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A longitudinal study of changing characteristics of self-reported taste and smell alterations in patients treated for lung cancer

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ABSTRACT

Purpose: Taste and smell alterations (TSAs) are common symptoms in patients with cancer that may interfere with nutritional intake and quality of life. In this study, we explore and describe how characteristics of self-reported TSAs change in individuals with lung cancer over time using a multiple case study approach to present longitudinal data from individuals.
Methods: Patients under investigation for lung cancer were recruited from one university hospital in Sweden. The 52 patients providing data eligible for the analyses presented here were those treated for primary lung cancer with three measurement time-points, of which one was prior to treatment and two after treatment start. Four self-report instruments were used for data collection. These included the Taste and Smell Survey, used to characterize TSAs for each individual at the three time-points and instruments measuring nutritional status, symptom burden and well-being. Three patient cases are described in detail to illustrate variation in individual experiences of TSAs.
Results: The characteristics of the TSAs experienced changed over time for many of the individuals in this study, including those undergoing surgery or stereotactic radiotherapy. The case descriptions show how the individual experiences of TSAs and the impact on daily life of these symptoms not only depend on TSA characteristics, but may be influenced by contextual factors, e.g. other symptoms and life situation.
Conclusions: Our results suggest that healthcare professionals need to consider the variation in characteristics of TSAs among and within patients over time, and be attentive to individual experiences of TSAs.

1. Introduction

Taste and smell alterations (TSAs) are recognized as common symptoms in patients with cancer that may interfere with nutritional intake and quality of life (Hutton et al., 2007; Zabernigg et al., 2010). Although TSAs have most often been studied in relation to cancer treatments such as chemotherapy and radiotherapy to the head-neck area, they have also been reported at the time of diagnosis and in palliative phases of cancer (Belqaid et al., 2014; Gamper, Zabernigg et al., 2012; Hutton et al., 2007; Yamashita et al., 2006).

One research strategy to assess taste function is to clinically test recognition and detection thresholds of the basic taste qualities (sweet, sour, salt, bitter and umami) or odours (Wismer, 2008). However, in the Swedish study presented here we were interested in patients' experiences of TSAs rather than their taste and smell acuity and we therefore used a self-report instrument to

Abbreviations: ESAS, Edmonton Symptom Assessment System; FAACT, Functional Assessment of Anorexia-Cachexia Therapy; M1, measurement time-point before treatment start; M2, first measurement time-point after treatment start; M3, second measurement time-point after treatment start; PG-SGA SF, Short form of Patient-Generated Subjective Global Assessment; SRT, stereotactic radiotherapy; TSA, taste and smell alteration; TSS, Taste and Smell Survey.

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investigate TSAs in patients treated for lung cancer. Recent research has acknowledged the lack of consensus surrounding the concepts and words used for describing altered taste and smell experiences during cancer (Boltong and Keast, 2015). For instance, 'taste' is often confused with flavour making it difficult to differentiate these concepts. Furthermore, flavour is a term which does not exist in the Swedish language. Based on that and in line with previous research (Bernhardson et al., 2008a; Steinbach et al., 2009; Gamper, Zabernigg et al., 2012) we have used the words "taste" and "taste and smell" in their colloquial sense to encompass flavour, taste and/or smell. When we refer to the sense of taste in terms of the basic taste qualities, we use the term "basic taste".

Prior longitudinal studies of TSAs have shown that, at group level, mean intensity scores of self-reported taste changes measured on a 4-point Likert scale, increase during the patient's course of chemotherapy (Gamper, Giesinger et al., 2012; Zabernigg et al., 2010). Steinbach et al. (2009) provided complementary information by clinically testing senses of taste and smell, and found, also at group level, increasingly impaired basic taste and smell function during chemotherapy. Similar results were presented by Boltong et al. (2014), who found an overall reduced taste function in patients undergoing chemotherapy and a cyclical change associated with proximity to chemotherapy administration; however they also reported taste function being restored eight weeks after completed chemotherapy. In a qualitative study by Bernhardson et al. (2007), patients undergoing chemotherapy were interviewed about their TSAs. They found that problems with taste and smell improved gradually after completed treatment, ceasing completely after 0.5–14 weeks. Brisbois et al. (2011) addressed differences in qualities of TSAs by grouping patients according to self-reported increased or decreased sensitivity to basic taste qualities (sweet, salt, sour and bitter) or smell. Our recent research developed this further to also account for self-reported TSAs that do not involve intensity changes, such as metallic taste or reduced enjoyment of specific foods (McGreevy et al., 2014). In that cross-sectional study, we observed gender differences among the groups describing different TSA qualities.

Although studies of groups of patients present important information about TSAs in patients with cancer, they do not reveal the nature of the individual experiences underlying group averages. Systematic study of individual experiences of TSAs may thus provide information of particular relevance for healthcare professionals dealing with symptomatic individuals in their daily practice. In addition, while the previously mentioned longitudinal studies using symptom intensity scoring provide descriptive information about some central aspects of TSAs, they do not give insight into other types of changes in taste and smell. Few studies to date have investigated the many different qualities of perceived TSAs, such as increased or decreased sensitivity in basic taste qualities or smell, and longitudinal data on this is particularly lacking. It is also important to consider that many of the different qualities of TSAs are not mutually exclusive, as an individual patient can experience several changes simultaneously.

This complexity led us to recognize that our previous results (Belqaid et al., 2014; McGreevy et al., 2014) did not adequately represent patients' individual experiences of TSAs. In the study presented here, we address these knowledge gaps by exploring and describing how characteristics of TSAs change in individuals treated for lung cancer over time. For this purpose, we have chosen a multiple case study design (Yin, 2014), allowing the combination of complementary data types to further understanding of individuals' experiences of TSAs.

2. Methods

The data presented here derive from the longitudinal "Taste and Smell project" which was approved by the Regional Ethical Review Board, Stockholm (2009/1463-31/3; 2010/1849-32; 2011/1324-32).

2.1. Patients and data collection procedure

Patients under investigation for lung cancer were recruited consecutively between January 2011 and July 2012 from one university hospital in Stockholm, Sweden. Patients were informed about the study by a staff nurse during their first visit at the outpatient clinic. If patients expressed interest in study participation, their contact information was forwarded to the researchers who contacted them by telephone. After a patient had agreed to participate and provided informed consent, one of four interviewers (either a nurse or dietitian) carried out structured face-to-face interviews based on the four questionnaires described below. Patients were first interviewed before treatment start, with three follow-up interviews conducted thereafter at two-month intervals. When feasible, the same interviewer conducted all interviews, reading the questions aloud and documenting the patient's responses. After each interview, the research interviewer compiled field notes with information about the context of the interview and other details of importance beyond that documented in the questionnaires. Additional clinical and background information was obtained from medical records with patients' consent.

Data for the analyses presented here were derived from patients participating in the "Taste and Smell project" who were treated for primary lung cancer, and had documented interviews conducted at a minimum of three of the four measurement time-points. Patients' treatment modalities were dichotomized as those receiving 1) systemic therapy, i.e. targeted therapy or chemotherapy, including concomitant chemo-radiotherapy, and adjuvant chemotherapy after surgery; or 2) localized therapy, i.e. surgery or stereotactic radiotherapy (SRT). Treatment start was registered as the first day of the targeted therapy or first chemotherapy cycle, day of surgery or first day of SRT.

In this study, the first measurement time-point, here referred to as M1, was held before treatment start. The second measurement time-point (M2) took place within 30–99 days after treatment start, so that patients on chemotherapy should have received at least two of their planned treatment cycles. The third measurement time-point (M3) took place $\geq$100 days after treatment start, to avoid overlap between time frames for M2 and M3. The exact number of days between measurement time-point and the previous treatment for individual patients is not presented here as the purpose of this study is to explore and describe changes in characteristics of TSAs rather than establish patterns of effects of cancer treatment on TSAs.

2.2. Questionnaires

The four self-report instruments used for data collection were presented in the same order to all patients.

The first instrument was the Swedish version of The Taste and Smell Survey (TSS) (Heald et al., 1998; McGreevy et al., 2013). The TSS is a 16-item TSA symptom-specific questionnaire, originally developed for patients with HIV, but used in research settings with patients with cancer in both Canada (Bernhardson et al., 2012; Brisbois et al., 2011; Hutton et al., 2007) and Sweden (Belqaid et al., 2014; McGreevy et al., 2013). The TSS consists both of items with fixed response alternatives and open-ended items to explore perceived changes in taste and smell sequentially.

The second self-report instrument was the Edmonton Symptom Assessment System (ESAS) (Bruera et al., 1991), which uses visual analogue scales to assess nine symptoms: pain, tiredness, nausea, depression, anxiety, drowsiness, loss of appetite, shortness of breath and "other". An additional item assesses general well-being. Higher scores indicate greater symptom intensity.

The third instrument, the Functional Assessment of Anorexia-Cachexia Therapy (FAACT), assesses aspects of well-being (Ribaudo et al., 2000). Patients rate their level of agreement with each of 40 statements on a five-point Likert scale. The statements are grouped into five domains of which four concern physical, social, emotional and functional well-being, and the fifth assesses other eating-related problems.

The short form of the Scored Patient-Generated Subjective Global Assessment (PG-SGA SF) (Bauer et al., 2002; Ottery, 1996; Persson et al., 1999; Vigano et al., 2014) was the final instrument used to assess weight change, food intake at present compared to "normal", symptoms that may have interfered with food intake, and perceived physical function.

2.3. Analysis and presentation of data

Traditional scoring of the TSS results in a "chemosensory complaint score" of 0–16 (Heald et al., 1998), with items reflecting TSAs' perceived nature and severity. In the study presented here, we seek to disentangle these different aspects of TSAs. We therefore adapted the use of TSS items and score to reflect TSA characteristics. We used seven items from the TSS addressing qualities of TSAs to categorise characteristics: five items assessing general changes in perceptions of taste or smell including persistent bad taste in mouth, and two items concerning changes in perception of intensity in four basic taste qualities (sweet, salt, sour and bitter) and/or smell.

Using the responses to these items, patients' TSAs were categorised into five *TSA intensity categories* according to their reported change in perceived intensity of TSAs qualities as follows: 1) *no TSAs*, 2) TSAs with *stronger intensity* of any or all of the basic taste qualities and/or smell, 3) TSAs with *weaker intensity* of any or all of the basic taste qualities and/or smell, 4) TSAs with *mixed changes in intensity* including both stronger and weaker intensity of different basic taste qualities and/or smell, and 5) *other TSAs*, including those reporting general changes in perception of taste or smell, but without specification of intensity changes in basic taste qualities or smell.

An additional strategy used here to present the data on characteristics of TSAs is calculation of a summed score from the seven TSS items described above. This score reflects the number of different qualities of TSAs reported by one patient at a specific time-point, giving an indication of what we here call the *multiplicity* of TSAs. The *TSA multiplicity score* was calculated using the standard TSS scoring, in which six items each yield either zero or one point, and one item has four sub-items and therefore yields between 0 and 4 points, giving a total TSA multiplicity score ranging between 0 and 10.

We present the case study data in two different forms. First, changes in TSA characteristics between different time-points are cumulatively explored based on each individual; this is done by graphically charting both the TSA intensity category and the TSA multiplicity score for individual patients at each time point (M1, M2 and M3). These data are presented by treatment type and gender to allow visual overview of changes over time which might facilitate hypothesis generation. For example, systemic and localized treatment might be postulated to affect TSAs through different mechanisms, and results from our previous research (McGreevy et al., 2014) have suggested differences in TSA qualities between men and women.

We thereafter present narrative descriptions of three individual cases to provide richer information about different experiences of having TSAs in the context of a lung cancer disease and its treatment. The case descriptions were summarized using data from the interviewer's field notes, responses to open-ended questions, and answers to, or ratings of, selected items in the four questionnaires. The names used here are fictitious.

For demographic purposes, patients' smoking status was categorised as smoker, former smoker (quit >1 year ago) and non-

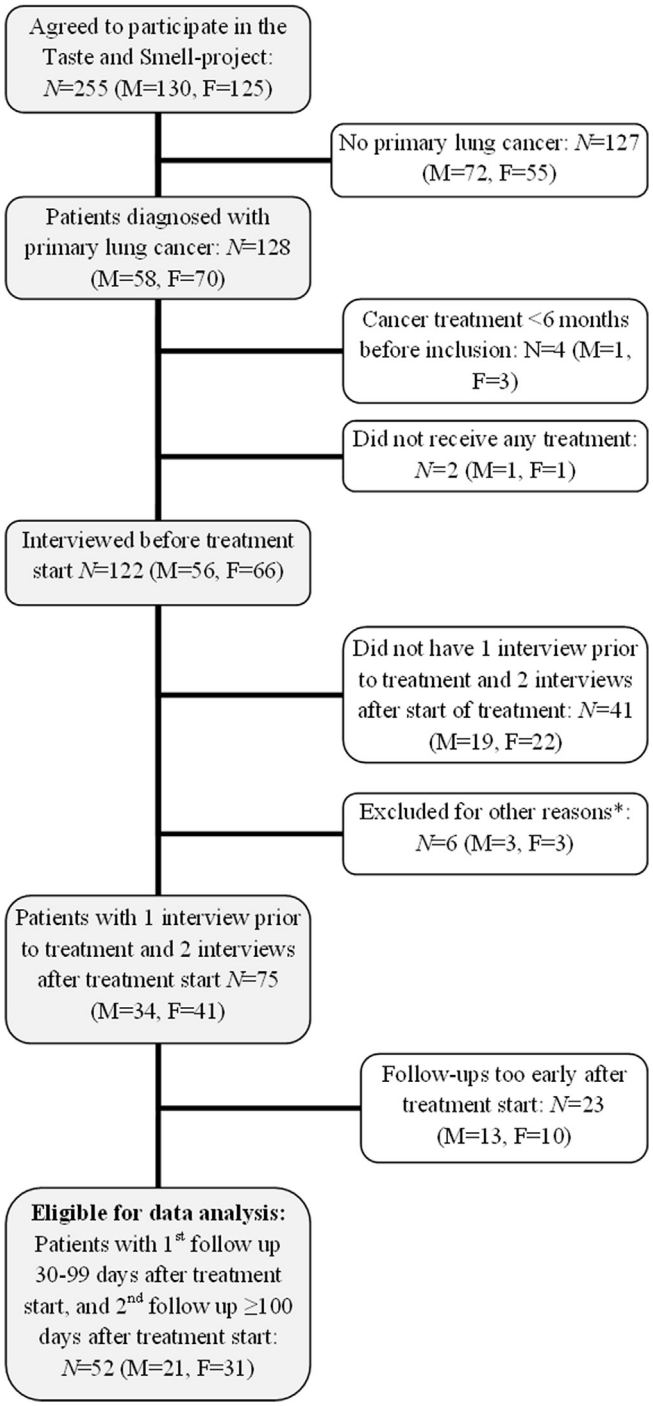

Fig. 1. Overview of the selection process. M, male; F, female. *Other reasons, e.g. major co-morbidities, cognitive impairments, withdrawn consent.

Table 1
Patient demographics and clinical characteristics.

		Total $N = 52$
Age (years)	Mean; SD	66.8; 8.7
Gender, *N* (%)	Men	21 (40)
	Women	31 (60)
Education, *N* (%)	Elementary school	13 (25)
	High school	22 (42)
	University	15 (29)
	Other	2 (4)
Smoking status, *N* (%)	Smoker	18 (35)
	Former smoker	28 (54)
	Non-smoker	6 (11)
Tumour type, *N* (%)	NSCLC	44 (85)
	SCLC	1 (2)
	Other	7 (13)
Disease stage, *N* (%)	I-IIIA	24 (46)
	IIIB-IV	28 (54)
Treatment, *N* (%)	Systemic	34 (65)
	Localized	18 (35)
Days between M1 and treatment start	Median	30.5
	Min; max	1; 77
Days between treatment start and M2	Median	55.5
	Min; max	30; 97
Days between treatment start and M3	Median	132
	Min; max	100; 172
Days between M2 and M3	Median	65.5
	Min; max	41; 137

NSCLC, non-small cell lung cancer; *SCLC*, small-cell lung cancer; *Other* includes unverified tumours, multiple tumours of different kinds, carcinoids and mesothelioma.
M1, measurement time-point before treatment start; *M2*, first measurement time-point after treatment start; *M3*, second measurement time-point after treatment start.
Systemic treatment includes targeted therapy, chemotherapy, chemotherapy following surgery and combined chemoradiotherapy.
Localized treatment includes surgery and stereotactic radiotherapy.

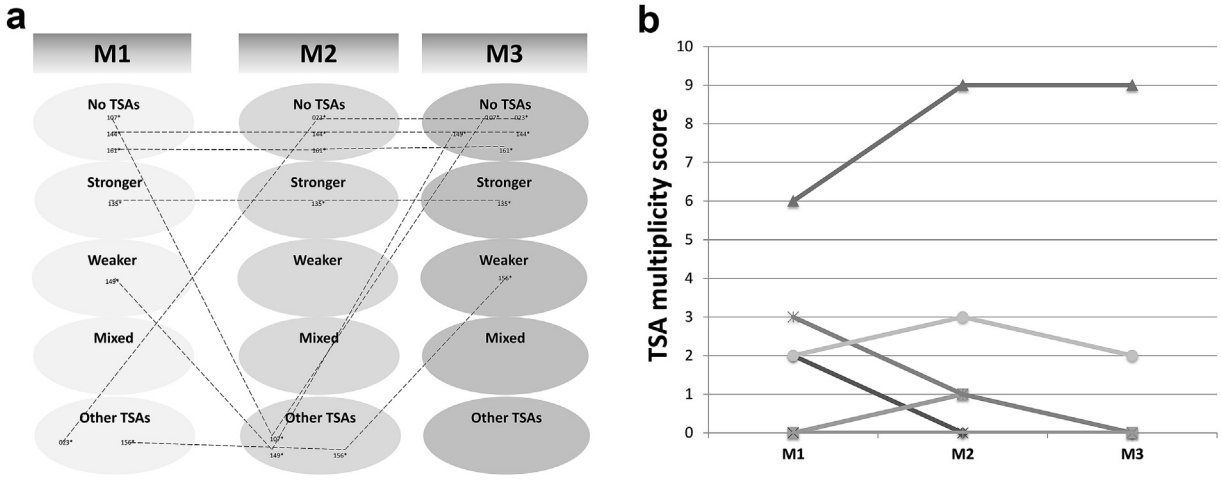

Fig. 2. a and b. Individual changes over time in characteristics of TSAs in men treated with localized therapy (n = 7), regarding a) TSA intensity categories and b) TSA multiplicity scores (0–10). TSAs, taste and smell alterations M1, measurement time-point before treatment start; M2, first measurement time-point after treatment start; M3, second measurement time-point after treatment start. *No TSAs*: Patients not reporting any TSAs; *Stronger*: Patients reporting stronger intensity in any or all of the basic taste qualities or smell; *Weaker*: patients reporting weaker intensity in any or all of the basic taste qualities or smell; *Mixed*: patients reporting mixed changes in intensity including both stronger and weaker intensity of different basic taste qualities or smell; *Other TSAs*: patients reporting TSAs but with no specification in intensity changes in basic taste qualities or smell.

smoker (includes occasional smoking), based on the distinctions made by the Swedish National Lung Cancer Registry (Swedish Lung Cancer Registry Board, 2010).

3. Results

Of the 255 patients interviewed for the Taste and Smell Project, 52 patients met inclusion criteria with data at three time-points eligible for analysis. See Fig. 1 for an overview of the selection process. Patients' demographic and clinical characteristics are shown in Table 1.

3.1. Individual changes in characteristics over time

Figs. 2a–5a graphically represent individual changes in TSA intensity categories over time according to gender and treatment type. Only 14 of the 52 individuals included in the study remained in the same TSA intensity category at all three time-points, with 11 of these patients reporting no TSAs at each time-point. Eighteen individuals shifted TSA intensity category (no TSAs, stronger intensity, weaker intensity, mixed changes in intensity or other TSAs) both between M1–M2 and between M2–M3. Figs. 2b–5b present the corresponding individual

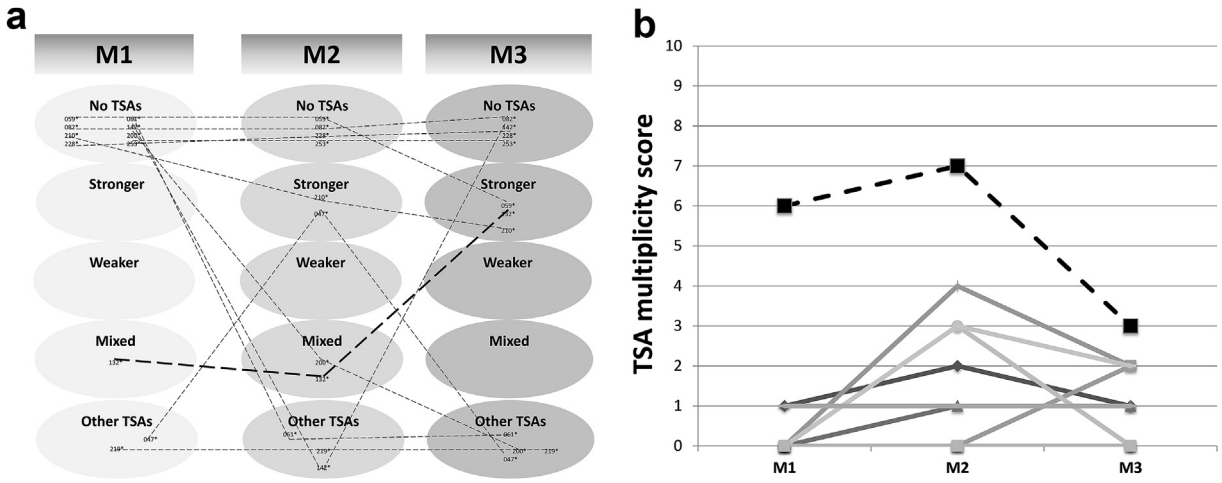

Fig. 3. a and b. Individual changes over time in characteristics of TSAs in women with localized therapy (n = 11), regarding a) TSA intensity categories and b) TSA multiplicity scores (0–10). TSAs, taste and smell alterations M1, measurement time-point before treatment start; M2, first measurement time-point after treatment start; M3, second measurement time-point after treatment start *No TSAs*: Patients not reporting any TSAs; *Stronger*: Patients reporting stronger intensity in any or all of the basic taste qualities or smell; *Weaker*: patients reporting weaker intensity in any or all of the basic taste qualities or smell; *Mixed*: patients reporting mixed changes in intensity including both stronger and weaker intensity of different basic taste qualities or smell; *Other TSAs*: patients reporting TSAs but with no specification in intensity changes in basic taste qualities or smell. ■——— represents *Beata*, see case description in Box 1.

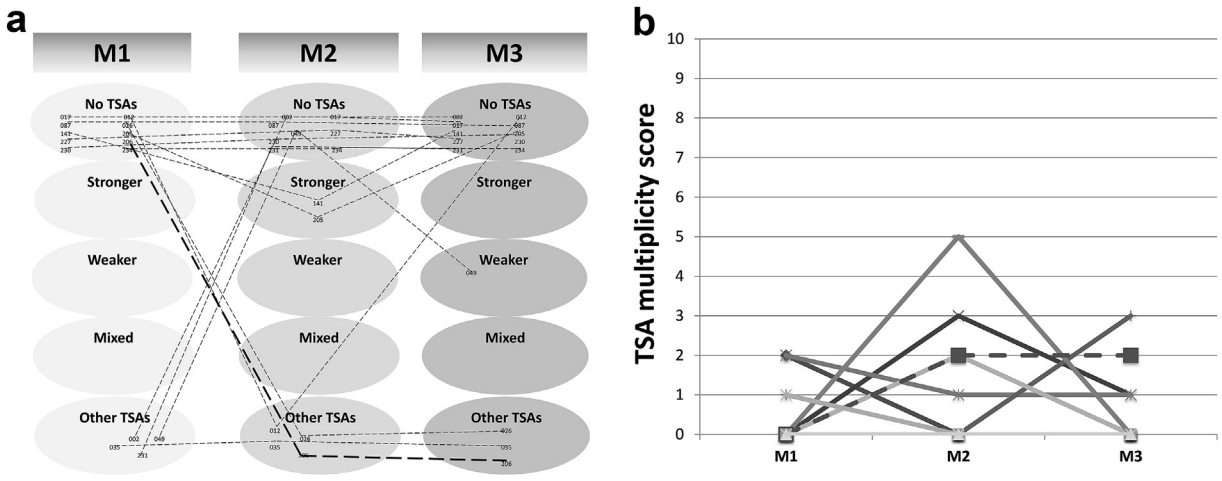

Fig. 4. a and b. Individual changes over time in characteristics of TSAs in men with systemic therapy (n = 14), regarding a) TSA intensity categories and b) TSA multiplicity scores (0–10). TSAs, taste and smell alterations M1, measurement time-point before treatment start; M2, first measurement time-point after treatment start; M3, second measurement time-point after treatment start No TSAs: Patients not reporting any TSAs; Stronger: Patients reporting stronger intensity in any or all of the basic taste qualities or smell; Weaker: patients reporting weaker intensity in any or all of the basic taste qualities or smell; Mixed: patients reporting mixed changes in intensity including both stronger and weaker intensity of different basic taste qualities or smell; Other TSAs: patients reporting TSAs but with no specification in intensity changes in basic taste qualities or smell. ■——— represents *Carl*, see case description in Box 2.

changes in TSA multiplicity scores over time. In general, the TSA multiplicity scores were relatively low among those who reported experiencing any TSAs. Twenty-eight of the 52 individuals in the study had TSA multiplicity scores of 0–2 at all time-points; it was only at the time-points after start of treatment (M2, M3) that seven individuals reported TSA multiplicity scores as high as 7–10. This also indicates that many of the individuals in this study reported an increase in TSA multiplicity scores after treatment start, that is between M1–M2. This was expected for the patients undergoing systemic treatment, but Figs. 2b and 3b suggest that several of the men and women treated with localized therapy also report increases in TSA multiplicity scores between M1 and M2. However, many of these individuals also report decreases in TSA multiplicity scores between M2 and M3.

3.2. Narrative case descriptions

The cases of Beata, Carl and Gunilla are described in depth in Boxes 1, 2 and 3, respectively; their reported TSA trajectories are also indicated in Figs. 3a,b (Beata), 4a–4b (Carl), and 5a–5b (Gunilla) with bold, broken lines.

Beata's case illustrates that patients may experience TSAs prior to treatment. She is one of the individuals in our study who underwent localized treatment and reported TSAs afterwards. *Carl* was chosen to exemplify those persons who experienced TSAs without intensity changes in basic taste qualities and smell during chemotherapy treatment. *Gunilla* represents a typical scenario with subtle TSAs before treatment start, but problems from alterations in both taste and smell during concomitant chemo-radiotherapy. These three case descriptions demonstrate that the consequences

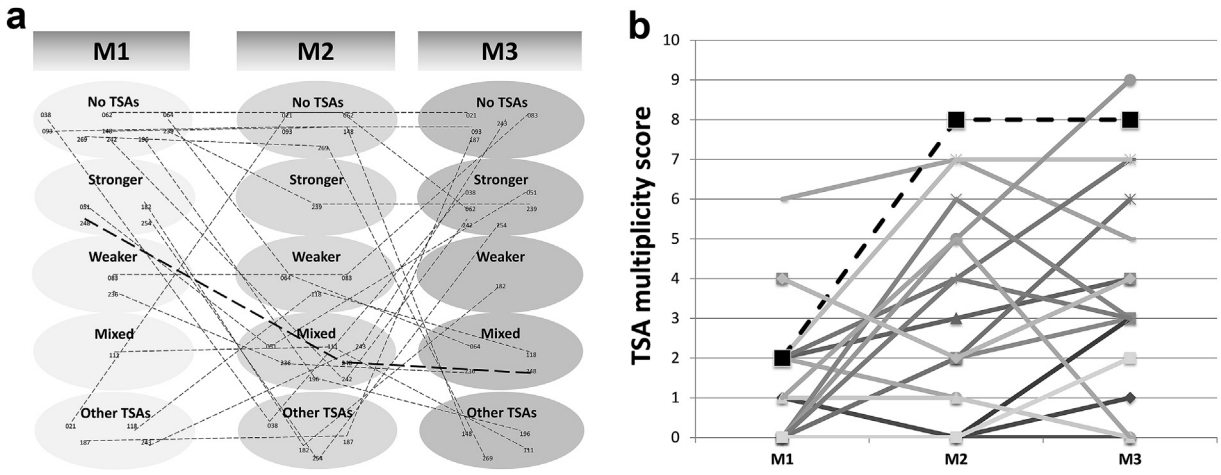

Fig. 5. a and b. Individual changes over time in characteristics of TSAs in women with systemic therapy (n = 20), regarding a) TSA intensity categories and b) TSA multiplicity scores (0–10). TSAs, taste and smell alterations M1, measurement time-point before treatment start; M2, first measurement time-point after treatment start; M3, second measurement time-point after treatment start *No TSAs*: Patients not reporting any TSAs; *Stronger*: Patients reporting stronger intensity in any or all of the basic taste qualities or smell; *Weaker*: patients reporting weaker intensity in any or all of the basic taste qualities or smell; *Mixed*: patients reporting mixed changes in intensity including both stronger and weaker intensity of different basic taste qualities or smell; *Other TSAs*: patients reporting TSAs but with no specification in intensity changes in basic taste qualities or smell. ■––– represents *Gunilla*, see case description in Box 3.

of TSAs on daily life are individual, and depend not only on the characteristics of TSAs, but on an individual person and his/her general life-situation as well as other symptoms and treatment side-effects.

4. Discussion

Through this multiple case study approach, we are able to expand further on our previous findings about the diversity of characteristics of TSAs between individuals treated for primary lung cancer (McGreevy et al., 2014) to also show that characteristics of TSAs change over time within many individuals in our study. However, our results also suggest that the individual experiences of TSAs and the impact of these symptoms on daily life may be influenced by individual and contextual factors such as other symptoms, treatment side-effects and general life-situation.

Previous longitudinal research has also demonstrated changes in TSAs over time in relation to treatment, but studies have primarily addressed TSAs in terms of self-reported symptom intensity or as changes in thresholds of basic taste and smell function at group level (Boltong et al., 2014; Gamper, Giesinger et al., 2012; Steinbach et al., 2009; Zabernigg et al., 2010). Our results suggest that not only intensity but also the characteristics of TSAs may change over time in individuals in relation to treatment. This is important information for health-care professionals, as the characteristics of TSAs should be taken into consideration when providing guidance and advice to patients for managing TSAs. For example, a patient experiencing a general decrease in taste function would not benefit from the same recommendations as someone who is bothered by a persistent bad taste in the mouth. Few research studies to date have addressed management strategies for TSAs (Thorne et al., 2015); our results suggest that follow-up of patients experiencing TSAs is of critical importance in order to adjust strategies to manage TSAs according to their changing characteristics.

Based on previous research on TSAs in patients with cancer (Bernhardson et al., 2008a; Joussain et al., 2013) we anticipated that TSAs would present after start of systemic treatment. Interestingly, several of the individuals in our study undergoing localized treatment with surgery or SRT also reported perceiving TSAs after this treatment (at M2 and M3). There are research reports of patients experiencing TSAs after surgery in the head-neck and gastric area (Heiser et al., 2010; Wikman et al., 2014) and a number of case reports of patients experiencing TSAs after general anesthesia (Dhanani and Jiang, 2012; Konstantinidis et al., 2009). The authors of these studies present theories for underlying mechanisms, which are often neurological, but also include factors such as wound healing, postoperative changes in nutritional intake, and side-effects of medications, all of which may be applicable to the patients included in our study. To the best of our knowledge, no previous study has reported changes in taste or smell following surgery for lung cancer, which might thus be a relevant topic for further investigation. Our results also show that TSAs present not only following treatment, as focused on in previous research, but also prior to treatment. This has been investigated in more detail in our previous work (Belqaid et al., 2014).

The narrative descriptions found in the three individual cases of Beata, Gunilla and Carl also suggest that although the characteristics of TSAs and changes in these, presented in Figs. 2–5a and 2–5b, reveal some aspects of the patient's individual experiences of TSAs, they do not capture the whole picture. The case reports illustrate different qualities of TSAs and the consequences of TSAs on daily life, such as impaired food enjoyment, restricted social life, and how the experience of TSAs are influenced by other symptoms and side-effects from treatment. These results are in line with previous research investigating the nature of TSAs and their impact on daily life (Bernhardson et al., 2008b; Boltong et al., 2012).

The case descriptions also provide additional information about the individual experience of TSAs in relation to food intake: Gunilla and Beata report similar characteristics of TSAs at the first follow-up after treatment start (M2), with both of them having TSAs with mixed changes in intensity and rather high TSA multiplicity scores of eight and seven, respectively. However their ratings on the PG-SGA SF checklist of symptoms interfering with food intake differ. Whereas Gunilla reports that TSAs along with other symptoms have affected food intake after treatment start, Beata, who also reports eating problems, instead indicates symptoms other than TSAs on this checklist. In our previous study we found that although 38% of the 117 patients prior to treatment

Box 1
Case description, Beata.

Beata is 66 years. Although she had retired, she has since returned to her previous employment at a residential centre for drug addicts. Beata says she is a former addict, but has been "clean" for 25 years. She lives alone but tells the interviewer about her close relationship with her daughter. At the first interview (M1), when asked about taste alterations using the TSS, Beata reflects that a specific type of candy no longer tastes as good as it used to. She used to eat a bag of candy all at once, but they are now left unopened in the cupboard. She responds to the item about being bothered by a persistent bad taste in her mouth, saying that this is sometimes the case, describing this taste as bitter. When asked about intensity changes in basic taste qualities, Beata rates tasting 'sour' as usual, 'salt' and 'sweet' as tasting weaker, and 'bitter' as tasting more intense. She exemplifies this, saying that she salts her food more now and that the coffee from the machine at work does not taste as good as it used to. Based on these ratings, Beata's TSAs are categorized as 'mixed changes in intensity'. She has a TSA multiplicity score of six but rates her taste changes as mild and says that her quality of life is only affected by no longer drinking coffee and not eating as many sweets as she used to. According to responses on ESAS and FAACT, she is not burdened by many symptoms and she assesses her well-being as good, although she reports loss of appetite on both these instruments. On the PG-SGA SF she reports having lost weight and indicates loss of appetite as the symptom that has kept her from eating sufficiently.

The second interview (M2) took place nearly one and a half months after the surgical resection of Beata's lung tumour. She says she was in terrible pain when she woke up after surgery as a rib was broken during the procedure and at M2 she is still feeling weak and bothered by this pain. On ESAS she reports several symptoms apart from pain: tiredness, anxiety, shortness of breath and cough. In response to the items about general changes in taste and smell on the TSS, Beata responds that her taste alterations have worsened following surgery. She describes this as a general lack of taste, with everything tasting the same. Beata also describes a lot of things smelling bad after the surgery, causing her nausea and vomiting. She confirms that she still sometimes has a persistent bad taste in her mouth, but now has difficulties defining this taste. Beata rates intensity changes in basic taste qualities similarly to her reports during the first interview, but now says that she cannot perceive salty taste at all. While her underlying taste sensations have changed, her TSAs remain in the TSA intensity category of mixed changes in intensity. Her TSA multiplicity score has increased from six to seven, but she still rates her altered sense of taste as mild, saying that it has not affected her quality of life much. However, she rates her altered sense of smell following surgery as severe. Despite this, at the time of the second interview, Beata rates her intensity of smell as normal, giving the interviewer the impression that the smell changes following surgery have decreased. In the PG-SGA SF, Beata's weight is reported to have stabilised although she reports symptoms of loss of appetite, early satiety and pain as having interfered with food intake.

By the third interview (M3), almost five and a half months have passed since Beata's surgery. She says she feels better than at the time of the second interview but is still not fully recovered. Her cough is slowly improving, but is not completely gone yet. On the ESAS, Beata reports symptoms such as pain, tiredness and shortness of breath. At this interview, Beata answers questions about general changes in taste or smell by saying she has no such changes, but adds that food and eating is not what it used to be. Again, she gives the example of having sweets at home but not feeling like eating them. Beata indicates that she often has a persistent bad taste in her mouth and she also describes a sensation of something moving from her nose down her throat. In contrast to previous interviews, Beata now rates the basic tastes of 'sour' and 'bitter' as tasting as usual and 'salt' and 'sweet' as tasting stronger; this means that her TSAs are now in the TSA intensity category 'stronger intensity change'. Although Beata has a TSA multiplicity score of three at this interview, there are no documented responses to the items concerning ratings of altered sense of taste or impact of taste change on quality of life, although the reason for this is unclear. It is possible that the interviewer omitted these questions or that Beata did not perceive her experiences as a change in taste. At this time-point, Beata reports on the PG-SGA SF that her weight is stable and that no symptoms keep her from eating enough.

TSA, taste and smell alteration
M1, measurement time-point before treatment start; M2, first measurement time-point after treatment start; M3, second measurement time-point after treatment start
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for lung cancer reported TSAs on the TSS, as few as eight of these indicated on the PG-SGA SF checklist that "taste changes" or "being bothered by smells" had interfered with food intake (Belqaid et al., 2014). When "taste changes" or "being bothered by smells" were indicated on the PG-SGA SF symptoms checklist, it was in conjunction with loss of appetite and/or nausea, which are symptoms well known to impair food intake. This suggests that other symptoms such as loss of appetite and nausea may be more powerful drivers of reducing food intake, but that TSAs may contribute and worsen the situation when presenting with these

Box 2
Case description, Carl.

Carl is 46 years old and lives with his partner and their two children. At the first interview (M1), he says the tumour is something that "must be removed" but that he does not feel like he is sick, which is also reflected in his responses to ESAS and FAACT. In his responses to the TSS questionnaire, Carl makes it clear that he experiences no taste or smell alterations.

The second interview (M2) took place a little more than three months after Carl's lung tumour was surgically resected. He had begun adjuvant chemotherapy about a month after surgery and was receiving his last cycle at the time of the interview. Carl tells the interviewer about his anxiety before each treatment, since he knows he will feel so sick afterwards. He reports anxiety, tiredness, loss of appetite and shortness of breath on ESAS, but with relatively low scores, indicating little disturbance in his sense of well-being.

When asked specifically about changes in taste, Carl describes experiencing taste alterations in the form of a metallic, "poisonous" taste, which presents two days after treatment and usually remains for two days. During these periods, he says everything tastes bad, even water. Since, despite this, Carl rates the intensity of all basic taste qualities and smell being as usual, his TSAs are categorized as 'other TSAs'. He also reports that the taste of different foods has not changed in themselves, but that he no longer finds the tastes good. It seems that his liking of the taste of food has changed, rather than the sense of basic taste in itself. His TSA multiplicity score is two, but he rates his altered sense of taste as severe; he responds to the TSS question about how it has affected his quality of life by saying it is ruining his appetite. Carl responds "somewhat" to the FAACT item about having a good appetite.

Another two months go by before the third interview (M3). At this time, Carl tells the interviewer that he started targeted therapy just a few days previously. He says he has been working quite a lot despite being on sick leave, as it makes him feel better. Carl's very positive assessments on ESAS and FAACT suggest that he is feeling well. He reinforces this impression by choosing not to respond to the FAACT statement about if his condition is improving, as he says he cannot imagine that he could feel better than he does now. However, as in the second interview, in this third interview Carl talks about changes in his enjoyment of foods that he previously liked. He exemplifies this by saying he no longer feels like eating fast foods like hamburgers and that he lost his desire to eat sweets for a while. He, once again, has a TSA multiplicity score of two and his TSAs remain in the intensity category of 'other TSAs', but this time he rates these taste changes as insignificant, responding that they are not affecting his quality of life. He points out that he is happy to not eat fast foods or sweets.

TSA, taste and smell alteration
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other symptoms.

The interaction between TSAs and other concurring symptoms should also include mention of the hedonic aspect of foods, which can be difficult to distinguish from the purely sensory perception of basic taste and smell. Hedonics is a concept which refers to the pleasantness and unpleasantness of sensory experience, for example from the taste of foods (Boltong and Keast, 2012). For instance, although different individuals may have the same sensory experience of the taste of coffee, some people enjoy it whilst others may not. The hedonic experience of foods has also been reported to encompass hunger and appetite (Boltong and Keast, 2012), which adds to the complexity of food enjoyment when experiencing multiple symptoms. The case description of Carl exemplifies this, as he says that it is not really his basic taste function that has changed, but his liking of familiar foods.

The concepts used here of TSA intensity categories and TSA multiplicity score have several limitations that should be considered. The TSA intensity categories indicate the type and direction of a patient's perceived TSAs and allowed us to show how characteristics of TSAs may change over time in individual patients in relation to treatment start. However, the TSA intensity categories do not contain information about the magnitude of the changes or how bothersome they are perceived to be. Also note that for consistency in categorization of TSA data, we used a strategy where we prioritized reports of changes in perceived intensity of the basic taste qualities or smell, such that only when no such changes were reported did we use the category "other TSAs" for other reported changes. The use of the TSA intensity categories is probably not appropriate in clinical practice, as successful management of TSAs demands more detailed information about an individual patient's TSAs. The TSA multiplicity score reflects the number of different TSAs reported by one patient and allowed us to show that many individuals in our study reported a larger number of TSAs after start of treatment. Limitations here include the TSS items used not being mutually exclusive, as some are open-ended while others have fixed answer alternatives. Therefore, a patient could report the same type of change in more than one item.

In this study, we chose a multiple case study approach to focus on individuals. We do not claim that these individuals are necessarily representative of the general lung cancer population; instead

Box 3
Case description, Gunilla.

Gunilla, a 53 year old woman, lives with her husband. The first interview (M1) takes place at the hospital before her appointment there. She scores rather high on the ESAS symptoms of tiredness, depression, anxiety and drowsiness, and on FAACT she endorses the statements about feeling nervous, worrying about death, and worrying that her condition will worsen. Gunilla reports no taste changes; however, she describes experiencing an improved sense of smell since she quit smoking about two months earlier. Although this results in a TSA multiplicity score of two and places Gunilla's TSAs in the 'stronger' TSA intensity category, the interviewer's impression is that she does not consider this a general smell alteration. On the FAACT domain concerning problems related to eating, Gunilla reports being worried about her weight, saying she has lost 10 kilograms during the last month. In response to the relevant PG-SGA SF items she reports having eaten less than normal, but does not indicate any symptoms as preventing her from eating enough.

Gunilla started chemotherapy a little more than a month before the second interview (M2) and had also received radiotherapy during the two weeks prior to M2. She tells the interviewer about being bothered by treatment side-effects. Compared to the first interview, at the second interview Gunilla scores higher on the ESAS symptoms of tiredness, drowsiness and loss of appetite, but lower on depression and anxiety. When asked about changes in her sense of taste, she describes feeling a greasy coating in the roof of her mouth, which interferes with her appetite. She says she cannot stand the taste of coffee and that even water tastes bad. She reports sometimes being bothered by a persistent bad taste and refers to the greasy coating in her mouth. When asked about intensity changes in basic taste qualities, Gunilla says 'sweet' and 'bitter' taste the same as usual, 'salt' tastes weaker and 'sour' tastes stronger, with these sensations thus categorized as 'mixed changes in intensity'. She rates her altered sense of taste as severe, responding to the question on how the taste change has affected her quality of life by talking about how she used to enjoy food, but now has to force herself to eat and drink. Gunilla also reports that everything smells bad the week following treatment. She is bothered by the smells of coffee, cooking and water, which she says has a metallic smell. She even says that her body smells differently during this period. Gunilla reports perceiving the intensity of odours as stronger than usual, rating the smell changes as moderate. However, she says that her altered sense of smell has hardly affected her quality of life. As Gunilla reports many different qualities of TSAs in the TSS, she has a TSA multiplicity score of eight out of ten at this interview. On the PG-SGA SF, she reports eating less than usual, indicating loss of appetite, nausea, taste change and being bothered by smells as symptoms that have kept her from eating enough. However, she reports her weight as stable during the last month. She says that despite her eating problems, the corticosteroids she is currently taking are increasing her drive to eat.

The third interview (M3) was conducted two months after Gunilla had completed chemotherapy and one month after she had finished radiotherapy. She says several metastases have been found in her brain so she will now receive radiation to her head. The interviewer perceives Gunilla to be upset about this, which is also reflected in Gunilla's high anxiety and depression scores on the ESAS, as well as reporting symptoms like tiredness, drowsiness and appetite loss. From her responses to the items in the TSS, it becomes clear that Gunilla still has taste changes although it is some time since she completed the combined chemo-radiotherapy. As at the previous interview, her TSAs are categorized as 'mixed changes in intensity' with a TSA multiplicity score of eight, although her descriptions of the TSAs differ somewhat from the previous interview. She says that she still cannot stand coffee or sour drinks as they leave her with a strange aftertaste. She says she often has a persistent bad taste in her mouth and describes this taste as sour, adding that it feels like this sour taste comes from her salivary glands somewhere in the back of her mouth. At this time-point, Gunilla rates the basic taste quality of 'bitter' tasting as usual, 'sour' tasting stronger but 'salt' and 'sweet' tasting weaker. She needs to add more salt and sugar to her food. She rates her altered sense of taste as moderate and, when asked how it has affected her quality of life, she responds that she no longer wants to cook and does not feel like eating. She says she no longer enjoys a nice meal with her husband in the evenings and avoids inviting people over as such activities usually involve food. She describes how she feels like a grumpy old lady when she refuses to eat. Despite this, she says that she usually does manage to eat when food is served. Gunilla also describes experiencing smell changes as she is still bothered by cooking odours. However, she reports perceiving the intensity of smell as normal and rates the smell alteration as insignificant. On the PG-SGA SF, just as at the previous interview, Gunilla reports her weight to be stable, although she is eating less than normal. This time, she indicates that loss of appetite and taste changes have kept her from eating sufficiently.

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we believe that our results demonstrate the importance of being aware of the variation of the individual symptom experience. This concerns both clinical practice and research, where individual changes may be concealed in results reported at group level. We argue that the case study approach is of particular interest for health-care professionals, as they deal with the individual experiences of disease and symptoms in their daily practice.

5. Conclusion

The results from this study further our understanding of cancer-related TSAs by illustrating that the characteristics of TSAs changed relative to the start of both systemic and localized therapy. Furthermore, the complexity of the individual experiences of TSAs suggest that health-care professionals should be attentive to changes in characteristics of TSAs to adapt advice and support to the individual needs and experiences of patients with TSAs.

Conflict of interest statement

None of the authors declare any conflict of interest.

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