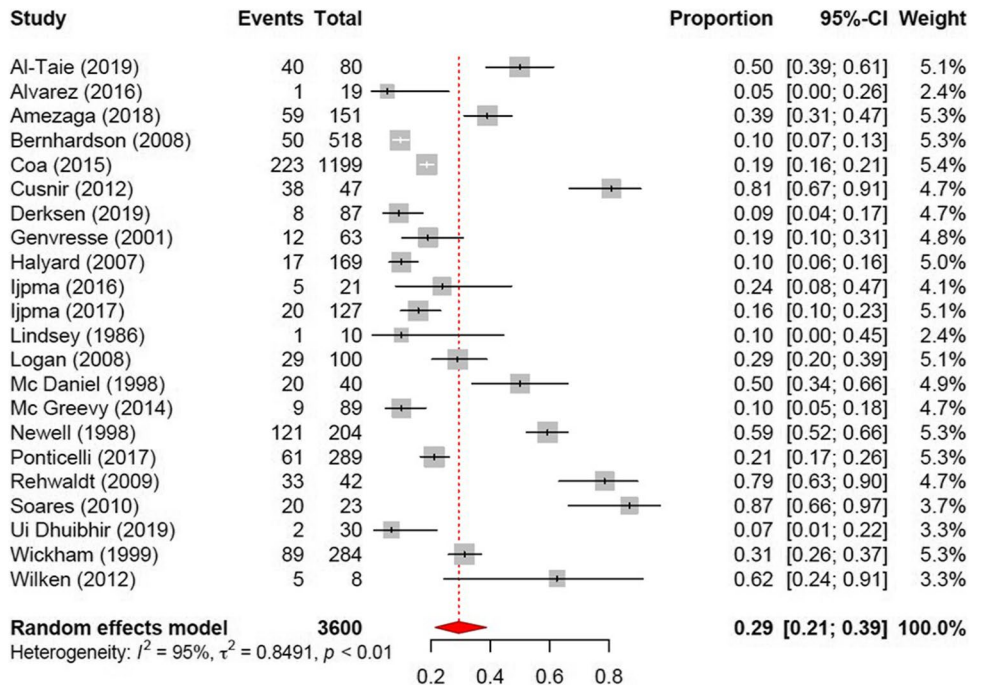


Fig. 3 Random effect meta-analysis of MT prevalence in cancer patients. The red dotted line represents the estimated pooled random effects



in the mouth, and medical treatments. However, no clear mechanism explaining MT has been reported.

Impact of MT on nutritional status and quality of life of cancer patients

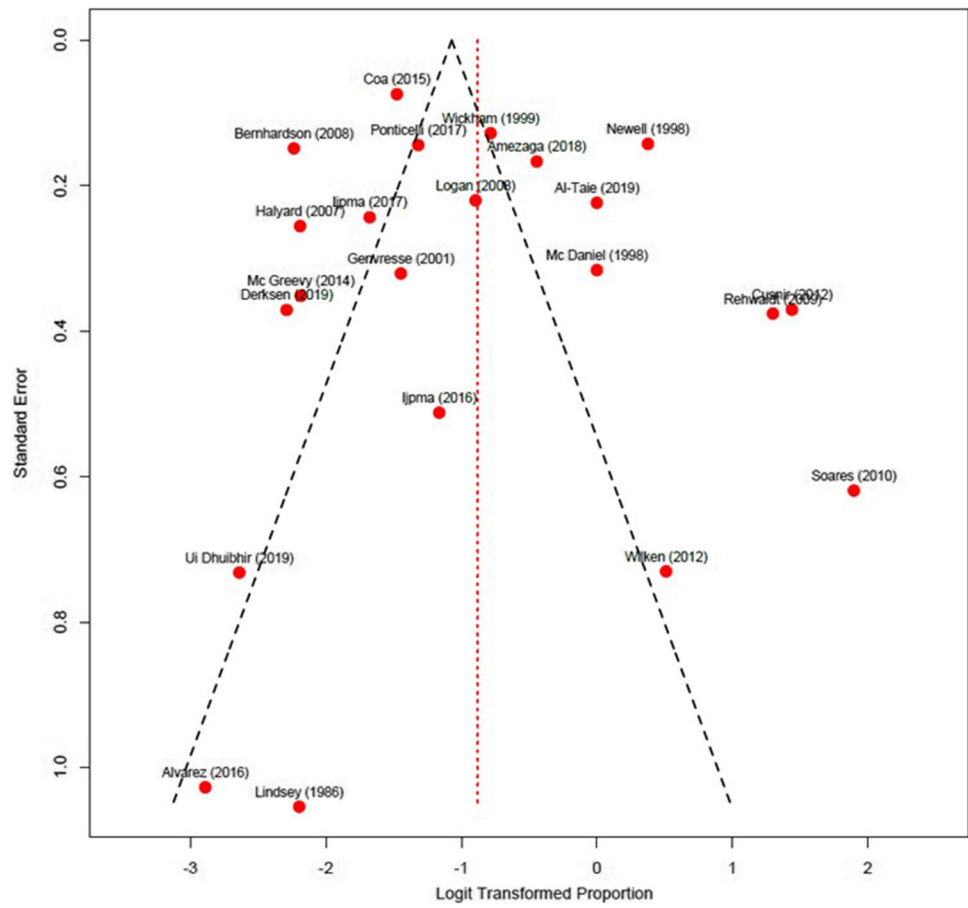
There was a presumed impact of MT on weight and/or quality of life in several of the included studies; however, only five studies reported weight changes in the investigated population [8, 22, 41, 43, 49]. Although every included study reported TSAs in cancer patients, none of the studies was

dedicated to MT. Therefore, we were not able to evaluate the specific impact of MT on nutritional status and weight in patients treated for cancer. Similarly, neither of the two studies in which TSAs were mentioned as affecting the quality of life [38, 39] reported a specific impact of MT on quality of life.

Quality of evidence

The quality of evidence for MT prevalence in the cancer patient population was considered to be low for different

Fig. 4 Funnel plot for random effects of meta-analysis of MT prevalence rate versus standard error. The dotted black triangle line represents the 95% confidence interval. The red dotted line represents the pooled random effects estimate



reasons. First, the substantial heterogeneity observed among studies could reflect the influence of the different types of cancer and/or of the different types of treatments considered in the included studies. Moreover, for several studies, the absence of a description of the location and dose used for the treatment might also contribute to the discrepancies among studies. Second, most of the included studies were unclear regarding MT evaluation or had a high risk of bias in the MT evaluation. These findings highlight the necessity of using a more rigorous and/or standardized methodology for MT evaluation.

The perceptual status of MT

This systematic review addresses the question of MT as a symptom of cancer patient treatments and highlight the difficulty to evaluate this symptom in an adequate manner. Indeed, it is likely that MT is not a basic taste since its perception vanished when retro-olfaction was suppressed in many studies [14, 15, 28, 29, 56, 57, 58, 59, 60]; MT is thus more in line with the concept of flavor that could involve the activation of several chemosensory systems [61]. Therefore, we suggest the need to introduce

an appropriate testing methodology of MT as a flavor. We decided to explore, in healthy volunteers, if there was a significant difference of intensity in the perception of MT when a ferrous sulfate solution is specifically applied by swabs to the anterior portion (facial nerve) or to the posterior portion (glossopharyngeal nerve) of the tongue. Another prospective line of study is currently led by our team, the TORCAD program (NCT03558789), and tries to better objectify the MT in head and neck cancers by a study of saliva composition, basic tastes, and MT testing [42] as well as employing serial quality of life [62, 63] questionnaires at specific times of treatments. This prospective study shall enable to clarify potential causes of MT, namely oxidation between Fe^{2+} and oral lipids in the mouth [14], removal of inhibition of the facial nerve on the glossopharyngeal nerve [16, 17, 18]. In addition, such a study would further explore implications for patient care and potential management strategies identified by IJpma et al. [42], such as the use of plastic cutlery, the addition of herbs, spices, sweetener, or acid to foods; to eat cold or frozen foods; to use “miracle fruit” supplements; and to rinse the mouth with chelating agents (e.g., bovine lactoferrin).

Limitations

Bias in the selection phase cannot be excluded. First, all relevant studies may not have been indexed in the three searched databases (WoS, PubMed, Embase). Second, the search was based on a specific list of terms related to the subject of this review. The possibility that additional articles may have been identified using other terms cannot be excluded, although the search was intended to be as extensive as possible.

Another limitation is the systematic absence of evaluations of oral health status and *Candida* in the selected articles. These health factors may not affect the incidence of MT, although they could be critically related to the etiology of MT. To clarify this, they should be considered in future MT studies.

Conclusion

This systematic review and meta-analysis revealed that approximately one-third of cancer patients suffer from MT disorder. However, these results should be interpreted with caution due to the low quality of the included studies which evaluated MT. The findings of this review highlight that a standardized procedure needs to be employed to evaluate MT in order to obtain high-quality results. Moreover, sensory and/or survey protocols should be followed to maximally reduce confounding MT with other tastes, particularly the bitter taste. The timing of MT evaluation should also be systematically reported to reduce the heterogeneity among studies. One of the initial objectives of this review was to evaluate the relationship between MT prevalence and the nutritional and quality-of-life status of cancer patients. However, insufficient information was available in the literature to accomplish this objective, revealing a gaping lack of knowledge in this field. This analysis clearly demonstrated that taste disorders, particularly MT, are considered independently of the quality of life and nutritional issues in prospective clinical studies. Therefore, it appears to be necessary to (i) promote rigorous evaluation of both nutritional status and quality of life in prospective clinical and biological studies, (ii) consider oral health and treatment in cases of mucositis or candidiasis, and (iii) conduct high-quality controlled trials to account for MT as well as other taste and smell disorders to improve the nutritional status and quality of life of patients treated for cancer. To this end, we are currently conducting a prospective study implementing these recommendations in patients with head and neck neoplasms. We expect that the results will provide better insights into the causes and possible treatments of MT.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00520-022-06904-y>.

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Author contribution All three authors contributed to the study conception and design. G. Buiret and G. Féron conceptualized the writing of the article, and all three authors performed the literature search and data analysis (as described in the Methods section). The first draft of the manuscript was written by G. Buiret, and all authors commented on subsequent versions of the manuscript.

Data availability Data are provided in Table 1 and the supplementary files.

Code availability Provided in the supplementary files.

Declarations

Ethics approval N/A.

Competing interests The authors declare no competing interests.

Consent for publication All authors read and approved the final manuscript.

Consent to participate N/A.

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