

**Investigation of oral problems using a
novel oral symptom assessment tool in
patients with advanced cancer and older
patients with frailty**

A thesis presented to Trinity College
Dublin, the University of Dublin, for the
degree of Doctor of Medicine (M.D.)

2024

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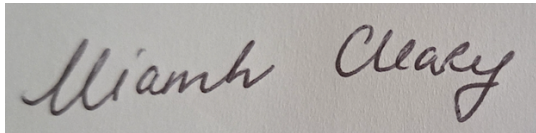
Supervisor: Professor Andrew Davies

DECLARATION

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university and it is entirely my own work.

I agree to deposit the thesis in the University's open access institution repository or allow the Library to do so on my behalf, subject to Irish Copyright Legislation and Trinity College Library conditions of use and acknowledgement.

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A photograph of a handwritten signature in dark ink on a light-colored surface. The signature is written in a cursive style and reads "Niamh Cleary".

Niamh Mairéad Cleary

29 February 2024

DECLARATION AND STATEMENT OF PLAGIARISM

Under the guidance of my supervisor Professor Andrew Davies, I am solely responsible for the design, implementation, analysis and presentation of the data in this thesis. Professor Davies advised on the design of the studies and contributed to the various outputs which arose from this research.

Full and informed consent was obtained for all participants for both studies.

Professor Suzanne Guerin is a Professor of Psychology at University College Dublin who provided guidance on the relevant statistical software for the study in patients in advanced cancer and contributed to the manuscript published from this study.

Professor Roman Romero-Ortuño and Dr Amanda Lavan are both Consultant Physicians in Medical Gerontology in St James' Hospital, Dublin and contributed to the design of the study in older patients with frailty.

Norah Fagan, Elaine Hyland and Muireann O'Donnell are research nurses and Dr Síofra Hearne is a research fellow in the Academic Department of Palliative Medicine all of whom assisted in patient recruitment for both studies. Norah Fagan also contributed to the manuscript published from the study in patients with advanced cancer.

Olivia Munnelly Mulkerrin is a Trinity College Dublin medical student who assisted as the second reviewer in the scoping review.

SUMMARY

This thesis reports a scoping review of the literature and two prospective observational studies with the Oral Symptom Assessment Scale (OSAS) as the central theme of the two observational studies.

STUDY 1: ORAL SYMPTOM ASSESSMENT TOOLS IN PATIENTS WITH ADVANCED CANCER: A SCOPING REVIEW.

The aim of this scoping review of the literature was to identify and describe oral symptom assessment tools that have been specifically utilised in patients with advanced cancer. The search strategy identified 1179 unique references. Fourteen papers were included in the full data extraction. The review identified four validated symptom assessment scales that could be utilised to assess oral symptoms in patients with advanced cancer, including one cancer-specific quality of life scale, one generic tool for assessing the “social impact” of specific oral problems, one cancer-specific generic symptom assessment scale, and one cancer-specific oral symptom assessment scale.

STUDY 2: THE ORAL SYMPTOM ASSESSMENT SCALE (OSAS): CRITERION VALIDATION WITH THE EORTC QLQ-OH15 AND RELIABILITY TESTING (CLINICALTRIALS.GOV TRIAL IDENTIFICATION NUMBER: NCT04932317).

The aim of this study was to carry out further testing of the psychometric properties of the original OSAS, with the objectives being to assess its reliability, and to further assess its criterion validity using a cancer-related oral quality of life instrument (the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Oral Health 15 /EORTC QLQ-OH15). 51 completed tests were obtained. The study data suggested at least moderate agreement between analogous questions on the OSAS and the EORTC QLQ-OH15. The test-retest results for the presence of symptoms were good, with one symptom having “almost perfect” agreement, 12 symptoms having “substantial” agreement, and six symptoms having “moderate” agreement. However, the test-retest results for the symptom domains (i.e. frequency, severity, and amount of distress / bothersomeness) were not quite as good. This study supports the validity of the OSAS, and provides evidence for the reliability of this novel oral symptom assessment tool, in patients with advanced cancer. Further research is needed to corroborate the findings of this study.

STUDY 3: ORAL SYMPTOM ASSESSMENT IN OLDER PATIENTS WITH FRAILTY USING THE ORAL SYMPTOM ASSESSMENT SCALE (CLINICALTRIALS.GOV TRIAL REGISTRATION NUMBER: NCT06286982)

The specific aims of this study were to determine the prevalence of oral symptoms in older patients with frailty and to determine the clinical features of these oral symptoms (i.e. frequency, severity, and level of distress) using a slightly modified OSAS (with the addition of the symptom of drooling). The results presented are from the initial 100 participants, and so they need to be viewed with caution. However, the data suggests that oral symptoms are common in this cohort of patients. Xerostomia and drooling were the most common reported symptoms on the modified OSAS. The results demonstrate that the OSAS is comprehensive and patient friendly in older patients with frailty. The results provide a novel insight into the prevalence and clinical features of oral symptoms not previously investigated in this patient population using a multi-dimensional symptom-specific assessment tool.

ACKNOWLEDGEMENTS

I am extremely thankful to my supervisor Professor Andrew Davies for his unwavering support and guidance in conducting this research. He has been exceptionally encouraging and supportive throughout this experience.

I am very grateful for the support provided by the research team in the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Services, Dublin for their support especially with recruitment. I would also like to thank Fiona Lawler, librarian at Our Lady's Hospice and Services, Harold's Cross for her advice and guidance.

I am especially thankful to all the patients who generously gave their time to participate in both of the studies.

Finally to my family – my wonderful husband James, my Mam and my two beautiful boys, Bobby and Conall- your never-ending love, support and encouragement I am forever grateful for.

OUTPUTS

PUBLICATIONS

Oral symptom assessment tools in patients with advanced cancer: a scoping review. **Cleary, N**, Munnelly Mulkerrin, O, Davies, A. Supportive Care in Cancer. 2022.

DOI: <https://doi.org/10.1007/s00520-022-07169-1> (Appendix 14)

The Oral Symptom Assessment Scale (OSAS): criterion validation with the EORTC QLQ-OH15 and reliability testing. **Cleary, N**, Guerin, S, Fagan, N. Davies, A. Supportive Care in Cancer. 2023.

DOI: <https://doi.org/10.1007/s00520-023-08118-2> (Appendix 15)

RELATED PUBLICATIONS

Taste disturbance in patients with advanced cancer: who gets it? Supportive Care in Cancer. Davies, A, **Cleary, N**, Hannon, M, Webber, K. 2024.

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ORAL PRESENTATIONS

Cleary, N. Oral symptom assessment scale (OSAS): validity and reliability. Oral presentation, Dr Mary Redmond Medal, Virtual 20 April 2023.

Cleary, N. Oral symptom assessment. Oral presentation, Trinity St James' Cancer Institute (TSJCI) Christmas Research Blitz, 8 December 2023.

POSTER PRESENTATIONS – NATIONAL

Cleary N, Davies, A, Munnelly Mulkerrin O, Oral symptom assessment tools in patients with advanced cancer: a scoping review. Poster presentation, Irish Association of Palliative Care, Virtual 2 February 2023.

POSTER PRESENTATIONS – INTERNATIONAL

Cleary N, Guerin S, Fagan, N, Hyland E, Davies, A. P 17.008. Oral symptom assessment scale (OSAS) : reliability and validity. Poster presentation, European Association of Palliative Care, Rotterdam 15-17 June 2023.

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LIST OF ABBREVIATIONS

% Percentage

± plus or minus

≥ Greater than or equal to

= equal to

ACE I Angiotension converting enzyme inhibitor

ADPM Academic Department of Palliative Medicine

α alpha

AMT 4 Abbreviated Mental Test 4

β beta

CFS Clinical Frailty Scale

CI Confidence Interval

CINAHL Cumulated Index to Nursing and Allied Health Literature

CIRS-G Cumulative Illness Rating Scale – Geriatric

CGA Comprehensive Geriatric Assessment

ECOG Eastern Cooperative Oncology Group

e.g. *exempli gratia* / for example

EMBASE Excerpta Medica database

EORTC QLQ- C30 European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire

EORTC QLQ- OH15/17 European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Oral Health 15/17

ESAS Edmonton Symptom Assessment Scale

FDI Fédération dentaire internationale /World Dental Federation

GOHAI Geriatric Health Assessment Index

h hour

HRQoL Health Related Quality of Life

IBM International Business Machines (Corporation)

ICC Intraclass Correlation Coefficient

ICHOM International Consortium for Health Outcomes Measurement

ICFSR International Conference of Frailty and Sarcopenia Research

κ Kappa

MDASI MD Anderson Symptom Inventory

MRONJ Medication-related osteonecrosis of the jaw

MSAS-HF Memorial Symptom Assessment Scale- Heart Failure

MSAS-SF Memorial Symptom Assessment Scale – Short Form

NCI National Cancer Institute

OED Oxford English Dictionary

OHIP-14 Oral Health Impact Profile -14

OHIP-49 Oral Health Impact Profile -49

OIDP Oral Impacts on Daily Performance

OPS Oral Problem Scale

OSAS Oral symptom assessment scale

QoL Quality of Life

PICOS Population, Intervention, Comparator/control, Outcome and Study design

PRISMA-ScR Prisma Extension for Scoping Reviews

PRN pro re nata (or as 'as required')

QUAL-E Quality of life at the end of life

r_s Spearman's rank correlation coefficient

SNRI Selective Noradrenaline Reuptake Inhibitor

SPSS Statistical Package for the Social Sciences

SSS – 8 Somatic Symptom Scale-8

SSRI Selective Serotonin Reuptake Inhibitor

WHO World Health Organisation

XI Xerostomia Inventory

Z-drug non-benzodiazepine

CHAPTER 1 INTRODUCTION

1.1 CHAPTER OVERVIEW

This chapter presents an introduction, contextualisation and overview of the structure of this dissertation. It begins with an overview of the definitions of the terms that will be used within the text. It will then be followed by a statement of the problem that this research - the investigation of oral problems using a novel oral symptom assessment tool in patients with advanced cancer and older patients with frailty - endeavours to address. Next, the chapter will discuss symptom assessment and measurement, including generic versus symptom-specific assessment. The focus then moves to a description of the Oral Symptom Assessment Scale (OSAS). The final section will provide an overview of the remainder of the dissertation.

1.2 DEFINITIONS

The Oxford English Dictionary (OED) defines 'oral' as "connected with the mouth" (1). The mouth extends from the oral fissure (opening between the lips) to the oropharyngeal isthmus (opening of the oropharynx), and is divided into the vestibule (space between the cheeks / lips and the gums / teeth), and the mouth cavity proper. The mouth plays a fundamental role in numerous essential daily functions, including communication (speech, facial gestures), respiration, digestion (chewing, swallowing), and infection control (2) (3) (4). The OED defines 'symptom' as "a change in your body or mind that shows you are not healthy" (5).

The National Cancer Institute define 'advanced cancer' as cancer that is "unlikely to be cured or controlled with treatment" (6). The definition for 'older' patient is more complex. However, traditionally, people with a chronological age of ≥ 65 years old have been generally referred to as "elderly" (7, 8), and for the purposes of this research an 'older' patient was considered to be ≥ 65 years old, which aligns with the referral criteria to Gerontology services at the sites of recruitment. In terms of 'frailty', this can be defined as a dynamic, multi-faceted syndrome of "multi-system reduction in physiological capacity as a result of which an older person's function may be severely compromised by minor environmental challenges" (9) or more simply put a "a group vulnerable to adverse outcomes" (10). Various interconnecting domains may be considered when examining frailty including cognitive, psychological, physical, social, and functional domains. There may be an indirect interplay between oral problems and several of these domains. Oral frailty is a novel individual domain and refers to a gradual reduction in oral function accompanied by a decline in physical and cognitive functions (2, 11).

Factors that may contribute to this include oral health status deterioration (for example number of teeth and periodontal disease), deterioration of oral motor skills (for example tongue pressure, masticatory function, and occlusal force), oral pain and disorders associated with chewing, swallowing and saliva (2).

1.3 STATEMENT OF THE PROBLEM

1.3.1 Prevalence of oral symptoms

Oral symptoms are common in patients with advanced cancer (12-15). Xerostomia (or dry mouth) is the most common reported oral symptom (13, 16, 17). Teunissen et al. (18) conducted a systematic review of symptom prevalence in patients with advanced cancer, and xerostomia was identified as the eighth most prevalent symptom in patients who were not in the final one to two weeks of their lives (20 studies; 6359 individuals; pooled prevalence 40%; 95% CI 29 %, 52 %). However, individual studies have reported a much higher prevalence of xerostomia in this cohort of patients (with certain studies confirming it to be one of the most common symptoms) (19).

In 2021, Davies et al (13) published the results of an observational study examining a novel oral symptom assessment scale (the “OSAS”): the results of this study (see Table 1-1 & 1-2) demonstrated that when asked directly about a range of oral symptoms, most (244/250, 97.5%) patients reported experiencing at least one oral symptom, and many patients were experiencing multiple oral symptoms (median five symptoms; range 1- 18 symptoms) (13). Moreover, this study uniquely demonstrated that certain other “orphan” oral symptoms were also relatively common (e.g. dental-related symptoms, denture problems, and altered sensation within the mouth).

SYMPTOM	NUMBER PATIENTS (n = 250)	AMOUNT OF DISTRESS / BOTHERSOMENESS				
		“Not at all”	“A little bit”	“Somewhat”	“Quite a bit”	“Very much”
Dry mouth	209 (83.5%)	38 (18.0%)	63 (30.0%)	43 (21.0%)	40 (19.0%)	25 (12.0%)
Taste disturbance*	139 (55.5%)	23 (16.5%)	42 (30.5%)	26 (19.0%)	33 (24.0%)	14 (10.0%)
Coating of tongue	117 (47.0%)	21 (18.0%)	39 (33.0%)	22 (19.0%)	22 (19.0%)	13 (11.0%)
Lip discomfort	96 (38.5%)	16 (16.5%)	29 (30.0%)	20 (21.0%)	21 (22.0%)	10 (10.5%)
“Dirty” mouth	88 (35.0%)	12 (13.5%)	28 (32.0%)	21 (24.0%)	15 (17.0%)	12 (13.5%)
Difficulty swallowing	86 (34.5%)	8 (9.5%)	25 (29.0%)	21 (24.5%)	16 (18.5%)	16 (18.5%)
Cracking of lips	85 (34.0%)	21 (24.5%)	31 (36.5%)	14 (16.5%)	9 (10.5%)	10 (12.0%)
Mouth discomfort / pain*	76 (30.5%)	1 (1.5%)	20 (26.5%)	23 (30.5%)	22 (29.5%)	9 (12.0%)
Difficulty speaking	68 (27.0%)	10 (15.0%)	17 (25.0%)	11 (16.0%)	16 (23.5%)	14 (20.5%)
Difficulty chewing	57 (23.0%)	3 (5.5%)	15 (26.5%)	12 (21.0%)	18 (31.5%)	9 (15.5%)
Cracking of corner of mouth	56 (22.5%)	11 (19.5%)	19 (34.0%)	11 (19.5%)	7 (12.5%)	8 (14.5%)
Sensitivity of teeth	52 (21.0%)	17 (32.5%)	21 (40.5%)	8 (15.5%)	4 (7.5%)	2 (4.0%)
Ulcers in mouth	42 (17.0%)	3 (7.0%)	14 (33.5%)	7 (16.5%)	8 (19.0%)	10 (24.0%)
Bad breath	41 (16.5%)	2 (5.0%)	14 (34.0%)	11 (27.0%)	9 (22.0%)	5 (12.0%)
Jagged teeth**	41 (16.5%)	15 (38.5%)	11 (28.0%)	5 (13.0%)	6 (15.5%)	2 (5.0%)
Altered sensation in mouth	27 (11.0%)	3 (11.0%)	6 (22.0%)	8 (30.0%)	6 (22.0%)	4 (15.0%)
Denture fitting problems	26 (10.0%)	6 (23.0%)	5 (19.0%)	5 (19.0%)	8 (31.0%)	2 (8.0%)
Toothache / pain in teeth	25 (10.0%)	2 (8.0%)	11 (44.0%)	4 (16.0%)	6 (24.0%)	2 (8.0%)
Burning sensation in mouth	24 (9.5%)	3 (12.5%)	7 (29.0%)	5 (21.0%)	6 (25.0%)	3 (12.5%)
Bleeding from mouth	19 (7.5%)	6 (32.0%)	10 (53.0%)	1 (5.0%)	1 (5.0%)	1 (5.0%)

Table 1-1: Amount of distress caused by oral symptoms. Reproduced from Davies et al (13) with permission from Springer Nature.

*Missing distress data for 1 patient; **Missing distress data for 2 patients

SYMPTOM	NUMBER PATIENTS (n = 250)	SYMPTOM FREQUENCY				SYMPTOM SEVERITY			
		“Rarely”	“Occasionally”	“Frequently”	“Almost constantly”	“Slight”	“Moderate”	“Severe”	“Very severe”
Dry mouth**	209 (83.5%)	19 (9.0%)	39 (18.5%)	81 (39.0%)	70 (33.5%)	48 (23.0%)	85 (41.0%)	55 (26.5%)	20 (9.5%)
Taste disturbance	139 (55.5%)	7 (5.0%)	41 (29.5%)	32 (23.0%)	59 (42.5%)	33 (23.5%)	63 (45.5%)	27 (19.5%)	16 (11.5%)
Coating of tongue	117 (47.0%)	8 (7.0%)	36 (30.5 %)	34 (29.0%)	39 (33.5%)	38 (32.5%)	44 (37.5%)	29 (25.0%)	6 (5.0%)
Lip discomfort	96 (38.5%)	7 (7.0%)	25 (26.0%)	32 (33.5%)	32 (33.5%)	34 (35.5%)	36 (37.5%)	19 (19.5%)	7 (7.5%)
“Dirty” mouth*	88 (35.0%)	7 (8.0%)	25 (29.0%)	28 (32.0%)	27 (31.0%)	21 (24.0%)	36 (41.0%)	23 (26.0%)	8 (9.0%)
Difficulty swallowing*	86 (34.5%)	11 (13.0%)	28 (32.5%)	25 (29.0%)	22 (25.5%)	19 (22.0%)	35 (40.5%)	24 (28.0%)	8 (9.5%)
Cracking of lips	85 (34.0%)	14 (16.5%)	29 (34.0%)	20 (23.5%)	22 (26.0%)	31 (36.5%)	33 (39.0%)	13 (15.0%)	8 (9.5%)
Mouth discomfort / pain	76 (30.5%)	6 (8.0%)	20 (26.5%)	26 (34.0%)	24 (31.5%)	15 (20.0%)	29 (38.0%)	24 (31.5%)	8 (10.5%)
Difficulty speaking	68 (27.0%)	8 (12.0%)	20 (29.0%)	21 (31.0%)	19 (28.0%)	21 (31.0%)	22 (32.0%)	21 (31.0%)	4 (6.0%)
Difficulty chewing*	57 (23.0%)	4 (7.0%)	10 (18.0%)	20 (35.5%)	22 (39.5%)	11 (19.5%)	21 (37.0%)	16 (28.0%)	9 (15.5%)
Cracking of corner of mouth	56 (22.5%)	9 (16.0%)	21 (37.5%)	10 (18.0%)	16 (28.5%)	19 (34.0%)	23 (41.0%)	12 (21.5%)	2 (3.5%)
Sensitivity of teeth	52 (21.0%)	11 (21.0%)	24 (46.0%)	9 (17.5%)	8 (15.5%)	24 (46.0%)	22 (42.5%)	5 (9.5%)	1 (2.0%)
Ulcers in mouth	42 (17.0%)	2 (4.5%)	16 (38.0%)	10 (24.0%)	14 (33.5%)	10 (24.0%)	14 (33.0%)	10 (24.0%)	8 (19.0%)
Bad breath	41 (16.5%)	3 (7.5%)	12 (29.0%)	19 (46.5%)	7 (17.0%)	9 (22.0%)	22 (53.5%)	8 (19.5%)	2 (5.0%)
Jagged teeth	41 (16.5%)	9 (22.0%)	7 (17.0%)	5 (12.0%)	20 (49.0%)	17 (41.5%)	14 (34.0%)	3 (7.5%)	7 (17.0%)
Altered sensation in mouth	27 (11.0%)	5 (18.5%)	9 (33.5%)	8 (29.5%)	5 (18.5%)	11 (41.0%)	10 (37.0%)	3 (11.0%)	3 (11.0%)
Denture fitting problems	26 (10.0%)	2 (8.0%)	2 (8.0%)	5 (19.0%)	17 (65.0%)	5 (19.5%)	11 (42.5%)	8 (30.5%)	2 (7.5%)
Toothache / pain in teeth	25 (10.0%)	6 (24.0%)	8 (32.0%)	7 (28.0%)	4 (16.0%)	11 (44.0%)	7 (28.0%)	7 (28.0%)	0 (0.0%)
Burning sensation in mouth	24 (9.5%)	6 (25.0%)	9 (37.5%)	6 (25.0%)	3 (12.5%)	7 (29.0%)	11 (46.0%)	4 (16.5%)	2 (8.5%)
Bleeding from mouth	19 (7.5%)	7 (37.0%)	9 (47.0%)	3 (16.0%)	0 (0.0%)	10 (52.5%)	8 (42.0%)	1 (5.5%)	0 (0.0%)

Table 1-2: Frequency and severity caused by oral symptoms. Reproduced from Davies et al (13) with permission from Springer Nature.

*Missing distress data for 1 patient; **Missing distress data for 2 patients

Oral symptoms like xerostomia, difficulty chewing, difficulty swallowing (20-23), and mouth discomfort/pain (24, 25) are common in older people. In a 2012 literature review from Liu et al. (22) examining the prevalence of xerostomia in “vulnerable elders”, the prevalence of xerostomia ranged from 17-49% in “community-dwelling” older people and 20-72% in “institutionalised elders”. There was no examination of the assessment methods for the individual studies included in the review. One recent study (20) identified the prevalence of dry mouth, chewing problems and swallowing difficulties as 15% (462/3188), 26% (817/3188) and 17% (548/3188) respectively among residents living in assisted facilities and nursing homes in Helsinki. The presence (or absence) of these symptoms was however recorded by the nurses caring for the residents and not by the residents themselves.

There is a paucity of research examining oral symptoms specifically in older patients with frailty. Thus, the prevalence of many oral symptoms is not known in this patient group.

1.3.2 Impact of oral symptoms

Oral problems are a direct cause of morbidity in patients with advanced cancer (13), and often have a significant effect on quality of life. However, they can also lead to further problems, which themselves have a negative impact on the patient. For example, patients with xerostomia often resort to drinking to relieve the problem, and this polydipsia results in polyuria (and often nocturia / sleep disturbance). Additionally, oral problems may also be an indirect cause of mortality in this patient cohort (26, 27) e.g. oral colonisation/infection causing respiratory or systemic infection (3).

Similarly, oral problems in older people may also be associated with increased morbidity and increased mortality (20, 21). For example, difficulty chewing (resulting from various causes) may necessitate changes in food selection, which may contribute to inadequate dietary intake leading to increased frailty and physical decline (28, 29). Oral problems in older people may also be associated with reduced oral health-related quality of life in particular in older people who have incremental tooth loss, dental caries, edentulism and xerostomia (30). Importantly, frailty may impact on the ability to undertake oral hygiene, which will result in numerous oral symptoms (e.g. halitosis) and problems (e.g. periodontal disease, dental caries and/or subsequent tooth loss). The same is true of fatigue, which is a common problem in patients with advanced cancer.

1.3.3 Aetiology of oral symptoms

There are a number of factors that may contribute to patients with advanced cancer (3, 13, 31) and older patients with frailty developing oral symptoms. These include:

1.3.3.1 Salivary gland hypofunction

Saliva is an integral component in maintaining oral homeostasis (32, 33). Saliva is composed of fluid secreted from the three pairs of major salivary glands – the parotid, submandibular and sublingual glands as well as from numerous minor salivary glands as well as gingival crevicular fluid (which is derived from periodontal tissue (34)). The majority (99%) of saliva is made up of water and the remaining components include electrolytes, immunoglobulins, proteins, enzymes, mucins, and nitrogenous products (33, 35, 36).

Saliva secretion is triggered by mechanical movements (like chewing and lip and tongue movements), alongside taste, smell, and specific visual stimuli. In response to these prompts, signals from the involved cranial nerves are carried to the central nervous system by afferent sensory nerves, with efferent signals then transmitted in parasympathetic and sympathetic autonomic nerves which are carried to the salivary glands (37). Disruptions to normal oral homeostasis caused by various aetiologies (discussed in the next subsections) results in salivary gland dysfunction which may alter saliva flow rate and/or its composition (see Figure 1-1). The latter may give rise to oral symptoms like xerostomia, mouth discomfort/pain, taste disturbance, difficulty chewing, difficulty swallowing, and difficulty speaking. Salivary gland dysfunction may also predispose to oral infections (oral candidosis, dental caries) (19), and to dental problems (enamel erosion, sensitivity) (19, 38), which in turn may give rise to many other oral symptoms/problems.

In terms of older patients, histological structural changes in salivary glands occur with advancing age, and a recent meta-analysis (33) demonstrated an age-dependent reduction in unstimulated salivary flow (independent of polypharmacy).

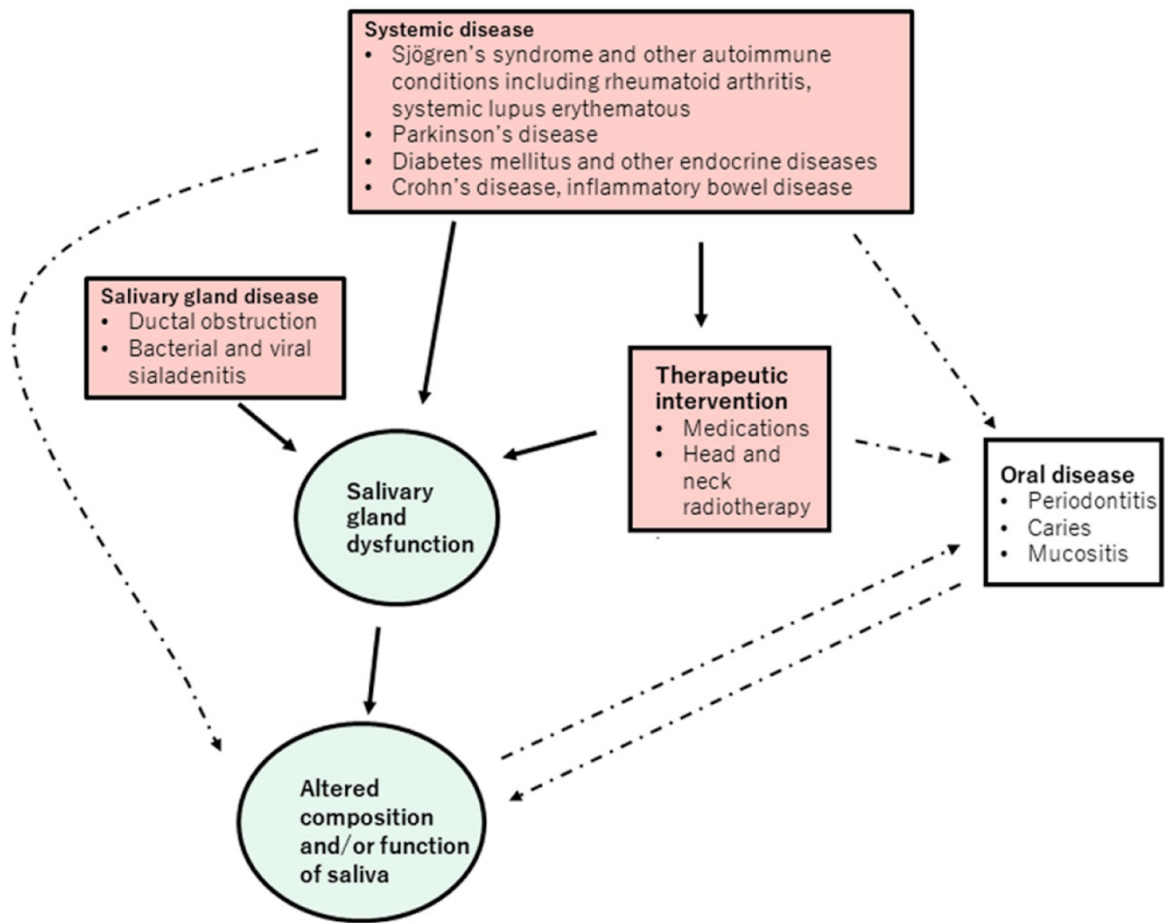


Figure 1-1: Relationship between disease, salivary gland dysfunction, and composition of saliva.
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1.3.3.2 Effects of the primary disease (direct and indirect)

1.3.3.2.1 Direct effects of the primary disease

Cancers involving the oral cavity or head and neck region (primary and secondary) may be a direct cause of oral symptoms (e.g. oral discomfort, trismus). Oral pre-cancerous lesions like lichen planus, leukoplakia and erythroplakia may cause oral symptoms similarly (30).

Conditions or diseases that result in neurological deficits, like stroke or Parkinson's disease, may cause drooling (due to facial weakness), and chewing or swallowing problems/disorders. Similarly, diabetes mellitus is associated with periodontitis (4, 39) which may cause various oral symptoms like mouth discomfort or pain or jagged teeth (23, 40).

1.3.3.2.2 Indirect effects of the primary disease

Certain physiological and psychological effects of cancer may contribute to a patient experiencing oral symptoms. Cancer-related fatigue may cause an inability to undertake adequate regular oral care, which may result in oral symptoms like bad breath, coating of the

tongue, or mouth pain/discomfort. Psychological effects like low mood or anhedonia may also contribute to patients having reduced motivation to conduct regular oral hygiene. Similarly, there is an association between depression and frailty, which may also have a negative impact on oral care, and so lead to further oral symptoms and problems (41, 42).

Significant functional impairment may result in an older person with frailty becoming homebound. This creates challenges in terms of accessing dental care in a dental surgery outside of their home for example having access to a wheelchair, wheelchair-accessible transport and being able to transfer into a dental chair (43-45). Ornstein et al. (46) in their study examining the oral health needs of older homebound adults (n=125) found that although 76% of the dentate participants (95/125) had at least one decayed tooth, 40% (50/125) required restorative dental treatment and 46% (57/125) required dental extractions, 60% (76/125) of the participants had not visited their dentist in over three years ago.

1.3.3.3 Treatment of the primary disease

1.3.3.3.1 Chemotherapy and radiation therapy

The oral mucosa is highly susceptible to the toxicities associated with chemotherapy and radiotherapy due to the fast rate of cell replacement (47, 48). Oral problems like mucositis, infection and dysgeusia may arise from direct injury to the oral mucosa or indirect injury through the loss of protective salivary components (47, 49). Whereas chemotherapy-induced oral problems often resolve upon cessation or dose reduction of the treatment, radiotherapy-induced problems often persist beyond the treatment (e.g. salivary gland dysfunction) (50).

1.3.3.3.2 Other treatments

Other treatments used to treat or manage symptoms of advanced cancer may also cause oral sequelae. For example, osteoclast inhibitors like high dose intravenous bisphosphonates and denosumab (used to treat bone pain from skeletal metastases, reduce skeletal-related events or to treat malignancy-induced hypercalcaemia) are a risk factor for the development of medication-related osteonecrosis of the jaw (51-53). The resultant oral problems may cause oral symptoms like mouth pain/discomfort, and difficulty chewing. Likewise, opioids used to manage cancer pain, may cause xerostomia, and taste disturbance (54).

1.3.3.4 Direct or indirect effect of a concomitant disease (or the treatment of the disease)

Certain systemic diseases may have oral manifestations causing oral symptoms (55). Some specific examples include mouth ulcers caused by Crohn's (or less commonly Behçet disease), and bad breath caused by hepatic or renal disease or diabetic ketoacidosis. Certain

rheumatological conditions are also associated with Sjogren's syndrome (and so salivary gland dysfunction).

1.3.3.4.1 Treatment of concomitant disease

Adverse side effects of many medications used to treat concomitant diseases are associated with oral symptoms (and especially xerostomia). Examples of medications that may cause xerostomia include antidepressants or anxiolytics used to treat depression or anxiety, antihistamines used to treat allergies or hay fever, and antihypertensives particularly diuretics and β blockers used to treat hypertension (30, 56).

Polypharmacy may be associated with xerostomia particularly in older patients (50, 57). The exact mechanism of polypharmacy as a risk factor for xerostomia in this patient population is unclear (58). However, one factor may be the cumulative effect (in terms of dosage and number) of taking medications with anticholinergic properties (i.e. the concept of 'anticholinergic burden') (30, 59).

1.3.3.5 A combination of these factors

One or more of these factors combined may be risk factors for these two patient cohorts developing oral symptoms.

1.4 COMPREHENSIVE SYMPTOM ASSESSMENT

Symptoms are often the primary reason for patients seeking medical advice and help the clinician formulate a differential diagnosis (60). The systematic review by Teunissen et al. (18) examined symptom prevalence in patients with advanced cancer using three assessment methods – standardised interview, questionnaires, and the medical record. Importantly, there were significant differences in mean percentages for dry mouth (questionnaire - 69%; standardised interview - 36%; medical record - 9%, $P = 0.008$), and also taste changes (questionnaire - 41%; standardised interview - 26%; medical record - 2%, $P = 0.043$). In other words, the mean percentages for both of these oral symptoms was highest when they were assessed by a questionnaire.

A symptom assessment tool should be "comprehensive, accurate and reliable" (61), and aim to capture the "symptom experience" (62). Many symptom assessment instruments are unidimensional (e.g. symptom present or absent). However, by assessing only one dimension, the nuances of how individual symptoms are experienced, and especially the burden of the symptom, may not be captured. Symptom assessment tool may assess symptom duration,

frequency, severity, distress (or bothersomeness) alone or in combination (61, 63). Li et al. (64) demonstrated that the severity of a symptom did not correlate consistently with symptom bothersomeness when patients with advanced cancer reported the severity of their symptoms on the Edmonton Symptom Assessment Scale (ESAS), and level of bother on the Quality of Life at the End of Life (QUAL-E) measure. Hence, multidimensional symptom assessment tools can be more reflective of symptom burden. Importantly, quality of life (QoL) is not determined solely by symptoms and is instead a multidimensional concept that measures “aspects of an individual’s sense of well-being and ability to carry out activities of daily living” (65). QoL measurement tools are not intended as symptom assessment tools, although several do contain some symptom assessment components.

1.4.1 Generic versus symptom-specific symptom assessment instruments

Generic cancer-specific symptom assessment tools invariably contain few oral symptoms (e.g. MD Anderson Symptom Inventory contains only one oral symptom, i.e. xerostomia) (66). Furthermore, many do not contain any oral symptoms (e.g. standard ESAS). Similarly, generic multi-symptom assessment tools that have been utilised to examine symptoms in studies involving older people with chronic diseases often only contain one oral symptom (e.g. xerostomia in the Memorial Symptom Assessment Scale- Heart Failure (or MSAS-HF) (67, 68)) and some do not contain any oral symptom (e.g. the Somatic Symptom Scale-8 (69)).

As discussed, oral health-related QoL measurement tools are not intended as oral symptom assessment tools, although several do contain some oral symptom assessment components like the Geriatric Oral Health Assessment Index (GOHAI) (70), Oral Health Impact Profile (OHIP) (71), and Oral Impacts on Daily Performance (OIDP) (72).

Symptom measurement in patients with advanced cancer and in older patients with frailty can be challenging due to the population, underlying (ever-changing) primary condition (61), and co-morbidities. So, the comprehensiveness of a symptom assessment tool must be balanced with overburdening patients with lengthy questionnaires, therein risking a reduction in patient acceptance and compliance (61).

1.5 THE ORAL SYMPTOM ASSESSMENT SCALE

The Oral Symptom Assessment Scale (see Figures 1-2, 1-3, 1-4) is a twenty-item, patient-rated oral symptom assessment tool (13). The design of this novel oral symptom assessment tool was modelled on the Memorial Symptom Assessment Scale (73). If a patient reports that a

symptom has been present in the last week, they then rate the frequency, severity and amount of distress (or bothersomeness) that the symptom has caused. The developers of the OSAS state that the twenty items were based on “a review of the medical literature on oral symptoms and problems in patients with advanced cancer/patients receiving palliative care, consultation with experts in the field (i.e. palliative medicine, dentistry/oral medicine), and discussion with patients, carers, and healthcare professionals regarding the specific wording of the questionnaire” (13). The results of the initial observational study provided preliminary validation of the symptom assessment tool. It was, however, recognised that further psychometric testing was necessary, including assessing criterion validity, and test-retest reliability.

ORAL SYMPTOM ASSESSMENT SCALE														
Name:								Date:						
SECTION 1														
Instructions: We have listed a number of symptoms below. Read each one carefully. If you have had the symptom during this past week, let us know how OFTEN you had it, how SEVERE it was usually and how much it DISTRESSED or BOTHERED you by putting an X in the appropriate box. If you DID NOT HAVE the symptom, put an "X" in the box marked "DID NOT HAVE"														
DURING THE PAST WEEK Did you have any of the following symptoms?	DID NOT HAVE	IF YES How OFTEN did you have it?				IF YES How SEVERE was it?				IF YES How much did it DISTRESS or BOTHER you?				
		Rarely	Occasionally	Frequently	Almost constantly	Slight	Moderate	Severe	Very severe	Not at all	A little bit	Somewhat	Quite a bit	Very much
Dry mouth														
Mouth discomfort / pain														
Lip discomfort														
Cracking of lips														
Cracking of corner of mouth														
Taste disturbance														
Difficulty chewing														
Difficulty swallowing														
Difficulty speaking														

Figure 1-2: OSAS section 1.

SECTION 1 continued														
Instructions: We have listed a number of symptoms below. Read each one carefully. If you have had the symptom during this past week, let us know how OFTEN you had it, how SEVERE it was usually and how much it DISTRESSED or BOTHERED you by putting an X in the appropriate box. If you DID NOT HAVE the symptom, put an "X" in the box marked "DID NOT HAVE"														
DURING THE PAST WEEK Did you have any of the following symptoms?	DID NOT HAVE	IF YES How OFTEN did you have it?				IF YES How SEVERE was it?				IF YES How much did it DISTRESS or BOTHER you?				
		Rarely	Occasionally	Frequently	Almost constantly	Slight	Moderate	Severe	Very severe	Not at all	A little bit	Somewhat	Quite a bit	Very much
"Dirty" mouth														
Coating of tongue														
Bad breath														
Toothache / pain in teeth														
Sensitivity of teeth														
Jagged teeth														
Denture fitting problems														
Bleeding from mouth														
Burning sensation in mouth														
Altered sensation in mouth (e.g. numbness, pins and needles)														
Ulcers in mouth														

Figure 1-3: OSAS section 1 continued.

SECTION 2														
If you had any other symptoms relating to your mouth during the past week, please list below, and let us know how OFTEN you had it, how SEVERE it was usually and how much it DISTRESSED or BOTHERED you by putting an X in the appropriate box.														
DURING THE PAST WEEK	Other mouth symptoms (list)	IF YES How OFTEN did you have it?				IF YES How SEVERE was it?				IF YES How much did it DISTRESS or BOTHER you?				
		Rarely	Occasionally	Frequently	Almost constantly	Slight	Moderate	Severe	Very severe	Not at all	A little bit	Somewhat	Quite a bit	Very much
1.														
2.														
3.														

Figure 1-4: OSAS section 2.

Currently, there is no analogous validated oral symptom assessment tool for older patients with frailty.

1.6 THESIS OUTLINE

Having provided a background to this research in the opening chapter, Chapter 2 will present a scoping review of the literature on oral symptom assessment tools utilised in studies with patients with advanced cancer. The focus of this scoping review was to identify a suitable validated instrument against which to measure the criterion validity of the OSAS in the subsequent observational study investigating the psychometric properties of the OSAS in patients with advanced cancer. Chapter 3 describes results of the initial observational study, whilst Chapter 4 describes the results of the subsequent observational study (to determine the prevalence and clinical features of oral symptoms in older patients with frailty using the OSAS). The dissertation concludes with Chapter 5, which discusses the findings of the studies, and implications for clinical practice and future research.

CHAPTER 2 ORAL SYMPTOM ASSESSMENT TOOLS IN PATIENTS WITH ADVANCED CANCER: A SCOPING REVIEW

2.1 INTRODUCTION

This scoping review identified and described oral symptom assessment tools that have been specifically utilised in patients with advanced cancer, and particularly in cancer patients receiving symptom-oriented treatment (i.e. palliative care).

2.2 ORAL SYMPTOMS IN PATIENTS WITH ADVANCED CANCER

The cornerstone of palliative care is the management of “distressing” symptoms (74). Patients with advanced cancer experience a range of different symptoms, including a variety of different oral symptoms (18). Davies et al. (13) reported that 97.5% (244/250) of participants in their multicentre study experienced at least one oral symptom on the OSAS, and that the median number of oral symptoms experienced was five (range 1–18 oral symptoms).

Moreover many of the oral symptoms were of high frequency, high severity and caused high levels of distress. The symptom of xerostomia for example, was reported by 83.5% (209/250) of participants using the OSAS: of those with xerostomia, 72.5% (151/209) reported that it occurred “frequently” or “almost constantly”, 77% (160/209) reported that severity was “moderate”, “severe” or “very severe”, and 52% (108/209) reported the level of distress caused by it as “somewhat”, “quite a bit” or “very much”. Moreover, the participants in this study separately reported xerostomia (79.6%, 199/250) was the third most common symptom overall after “lack of energy” and “feeling drowsy”.

2.2.1 Discrepancies in oral symptom prevalence

Investigators have identified discrepancies between the recorded prevalence of oral symptoms and the true (higher) prevalence of these symptoms in patients with advanced cancer (75).

The reasons for the latter are unclear. Healthcare professionals may not enquire about a symptom if: (a) they perceive the symptom to be uncommon; (b) they perceive the symptom to be unimportant; (c) they perceive there is no treatment for the symptom; and/or (d) time does not permit. Similarly, patients may not volunteer a symptom if: (a) they perceive the symptom to be inevitable; (b) they perceive there is no treatment for the symptom; (c) they sense that healthcare professionals consider the symptom to be unimportant; and/or (d) other symptoms predominate.

2.3 SYMPTOM ASSESSMENT TOOLS

Symptom assessment tools can facilitate good clinical practice by improving the thoroughness of the assessment (and re-assessment) of common symptoms. Furthermore, validated symptom assessment tools are essential in undertaking robust research studies. However, many generic symptom assessment scales contain no oral symptoms (e.g., Edmonton Symptom Assessment Scale/ESAS (76)), or only a limited number of oral symptoms (e.g., Memorial Symptom Assessment Scale/MSAS (73)). For example, the MSAS, which consists of 32 symptoms (26 physical, 6 psychological), includes only four oral symptoms, i.e. “dry mouth”, “change in the way food tastes”, “difficulty swallowing”, and “mouth sores”. Interestingly, the Norwegian version of ESAS does include xerostomia, as this is one of the “10 common symptoms of advanced cancer” (12).

2.4 METHODS

The function of a scoping review is to identify the available evidence rather than to produce critically appraised answers to research questions (77). The Arksey and O'Malley methodological framework (78), which has been enhanced/developed by Levac et al (79) and the Joanna Briggs Institute (80), was used as a framework to conduct this scoping review. The PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist was used as a guide in reporting this scoping review (81).

2.4.1 Literature search

2.4.1.1 Study eligibility criteria

The Population, Intervention, Comparator/control, Outcome and Study design (PICOS) framework was used to identify relevant research studies (82). Eligible studies included adult (> 18 years) patients with advanced cancer (as defined by the National Cancer Institute/NCI, USA): “cancer that is unlikely to be cured or controlled with treatment” (6). Studies involving patient-rated oral symptom assessment tools, as well as quality of life (QoL) instruments that contain oral symptom items, were included. However, studies involving assessment of a single oral symptom (e.g., xerostomia), or a single cancer site (e.g., head and neck cancer), were not included. Observational and experimental studies were included. Perspective, commentary or opinion articles without original data were excluded.

2.4.1.2 Search strategy

A comprehensive search of three electronic databases including PubMed, Embase, and CINAHL was conducted from their inception to 11 June 2021 (see Appendix 1 for the database

search strategy). The literature review was adapted to meet the requirements of each database searched. The search was limited to English language articles. Reference lists of all eligible full texts were hand searched for other relevant articles. In addition, handsearching of reference lists of relevant chapters in academic palliative care textbooks was undertaken to ensure a comprehensive search of the literature was conducted.

2.4.1.3 Data management and synthesis

The EndNote 20™ (Clarivate) bibliographic software was used to store the records retrieved from the literature searches. This software removes similarly identified duplicate entries automatically. The records were then imported to Covidence software, which is an online screening and data extraction software tool. Two reviewers independently screened the titles and abstracts using the PICOS criteria. Where an abstract was unavailable, the paper was included in the full text review process. If there was any conflict between the two reviewers, a third reviewer was available to determine inclusion. The same two reviewers independently reviewed the full texts, and extracted the relevant information using a review-specific proforma which included:

- the reference
- study type
- symptom assessment tool
- symptoms assessed
- symptom dimensions assessed
- time frame of assessment

Again, if there was any conflict between the two reviewers, a third reviewer was available to determine inclusion.

2.5 RESULTS

2.5.1 Search results

The search strategy identified 1179 unique references (see Figure 2-1). Fourteen papers were included in the full data extraction. One reference was a conference abstract and the authors confirmed that this was the same study as an included article. Five further articles were included following handsearching of the included full text articles. No further articles were included following handsearching of relevant chapters in academic textbooks. Table 2-1 summaries the data extraction.

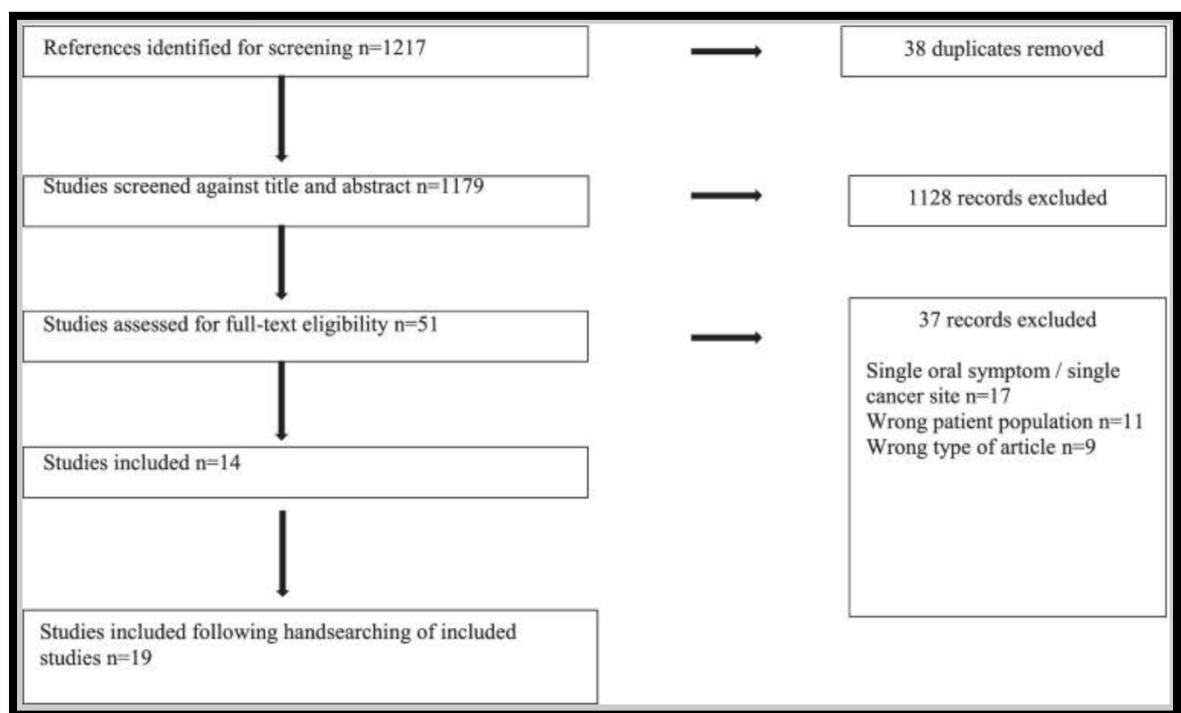


Figure 2-1: Study flow.

2.5.2 Symptoms assessed

The number of oral symptoms assessed in each study varied from two (15, 83) to 20 (13, 84). Xerostomia was universally assessed, which is unsurprising as studies in patients with advanced cancer demonstrate a very high prevalence (i.e. 82–83.5%)(13, 84, 85). Other commonly assessed symptoms included oral discomfort (18/18 studies), taste disturbance (15/18 studies), and denture problems (8/18 studies).

REFERENCE	STUDY TYPE	NUMBER OF ORAL SYMPTOMS ASSESSED	SYMPTOMS ASSESSED	SYMPTOM DIMENSIONS ASSESSED	TIME FRAME	SYMPTOM ASSESSMENT TOOL
Pople et al, 1986 (86)	Observational	3	"Dry mouth"; "altered taste"; "sore mouth"	Present/absent	Not described (but assessments performed on day 1, day 3, and day 5 after admission)	Non validated questionnaire
Clarke et al, 1987 (87)	Observational	5	"Xerostomia"; "glossodynia"; "painful gums"; "dysphagia"; "sour taste"	Present/absent	Not described	Non validated questionnaire
Aldred et al, 1991 (88)	Observational	6	"Disturbance of taste"; "dysphagia"; "oral soreness"; "dryness of the mouth"; "difficulty in wearing dentures"; "any other miscellaneous problems"	Present/absent	Not described	Non validated questionnaire

Jobbins et al, 1992 (89)	Observational	5	"Xerostomia"; "denture problems"; "taste disturbance"; "swallowing difficulty"; "oral soreness"	Present/absent	Not described	Non validated questionnaire
Sweeney et al, 1997 (16)	Interventional – clinical trial in patients with xerostomia	7	"Oral dryness during the day"; "dryness at night"; "soreness of the mouth"; "unpleasant or altered taste sensation"; "difficulty talking"; "difficulty eating"; "denture problems"	Present/absent Visual analogue scales used to assess response (no details provided)	Not described	Non validated questionnaire
Sweeney et al, 1998 (90)	Observational	7	"Dry mouth during the day"; "dry mouth at night"; "soreness of the mouth"; "bad or altered taste"; "difficulty talking"; "difficulty eating"; "problems with dentures"	Present/absent "Grading" - visual analogue scale 0-6 (no problem-severe problem)	Not described	Non validated questionnaire

Oneschuk et al, 2000 (15)	Observational	2	"Mouth pain"; "mouth dryness"	Presence/absence Intensity – numerical rating scale 0-10 (low- high) "Importance" (relative to other symptoms / problems) – not important, slight importance, some importance, moderate importance, considerable importance, very important, great importance	Not described (but symptoms reported present from 1 day to > 1 year)	Non validated questionnaire
Milligan et al, 2001 (83)	Interventional – oral care regimen	2	"Oral pain"; "oral dryness"	Presence/absence	Not described (but assessments performed on day 1, and day 7)	Non validated questionnaire

Davies et al, 2001 (91)	Observational	4 ("standard" symptoms) 3 ("additional" symptoms)	"Dry mouth"; "difficulty swallowing"; "mouth sores"; "change in the way food tastes" "Oral discomfort"; "difficulty chewing"; "difficulty speaking"	Presence/absence Frequency – rarely, occasionally, frequently, almost constantly Intensity – slight, moderate, severe, very severe Amount of distress caused – not at all, a little bit, somewhat, quite a bit, very much	Previous week	Validated questionnaire (with additional questions) - Memorial Symptom Assessment Scale / MSAS (73)
Alt-Epping et al, 2012 (17)	Observational	5	"Dry mouth"; "taste disturbances"; "dysphagia"; "halitosis"; "pain of the oral cavity"	Presence/absence Intensity – numerical rating scale 0-10 (low-high)	Not described	Non validated questionnaire
Wilberg et al, 2012 (12)	Observational	5	"Oral discomfort"; xerostomia"; "taste disturbances"; "problems eating"; "dental health"	Presence/absence	Not described (but xerostomia reported present for > 3 months)	Non validated questionnaire

Hjermstad et al, 2012 (92)	Observational	14	“Pain in gums”; “bleeding gums”; “lip sores”; “problems with teeth”; “sore mouth”; “sores in mouth corners”; “dry mouth”; “sticky saliva”; “sensitive mouth”; “taste change”; “problems with solid food”; “trouble enjoying meals”; “worn dentures”; “ill-fitting dentures”	Presence/absence “Extent to which you have experienced these symptoms” – not at all, a little, quite a bit, very much	Previous week	Development study - EORTC QLQ-OH17
Fischer et al, 2014 (93)	Observational	3 main symptoms (with extra questions about related oral symptoms)	“Xerostomia” (with extra question about dry lips); “orofacial pain” (separate questions about intraoral and facial pain, with extra question about mouth sores); “taste change”	Presence/absence Frequency – Likert scale 0-4 (never-always) Severity (xerostomia, orofacial pain) – numerical rating scale 0-10 (low-high)	Not described	Non validated questionnaire (Oral Problem Scale) – based upon questions from other tools, including Oral Health Impact Profile / OHIP (94), and Oral Symptom and Function Scale (95)

Mercadante et al, 2015 (96)	Observational	3	"Limitation on nutrition or hydration" (due to mucositis); "dry mouth"; "dysphagia"	Presence/absence Mucositis intensity – no limitation, mucositis partially preventing nutrition or hydration, mucositis severely limiting nutrition or hydration, mucositis completely preventing nutrition or hydration Dry mouth / dysphagia intensity – numerical rating scale 0-10 (low-high)	Not described	Non validated questionnaire
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Nikles et al, 2015 (97)	Interventional – clinical trial in patients with xerostomia	3 generic symptoms	“Dry mouth”; “difficulty in swallowing”; “altered taste”	Presence/absence Severity – numerical rating scale 0-10 (low- high), and summated score from Xerostomia Inventory (see below)	Previous 24 hours	Non validated questionnaire – patients were also asked to complete Xerostomia Inventory / XI (98), and OHIP (94). The XI is a validated single symptom assessment tool. The OHIP is a validated assessment tool that measures “the social impact of oral disorders”. The protocol paper states that the OHIP-14 (14 questions) would be used (99) but the main paper suggests that the OHIP-49 (49 questions) was used (97)
		4 symptoms from Xerostomia Inventory (see final column)	“Mouth feels dry”; “difficulty eating dry food”; difficulties swallowing certain foods; “lips feel dry”	Frequency – never, hardly ever, occasionally, fairly often, very often	Not described	
		? number symptoms from OHIP-49 (see final column)	Symptoms different for different versions	Frequency - scales different for different versions (see final column)	Not described	

Hjermstad et al, 2016 (56)	Observational	12	“Pain in your gums”; “problems with bleeding gums”; “lip sores”; “problems with your teeth”; “soreness in your mouth”; “sores in the corners of your mouth”; “dry mouth”; “sticky saliva”; “mouth been sensitive to food and drink”; “food and drink tasted different than usual”; “problems eating solid foods”; “problems with an ill-fitting denture”	Presence/absence “Extent to which you have experienced these symptoms” – not at all, a little, quite a bit, very much	Previous week	Validation study - EORTC QLQ-OH17 (leading to EORTC QLQ-OH15)
Magnani et al, 2019 (100)	Interventional – oral care regimen	3	“Xerostomia/dry mouth”; “dysgeusia”; “orofacial pain”	Presence/absence Intensity – numerical rating scale 0-10 (low-high)	Not described (but assessments performed on day 1, and day 3)	Non validated questionnaire

Davies et al, 2021 (13, 84)	Observational	20 (with option to report additional oral symptoms)	"Dry mouth"; "mouth discomfort/pain"; "lip discomfort"; "cracking of lips"; "cracking of corner of mouth"; "taste disturbance"; "difficulty chewing"; "difficulty swallowing"; "difficulty speaking"; "dirty mouth"; "coating of tongue"; "bad breath"; "toothache/pain in teeth"; "sensitivity of teeth"; "jagged teeth"; "denture fitting problems"; "bleeding from mouth"; "burning sensation in mouth"; "altered sensation in mouth"; "ulcers in mouth"	Presence/absence Frequency – rarely, occasionally, frequently, almost constantly Intensity – slight, moderate, severe, very severe Amount of distress caused – not at all, a little bit, somewhat, quite a bit, very much	Previous week	Oral Symptom Assessment Scale/OSAS Initial validation of OSAS undertaken as part of this study
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Table 2-1: Summary of data extraction

It should be noted that the wording of the questions differed amongst the oral assessment tools: for example, taste disturbance was variously described as “altered taste”, “sour taste”, “disturbance of taste”, “taste disturbance(s)”, “unpleasant or altered taste sensation”, “bad or altered taste”, “change in the way food tastes”, “taste change”, “food and drink tasted different from usual”, and “dysgeusia” (although it was unclear as to the wording used with the participants) (100).

Davies et al. (13) assessed 20 oral symptoms, many of which were not included in other studies (e.g. “sensitivity of teeth”, “altered sensation in mouth”, “burning sensation in mouth”, “bleeding from mouth”), and all of which were present in $\geq 7.5\%$ of participants.

2.5.3 Dimensions assessed

Many of the (generally older) studies simply assessed the presence or absence of specific oral symptoms (12, 83, 86-89). However, many of the (generally newer) studies assessed one or more dimensions, including frequency (13, 84, 91, 93, 97), intensity/severity (13, 15, 17, 84, 90, 91, 93, 96, 97, 100), level of distress or bothersomeness (13, 84, 91), level of limitation (96), and relative importance (15).

2.5.4 Symptom time frames

Many of the studies did not specify the time frames used in the questions. Of the studies that did specify a time frame, this varied from “in the previous 24 h” (97), to “during the past week” (12, 13, 56, 84). Nevertheless, some studies appear to have used longer time frames based upon the results reported (e.g., up to 1 year (15)).

2.6 DISCUSSION

As highlighted, oral symptoms are common in patients with advanced cancer. Furthermore, these symptoms are often frequent in occurrence, moderate to severe in intensity, and cause significant levels of distress (and so have a negative impact on quality of life). However, observational studies suggest that oral problems are not well-managed in this group of patients (101). The reasons for the latter are several, and include inadequate assessment (including non-identification of oral symptoms/problems), inappropriate treatment, and inadequate re-assessment.

Symptom assessment tools can improve clinical practice through the improved/earlier identification of troublesome “orphan” symptoms (i.e. symptoms not usually reported or assessed) (102). The “ideal” symptom assessment tool should be valid, reliable, relevant (for

the population/specific scenario), comprehensive (for the specific scenario), multidimensional, and easy to administer/complete (103). Symptom assessment tools also have a role in research, in both observational studies, and in interventional studies (as a means of demonstrating improvements in symptom control).

Currently, there is no consensus on the number of symptoms that should be included in symptom assessment tools. Longer (more comprehensive) symptom assessment tools may be more suited to research settings, whilst shorter assessment tools may be preferable for clinical practice due to related issues of patient burden, and inadequate completion.

Symptom assessment tools that only ask about the presence (or absence) of a symptom, or are limited to the assessment of a single dimension (e.g. frequency), risk underestimating, and equally overestimating, the importance of certain symptoms. For example, although a symptom may be frequent in nature, it may not cause significant distress (and so may not require any intervention). It should be noted that the level of distress of a symptom is often a very good indicator of its impact on the person's quality of life (although frequency, and especially intensity/severity, are also important) (103).

Many of the included studies used study-specific questionnaires, which had not been validated, although some contained elements from other validated assessment tools. Validated tools included the MSAS (91), the EORTC QLQ-OH17 (12), the EORTC QLQ-OH15 (56), and the OSAS (13, 84). One study used the OHIP (97), although related results were not presented (and it was unclear which version was used). Of note, another study used selected elements from the OHIP (93).

The MSAS is a 32-item multidimensional generic symptom assessment scale, which has been extensively validated in cancer patients (73). It contains four oral symptoms (i.e. "dry mouth", "difficulty swallowing", "mouth sores" and "change in the way food tastes"). The MSAS also provides blank spaces for the patient to add additional symptoms not mentioned within the tool. Davies et al. (91) supplemented the MSAS with three further oral symptoms ("oral discomfort", "difficulty chewing" and "difficulty speaking") in their study. The MSAS involves patients rating the frequency, severity, and distress caused by each of 24 symptoms and then the severity and distress caused by a further 8 symptoms (which includes "mouth sores" and "change in the way food tastes").

The EORTC QLQ oral health module is a validated quality of life instrument, which includes a number of oral symptoms. It was initially developed as the EORTC QLQ OH-17 (a 17-item tool) (12), but was subsequently refined to the EORTC QLQ-15 (a 15-item tool) (56). This oral health module must be completed alongside the core EORTC QLQ C-30 instrument. The EORTC QLQ-15 assesses 12 oral symptoms with three further items pertaining to the wearing of dentures, and information received about dental or mouth problems.

As previously described, the OSAS is a 20-item multidimensional oral symptom assessment tool. The OSAS was modelled on the design of the MSAS. The symptoms assessed are shown in Figure 5, and it also provides blank spaces for the patient to add any additional oral symptoms not mentioned within the tool. The OSAS involves patients rating the frequency, severity, and distress caused by each of the oral symptoms.

2.7 CONCLUSION

Symptom assessment tools can facilitate good symptom control in clinical practice, and are an integral component of clinical research. This scoping review identified four validated symptom assessment scales that could be utilised to assess oral symptoms in patients with advanced cancer, including one cancer-specific quality of life scale (EORTC QLQ OH-15), one generic tool for assessing the “social impact” of specific oral problems (OHIP), one cancer-specific generic symptom assessment scale (MSAS), and one cancer-specific oral symptom assessment scale (OSAS).

With these results, the EORTC QLQ OH-15 was identified as a suitable, validated symptom assessment instrument that could be used to examine the criterion validity of the OSAS.

CHAPTER 3 THE ORAL SYMPTOM ASSESSMENT SCALE (OSAS): CRITERION VALIDATION WITH THE EORTC QLQ-OH15 AND RELIABILITY TESTING

3.1 INTRODUCTION

This prospective observational study evaluated the reliability of the OSAS, and its criterion validity with the EORTC QLQ-OH15, in a cohort of adult patients with advanced cancer admitted to hospice.

3.2 ORAL SYMPTOM AND ORAL SYMPTOM ASSESSMENT IN PATIENTS WITH ADVANCED CANCER

Oral symptoms are common in patients with advanced cancer (3), and are often associated with significant distress / “bothersomeness” and a negative impact on quality of life (13). However, many generic symptom assessment tools contain no or only a few oral symptoms (61). The commonly-employed MSAS (73), for example, is a multidimensional patient-rated instrument that evaluates a diverse set of common symptoms in patients with cancer. It consists of 32 symptoms (26 physical, six psychological), but includes only four oral symptoms, i.e., “dry mouth”, “change in the way food tastes”, “difficulty swallowing”, and “mouth sores.

The scoping review of the literature outlined in Chapter 2 identified a limited number of validated oral symptom assessment tools in patients with advanced cancer including the EORTC QLQ OH-15, the OHIP, the MSAS, and the OSAS (104). The OSAS was specifically developed to assess oral symptoms in this cohort of patients (13). It is a patient-rated tool, which asks about twenty oral symptoms. The OSAS was modelled on the MSAS. Patients are asked about the presence of each oral symptom in the preceding week. If a symptom is not experienced, the patient marks a column labelled ‘did not have’. If a symptom is present, the frequency and severity of the symptom is rated on a 4-point Likert-type scale i.e. “rarely”, “occasionally”, “frequently”, “almost constantly” and “slight”, “moderate”, “severe”, “very severe”, respectively. In addition, the amount of distress or bothersomeness that the symptom causes is rated on a five-point Likert-type scale i.e., “not at all”, “a little bit”, “somewhat”, “quite a bit”, “very much”. Patients are also asked about the presence of any other oral symptoms and the rate them in the same way.

The OSAS has undergone a degree of validation during its development, including content validity, and the initial observational study in patients with advanced cancer established

criterion validity (13). However, it has not previously undergone any reliability testing, including test-retest reliability.

The aim of this study was to carry out further testing of the psychometric properties of the original OSAS, with the objectives being to assess its reliability, and to further assess its criterion validity using a cancer-related oral quality of life instrument (the EORTC QLQ-OH15) (56). The EORTC QLQ-OH15 was developed for patients with cancer, but not specifically for patients with advanced cancer.

3.3 METHODS

3.3.1 Study design and ethics committee approval

This prospective observational study was conducted at Our Lady's Hospice and Care Services in Dublin (Ireland). The study was sponsored by Our Lady's Hospice and Care Services, and received ethical approval from the St Vincent's University Hospital Ethics Committee (reference number: RS21-044) (Appendix 2). The study was registered on ClinicalTrials.gov (protocol ID: PM202166/ ClinicalTrials.gov trial identification number: NCT04932317).

3.3.2 Patient recruitment and criteria for study inclusion

All patients with advanced cancer admitted to Our Lady's Hospice and Care Services were potentially eligible for participation. Potential participants were identified by the clinical team, and then screened by the researcher (or other members of the research team) using the following inclusion and exclusion criteria:

Inclusion criteria:

- cancer diagnosis
- aged ≥ 18 years old
- in a 'stable' clinical phase
- able to understand and speak English
- able to provide a signed written consent form

Exclusion criteria included:

- in the judgment of the palliative care physician study participation was not appropriate
- in the 'unstable', 'deteriorating' or 'terminal' phase
- unable to complete the study assessments in entirety

3.3.3 Consent process

The clinical team introduced the study to any eligible patients and sought permission for further discussion with the researcher. Those who agreed to further discussion met with one of the research team who provided information about the study and a copy of the patient information leaflet (Appendix 4). If the patient agreed to consent, the consent form (Appendix 3) was signed in the presence of the researcher. There was no 'cooling off period', i.e. the participant could enter the study at the time of the initial approach, assuming the participant was happy to enter the study at that point in time.

Upon recruitment each participant was assigned a unique study number (e.g. 1,2,3) to maintain anonymity and confidentiality. The collected data was stored on a password-protected Microsoft Excel spreadsheet. All paper copies were stored in a locked cabinet in a fob access-only office in the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Services in Harold's Cross (and will be securely destroyed after 5 years).

3.3.4 Study procedures

The study was undertaken on two consecutive days in order to assess the reliability of the OSAS. This time scale was chosen because of the clinical instability of this cohort of patients, and is supported by a systematic review of validation studies in patients with advanced cancer (105). On the first day, demographic (age, sex) and other relevant information (cancer diagnosis, Eastern Cooperative Oncology Group/ECOG performance status) were collected (Appendix 5), and the participants were asked to complete the OSAS, the EORTC QLQ-C30, and the EORTC QLQ-OH15 and asked if both were easy to complete. On the second day, the participants were asked to complete the OSAS again. The time taken to complete the questionnaires was recorded.

The OSAS has been previously described in Chapter 1, and is reproduced in Figures 1-2, 1-3, 1-4.

The EORTC QLQ-C30 (see Figures 3-1 and 3-2) is a health-related quality of life (HRQoL) measurement instrument, which has been extensively validated in patients with cancer (106). It is a 30-item tool and contains five functional scales, three symptom scales, six single items, and a global health status /quality of life scale. Permission was granted to use the EORTC QLQ C30 (permission reference ID: 73877/ Appendix 6).

The EORTC QLQ-OH15 (see Figure 3-3) is a 15-item tool, and patients are asked to rate the “extent” to which the fifteen symptoms or problems have been experienced in the past week (56). It contains an eight-item oral health quality of life scale, three single items (i.e. sticky saliva, mouth soreness, sensitivity to food/drink), and two two-item scales: the first scale relates to the use (yes/no) and problems with dentures, whilst the second scale relates to the reception (yes/no) and satisfaction of information received about dental or mouth problems. The EORTC QLQ-OH15 is the oral health module of the EORTC QLQ-C30, and as such it must be completed in conjunction with the EORTC QLQ-C30. Permission was granted to use the oral health module in this study (Permission reference ID: 74963/ Appendix 7).



EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials:

--	--	--	--	--

Your birthdate (Day, Month, Year):

--	--	--	--	--	--	--	--	--	--

Today's date (Day, Month, Year):

31

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	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a <u>long</u> walk?	1	2	3	4
3. Do you have any trouble taking a <u>short</u> walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

Figure 3-1: EORTC QLQ-C30.

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor

Excellent

Figure 3-2: EORTC QLQ-30 continued.



EORTC QLQ – OH15

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:		Not at all	A little	Quite a bit	Very much
31.	Have you had pain in your gums?	1	2	3	4
32.	Have you had problems with bleeding gums?	1	2	3	4
33.	Have you had lip sores?	1	2	3	4
34.	Have you had problems with your teeth?	1	2	3	4
35.	Have you had soreness in your mouth?	1	2	3	4
36.	Have you had sores in the corners of your mouth?	1	2	3	4
37.	Have you had a dry mouth?	1	2	3	4
38.	Have you had sticky saliva?	1	2	3	4
39.	Has your mouth been sensitive to food and drink?	1	2	3	4
40.	Have food and drink tasted different than usual?	1	2	3	4
41.	Have you had problems eating solid foods?	1	2	3	4

During the past week:		Yes	No
42.	Have you worn dentures?	1	2

Answer question 43 only if you used dentures:		Not at all	A little	Quite a bit	Very much
43.	Have you had problems with an ill-fitting denture?	1	2	3	4

In the course of your current illness or its treatment, not only the past week:		Yes	No
44.	Have you received any information about possible dental or mouth problems?	1	2

Answer question 45 only if you have received information:		Not at all	A little	Quite a bit	Very much
45.	Have you been satisfied with the amount of information you received about possible dental or mouth problems?	1	2	3	4

Figure 3-3: EORTC QLQ OH-15.

3.3.5 Statistical analysis/considerations

The estimation method (107) for sample size calculation for intraclass correlation coefficient was used to determine the sample size for this study: an expected reliability of 0.8 with a precision of ± 0.1 was determined after review of the relevant literature (105), and from researcher experience (based upon a confidence level: 95%; the number of repetitions per subject(k): 2; and an expected dropout rate: 20%). A sample size of 51 complete datasets was determined based on this calculation method. Three participants did not complete both days, and so recruitment continued until 51 completed tests were obtained.

IBM®SPSS® Statistics (Version: 28.0.1.1(14)) software was used to undertake the statistical analysis. The OSAS responses were scored as follows for the statistical analysis: if a symptom is not present it is assigned a score of zero. If present, the frequency was scored as “rarely” (= 1), “occasionally” (= 2), “frequently” (= 3), “almost constantly” (= 4); the severity was scored as “slight” (= 1), “moderate” (= 2), “severe” (= 3), “very severe” (= 4); and the level of distress / bothersomeness was scored as “not at all” (= 0.8), “a little bit” (= 1.6), “somewhat” (= 2.4), “quite a bit” (= 3.2), “very much” (=4).). Similarly, the EORTC QLQ-OH15 “extent” experienced responses were scored as follows: “not at all” (= 1), “a little bit” (= 2), “quite a bit” (= 3), “very much” (= 4).

Reliability testing: Cohen’s kappa test was used to evaluate the agreement for the presence / absence of symptoms on the OSAS on the first and second days. Intraclass correlation coefficient (ICC) analysis was used to evaluate the agreement for the frequency, severity, and degree of distress / bothersomeness of symptoms on the first and second days. The evaluation of ICC in this study was based on a single-rating (type), absolute agreement (definition), two-way mixed effects model (model) (108).

Concurrent validity testing: Spearman’s rank correlation coefficients were used to evaluate agreement between similar questions on the OSAS from day one and the EORTC QLQ-OH15 (also from day one).

3.4 RESULTS

3.4.1 Baseline demographics and characteristics of participants

Sixty-six patients were screened non-consecutively. Fifty-four patients were recruited, and 51 completed both assessments. The reasons for the three patients not completing the second assessment were one patient transitioned into the ‘deteriorating’ phase and two patients declined. Table 3-1 shows the characteristics of the recruited patients.

Characteristic	Number of participants (n=54)
Age	
Median (range)	70 years (35-93 years)
Gender	
Female	26 (48.1%)
Male	28 (51.9%)
Cancer diagnosis	
Breast	6 (11.1%)
Gastrointestinal	13 (24.1%)
Gynaecological	1 (1.9%)
Haematological	3 (5.6%)
Head and neck	4 (7.4%)
Lung	12 (22.2%)
Neurological	2 (3.7%)
Skin	1 (1.9%)
Urological	11 (20.4%)
Primary of unknown origin	1 (1.9%)
ECOG performance status (self-reported)	
0	0 (0%)
1	4 (7.4%)
2	23 (42.6)
3	26 (48.1%)
4	1 (1.9%)

Table 3-1: Characteristics of participants.

3.4.2 OSAS data

Fifty three patients (98.1%) reported at least one oral symptom on the OSAS, and the median number of oral symptoms was four (range 1-12). Table 3-2 shows the prevalence of oral symptoms and the level of distress associated with these symptoms. Dry mouth was the most common symptom (77.8% / 42/54), with 57.1% (24/42) reporting that it occurred “frequently” or “almost constantly”, 83.4% (35/42) reporting that it was “moderate”, “severe” or “very severe”, and 40.5% (17/42) reporting that the distress it caused was “quite a bit” or “very much”. Tables 3-3 and 3-4 demonstrate the frequency and severity of these symptoms.

The median time to complete the OSAS was 5.15 minutes (range 2.24-14.35 minutes).

SYMPTOM	NUMBER PATIENTS (n = 54)	AMOUNT OF DISTRESS / BOTHERSOMENESS				
		Not at all	A little bit	Somewhat	Quite a bit	Very much
Dry mouth	42 (77.8%)	6 (14.3%)	12 (28.6%)	7 (16.7%)	12 (28.6%)	5 (11.9%)
Mouth discomfort/pain	17 (31.5%)	2 (11.8%)	2 (11.8%)	6 (35.3%)	3 (17.6%)	4 (23.5%)
Lip discomfort	24 (44.4%)	7 (29.2%)	6 (25%)	6 (25%)	3 (12.5%)	2 (8.3%)
Cracking of lips	15 (27.8%)	4 (26.7%)	4 (26.7%)	2 (13.3%)	4 (26.7%)	1 (6.7%)
Cracking of corner of mouth	14 (25.9%)	3 (21.4%)	3 (21.4%)	3 (21.4%)	5 (35.7%)	0 (0%)
Taste disturbance	21 (38.9%)	3 (14.3%)	7 (33.3%)	3 (14.3%)	5 (23.8%)	3 (14.3%)
Difficulty chewing	18 (33.3%)	2 (11.1%)	3 (16.7%)	1 (5.6%)	7 (38.9%)	5 (27.8%)
Difficulty swallowing	15 (27.8%)	3 (20%)	2 (13.3%)	4 (26.7%)	2 (13.3%)	4 (26.7%)
Difficulty speaking	17 (31.5%)	1 (5.9%)	8 (47.1%)	2 (11.8%)	4 (23.5%)	2 (11.8%)
“Dirty mouth”	25 (46.3%)	1 (4%)	8 (32%)	6 (24%)	4 (16%)	6 (24%)
Coating of tongue	17 (31.5%)	5 (29.4%)	3 (17.6%)	2 (11.8%)	3 (17.6%)	4 (23.5%)
Bad breath	7 (13%)	2 (28.6%)	1 (14.3%)	0 (0%)	3 (42.9%)	1 (14.3%)
Toothache / pain in teeth	5 (9.3%)	0 (0%)	1 (20%)	1 (20%)	3 (60%)	0 (0%)
Sensitivity of teeth	6 (11.1%)	0 (0%)	3 (50%)	2 (33.3%)	1 (16.7%)	0 (0%)
Jagged teeth	12 (22.2%)	5 (41.7%)	3 (25%)	1 (8.3%)	2 (16.7%)	1 (8.3%)
Denture fitting problems	2 (3.7%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)
Bleeding from mouth	1 (1.9%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Burning sensation in mouth	7 (13%)	3 (42.9%)	1 (14.3%)	2 (28.6%)	0 (0%)	1 (14.3%)
Altered sensation in mouth	3 (5.6%)	1 (33.3%)	0 (0%)	1 (33.3%)	1 (33.3%)	0 (0%)
Ulcers in mouth	3 (5.6%)	1 (33.3%)	0 (0%)	1 (33.3%)	0 (0%)	1 (33.3%)

Table 3-2: Amount of distress caused by oral symptoms on the OSAS.

SYMPTOM	NUMBER OF PATIENTS n = 54	FREQUENCY			
		Rarely	Occasionally	Frequently	Almost constantly
Dry mouth	42 (77.8%)	7 (16.7%)	11 (26.2%)	10 (23.8%)	14 (33.3%)
Mouth discomfort/pain	17 (31.5%)	2 (11.8%)	3 (17.6%)	8 (47.1%)	4 (23.5%)
Lip discomfort	24 (44.4%)	9 (37.5%)	5 (20.8%)	5 (20.8%)	5 (20.8%)
Cracking of lips	15 (27.8%)	4 (26.7%)	4 (26.7%)	4 (26.7%)	3 (20%)
Cracking of corner of mouth	14 (25.9%)	3 (21.4%)	3 (21.4%)	3 (21.4%)	5 (35.7%)
Taste disturbance	21 (38.9%)	6 (28.6%)	2 (9.5%)	5 (23.8%)	8 (38.1%)
Difficulty chewing	18 (33.3%)	2 (11.1%)	4 (22.2%)	3 (16.7%)	9 (50%)
Difficulty swallowing	15 (27.8%)	6 (40%)	4 (26.7%)	1 (6.7%)	4 (26.7%)
Difficulty speaking	17 (31.5%)	4 (23.5%)	7 (41.2%)	4 (23.5%)	2 (11.8%)
“Dirty mouth”	25 (46.3%)	5 (20%)	7 (28%)	7 (28%)	6 (24%)
Coating of tongue	17 (31.5%)	5 (29.4%)	1 (5.9%)	3 (17.6%)	8 (47.1%)
Bad breath	7 (13%)	0 (0%)	2 (28.6%)	2 (28.6%)	3 (42.9%)
Toothache/pain in teeth	5 (9.3%)	1 (20%)	2 (40%)	1 (20%)	1 (20%)
Sensitivity of teeth	6 (11.1%)	4 (66.7%)	0 (0%)	1 (16.7%)	1 (16.7%)
Jagged teeth	12 (22.2%)	1 (8.3%)	3 (25%)	1 (8.3%)	7 (58.3%)
Denture fitting problems	2 (3.7%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
Bleeding from mouth	1 (1.9%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Burning sensation in mouth	7 (13%)	4 (57.1%)	1 (14.3%)	1 (14.3%)	1 (14.3%)
Altered sensation in mouth	3 (5.6%)	0 (0%)	1 (33.3%)	2 (66.7%)	0 (0%)
Ulcers in mouth	3 (5.6%)	1 (33.3%)	0 (0%)	0 (0%)	2 (66.7%)

Table 3-3: Frequency of oral symptoms on the OSAS.

SYMPTOM	NUMBER OF PATIENTS n = 54	SEVERITY			
		Slight	Moderate	Severe	Very severe
Dry mouth	42 (77.8%)	7 (16.7%)	16 (38.1%)	12 (28.6%)	7 (16.7%)
Mouth discomfort / pain	17 (31.5%)	3 (17.6%)	9 (52.9%)	4 (23.5%)	1 (5.9%)
Lip discomfort	24 (44.4%)	10 (41.7%)	7 (29.2%)	6 (25%)	1 (4.2%)
Cracking of lips	15 (27.8%)	3 (20%)	5 (33.3%)	7 (46.7%)	0 (0%)
Cracking of corner of mouth	14 (25.9%)	4 (28.6%)	3 (21.4%)	6 (42.9%)	1 (7.1%)
Taste disturbance	21 (38.9%)	3 (14.3%)	8 (38.1%)	7 (33.3%)	3 (14.3%)
Difficulty chewing	18 (33.3%)	2 (11.1%)	7 (38.9%)	5 (27.8%)	4 (22.2%)
Difficulty swallowing	15 (27.8%)	6 (40%)	3 (20%)	4 (26.7%)	2 (13.3%)
Difficulty speaking	17 (31.5%)	6 (35.3%)	8 (47.1%)	3 (17.6%)	0 (0%)
“Dirty mouth”	25 (46.3%)	5 (20%)	9 (36%)	7 (28%)	4 (16%)
Coating of tongue	17 (31.5%)	4 (23.5%)	5 (29.4%)	3 (17.6%)	5 (29.4%)
Bad breath	7 (13%)	1 (14.3%)	4 (57.1%)	0 (0%)	2 (28.6%)
Toothache / pain in teeth	5 (9.3)	1 (20)	4 (80)	0 (0)	0 (0)
Sensitivity of teeth	6 (11.1)	3 (50)	2 (33.3)	0 (0)	1 (16.7)
Jagged teeth	12 (22.2)	4 (33.3)	7 (58.3)	0 (0)	1 (8.3)
Denture fitting problems	2 (3.7)	0 (0)	0 (0)	2 (100)	0 (0)
Bleeding from mouth	1 (1.9)	1 (100)	0 (0)	0 (0)	0 (0)
Burning sensation in mouth	7 (13)	3 (42.9)	2 (28.6)	0 (0)	2 (28.6)
Altered sensation in mouth	3 (5.6)	1 (33.3)	1 (33.3)	0 (0)	1 (33.3)
Ulcers in mouth	3 (5.6)	1 (33.3)	2 (66.7)	0 (0)	0 (0)

Table 3-4: Severity of oral symptoms on the OSAS.

3.4.3 EORTC data

Table 3-5 shows the extent of the oral symptoms / problems experienced by the patients on the EORTC QLC-OH15. The data from the EORTC QLQ-C30 is reported in Table 3-6, 3-7, 3-8. Dry mouth was reported by 75.9% (41/54) i.e. participants reported “a little”, “quite a bit” or “very much” to the dry mouth question. This is similar to the OSAS data. 14 patients reported problems with ill-fitting dentures, although only 2 patients reported “denture fitting problems” on the OSAS. The reason for this difference is unclear.

SYMPTOM	"EXTENT TO WHICH YOU HAVE EXPERIENCED"			
	Not at all	A little	Quite a bit	Very much
Have you had pain in your gums?	46 (85.2%)	4 (7.4%)	4 (7.4%)	0 (0%)
Have you had problems with bleeding gums?	52 (96.3%)	2 (3.7%)	0 (0%)	0 (0%)
Have you had lip sores?	44 (81.5%)	5 (9.3%)	2 (3.7%)	3 (5.6%)
Have you had problems with your teeth?	48 (88.9%)	2 (3.7%)	2 (3.7%)	2 (3.7%)
Have you had soreness in your mouth?	37 (68.5%)	10 (18.5%)	4 (7.4%)	3 (5.6%)
Have you had sores in the corners of your mouth?	44 (81.5%)	4 (7.4%)	2 (3.7%)	4 (7.4%)
Have you had a dry mouth?	13 (24.1%)	12 (22.2%)	10 (18.5%)	19 (35.2%)
Have you had sticky saliva?	29 (53.7%)	9 (16.7%)	9 (16.7%)	7 (13%)
Has your mouth been sensitive to food and drink?	31 (57.4%)	9 (16.7%)	7 (13%)	7 (13%)
Have food and drink tasted different than usual?	34 (63%)	8 (14.8%)	5 (9.3%)	7 (13%)
Have you had problems with eating solid foods?	23 (42.6%)	12 (22.2%)	7 (13%)	12 (22.2%)
Have you had problems with an ill-fitting denture? (n = 14)	11 (78.6%)	0 (0%)	0 (0%)	3 (21.4%)

Table 3-5: "Extent" oral symptoms experienced on the EORTC QLQ-OH15.

n=54	Not at all	A little bit	Quite a bit	Very much
Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	5 (9.3%)	5 (9.3%)	9 (16.7%)	35 (64.8%)
Do you have any trouble taking a long walk?	5 (9.3%)	7 (13%)	5 (9.3%)	37 (68.5%)
Do you have any trouble taking a short walk outside of the house?	20 (37%)	7 (13%)	7 (13%)	20 (37%)
Do you need to stay in bed or a chair during the day?	6 (11.1%)	11 (20.4%)	8 (14.8%)	29 (53.7%)
Do you need help with eating, dressing, washing yourself or using the toilet?	24 (44.4%)	10 (18.5%)	8 (14.8%)	12 (22.2%)

Table 3-6: EORTC QLQ-C30 results.

During the past week:

n=54	Not at all	A little bit	Quite a bit	Very much
Were you limited in doing either your work or other daily activities?	11 (20.4%)	13 (24.1%)	12 (22.2%)	18 (33.3%)
Were you limited in pursuing your hobbies or other leisure time activities?	15 (27.8%)	8 (14.8%)	13 (24.1%)	18 (33.3%)
Were you short of breath?	24 (44.4%)	14 (25.9%)	10 (18.5%)	6 (11.1%)
Have you had pain?	13 (24.1%)	5 (9.3%)	13 (24.1%)	23 (42.6%)
Did you need to rest?	0 (0%)	9 (16.7%)	24 (44.4%)	21 (38.9%)
Have you had trouble sleeping?	19 (35.2%)	11 (20.4%)	12 (22.2%)	12 (22.2%)
Have you felt weak?	18 (33.3%)	11 (20.4%)	11 (20.4%)	14 (25.9%)
Have you lacked appetite?	24 (44.4%)	11 (20.4%)	9 (16.7%)	10 (18.5%)
Have you felt nauseated?	28 (51.9%)	11 (20.4%)	9 (16.7%)	6 (11.1%)
Have you vomited?	37 (68.5%)	11 (20.4%)	3 (5.6%)	3 (5.6%)
Have you been constipated?	18 (33.3%)	14 (25.9%)	12 (22.2%)	10 (18.5%)
Have you had diarrhea?	29 (53.7%)	11 (20.4%)	5 (9.3%)	9 (16.7%)
Were you tired?	2 (3.7%)	12 (22.2%)	18 (33.3%)	22 (40.7%)
Did pain interfere with your daily activities?	20 (37%)	6 (11.1%)	13 (24.1%)	15 (27.8%)
Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	16 (29.6%)	11 (20.4%)	15 (27.8%)	12 (22.2%)
Did you feel tense?	26 (48.1%)	10 (18.5%)	13 (24.1%)	5 (9.3%)
Did you worry?	16 (29.6%)	10 (18.5%)	16 (29.6%)	12 (22.2%)
Did you feel irritable?	27 (50%)	10 (18.5%)	12 (22.2%)	5 (9.3%)
Did you feel depressed?	31 (57.4%)	13 (24.1%)	8 (14.8%)	2 (3.7%)
Have you had difficulty remembering things?	21 (38.9%)	18 (33.3%)	12 (22.2%)	3 (5.6%)
Has your physical condition or medical treatment interfered with your family life?	14 (25.9%)	9 (16.7%)	16 (29.6%)	15 (27.8%)
Has your physical condition or medical treatment interfered with your social activities?	11 (20.4%)	9 (16.7%)	10 (18.5%)	24 (44.4%)
Has your physical condition or medical treatment caused you financial difficulties?	39 (72.2%)	7 (13%)	3 (5.6%)	5 (9.3%)

Table 3-7: EORTC QLQ-C30 results continued.

n=54	1 (very poor)	2	3	4	5	6	7 (excellent)
How would you rate your overall health during the past week?	7 (13%)	15 (27.8%)	7 (13%)	13 (24.1%)	7 (13%)	4 (7.4%)	1 (1.9%)
How would you rate your overall quality of life during the past week?	5 (9.3%)	8 (14.8%)	10 (18.5%)	15 (27.8%)	7 (13%)	4 (7.4%)	5 (9.3%)

Table 3-8: EORTC QLQ-C30 results continued.

3.4.4 Criterion validation

Table 3-9 shows the correlations between the scores derived from the EORTC QLQ-OH15 and the scores derived from the OSAS for the seven analogous questions. There was a very strong correlation between the extent of “soreness in your mouth” experienced on the EORTC QLQ-OH15 and the frequency of “mouth discomfort / pain” ($n = 17$; $r_s = .830$, $P = <.001$) on the OSAS (with a strong correlation with the distress caused: $r_s = .689$; $P = .002$, but a weak correlation with the severity $r_s = .294$; $P = .251$). Similarly, there was a strong correlation between the extent “dry mouth” experienced on the EORTC QLQ-OH15 and the frequency of “dry mouth” ($n = 42$; $r_s = .643$; $P = <.001$) on the OSAS (with a moderate correlation with the distress caused ($r_s = .481$; $P = .001$) and the severity $r_s = .522$; $P = <.001$). It was not possible to determine any correlation for denture fitting problems, or bleeding from the mouth, due to limited number of patients with these oral problems.

EORTC symptom / problem	OSAS symptom			
	Prevalence	Frequency	Severity	Amount of distress / bothersomeness
'Have you had a dry mouth?'	"Dry mouth" (n=42)	$r_s = .643$ ($P = <.001$)	$r_s = .522$ ($P = <.001$)	$r_s = .481$ ($P = .001$)
'Have you had soreness in your mouth?'	"Mouth discomfort/pain" (n=17)	$r_s = .830$ ($P = <.001$)	$r_s = .294$ ($P = .251$)	$r_s = .689$ ($P = .002$)
'Have you had lip sores?'	"Lip discomfort" (n=24)	$r_s = .590$ ($P = .002$)	$r_s = .447$ ($P = .028$)	$r_s = .378$ ($P = .068$)
'Have you had lip sores?'	"Cracking of lips" (n=15)	$r_s = .534$ ($P = .040$)	$r_s = .642$ ($P = .010$)	$r_s = .056$ ($P = .842$)
'Have you had sores in the corners of your mouth?'	"Cracking of corner of mouth" (n=14)	$r_s = .585$ ($P = .028$)	$r_s = .304$ ($P = .291$)	$r_s = .652$ ($P = .012$)
'Have food and drink tasted different than usual?'	"Taste disturbance" (n=21)	$r_s = .312$ ($P = .169$)	$r_s = .411$ ($P = .064$)	$r_s = .528$ ($P = .014$)
'Have you had problems eating solid foods?'	"Difficulty chewing" (n=18)	$r_s = .311$ ($P = .209$)	$r_s = .214$ ($P = .394$)	$r_s = .287$ ($P = .248$)

Table 3-9: Correlation between responses to analogous questions on the EORTC QLQ-C30 and the OSAS.

r_s = Spearman's rank correlation coefficient ; r_s of .00-.19 is considered "very weak", .20-.39 is "weak", .40-.59 is "moderate", .60-.79 is "strong", and .80-1.0 is "very strong"
(109)

3.4.5 Test-retest reliability

Table 3-10 shows the data relating to test-retest reliability of the OSAS. In terms of the presence of symptoms, “difficulty chewing” showed almost perfect agreement ($n = 17$; $\kappa = 0.914$; $P = <.001$), whilst 12 other symptoms showed substantial agreement, and six symptoms showed moderate agreement. It was not possible to assess “bleeding from the mouth” due to limited number of patients with this symptom ($n = 1$). “Ulcers in mouth” ($n=2$; $ICC = 1$) and “denture fitting problems” ($n=2$; $ICC = 1$) showed excellent reliability in the bothersomeness domain: two other symptoms showed excellent reliability, six good reliability, six moderate reliability, and four poor reliability (with no values calculable for two problems due to limited number of patients with these symptoms).

SYMPTOM	Cohen's Kappa (κ)	Intraclass correlation coefficient (ICC)		
	Presence [51]	Frequency	Severity	Bothersomeness
Dry mouth (n = 35)	$\kappa = 0.564$ ($P = <.001$)	ICC = 0.425 [95% CI: 0.113-0.661]	ICC = 0.503 [95% CI: 0.203-0.715]	ICC = 0.279 [95% CI: -0.064-0.560]
Mouth discomfort/pain (n = 13)	$\kappa = 0.647$ ($P = <.001$)	ICC = 0.576 [95% CI: 0.069-0.848]	ICC = 0.276 [95% CI: -0.214-0.688]	ICC = 0.536 [95% CI: 0.046-0.827]
Lip discomfort (n=16)	$\kappa = 0.598$ ($P = <.001$)	ICC = 0.791 [95% CI: 0.508-0.921]	ICC = 0.127 [95% CI: -0.412-0.583]	ICC = 0.242 [95% CI: -0.242-0.651]
Cracking of lips (n=11)	$\kappa = 0.622$ ($P = <.001$)	ICC = 0.739 [95% CI: 0.265-0.923]	ICC = 0.185 [96% CI: -0.271-0.651]	ICC = 0.713 [95% CI: 0.210-0.915]
Cracking of corner of mouth (n=11)	$\kappa = 0.622$ ($P = <.001$)	ICC = 0.704 [95% CI: 0.192-0.912]	ICC = 0.294 [95% CI: -0.378-0.749]	ICC = 0.638 [95% CI: 0.094-0.888]
Taste disturbance (n=14)	$\kappa = 0.620$ ($P = <.001$)	ICC = 0.684 [95% CI: 0.260-0.887]	ICC = 0.387 [95% CI: -0.182-0.755]	ICC = 0.604 [95% CI: 0.159-0.851]
Difficulty chewing (n=17)	$\kappa = 0.914$ ($P = <.001$)	ICC = 0.509 [95% CI: 0.068-0.787]	ICC = 0.509 [95% CI: 0.078-0.786]	ICC = 0.233 [95% CI: -0.206-0.618]
Difficulty swallowing (n=11)	$\kappa = 0.705$ ($P = <.001$)	ICC = 0.543 [95% CI: -0.070-0.854]	ICC = 0.882 [95% CI: 0.627-0.967]	ICC = 0.751 [95% CI: 0.291-0.927]
Difficulty speaking (n=10)	$\kappa = 0.528$ ($P = <.001$)	ICC = 0.591 [95% CI: -0.027-0.880]	ICC = 0.679 [95% CI: 0.144-0.909]	ICC = 0.897 [95% CI: 0.649-0.973]
"Dirty mouth" (n=16)	$\kappa = 0.559$ ($P = <.001$)	ICC = 0.368 [95% CI: -0.081-0.711]	ICC = 0.363 [95% CI: -0.164-0.723]	ICC = 0.739 [95% CI: 0.410-0.900]
Coating of tongue (n=14)	$\kappa = 0.735$ ($P = <.001$)	ICC = 0.307 [95% CI: -0.267-0.713]	ICC = 0.761 [95% CI: 0.407-0.916]	ICC = 0.888 [95% CI: 0.693-0.962]
Bad breath (n=6)	$\kappa = 0.766$ ($P = <.001$)	ICC = 0.898 [95% CI: 0.513-0.985]	ICC = 0.706 [95% CI: -0.019-0.952]	ICC = 0.536 [95% CI: -0.295-0.917]
Toothache/pain in teeth (n=4)	$\kappa = 0.778$ ($P = <.001$)	ICC = 0.889 [95% CI: 0.260-0.992]	ICC = 0.250 [95% CI: -0.363-0.907]	ICC = -.235 [95% CI: -1.598-0.864]

Sensitivity of teeth (n=5)	$\kappa = 0.670$ ($P = <.001$)	ICC = 0.806 [95% CI: -0.019-0.978]	ICC= 0.000 [95% CI: -1.272-0.843]	ICC = 0.824 [95% CI: 0.040-0.980]
Jagged teeth (n=8)	$\kappa = 0.652$ ($P = <.001$)	ICC = 0.234 [95% CI -0.551-0.783]	ICC = 0.887 [95% CI: 0.527-0.976]	ICC = 0.767 [95% CI: 0.263-0.947]
Denture fitting problems (n=2)	$\kappa = 0.790$ ($P = <.001$)	ICC = 0.000 [95% CI: -0.997-0.997]	ICC = 0.000 [95% CI : -0.997-0.997]	ICC = 1 [95% CI: -]
Burning sensation in mouth (n=3)	$\kappa = 0.558$ ($P = <.001$)	ICC = 1 [95% CI: -]	ICC = 0.833 [95% CI: -0.100-0.995]	ICC = 0.783 [95% CI: -0.154-0.993]
Altered sensation in mouth (n=2)	$\kappa = 0.646$ ($P = <.001$)	ICC = 0.800 [95% CI: -0.631-1]	ICC = -4.00 [95% CI: -9.000-0.967]	*Part of the scale showed zero variance
Ulcers in mouth (n=2)	$\kappa = 0.541$ ($P = <.001$)	ICC = 0.000 [95% CI: -0.997-0.997]	ICC = 0.000 [95% CI: -0.111-0.985]	ICC = 1 [95% CI: -]

Table 3-10: Test-retest reliability of the OSAS.

Cohen's kappa values of .41-.60 are considered "moderate", .61-.80 are considered "substantial", and .81-1.0 are considered "almost perfect" (110, 111).

ICC values <0.5 are considered to indicate "poor" reliability, values between 0.5-0.75 "moderate" reliability, values between 0.75- 0.9 "good" reliability, and values >0.9 "excellent" reliability.

3.5 DISCUSSION

The scoping review of the literature, as outlined in Chapter 2, identified a lack of validated oral symptom assessment tools in patients with advanced cancer. Thus, there was no gold standard to compare against the OSAS. The EORTC QLQ-OH15 is an adjunct to the EORTC QLQ-C30, and was developed to assess the impact of oral health problems on quality of life in patients with cancer (but not specifically patients with advanced cancer). However, the EORTC QLQ-OH15 has been extensively validated, and so we decided to use this tool to further validate the OSAS.

The validity of an instrument is the degree to which it measures what it claims to measure (112). Criterion (or concurrent) validity demonstrates evidence of the extent “to which scores of the instrument are related to a criterion measure” (112). The study data suggests at least moderate agreement between analogous questions on the OSAS and the EORTC QLQ-OH15. There was a weak correlation between the questions “difficulty chewing” (OSAS) and “problems eating solid foods” (EORTC QLQ-OH15), and this undoubtedly reflects that “problems eating solid foods” is often related to other oral symptoms, e.g. xerostomia, mouth discomfort. Indeed, the correlation between the EORTC QLQ-OH15 and the OSAS varied across the various domains, and there was no obvious pattern to the variation. Thus, the correlation was strongest with frequency for dry mouth, but strongest with bothersomeness for taste disturbance.

The EORTC QLQ-OH15 states: “Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week” (with the options being “not at all”, “a little”, “quite a bit”, and “very much”). However, it is unclear what is the meaning of the phrase “the extent” of the symptoms experienced – there is no guidance within this tool (or indeed the other EORTC tools that utilise this phrase). Does it relate to the severity of the problem or the degree of distress caused by the problem? In contrast, the OSAS is simple to interpret.

The reliability of an instrument is the extent to which it yields scores that are stable over time in “respondents who are assumed not to have changed” (112). The test-retest results for the presence of symptoms were good, with one symptom (“difficulty chewing”) having “almost perfect” agreement ($n = 17$; $\kappa = 0.914$; $P = <.001$), 12 symptoms having “substantial” agreement, and six symptoms having “moderate” agreement. However, the test-retest results

for the symptom domains (i.e. frequency, severity, and amount of distress / bothersomeness) were not quite as good. Nevertheless, in terms of amount of distress / bothersomeness, two symptoms showed “excellent” reliability, six showed “good” reliability, and four “moderate” reliability. It should be noted that the analysis was looking for absolute agreement, whilst many of the responses differed by a single category / point between the two test periods (e.g. a symptom’s severity rated as moderate on one day, and severe on another day).

The OSAS was modelled on the Memorial Symptom Assessment Scale (73), and importantly assesses the amount of distress or bothersomeness of the relevant oral symptoms. The latter is important since this is the domain most closely linked to quality of life (113). Indeed, these are the symptoms that should be prioritised by healthcare professionals. However, it is important to stress that some oral problems may be asymptomatic (initially), and so the OSAS should always be accompanied by a thorough clinical (oral) examination. For example, oral candidosis is frequently asymptomatic, even when the infection is widespread.

3.6 CONCLUSION

This study supports the validity of the OSAS, and provides evidence for the reliability of this novel oral symptom assessment tool, in patients with advanced cancer. Further research is needed to corroborate the findings of this study, and such research is being undertaken within the Academic Department of Palliative Medicine.

CHAPTER 4 ORAL SYMPTOM ASSESSMENT IN OLDER PATIENTS WITH FRAILTY USING THE ORAL SYMPTOM ASSESSMENT SCALE

4.1 INTRODUCTION

This prospective observational study evaluated oral symptoms in a cohort of older patients with frailty using a slightly modified version of the OSAS.

4.2 FRAILTY IN OLDER PATIENTS

The structure of the population of high- and middle-income countries across the world is undergoing a 'demographic shift' (30) as a consequence of both a decline in birth rates and an increase in life expectancy. Thus, older people account for an increasing proportion of the population of these countries (45). This structural shift has major implications for healthcare systems which must adapt to address their ageing populations' changing needs like frailty (114). Frailty is a common condition/syndrome in older people. A recent metanalysis of frailty prevalence in European countries (115) identified an estimated pooled prevalence across all settings (hospital inpatients, long-term care, primary care, and out-patient settings) of 18% (95% CI 15-21%; 68 datasets; 13 932 individuals; $P < 0.001$). This increases to over 25% in people aged over 85 years (116, 117). It is regarded as a "state of vulnerability" (118) that results in a "multi-system reduction in reserve capacity" (119) in which even a minor stressor may result in adverse health outcomes (10), need for long-term care (120) and mortality (121) independently of chronological age (119). Because frailty is "a dynamic process that changes over time" (118), a person may transition back and forth between the various frailty states (i.e. non-frail, pre-frail and frail – see Figure 4-1). Thus, regular screening and identification may potentially facilitate reversibility of frailty with a targeted intervention (119).

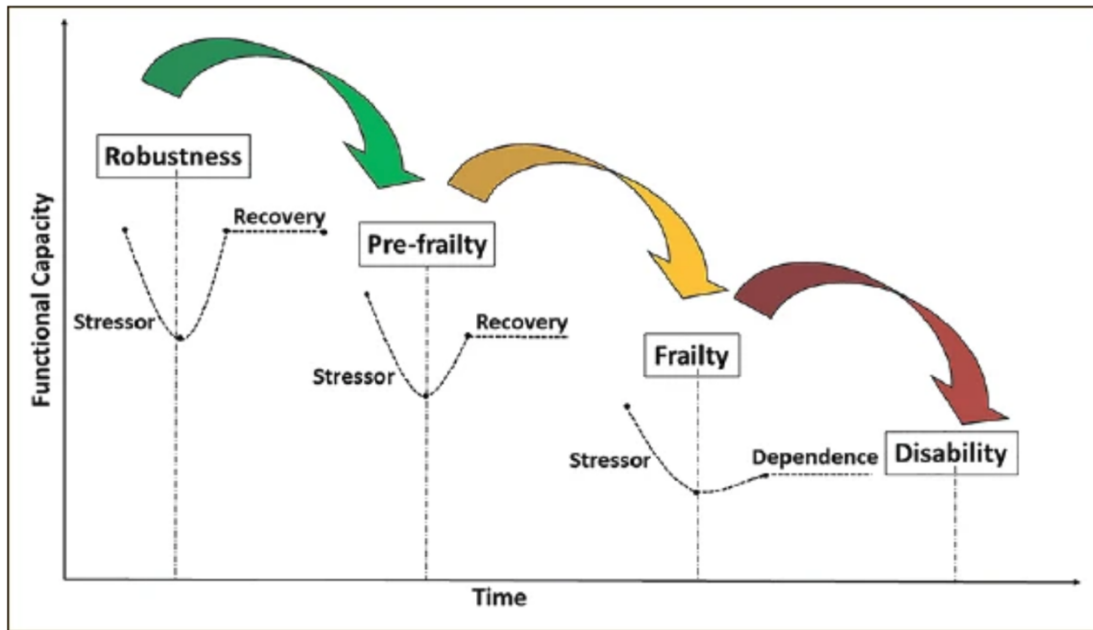


Figure 4-1: The cascade of functional decline in older adults from independence, through to frailty and disability (in the absence of intervention). Reprinted from Dent et al (111) and made available under Creative Commons Attribution 4.0 License.

4.2.1 Screening for frailty in older patients

An International Conference of Frailty and Sarcopenia Research (ICFSR) task force recommended that “all adults aged 65 years and over should be offered screening for frailty using a validated rapid frailty instrument suitable to the specific setting or context” (116). Amongst the screening tools endorsed by this task force was the Clinical Frailty Scale/CFS (see Figure 4-2). Furthermore, it has been recommended by the International Consortium for Health Outcomes Measurement (122) as part of its standard set of outcome measurements for studies of older people. The CFS (123) comprises a visual chart with nine graded illustrations with corresponding text describing frailty scores. The scoring involves the evaluation of domains including cognition, function, and co-morbidity (see Figure 4-3). The baseline of the patient in the two weeks prior to the acute presentation should form the basis of the score as opposed to the immediate presentation. The cut-off point for “frailty” is ≥ 5 (see Figure 4-2).

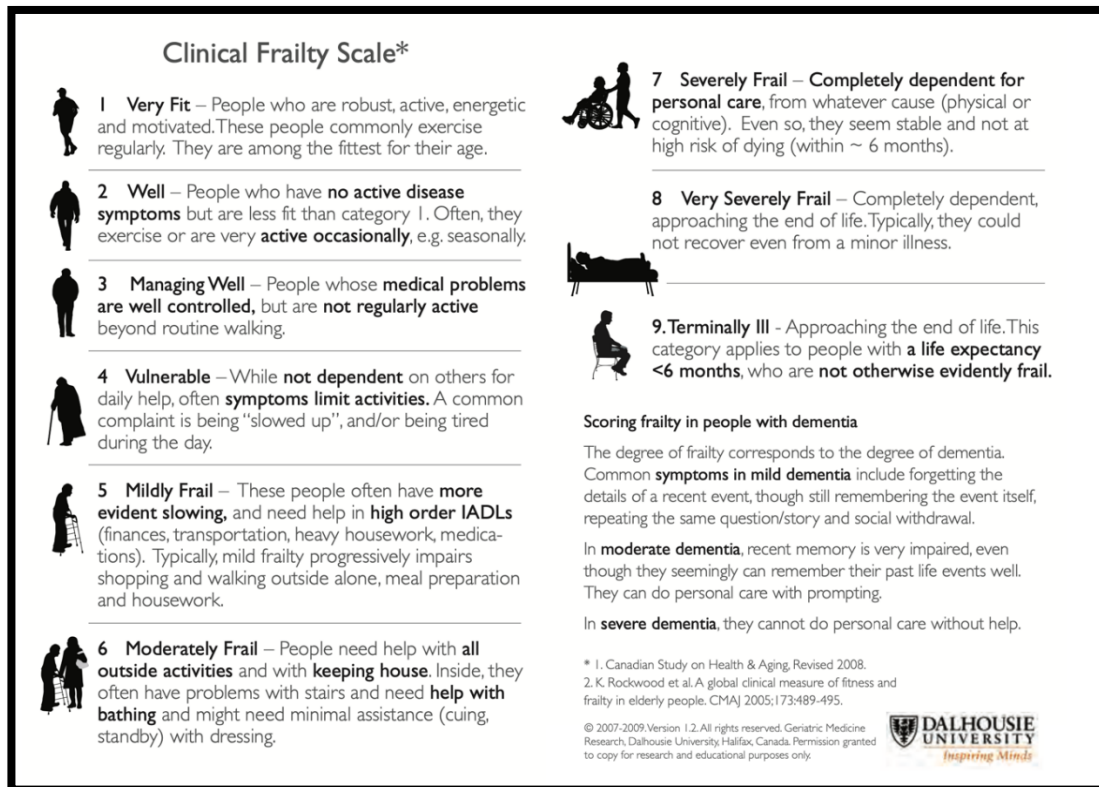


Figure 4-2: Clinical Frailty Scale from Rockwood et al (118). Permission for use granted by Dalhousie University (see Appendix 9).

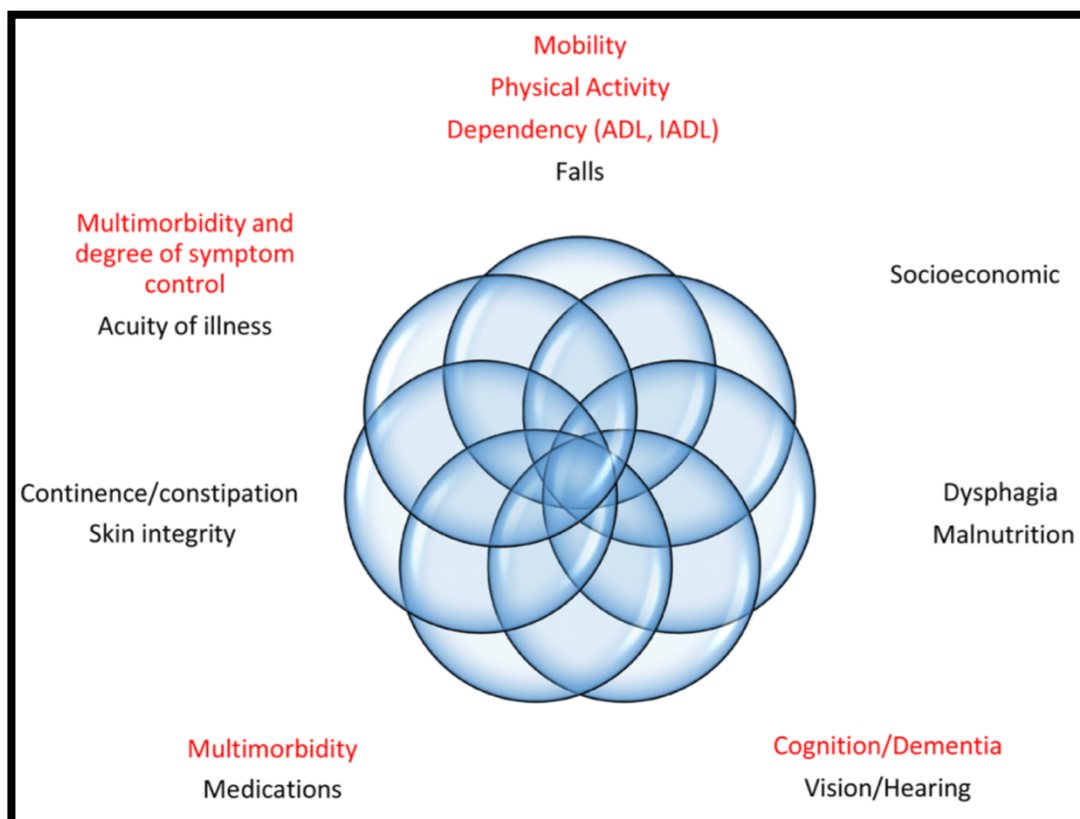


Figure 4-3: Geriatric dimensions assessed by the CFS in red. Reproduced from O'Halloran et al (113) and made available under Creative Commons Attribution 4.0 License.

A positive screening result should then prompt a thorough assessment of frailty by the multi-disciplinary team using the gold standard Comprehensive Geriatric Assessment (CGA). The CGA is a “multi-dimensional, multi-disciplinary, diagnostic and therapeutic process” (124). It comprises an assessment of the health and well-being of an older person with frailty, examining physical, psychological, social, and functional dimensions (125, 126).

4.2.2 Why assess oral symptoms in older patients with frailty?

Despite advances in dental healthcare resulting in fewer older people becoming edentulous (44), older dentate people with frailty continue to experience oral symptoms and problems as a result of the various causes (including salivary gland hypofunction and the direct (and indirect) effects of conditions as well as their treatments) discussed in Section 1.3.3. As a result, they will have a continuous requirement for preventative and restorative oral healthcare (44). Oral problems in older people may be associated with increased morbidity and mortality (20, 21) and with reduced oral health-related quality of life in particular in older people who have incremental tooth loss, dental caries, edentulism and xerostomia (30). Van der Putten et al. (44) suggest that oral health is “jeopardised” by frailty as a consequence of the sequelae of the condition/syndrome, including dietary requirements, medications and limitations to accessing professional oral/dental healthcare. These associations suggest that there may be an indirect interplay between oral problems and the various frailty domains (e.g. ill-fitting dentures causing restricted food choices and thus nutritional deficits). Hence, a comprehensive oral symptom assessment within a personalised CGA may be relevant for these patients.

Oral frailty as described in Chapter 1 is a novel frailty domain and is described as a gradual reduction in oral function accompanied by a decline in physical and cognitive functions (2, 11). As research into this novel frailty domain expands, a validated oral symptom assessment tool may be of benefit to augment its assessment and management. There appears to be no such tool currently, and oral symptoms are either not assessed, or only superficially assessed, in generic symptom assessment tools. Hence, many older patients with frailty have unrecognised oral problems despite regular contact with medical services, and when these oral problems are eventually identified, they are often advanced / chronic in nature, and therefore more difficult to manage.

Our hypothesis for this study was that oral symptoms are common in older patients with frailty, although the prevalence and clinical features of many oral symptoms has not been

reported. Furthermore, we hypothesised that the OSAS may be a useful research and/or clinical tool in examining oral symptoms in this patient cohort. Identification of oral symptoms should then trigger further assessment (to determine the aetiology of the symptom) followed by appropriate management of the symptom and underlying oral problem (including referral to dental and oral medicine specialists where necessary). Importantly, the management of oral problems in this cohort of patients may need to be adapted due to the person's frailty, and their individual needs (43).

4.2.3 Specific study objectives

- To determine the prevalence of oral symptoms in this group
- To determine the clinical features of these oral symptoms in this group (i.e. frequency, severity and level of distress)
- To determine the relationship between oral symptoms and Clinical Frailty Score / Cumulative Illness Rating Scale for Geriatrics / medications *
- To provide initial validation of OSAS in older patients with frailty *

*As recruitment for the study continues at the time of writing the focus of this research was to provide descriptive analysis for the first one hundred participants recruited.

4.3 METHODS

4.3.1 Study design and ethics committee approval

This prospective observational study was conducted at Our Lady's Hospice and Care Services in Dublin, and St James' Hospital in Dublin. The study received ethical approval from the St James' Hospital and Tallaght University Hospital Joint Research and Ethics Committee (Project ID 1935/ Submission number 2551). The study was registered on ClinicalTrials.gov (protocol ID OASIS III/ ClinicalTrials.gov trial identification number: NCT06286982).

4.3.2 Patient recruitment and criteria for study inclusion

Patient recruitment took place in the Robert Mayne Day Hospital in St James' Hospital, Dublin. This unit provides both rehabilitative and acute medical care to older persons. Recruitment at Our Lady's Hospice and Care Services, Harold's Cross, Dublin took place in Anna Gaynor House and the Community Rehabilitation Unit. The former is a residential unit for older persons located on the grounds of Our Lady's Hospice and Care Services in Harold's Cross. The latter is a short-stay in-patient unit for older persons where assessment and rehabilitation occurs in order to maintain community living. This is also located at Our Lady's Hospice and Care Services in Harold's Cross.

All patients were deemed eligible for recruitment using the following criteria:

Inclusion criteria:

- Age $\geq$ 65 years old
- Clinical Frailty Score $\geq$ 5

Exclusion criteria:

- Abbreviated Mental Test 4 (AMT4) score <4
- History of dementia
- Inability to provide informed consent
- Inability to complete the questionnaire

The AMT4 is a four-item version of the Abbreviated Mental Test Score, and is often used as an initial screening test for impaired cognition in older patients. The patient is asked their age, their date of birth, their current “place” / location and the current year, with each correct answer scoring 1, and a total score of < 4 indicating impaired cognition.

4.3.3 Consent Process

Written consent was sought from all eligible patients to participate in the study. The clinical team introduced the study to patients, and sought their permission for a further discussion with the research team. Those who agreed to further discussion then met with one of the researchers. The researcher carried out an initial screening assessment for cognitive impairment (AMT4). If the participant scored 4, then they were be provided with a patient information leaflet (Appendix 11) . Any queries the participant had were addressed by the researcher. If the participant scored < 4 , then they were excluded from the study.

If the participant agreed to participate, the consent form (Appendix 10) was signed in the presence of the researcher. It was deemed not necessary to have a 'cooling off' period, i.e. the participant could enter the study at the time of the initial approach, assuming the participant was happy to enter the study at that point in time.

4.3.4 Study procedures

Once informed consent was obtained, the participant completed a modified version of OSAS: the OSAS was only modified by the addition of the symptom of ‘drooling’. This was followed by feedback questions in relation to oral symptom assessment and the OSAS (see Figure 4-4).

Do you think it is important to ask patients about mouth problems?
Yes ☐ No ☐

Do you think the questionnaire was easy to complete?
Yes ☐ No ☐

If no, why not?

Do you think the questionnaire was quick to complete?
Yes ☐ No ☐

Do you think the questionnaire asked about all important mouth problems?
Yes ☐ No ☐

If no, why not?

Do you have any other comments about the questionnaire?

Figure 4-4: OSAS feedback questions.

The researcher also collected the following information from the participant themselves and/or their medical record:

- Demographic details - age and sex
- Medications - regular and “as required”
- Clinical Frailty Score
- Co-morbidities using the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) (127)

The Cumulative Illness Rating Scale for Geriatrics (CIRS-G) (127) is a scale designed to rate both the presence and severity of a disease in older persons. It encompasses information about both the long-term course and as well as current severity of a disease (128). It assesses co-morbidities in 14 organs or systems and rates each on a scale of 0-4. This yields a cumulative score with a maximum score of 56 (see Figure 4-5).

Scoring Sheet

CUMULATIVE ILLNESS RATING SCALE FOR GERIATRICS (CIRS-G)

Miller, Paradis, and Reynolds 1991

PATIENT _____ AGE _____

RATER _____ DATE _____

Instructions: Please refer to the CIRS-G Manual. Write brief descriptions of the medical problem(s) that justified the endorsed score on the line following each item. (Use the reverse side for more writing space).

RATING STRATEGY

0 - No Problem
 1 - Current mild problem or past significant problem
 2 - Moderate disability or morbidity/requires "first line" therapy
 3 - Severe/constant significant disability/"uncontrollable" chronic problems
 4 - Extremely Severe/immediate treatment required/end organ failure/severe impairment in function

	SCORE
<u>HEART</u>	_____
<u>VASCULAR</u>	_____
<u>HEMATOPOIETIC</u>	_____
<u>RESPIRATORY</u>	_____
<u>EYES, EARS, NOSE AND THROAT AND LARYNX</u>	_____
<u>UPPER GI</u>	_____
<u>LOWER GI</u>	_____
<u>LIVER</u>	_____
<u>RENAL</u>	_____
<u>GENITOURINARY</u>	_____
<u>MUSCULOSKELETAL/INTEGUMENT</u>	_____
<u>NEUROLOGICAL</u>	_____
<u>ENDOCRINE/METABOLIC AND BREAST</u>	_____
<u>PSYCHIATRIC ILLNESS</u>	_____
TOTAL NUMBER CATEGORIES ENDORSED	_____
TOTAL SCORE	_____
Severity Index: (total score/total number of categories endorsed)	_____
Number of categories at level 3 severity	_____
Number of categories at level 4 severity	_____

Figure 4-5 The original CIRS-G reprinted from Millar et al. (127) with permission from Professor Mark Miller.

4.3.5 Statistical analysis/considerations

A sample size of 250 patients was determined based on the sample size of the initial OSAS observational study (129). [The latter sample size calculation was based upon the fact that the developers wanted OSAS to include oral symptoms with a prevalence of at least $\geq 5\%$]. The sample size was calculated as being 250 patients (i.e. two-sided 95% confidence interval; expected proportion 5% +/- 2.7%).

As recruitment for the study is ongoing, the focus of this chapter is on a descriptive analysis of the first 100 participants recruited. Currently (as of the 29 February 2024), 110 participants have been recruited.

Statistical analysis was performed using IBM SPSS V.29 software. Descriptive statistics have been used to present the data, including counts and proportions for categorical variables and medians and ranges for continuous data.

4.4 RESULTS

4.4.1 Baseline demographics and characteristics of participants

Initial recruitment was completed between June 2023 and January 2024. One hundred participants were recruited. Table 4-1 outlines the characteristics of the participants. The median age was 81 years (range: 56- 99 years). Females accounted for 70% (70/100) of the participants. None of the participants had a CFS above 8. The median cumulative score on the CIRS-G was 12 (range: 3- 30).

Characteristics	No of participants (n = 100)
Age	
Median age (range)	81 years (65-99 years)
Gender	
Female	70 (70%)
Male	30 (30%)
Clinical Frailty Scale (CFS)	
5	57 (57%)
6	32 (32%)
7	11 (11%)
8	0 (0%)
9	0 (0%)
Cumulative Illness Rating Scale-Geriatric (CIR-G)	
Median score (range)	12 (3-30)
Regular medications	
Median number (range)	11 (3- 27)
'As required' medications	
Median number (range)	3 (0-12)

Table 4-1: Characteristics of participants.

4.4.2 Medications

The median number of regular medications was 11. One patient was prescribed 27 medications. The number of regular medications ranged from 3-27. In terms of individual oral, subcutaneous and transdermal drugs categories, proton pump inhibitor was the most common regular medication (62%, 62/100). Table 4-2 shows the regular individual drugs / classes of drugs prescribed.

Drug category	Number of participants (n=100) (%)
Proton pump inhibitor	62 (62%)
Statin	55 (55%)
Cholecalciferol (Vitamin D3)	52 (52%)
Paracetamol	40 (40%)
Conventional laxative	40 (40%)
Combination calcium/vitamin D	30 (30%)
Direct oral anticoagulant	28 (28%)
β blocker	27 (27%)
Anti-platelet agent	27 (27%)
Folic acid	27 (27%)
Loop diuretic	24 (24%)
Nutritional supplements	24 (24%)
Opioid for moderate to severe pain	23 (23%)
Mirtazepine	22 (22%)
Levothyroxine	21 (21%)
Selective Serotonin Reuptake Inhibitor (SSRI)	21 (21%)
Mirabegron	19 (19%)
Oral hypoglycaemic agent	18 (18%)
Angiotensin converting enzyme inhibitor (ACE inhibitor)	17 (17%)
Calcium channel blocker	13 (13%)
Denosumab	13 (13%)
Sinemet	13 (13%)
Benzodiazepine	12 (12%)

Selective Noradrenaline Reuptake Inhibitor (SNRI)	11 (11%)
Antimuscarinic agent	9 (9%)
Dopamine agonist e.g. ropinirole, rotigotine	9 (9%)
Pregabalin	9 (9%)
Antihistamine	8 (8%)
Ranolazine	7 (7%)
Anti-epileptic agent	6 (6%)
Atypical antipsychotic	6 (6%)
Digoxin	6 (6%)
Ezetimibe	5 (5%)
Amitriptyline	4 (4%)
Gabapentin	4 (4%)
Montelukast	4 (4%)
“Z-drug”	4 (4%)
α blocker	3 (3%)
Non-steroidal anti-inflammatory	3 (3%)
Insulin	2 (2%)
Opioid – for mild pain	2 (2%)
Thiazide diuretic	2 (2%)
Typical psychotic	2 (2%)
Spirolactone	0 (0%)
Tricyclic antidepressant	0 (0%)

Table 4-2: Regular medication drug categories.

4.4.3 OSAS results

Ninety-one participants reported at least one symptom on the 21-item OSAS (see Figure 4-6).

Two symptoms was the most frequent number of oral symptoms experienced (19%, 19/100).

The median number of oral symptoms present was 4 (range: 0–13 symptoms). Forty participants reported the “new” symptom of “drooling”.

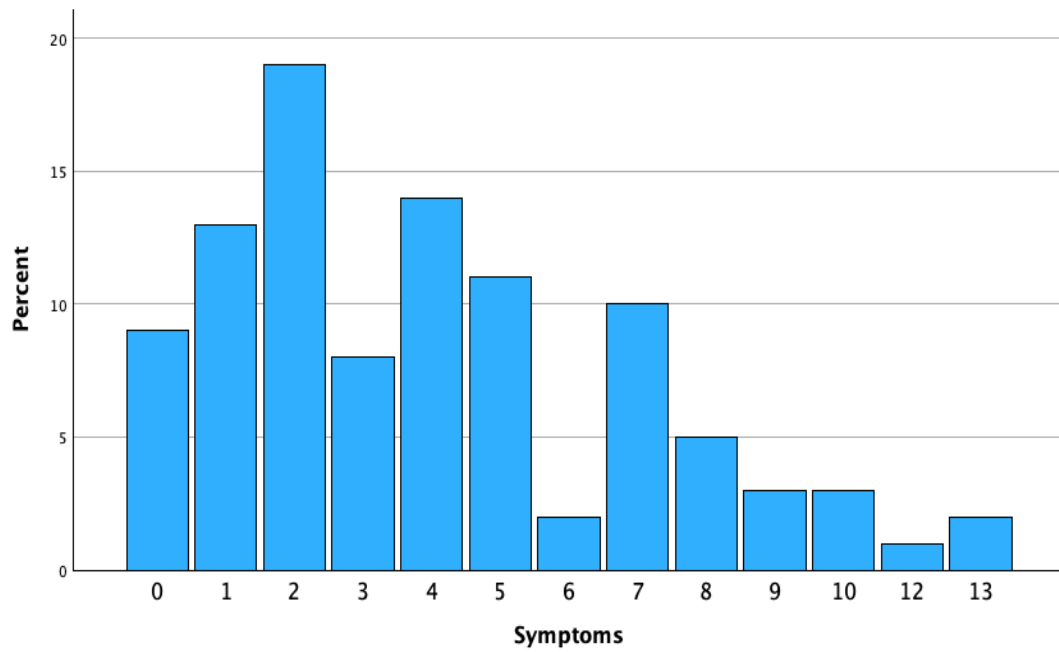


Figure 4-6: Number of oral symptoms experienced.

Tables 4-3, 4-4 and 4-5 show the frequency, severity, and “bothersomeness” of these oral symptoms respectively.

SYMPTOM	NUMBER PATIENTS (n = 100)	SYMPTOM FREQUENCY			
		“Rarely”	“Occasionally”	“Frequently”	“Almost constantly”
Dry mouth	57 (57.0%)	5 (8.8%)	10 (17.5%)	20 (35.1%)	22 (38.6%)
Mouth discomfort / pain	15 (15.0%)	5 (33.3%)	3 (20.0%)	4 (26.7%)	3 (20%)
Lip discomfort	21 (21.0%)	7 (33.3%)	5 (23.8%)	4 (19.0%)	5 (23.8%)
Cracking of lips	14 (14.0%)	2 (14.3%)	5 (35.7%)	4 (28.6%)	3 (21.4%)
Cracking of corner of mouth	22 (22.0%)	9 (40.9%)	6 (27.3%)	3 (13.6%)	4 (18.2%)
Taste disturbance	17 (17.0%)	4 (23.5%)	2 (11.8%)	3 (17.6%)	8 (47.1%)
Difficulty chewing	20 (20.0%)	4 (20.0%)	6 (30.0%)	6 (30.0%)	4 (20.0%)
Difficulty swallowing	21 (21.0%)	1 (4.8%)	9 (42.9%)	6 (28.6%)	5 (23.8%)
Difficulty speaking	22 (22.0%)	4 (18.2%)	4 (18.2%)	6 (27.3%)	8 (36.4.0%)
“Dirty mouth”	22 (22.0%)	3 (13.6%)	5 (22.7%)	11 (50.0%)	3 (13.6%)
Coating of tongue	26 (26.0%)	6 (23.1%)	12 (46.2%)	4 (15.4%)	4 (15.4%)
Bad breath	17 (17.0%)	3 (17.6%)	5 (29.4%)	5 (29.4%)	4 (23.5%)
Toothache / pain in teeth	13 (13.0%)	2 (15.4%)	6 (46.2%)	2 (15.4%)	3 (23.1%)
Sensitivity of teeth	18 (18.0%)	8 (44.4%)	4 (22.2%)	5 (27.8%)	1 (5.6%)
Jagged teeth	23 (23.0%)	3 (13.0%)	4 (17.4%)	3 (13.0%)	13 (56.5%)
Denture fitting problems	18 (18.0%)	3 (16.7%)	3 (16.7%)	3 (16.7%)	9 (50.0%)
Bleeding from mouth	6 (6.0%)	2 (33.3%)	1 (16.7%)	3 (50.0%)	0 (0%)
Burning sensation in mouth	3 (3.0%)	1 (33.3%)	0 (0%)	1 (33.3%)	1 (33.3%)
Altered sensation in mouth	1 (1.0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Ulcers in mouth	7 (7.0%)	3 (42.9%)	1 (14.3%)	2 (28.6%)	1 (14.3%)
Drooling	40 (40.0%)	10 (25.0%)	9 (22.5%)	11 (27.5%)	10 (25.0%)

Table 4-3: Frequency of oral symptoms on the OSAS.

SYMPTOM	NUMBER PATIENTS (n = 100)	SYMPTOM SEVERITY			
		“Slight”	“Moderate”	“Severe”	“Very severe”
Dry mouth	57 (57.0%)	5 (8.8%)	31 (54.4%)	15 (26.3%)	6 (10.5%)
Mouth discomfort / pain	15 (15.0%)	3 (20.0%)	8 (53.3%)	3 (1%)	1 (6.7%)
Lip discomfort	21 (21.0%)	6 (28.6%)	10 (47.6%)	3 (14.3%)	2 (9.5%)
Cracking of lips	14 (14.0%)	5 (35.7%)	7 (50.0%)	2 (14.3%)	0 (0%)
Cracking of corner of mouth	22 (22.0%)	8 (36.4%)	8 (36.4%)	4 (18.2%)	2 (9.1%)
Taste disturbance	17 (17.0%)	6 (35.3%)	7 (41.2%)	4 (23.5%)	0 (0%)
Difficulty chewing	20 (20.0%)	6 (30.0%)	8 (70.0%)	5 (25.0%)	1 (5.0%)
Difficulty swallowing	21 (21.0%)	3 (14.3%)	13 (61.9%)	4 (19.0%)	1 (4.8%)
Difficulty speaking	22 (22.0%)	6 (27.3%)	11 (50.0%)	5 (22.7%)	0 (0%)
“Dirty mouth”	22 (22.0%)	1 (4.5%)	16 (72.7%)	5 (22.7%)	0 (0%)
Coating of tongue	26 (26.0%)	12 (46.2%)	11 (42.3.0%)	3 (11.5%)	0 (0%)
Bad breath	17 (17.0%)	3 (17.6%)	12 (70.6%)	2 (11.8%)	0 (0%)
Toothache / pain in teeth	13 (13.0%)	5 (38.5%)	5 (38.5%)	3 (23.1%)	0 (0%)
Sensitivity of teeth	18 (18.0%)	4 (22.2%)	12 (66.7%)	2 (11.1%)	0 (0%)
Jagged teeth	23 (23.0%)	11 (47.8%)	6 (26.1%)	4 (17.4%)	2 (8.7%)
Denture fitting problems	18 (18.0%)	4 (22.2%)	7 (38.9%)	6 (33.3%)	1 (5.6%)
Bleeding from mouth	6 (6.0%)	1 (16.7%)	4 (66.7%)	1 (16.7%)	0 (0%)
Burning sensation in mouth	3 (3.0%)	1 (33.3%)	1 (33.3%)	1 (33.3%)	0 (0%)
Altered sensation in mouth	1 (1.0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
Ulcers in mouth	7 (7.0%)	4 (57.1%)	2 (28.6%)	1 (14.3%)	0 (0%)
Drooling	40 (40.0%)	13 (32.5%)	21 (52.5%)	5 (12.5%)	1 (2.5%)

Table 4-4: Severity of oral symptoms on the OSAS.

SYMPTOM	NUMBER PATIENTS (n = 100)	AMOUNT OF DISTRESS / BOTHERSOMENESS				
		“Not at all”	“A little bit”	“Somewhat”	“Quite a bit”	“Very much”
Dry mouth	57 (57.0%)	11 (19.3%)	19 (33.3%)	7 (12 .3%)	12 (21.1%)	8 (14.0%)
Mouth discomfort / pain	15 (15.0%)	2 (13.3%)	4 (26.7%)	2 (13.3%)	5 (33.3%)	2 (13.3%)
Lip discomfort	21 (21.0%)	5 (23.8%)	7 (33.3%)	3 (14.3%)	4 (19.0%)	2 (9.5%)
Cracking of lips	14 (14.0%)	4 (28.6%)	6 (42.9%)	1 (7.1%)	3 (21.4%)	0 (0%)
Cracking of corner of mouth	22 (22.0%)	7 (31.8%)	4 (18.2%)	3 (13.6%)	6 (27.3%)	2 (9.1%)
Taste disturbance	17 (17.0%)	3 (17.6%)	7 (41.2%)	2 (11.8%)	3 (17.6%)	2 (11.8%)
Difficulty chewing	20 (20.0%)	3 (15.0%)	11 (55.0%)	2 (10.0%)	1 (5.0%)	3 (15.0%)
Difficulty swallowing	21 (21.0%)	2 (9.5%)	3 (14.3%)	8 (38.1%)	6 (28.6%)	2 (9.5%)
Difficulty speaking	22 (22.0%)	2 (9.1%)	9 (40.9%)	3 (13.6%)	5 (22.7%)	3 (13.6%)
“Dirty mouth”	22 (22.0%)	2 (9.1%)	10 (45.5%)	8 (36.4%)	1 (4.5%)	1 (4.5%)
Coating of tongue	26 (26.0%)	5 (19.2%)	10 (38.5%)	7 (26.9%)	3 (11.5%)	1 (3.8%)
Bad breath	17 (17.0%)	4 (23.5%)	6 (35.3%)	2 (11.8%)	3 (17.6%)	2 (11.8%)
Toothache / pain in teeth	13 (13.0%)	2 (15.4%)	6 (46.2%)	3 (23.1%)	1 (7.7%)	1 (7.7%)
Sensitivity of teeth	18 (18.0%)	2 (11.1%)	14 (77.8%)	1(5.6%)	1 (5.6%)	0 (0%)
Jagged teeth	23 (23.0%)	10 (43.5%)	3 (13.0%)	4 (17.4%)	2 (8.7%)	4 (17.4%)
Denture fitting problems	18 (18.0%)	1 (5.6%)	4 (22.2%)	4 (22.2%)	4 (22.2%)	5 (27.8%)
Bleeding from mouth	6 (6.0%)	4 (66.7%)	0 (0%)	1 (16.7%)	1 (16.7%)	0 (0%)
Burning sensation in mouth	3 (3.0%)	0 (0%)	2 (66.7%)	0 (0%)	0 (0%)	1 (33.3%)
Altered sensation in mouth	1 (1%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ulcers in mouth	7 (7%)	2 (28.6%)	2 (28.6%)	1 (14.3%)	2 (28.6%)	0 (0%)
Drooling	40 (40.0%)	5 (12.5%)	14 (35.0%)	8 (20.0%)	10 (25.0%)	3 (7.5%)

Table 4-5: Amount of distress caused by oral symptoms on the OSAS.

“Dry mouth” was the most common oral symptom present among participants. Of the 57 participants who experienced dry mouth, 35% reported that it caused them “quite a bit” (21%, 12/57) or “very much” (14%, 8/57) distress, 74% reported that it occurred at least “frequently” (35%, 20/57) or “almost constantly” (38%, 22/57), and 91% (52/57) reported that it was at least moderate or above severity. “Drooling” accounted for the next most common symptom (40%, 40/100): 32.5% (13/40) reported that it caused them “quite a bit” (25%, 10/40) or “very much” (7.5%, 3/40) distress, 27.5% (11/40) reported that it occurred “frequently” or “almost constantly” (25%, 10/40) and 67.5% (27/40) reported that it was “moderate” or above in severity. 23/40 (57.5%) also reported xerostomia. The least frequent oral symptom recorded on the OSAS was “altered sensation in mouth” (n=1) and burning sensation in mouth (n=3).

4.4.4 Other oral symptoms not listed

Fifteen participants reported at least one additional oral symptom not listed in the OSAS (13 reported one symptom and 2 participants reported two symptoms). These symptoms are listed in Table 4-6, and it can be seen that many of them are related to symptoms on the OSAS (e.g. sore gums / gum discomfort and “mouth discomfort / pain”; dry lips with “dry mouth”; food tasting bland with “taste disturbance”; teeth feel rough with “jagged teeth”). The data of these participants was examined and in the two participants who listed “dry lips”, dry mouth was present, occurred frequently and was associated with at least “quite a bit” of distress for both. In the participants listing sore gums/gum discomfort only one participant (of the five who reported this additional symptom) listed the presence of mouth discomfort/pain on the OSAS. Until recruitment is complete it is difficult to interpret these findings but there appears to be some overlap with these additional symptoms and symptoms already listed in the OSAS.

Oral symptom	Amount of distress	Frequency	Severity
“teeth feel rough”	“a little bit”	“almost constantly”	“severe”
“tongue sensitive”	“a little bit”	“almost constantly”	“moderate”
“right lip numbness”	“quite a bit”	“almost constantly”	“moderate”
“food tasting bland”	“a little bit”	“frequently”	“moderate”
“upper palate coating”	“not at all”	“rarely”	“slight”
“loose teeth”	“not at all”	“occasionally”	“moderate”
“gum discomfort”	“a little bit”	“rarely”	“moderate”
“biting on inner cheek”	“somewhat”	“almost constantly”	“moderate”
“dry lips”	“not at all”	“rarely”	“slight”
“sore gums”	“a little bit”	“occasionally”	“slight”
“dry lips”	“not at all”	“almost constantly”	“slight”
“difficulty coughing when eating” *	“very much”	“almost constantly”	“severe”
“gum discomfort”	“quite a bit”	“occasionally”	“moderate”
“gum discomfort”	“very much”	“almost constantly”	“moderate”
“gum discomfort”	“quite a bit”	“occasionally”	“severe”

Table 4-6: Other oral symptoms not listed in the OSAS.

*One participant listed “difficulty coughing when eating” as an oral symptom however this is not considered an oral symptom

The median time taken to complete the OSAS was 4.47 minutes (range = 1.27 – 16.09 minutes). Most (97%, 97/100) participants felt it was important to ask about mouth problems, that the questionnaire was easy to complete (99%, 99/100), that the questionnaire was quick to complete (98%, 98/100), and that it asked about all the important mouth problems (97%, 97/100).

4.5 DISCUSSION

As discussed, the results presented are from the initial 100 participants, and so they need to be viewed with caution. However, the data suggests that oral symptoms are common in this cohort of patients with over 91 (91%) of the one hundred participants reporting at least one oral symptom. The OSAS provides data not just on prevalence, but also on frequency, intensity

(severity), and associated distress (“bothersomeness”). The latter is especially relevant, since this domain has been shown to be closely related to quality of life measures in other studies involving analogous symptom assessment scales (i.e. Memorial Symptom Assessment Scale) (130).

The symptom profile appears to be somewhat different however from that seen in the cohort of patients with advanced cancer. Compared to the advanced cancer patient cohort, participants reported less mouth discomfort/pain (15% vs 31.5%), less taste disturbance (15% vs 38.9%) but more denture-fitting problems (18% vs 3.7%). These preliminary results are unsurprising in the context of the different aetiologies of oral symptoms in the distinct patient cohorts as outlined in Chapter 1. Importantly, edentulism is more common in older people in Ireland (131), and the absence of teeth precludes the existence of certain oral symptoms (e.g. “toothache / pain in teeth”). However, “denture fitting problems” can lead to other symptoms, especially oral discomfort related to mucosal trauma. Nevertheless, many of the oral symptoms are common to both groups, and often reflect a shared aetiology, e.g. drug-induced xerostomia (“dry mouth”).

The modified OSAS appears to be a useful tool in this cohort of patients. The results from the first 100 participants indicate that it is comprehensive - most participants reported that the OSAS asked about all the important mouth problems in the participant feedback and furthermore only 15 participants reported an additional symptom and many of these overlapped with symptoms already on the OSAS. It also seems to be patient-friendly - most participants reported that it was easy and quick to complete and the median time to complete it was just over 4 minutes. Importantly, the OSAS data and patient feedback confirm that oral symptoms / problems need to be given a higher profile in clinical practice.

Xerostomia was unsurprisingly the most common oral symptom reported on the OSAS (57%, 57/100) and was of high impact in terms of frequency, severity, and the amount of distress it caused. Xerostomia has been identified as a predictor of poor oral health-related quality of life in older people (30) and our preliminary findings support this assertion in terms of its multi-dimensional impact. In terms of the prevalence for xerostomia in older people, Liu et al (22) in their review of the literature examining the prevalence and causes of xerostomia defined ‘vulnerable elderly’ as “ persons aged >65 years that have any or all of the following: limited mobility, limited resources, or complex health status”. Thus, yielding studies that included

older patients with frailty. Only one (132) of the included studies however described its study population as 'frail elderly' and the definition that the study's authors used for frailty was "people who have lost some of their independence but who continue to live in the community with the help of support services" (132) (the study's inclusion criteria was "75 years or older and receiving a home care nurses' visits at least once every fortnight"). In this study examining "oral health status", 66% (n=33) of participants reported xerostomia. Because of the significance differences in study design (frailty definition and inclusion criteria) it is difficult to compare the prevalence of xerostomia to our results.

The symptom of drooling was added to the OSAS based on investigator experience in this study which included experts in gerontology. In the original OSAS observational study (13), the authors stated that the 20 symptoms on the OSAS were based on a review of medical literature on oral symptoms and problems in advanced cancer patients and in consultation with experts including palliative medicine and dentistry/oral medicine. With the additional perspective and experience of experts in gerontology, drooling was added to the OSAS in this study. Drooling may be caused by neuromuscular dysfunction or much less commonly hypersalivation. It occurs in many neurological disorders that are common in older people with frailty. Examples include stroke, neurodegenerative diseases like Parkinson's disease, progressive supranuclear palsy, Lewy body dementia, multiple system atrophy and neuromuscular conditions like myasthenia gravis. Drooling accounted for the second most common oral symptom in our study. It was present for 40 participants. Of these, 18 (45%) had a recorded neurological illness of mild (9), moderate (7), or severe (2) severity. A disadvantage of the CIRS-G is that it calculates a cumulative illness risk score for individual organ systems as opposed to individual conditions. Of the 23 participants who had a recorded neurological illness of mild or above severity, 18 (78%) reported the symptom of drooling. One systematic review (133) examining the symptom of drooling in patients with Idiopathic Parkinson's disease reported a pooled prevalence estimate of 56% (95% CI 44-67) in patients with Parkinson's disease and 14% (95% CI 3-25) for healthy controls. All the studies involved patients who were community-dwelling. Our study provides new prevalence data on drooling in older patients with frailty with and without neuromuscular dysfunction who are both living at home or in a long-stay residential care facility.

More recent studies have evaluated certain oral health problems (which have included oral symptom evaluation) in older adults with frailty using validated frailty screening methods.

Hasegawa et al. (134) identified frail older adults using the Kihon Checklist (a self-rated screening tool that is used extensively in Japan to screen for frailty (135)). Xerostomia (and bad breath and drooling) was examined but it was measured using the Clinical Oral Assessment Chart. This is an objective measure and therefore does not give insight into the subjective nature of a symptom. Ramsay et al. (23) used the Fried frailty phenotype (136) to establish frailty status. Self-rated questionnaires were used to examine difficulty eating (yes/no), sensitivity to hot, cold, or sweet (yes/no) and xerostomia using the Xerostomia Inventory (98) (an 11-item subjective measure of xerostomia). An association (OR for ≥ 3 symptoms = 2.50, 95% CI = 1.77–3.53) between frailty and ≥ 3 dry mouth symptoms in the study's participants (older British men, aged 71-92) was demonstrated even after adjustments for smoking, social class, history of diabetes or cardiovascular disease and medication use. Hoeksema et al. (137) used the Groningen Frailty Indicator to measure frailty. Participants completed a 13-item questionnaire which included questions on "complaints related to pain or dry mouth and difficulties with chewing". Fifty-six (25%) of participants who were defined as frail in this study (n= 225) reported dry mouth at night and 17 (8%) reported dry mouth during the day. In terms of screening for frailty in our study, the CFS was chosen as it has been recommended by the recent ICHOM Older Person Working Group – a modified Delphi consensus – driven standard set of health outcomes measures for older persons (122).

As in patients with advanced cancer, oral symptom assessment should not be done in isolation in older people with frailty and should be accompanied by a thorough examination of the oral cavity to identify the cause of the symptom and guide its management. Van der Putten et al. (44) suggest a bi-directional process whereby when an older person has been identified as having 'frailty' that healthcare professionals should have an awareness that the older person's oral health is at risk which should prompt a referral to a dental healthcare professional. Similarly, if a dental healthcare professional observes a sudden decline in the oral health of an older person this may indicate the first signs of frailty and should prompt a referral to a physician for formal frailty screening. The Seattle Care Pathway (138) is a structured, evidence-based approach to maintain the oral health of older people that can be tailored to the jurisdiction in which it is being implemented. In terms of the frailty concept, categories were developed based on 'levels of dependency'. The care pathway provides a structure in terms of assessment, prevention, treatment and communication determined by the dependency level. The pathway relates to the individual patient being assessed and their treatment needs but can also be used to examine population-based interventions. When an older person is

identified as being frail through screening and referred for a personalised CGA, incorporating dental healthcare professionals into multidisciplinary teams should be a key priority in order to maintain the oral health of these patients.

4.6 CONCLUSION

Asking about oral symptoms is important for older people with frailty. Data from the first 100 participants recruited to the study suggest that many oral symptoms are common (and often of high impact) in older patients with frailty. Xerostomia and drooling were the most common reported symptoms. This study provides a novel insight into the prevalence and clinical features of oral symptoms not previously investigated using a multi-dimensional symptom-specific assessment tool.

CHAPTER 5 CONCLUSION AND FUTURE DIRECTIONS

OVERVIEW

This thesis describes three distinct, but related projects: 1) a scoping review of the literature of oral symptom assessment tools in patients with advanced cancer; 2) a validation study of the Oral Symptom Assessment Scale (OSAS) – the OSAS was specifically developed to assess oral symptoms in patients with advanced cancer; 3) an observational study of oral symptoms in frail older patients using a modified version of the OSAS. The latter (ongoing) study will not only provide data on the epidemiology of oral symptoms in the frail older population, but will also provide information about the possible utility of the OSAS in this different cohort of patients.

5.1 ORAL SYMPTOM ASSESSMENT TOOLS IN PATIENTS WITH ADVANCED CANCER: A SCOPING REVIEW

Symptom assessment tools can facilitate good symptom control in clinical practice, and are an integral component of clinical research. This is the first scoping review of the literature to identify and describe oral symptom assessment tools that have been specifically utilised in patients with advanced cancer. Four validated symptom assessment scales were identified that could be utilised to assess oral symptoms in patients with advanced cancer, including one cancer-specific quality of life scale (EORTC QLQ OH-15), one generic tool for assessing the “social impact” of specific oral problems (OHIP), one cancer-specific generic symptom assessment scale (MSAS), and one cancer-specific oral symptom assessment scale (OSAS).

With the results of this scoping review, the EORTC QLQ OH-15 was identified as a suitable, validated symptom assessment instrument that could be used to examine the criterion validity of the OSAS which formed part of the first observational study examining the psychometric properties of the OSAS in patients with advanced cancer.

5.2 OSAS IN PATIENTS WITH ADVANCED CANCER

This is the first study, excluding the initial OSAS observational study, to evaluate the psychometric properties of the OSAS in patients with advanced cancer. The study’s results support the validity of the OSAS, and provide evidence for its reliability in patients with advanced cancer. It is however necessary that more studies are conducted to corroborate the findings from the study (and these are ongoing within the ADPM, and other research groups).

In 2018 (139) the four leading causes of cancer deaths in Ireland were gastrointestinal (31%), respiratory and thoracic (20%), breast and gynaecological (14%) and genitourinary and testicular (12%). A strength of this study was that the participant cohort recruited to the study is representative of these national figures with the exception of a higher proportion of genitourinary and testicular cancers (“urological cancers” - 20%, 11/54). One reason for this may be the higher proportion of these cancers treated in the local cancer centres referring to the hospice where recruitment occurred.

A limitation of the study was that recruitment occurred using convenience sampling at a single site in-patient hospice. However, this site takes referral from the two main cancer centres in Dublin, and most of the teaching hospitals within the city, which means that the hospice inpatient population is drawn from a very broad and diverse population of patients with advanced cancer. Importantly, the results of this study were in keeping with the results of the initial OSAS observational study which was undertaken in a number of different settings (hospital and hospice- both inpatient and outpatient) in the United Kingdom.

Another limitation of the study was that there was a wide range of ages of those recruited to the study. 36/54 (67%) of the participants were aged ≥ 65 years old. In the older patients (i.e. those aged ≥ 65 years) recruited to the study there may have been a concomitant frailty syndrome, but this was not measured in this study. Frailty is not based on chronological age so similarly in the patients aged <65 there may have been a concomitant frailty syndrome. Therefore, there may have been an overlap in the aetiologies of these symptoms. The focus of this study was however not to determine causes or associations of oral symptoms in patients with advanced cancer. Further studies could examine the OSAS in patients with advanced cancer to include frailty.

5.3 OSAS IN OLDER PATIENTS WITH FRAILITY

The initial results of this study confirm that oral symptoms are common in older patients with frailty, and that they are often associated with significant morbidity. Moreover, it provides further evidence of the need for regular (and comprehensive) assessment of oral symptoms in this cohort of patients. Importantly, assessment of symptoms should be accompanied by examination of the oral cavity to determine the potential cause of the symptom, and to identify asymptomatic oral conditions that require intervention. However, this needs to be

confirmed by analysis of the full dataset (comprising 250 individuals), which will involve not only the use of descriptive statistics, but also appropriate statistical analyses.

The initial results of this study also suggest that the modified version of the OSAS (to include drooling) may have utility in older patients with frailty. However, the definitive results may identify further oral symptoms that are prevalent in this cohort of patients (and so need including in future iterations). Importantly, the modified version of the OSAS needs to be formally validated in this patient cohort, and in a similar manner to the validation of the OSAS in patients with advanced cancer (e.g. criterion validity, test-retest reliability). The latter would need to be undertaken before the tool could be considered for usage in clinical settings. Importantly, the criterion validity should be undertaken using assessment tools that has been validated in older patients with frailty (e.g., the Geriatric Oral Health Assessment Index (70)).

An aspect to be considered will be the time taken to complete the modified OSAS in this cohort of patients for whom fatigue is often a prominent feature. It may be necessary to consider adapting the tool to an abbreviated version that is either unidimensional, or assesses fewer symptoms, to ensure its acceptability in the clinical setting. Indeed, the Memorial Symptom Assessment Scale (MSAS), which was the template for the OSAS, has been adapted / shortened a number of times in order to make it suitable for clinical practice. Thus, the MSAS-short form only includes the “distress” domain (and not the frequency or severity domains) (140). Equally, the Condensed MSAS only includes symptoms most associated with impaired quality of life (and has 14 questions, rather than 32 questions) (130).

This study adds to the available literature on oral problems in older patients with frailty. However, there remains many unanswered questions, and further research is required in relation to the assessment, prevention, and management of oral problems in this cohort. Such research requires the input of both healthcare professionals (medical, nursing, dental, oral medicine), and also patients and family carers. Nevertheless, the routinisation of oral assessments, and the standardisation of oral hygiene regimens, will undoubtedly decrease morbidity from oral conditions, and improve oral health-related quality of life, in this vulnerable population.

5.4 NEXT STEPS

As discussed, the frailty study is ongoing and is expected to be completed in the third quarter of 2024. The aim is to publish the primary paper (main results) in a gerontology journal, and a

further paper comparing the results of this study and the original OSAS study (in patients with advanced cancer) in an oral health/ dental journal.

In terms of the OSAS, there are plans to publish a further validation paper (based upon further analysis of the data from the initial study in advanced cancer patients), and there are ongoing validation studies of the Japanese and Portuguese versions of the tools (again in patients with advanced cancer).

LIST OF APPENDICES

APPENDIX 1: DATABASE RESEARCH STRATEGY.

Database	Search strategy
PubMed	((((((((((((((oral care[Title/Abstract]) OR (oral symptom*[Title/Abstract])) OR ("oral health related quality of life"[Title/Abstract])) OR (oral disease*[Title/Abstract])) OR (mouth inflammation[Title/Abstract])) OR (dental disease[Title/Abstract])) OR (dental health[Title/Abstract])) OR (oral manifestations[MeSH Terms])) OR (oral health[MeSH Terms])) OR (oral candidiasis[MeSH Terms])) OR (mouth diseases[MeSH Terms])) OR (oral hygiene[MeSH Terms])) OR (stomatitis[MeSH Terms])) OR (xerostomia[MeSH Terms])) AND ((((((((((health impact assessment[MeSH Terms]) OR (patient reported outcome measures[MeSH Terms])) OR (patient outcome assessment[MeSH Terms])) OR (problem rating scale for outcomes[Title/Abstract])) OR (outcome measure*[Title/Abstract])) OR (outcome assessment*[Title/Abstract])) OR (outcome tool*[Title/Abstract])) OR (symptom assessment scale*[Title/Abstract])) OR (clinical assessment tool*[Title/Abstract])) AND ((((((((((advanced cancer[Title/Abstract]) OR (metastatic cancer[Title/Abstract])) OR (terminal cancer[Title/Abstract])) OR (care, palliative[MeSH Terms])) OR (medicine, palliative[MeSH Terms])) OR (end of life care[Title/Abstract])) OR (Neoplasms[MeSH Terms])) OR (neoplasm metastasis[MeSH Terms])) OR (neoplasm metastases[MeSH Terms])) OR (terminal care[Title/Abstract]))
CINAHL	patient outcome assessment* OR problem rating scale for outcome* OR

	outcome measure* OR outcome tool* OR outcome measurement tool* OR symptom assessment scale* OR MH outcome assessment OR MH clinical assessment tools OR MH patient assessment OR MH patient-reported outcomes OR MH health impact assessment AND MH palliative care OR MH palliative medicine OR MH Neoplasms OR MH terminal care OR MH Neoplasm metastasis OR advanced cancer OR terminal cancer OR metastatic cancer OR terminal care OR end of life care AND MH oral manifestations OR MH oral health OR MH oral candidiasis OR MH mouth diseases OR MH oral hygiene OR MH xerostomia OR MH stomatitis OR oral care OR oral symptom* OR "oral health related quality of life" OR oral disease OR dental disease OR dental health
Embase	health impact assessment or patient reported outcome measures or patient outcome assessment or clinical assessment tool* or "problem rating scale for outcomes" or outcome measure* or outcome assessment* or outcome tool* or outcome measurement tool* or symptom assessment scale*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] AND (oral care or oral symptom* or "oral health related quality of life" or oral disease or mouth inflammation or dental disease or dental health or oral

	manifestations* or oral health or oral candidiasis or mouth disease* or oral hygiene or stomatitis or xerostomia).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] AND (medicine, palliative or care, palliative or Neoplasms or Neoplasm metastasis or end of life care or terminal care or terminal cancer or advanced cancer or metastatic cancer).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
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APPENDIX 2: SVUH RESEARCH AND ETHICS COMMITTEE STUDY APPROVAL LETTER.



St. Vincent's University Hospital
Elm Park, Dublin 4,
D04 T6F4, Ireland

T +353 1 221 4000
www.stvincents.ie

Professor Andrew Davies,
Professor of Palliative Medicine,
Our Lady's Hospice and Care Services,
Harold's Cross
Dublin 6W

4th August 2021

Ref No: RS21-044
Oral Symptom Assessment Scale (OSAS): Validity and Reliability

Documentation:

Local Checklist V1 14.04.2021, Protocol V1 14.04.2021, Standard Application Form V1 14.04.2021,
Patient Information Leaflet V1 14.04.2021, Patient Consent Form V1 14.04.2021, Data Confidentiality
Agreement V1.0, ECOG, OSAS-LF, QLQ-C30, QLQ-OH15, Phases, Data Collection Sheet, Ease of Use
Questionnaire, GCP Cert Niamh Cleary, References

Dear Professor Davies

I refer to your attendance at the Research Ethics Committee meeting on the 9th June, 2021, at which the
above study was reviewed. Following review of the documentation received, this study has been granted full
Ethics approval.

Please note, it is the responsibility of the Principal Investigator to retain full file copies of all documentation
submitted and received in respect of this application submission.

Yours sincerely,

A handwritten signature in blue ink, appearing to read "Ronan Killeen".

Professor Ronan Killeen
Chairperson
SVHG Research Ethics Committee

Cc: Dr. Niamh Cleary



St. Vincent's Healthcare Group Board of Directors: Chairman: Mr. James Menton,
Dr. David Brophy, Mr. John Compton, Mr. Gerard Flood, Prof. Michael Keane, Mr. Myles Lee,
Ms. Sharen McCabe, Prof. Patrick Murray, Mr. Frank O'Riordan, Mr. William Shannon.
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Registered Office: Elm Park, Dublin 4.

APPENDIX 3: CONSENT FORM.



PLEASE TICK YOUR RESPONSE IN THE APPROPRIATE BOX

Please tick	Yes	No
I have read and understood the Participant Information Leaflet		
I had the opportunity to ask questions and discuss the study		
I have received satisfactory answers to all my questions		
I have received enough information about this study		
I understand that I am free to withdraw from the study at any time without giving a reason and without this affecting my future medical care		
I give my explicit consent to have my data processed as part of this research study		
I agree to allow the researchers access to my medical records as part of this study.		
I consent to take part in this research study having been fully informed of the risks, benefits and purpose of the study		
I consent for the researcher to inform my treating team if I have symptoms		

STORAGE & FUTURE USE OF INFORMATION:

Please tick	Yes	No
I give permission for material/data to be stored for <u>possible future research related</u> to the current study <u>only if consent is obtained</u> at the time of the future research but only if the research is approved by a Research Ethics Committee.		
I give permission for material/data to be stored for <u>possible future research related</u> to the current study <u>without further consent being required</u> but only if the research is approved by a Research Ethics Committee		
I give permission for material/data to be stored for <u>possible future research unrelated</u> to the current study <u>only if consent is obtained</u> at the time of the future research but only if the research is approved by a Research Ethics Committee		
I give permission for material/data to be stored for <u>possible future research unrelated</u> to the current study <u>without further consent</u> being required but only if the research is approved by a Research Ethics Committee.		
I agree that some future research projects may be carried out by researchers working for commercial/pharmaceutical companies		
I understand I will not be entitled to a share of any profits that may arise from the future use of my material/data or products derived from it.		

Participant's Signature: _____ Date: _____

Participant's Name in print: _____

Please tick	Yes	No
I have fully explained the purpose and nature (including benefits and risks) of this study to the participant in a way that he/she could understand. I have invited him/her to ask questions on any aspect of the study.		
I confirm that I have given a copy of the information leaflet and consent form to the participant.		

Investigator's Signature: _____ Date: _____

Investigator's Name in print: _____

APPENDIX 4: PATIENT INFORMATION LEAFLET.

STUDY TITLE: Oral Symptom Assessment Scale (OSAS): Validity and Reliability

NAME OF PRINCIPAL INVESTIGATORS: Professor Andrew Davies

You are invited to participate in a research study. Please read this document and ask any questions you may have before agreeing to participate in the study.

WHAT IS THE PURPOSE OF THIS STUDY?

Oral (mouth) symptoms are very common and often bothersome in patients with cancer. The best way to assess these symptoms is using a patient-rated symptom assessment scale. A new symptom assessment scale for oral symptoms has been developed and already tested in patients. The purpose of this study is to test the scale again to make sure it is reliable and accurate.

WHY HAVE I BEEN CHOSEN?

You have been invited to participate in this study because you are an in-patient in Our Lady's Hospice and Care Services. It is hoped that your participation in the study will inform our assessment of oral symptoms and contribute to how we ask about these symptoms in the future.

WHAT WILL HAPPEN IF I VOLUNTEER?

Your participation is entirely voluntary. If you initially decide to take part, you can subsequently change your mind without difficulty.

If you agree to participate, at the first meeting with the researcher you will be asked to complete two questionnaires. One will be entirely about oral symptoms. The second will be about lots of a different symptoms relating to your quality of life as well as about oral symptoms. You will

also be asked about how easy both questionnaires are to complete. This will take approximately 20 minutes. 24 hours later the researcher will return and you will be asked to complete the questionnaire on oral symptoms alone. It is anticipated that this will take 10 minutes.

ARE THERE ANY BENEFITS FROM MY PARTICIPATION?

You will not benefit directly from taking part in this study, but the information obtained may contribute to improving the assessment, diagnosis and management of oral symptoms. The ultimate goal of this study is to improve quality of life for those who suffer with oral symptoms. The data recorded will not be available to you. However, in the event of an abnormality being discovered e.g. dry mouth your doctor will then be informed so that appropriate steps can be taken to improve this.

ARE THERE ANY RISKS INVOLVED IN PARTICIPATING?

There are no risks associated with this study.

WHAT HAPPENS IF I DO NOT AGREE TO PARTICIPATE?

If you decide not to participate in this study, there will be no adverse consequences and it will not affect your current or future medical care. You do not need to give a reason to decline participation or to withdraw from the study.

CONFIDENTIALITY & DATA PROTECTION

1. INTRODUCTION

- 1.1 This Participant Information and Consent Form provides guidance and information to "Oral Symptom Assessment Scale: Validity and Reliability" research participants regarding the processing of the research participants' personal data. The Academic Department of Palliative Medicine at Our Lady's Hospice and Care Service is committed to protecting and respecting your privacy. This Participant Information and Consent Form together sets out the basis on which any personal data we collect from you or that you provide to us will be processed by us an independent data controller. Please read this Participant Information and Consent Form carefully to understand our treatment and use of your personal data.

- 1.2 The processing of your personal data will be in compliance with the Data Protection Acts 1988 to 2018 (as amended) and the General Data Protection Regulation (the "Data Protection Legislation").
- 1.3 Please note that agreeing to participate in a research program with the Academic Department of Palliative Medicine at Our Lady's Hospice and Care you acknowledge that you have read, understood and agree to this Participant Information and Consent Form.

2. IDENTITY OF THE CONTROLLER OF PERSONAL INFORMATION

For the purposes of the Data Protection Legislation, the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Service is an independent data controller in the following circumstances:

1.	Company/PI Name: Prof Andrew Davies Company/PI Type: Academic Department of Palliative Medicine Company Registration number: 20001827 Having its registered office at: <i>Our Lady's Hospice and Care Services, Harold's Cross</i>
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3. CONTACT DETAILS OF THE DATA PROTECTION OFFICER*

3.1

The data protection officer for Our Lady's Hospice and Care Services, Harold's Cross: Patricia Pierce, Our Lady's Hospice and Care Services, Harold's Cross, Dublin 6W, Contact 01 406 8725

4. PROCESSING OF YOUR PERSONAL DATA

The Academic Department of Palliative Medicine at Our Lady's Hospice and Care Service will process your personal data for the following purposes on the basis of your consent:

Personal data	Purpose of processing ¹
1. Identification e.g. name - A record of your name will be obtained; however, this will be kept in a separate area to maintain anonymity. Participants will be identified by a study number (please note this and subsequent information will be anonymised)	1. (a)Originally captured as part of medical care (b) used for purpose of carrying out research
2. Clinical History (not identifiable)	2. Past Medical History relevant to study outcomes
3. Questionnaires	3. Patient Reported Outcome Measures (PROMS) required to measure response to treatment

4.1 Where does the research team obtain my personal data from?

Most of the personal data we process is obtained from you directly but we also obtain personal data about you from your medical notes

5. SHARING OF PERSONAL DATA

Your personal data may be shared with other researchers who are conducting similar research. However, we will not pass on any personal data.

5.1 Service Providers

We use third party service providers who provide services including research services. In providing the services, your personal data will, where applicable, be processed by the service provider on our behalf.

We will check any third party that we use to ensure that they can provide sufficient guarantees regarding the confidentiality and security of your personal data. We will have written contracts with them which provide assurances regarding the protections that they will give to your personal data and their compliance with our data security standards and international transfer restrictions.

5.2 Disclosures to Third Parties

In certain circumstances, we share and/or are obliged to share your personal data with third parties outside the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Service for the purposes described above and in accordance with Data Protection Legislation.

These third parties include but are not limited to:

- the Health Service Executive
- the Health Products Regulatory Authority;
- others, where it is permitted by law, or where we have your consent.

6. TRANSFERS OUTSIDE THE EUROPEAN ECONOMIC AREA²

6.1b Your personal information may be transferred, stored and processed in one or more countries outside the European Economic Area ("EEA"). For transfers of your personal data to third parties outside of the EEA, we take additional steps in line with Data Protection Legislation. We have put in place adequate safeguards with respect to the protection of your privacy, fundamental rights and freedoms, and the exercise of your rights, e.g. we establish

an adequate level of data protection through EU Standard Contractual Clauses based on the EU commission's model clauses.

- 6.1 If you would like to see a copy of any relevant provisions, please contact your data protection officer (see "Contact Us" section below).

7. HOW IS MY PERSONAL DATA SECURED

- 7.1 The Academic Department of Palliative Medicine at Our Lady's Hospice and Care Service operates and uses appropriate technical and physical security measures to protect your personal data.

- 7.2 We have in particular taken appropriate security measures to protect your personal data from accidental or unlawful destruction, loss, alteration, ~~unauthorised disclosure~~ of, or access, in connection with this research study. Access is only granted on a need-to-know basis to those people whose roles require them to process your personal data. In addition, our service providers are also selected carefully and required to use appropriate protective measures.

8. STORAGE OF PERSONAL DATA

We will keep your personal data for 5 years.

9. YOUR RIGHTS

- 9.1 You may have various rights under Data Protection Legislation. However, in certain circumstances, these rights may be restricted³. In particular, your rights may be restricted where this is necessary: (i) for the prevention, detection, investigation and prosecution of criminal offences; (ii) in contemplation of or for the establishment, exercise or defence of a legal claim or legal proceedings (whether before a court, tribunal, statutory body or an administrative or out-of-court procedure); and/or (iii) for the performance of a task carried out in the public interest or in the exercise of official authority vested in the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Service These rights may include (as relevant):

- (i) **The right of access** enables you to check what type of personal data we hold about you and what we do with that personal data and to receive a copy of this personal data.
- (ii) **The right to object** to processing of your personal data where that processing is carried out on the basis of our legitimate interests. We will stop using your personal data unless we can demonstrate an overriding legitimate ground for the continued processing of this personal data.
- (iii) **The right to rectification** enables you to correct any inaccurate or incomplete personal data that we hold about you.
- (iv) **The right to erasure** enables you to request that we erase personal data held about you in certain circumstances.
- (v) **The right to restrict processing** of your personal data by us in certain cases, including if you believe that the personal data held about you is inaccurate or our use of the personal data is unlawful; and
- (vi) **The right to data portability** enables you to receive your personal data in a structured, commonly used and machine readable format and to have that personal data transmitted to another data controller

10. YOUR RIGHT TO LODGE A COMPLAINT WITH A SUPERVISORY AUTHORITY

- 10.1 Without prejudice to any other administrative or judicial remedy you might have, you may have the right under data protection legislation in your country (where applicable) to lodge a complaint with the relevant data protection supervisory authority in your country (i.e. the Office of the Data Protection Commissioner in Ireland) if you consider that we have infringed applicable data protection legislation when processing your personal data. This means the country where you are habitually resident, where you work or where the alleged infringement took place.

11. CHANGES TO THIS INFORMATION

- 11.1 We may decide to make changes to this Participant Information and Consent Form. If a change is made, we will notify you in person of such changes. An updated Participant Information and Consent Form will be provided to you in advance of any change actually taking effect.

12. CONTACT US

12.1 For further information or if you have any questions or queries about this Participant Information and Consent Form, please contact:

By address	Patricia Pierce, Our Lady's Hospice and Care Services, Harold's Cross, Dublin 6W
By telephone	(01) 4068725
By email address	PPierce@OLH.ie

COMPENSATION

You will not be paid for taking part in this study.

WHO IS ORGANISING AND FUNDING THIS RESEARCH?

This research is being organised by the Academic Department of Palliative Medicine in Our Lady's Hospice and Care Services. There is no commercial or pharmaceutical sponsorship of this research. This research is being conducted as part of research for an academic qualification in collaboration with Trinity College Dublin, University College Dublin and Our Lady's Hospice and Care Services.

HAS THIS STUDY BEEN REVIEWED BY AN ETHICS COMMITTEE?

St Vincent's University Hospital Research and Ethics Committee has reviewed and approved this study.

CONTACT DETAILS

Dr Niamh Cleary
01 406 8700
ncleary@olh.ie

Data Processors:

Dr Niamh Cleary Clinical Lecturer, Our Lady's Hospice and Care Services
Dr Jenny Power, Clinical Lecturer, Our Lady's Hospice and Care Services
Ms Michelle Barrett, Research Nurse, Our Lady's Hospice and Care Services
Ms Norah Fagan, Research Nurse, Our Lady's Hospice and Care Services
Ms Elaine Hyland, Research Nurse, Our Lady's Hospice and Care Services

I wish to thank you for taking the time to consider participating in the study.

APPENDIX 5: DATA COLLECTION SHEET/CASE REPORT FORM.

Study number:
Study Date:

Gender (identifies as):

Male ☐
Female ☐
Transgender ☐
Non-binary ☐
Intersex ☐
Would prefer not to say ☐

Age:

ECOG:

Cancer Primary Location: (Tick box)

Breast	
Gastrointestinal	
Gynaecological	
Haematological	
Head and Neck	
Lung	
Neurological	
Skin	
Urological	
Unknown primary	

Time 1		
OSAS	Yes	No
EORTC QLQ-C30 and EORTC QLQ-OH15	Yes	No
Ease of use questionnaire	Yes	No

Time to complete OSAS:

Time to complete EORTC QLQ- C30 and EORTC QLQ-OH15

Time 2		
OSAS	Yes	No

Time to complete OSAS:

APPENDIX 6: EORTC QLQ-C30 QUESTIONNAIRE APPROVAL TO USE.

Your request for an EORTC-questionnaire Request ID : 73877 External  

no-reply@eortc.be
to me ▼

Mon, 1 Mar 2021, 08:51

Dear Niamh Cleary ,

Thank you for registering on the EORTC Quality of Life Group website.

Your registration to obtain permission to use our tools has been approved. During the registration process you agreed to our terms and conditions regarding the academic use of our questionnaires. You can review the terms and conditions [here](#).

Please find below the links to the requested tools:

[QLQ-C30 Core Questionnaire - English](#)

APPENDIX 7: EORTC QLQ-OH15 QUESTIONNAIRE APPROVAL TO USE.

Your request for an EORTC-questionnaire Request ID : 74963 External  

no-reply@eortc.be
to me ▼

Fri, 16 Apr 2021, 11:02

Dear Niamh Cleary,

Thank you for registering on the EORTC Quality of Life Group website.

Your registration to obtain permission to use our tools has been approved. During the registration process you agreed to our terms and conditions regarding the academic use of our questionnaires. You can review the terms and conditions [here](#).

Please find below the links to the requested tools:

[Oral Health Module \(OH15\) - English](#)

APPENDIX 8: SJH/TUH JOINT RESEARCH AND ETHICS COMMITTEE STUDY APPROVAL LETTER.



**Tallaght
University
Hospital**
Ospidéal
Ollscoile
Thamhlachta
An Academic Partner of Trinity College Dublin



Research Office

Project ID: 1935

Dr Niamh Cleary,
Our Lady's Hospice and Care Services, Harold's Cross

Prof Andrew Davies, Our Lady's Hospice and Care Services, Harold's Cross and Trinity College Dublin

Approval Date: 16 March 2023

Submission Number: 2551

Submission Title: Oral symptoms in older patients with frailty: a prospective observational study using the Oral Symptom Assessment Scale
Submission Date: 16.Feb.2023 16:36

Dear Dr Cleary,

On behalf of the Chair and members of the SJH/TUH Joint Research Ethics Committee I wish to inform you that your study has received **FULL APPROVAL**. Your study can now proceed.

The following comments were made: Please ensure Prof updates his GDPR training.

The following documents were reviewed and approved:

Document Type	File Name	Date	Version
Principle Investigator C.V.	CVAndrewDavies20122021	14.Oct.2021	
Survey/Questionnaire	OSAS with drooling V9	20.May.2022	V9
Participant Consent Form	SJH-TUH_JREC_Consent_Form_13.10.2022	13.Oct.2022	1
Data Collection Case Report Form	Appendix 6_CRF_V1 14.10.22	14.Oct.2022	1

Document Type	File Name	Date	Version
Protocol	V10 14.10.2022_nc	14.Oct.2022	10
Participant Information Leaflet	SJH-TUH_JREC_Participant_Information_Leaflet_V1 14.10.2022	14.Oct.2022	1
Survey/Questionnaire	Appendix 9_feedback_V1 14.10.22	14.Oct.2022	1
Default	Minor Comments_JREC_Feb2023	15.Feb.2023	1

Please note that ethical approval for this study is only active under the following conditions:

1. Applicants must submit an annual report for ongoing projects.
2. Applicants must submit an end of study declaration/end of study report upon completion of the study.
3. All adverse events must be reported to the JREC.
4. All changes (minor and substantial) to documentation/study must be submitted to the JREC using the amendment request form and the changes must be tracked/highlighted clearly. Approval from the JREC is required before implementation of the changes.

It is the responsibility of the researcher/research team to ensure all aspects of the study are executed in compliance with the General Data Protection regulation (GDPR), Health Research Regulations and the Data Protection Act 2018.

Yours sincerely,

Dr Sadhbh O'Neill

Research Ethics & Clinical Trials Manager,

SJH/TUH Joint Research Ethics Committee

The SJH/TUH Joint Research and Ethics Committee operates in compliance with and is constituted in accordance with the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004 & ICH GCP guidelines.

APPENDIX 9: CFS PERMISSION TO USE LETTER.



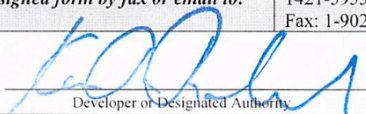
GERIATRIC MEDICINE
RESEARCH

FOR OFFICE USE ONLY

PF#: 20211223-05

PERMISSION TO USE THE CLINICAL FRAILTY SCALE (CFS)

The undersigned is granted permission to use, reproduce and distribute the Clinical Frailty Scale (CFS), developed by Dr. Kenneth Rockwood, in the format attached¹ for educational purposes and for non-commercially funded research and/or quality assurance projects. The CFS must be administered free of charge to patients and/or study participants. A formal Licensing Agreement is required for research funded by any commercial entity or pharma and, in some cases, for use in routine clinical care. The copyright holder reserves the right to prospectively follow-up at any time to determine whether use of the CFS meets the conditions described above. Reselling of the CFS or other commercial development without a license agreement is prohibited by copyright. The undersigned, their delegates and affiliated organization(s) agree that they will not claim ownership rights to the CFS, or any derivative, including translations, compilation, sequel or series. Nothing in this Agreement shall give the undersigned any right, title, or interest in the CFS other than the right to use in accordance with this Agreement. The CFS will not be modified unless explicit permission is granted.

USER INFORMATION:	
Full Name:	Dr Niamh Cleary
Position/Title:	Specialist Registrar
Institution/Organization:	Academic Department of Palliative Medicine
Mailing Address:	Our Lady's Hospice and Care Services, Harold's Cross, Dublin 6W
Telephone:	00353 87 6603466
Email:	clearynm@tcd.ie
Type of organization:	☐ For-profit ☒ Not-for-profit ☐ Other, please specify:
INTENDED USE (Select all that apply):	
☐ Reprint Provide publication details:	
☒ Research study/clinical trial Expected duration of study: ?Feb/March Start date 2021 End date 2022	
Describe use in study: I am assessing oral symptoms in older patients with frailty. The inclusion criteria is patients with a CFS >5	
Is research sponsored or funded by pharma or industry? ☐ Y ☒ N	
If yes, please specify:	
☐ Routine clinical care	
Will the CFS be incorporated into an electronic medical/health record (EMR)? ☐ Y ☐ N	
If yes, please identify whether an EMR company is involved (e.g., Epic, Meditech):	
☐ Other Specify:	
Are you planning to translate the CFS? ☐ Y ☒ N If yes, specify language(s):	
We request editable (e.g. MSWord) copies of all translations. We do not independently verify or validate translations.	
Are you planning any commercial development that would incorporate the CFS?	
☐ Y ☒ N If yes, please specify:	
By your signature below, you attest that you understand the conditions under which permission is granted.	
Signature:	
Date:	Niamh Cleary 14/12/2021
Send completed, signed form by fax or email to:	
Geriatric Medicine Research 1421-5955 Veterans' Memorial Lane, Halifax, NS B3H 2E1 Canada Fax: 1-902-473-1050 Email: gmru@dal.ca	
Approved by:	
Date:	2021/12/23

¹A copy of the CFS will be sent to the user upon review and approval of this permission form. Valid only when signed by all parties.

APPENDIX 10: CONSENT FORM.

CONSENT FORM
Oral symptoms in older patients with frailty: a prospective observational study using the Oral Symptom Assessment Scale

To be completed by the **PARTICIPANT**:

I confirm that I have read and understood the Information Leaflet for the above study and the Information within the Leaflet has been fully explained to me.	YES ☐	NO ☐
I have had the opportunity to discuss the study, ask questions about the study and I have received satisfactory answers to all my questions.	YES ☐	NO ☐
I understand that the study is entirely voluntary and, if I decide that I do not want to take part, I can stop taking part in this study at any time without giving a reason. I understand that not taking part will not affect my future medical care.	YES ☐	NO ☐
I understand that medical notes and records may be looked at by Professor Andrew Davies and his study team at Our Lady's Hospice and Care Services, Harold's Cross or St James' Hospital where it is relevant to do research. I agree that these individuals can access my medical records. I understand that all information will be kept private and confidential and that my name will not be disclosed.	YES ☐	NO ☐
I understand that I will not be paid for taking part in the study	YES ☐	NO ☐
I know how to contact the research team if I need to	YES ☐	NO ☐
I consent to take part in this research study having been fully informed of the risks, benefits and purpose of the study as set out in the information leaflet which I have been provided with.	YES ☐	NO ☐
I understand that there are no direct benefits to me from participating in this study. I understand that results from analysis of my personal information will not be given to me.	YES ☐	NO ☐
I consent for the researcher to inform my treating team if I have symptoms.	YES ☐	NO ☐

Participant's Name (Block Capitals):	
Participant's Signature:	
Date:	

To be completed by the **RESEARCHER**:

I have fully explained the purpose and nature (including benefits and risks) of this study to the participant in a way that he/she could understand. I have invited him/her to ask questions on any aspect of the study.	YES ☐	NO ☐
I confirm that I have given a copy of the information leaflet and consent form to the participant.	YES ☐	NO ☐

Researcher's Name (Block Capitals):	
Researcher's Title & Qualifications:	

APPENDIX 11: PATIENT INFORMATION LEAFLET.

PARTICIPANT INFORMATION LEAFLET

Oral symptoms in older patients with frailty: a prospective observational study using the Oral Symptom Assessment Scale

Principal investigator's name:	Andrew Davies
Principal investigator's title:	Professor
Telephone number of principal investigator:	01 406 8700
Co-investigator's name:	Niamh Cleary
Co-investigator's title:	Doctor
Other co-investigators:	Professor Roman Romero-Ortuno, Dr Amanda Lavan, Ms Norah Fagan, Dr Jenny Power, Dr Craig Gouldthorpe
Data Controller's/joint Controller's Identity:	Our Lady's Hospice and Care Services, Harold's Cross Dublin 6W
Data Controller's/joint Controller's Contact Details:	01 406 8700
Data Processors Identity: for this study	There are no third party data processors
Data Handler's Identity:	Dr Niamh Cleary, Ms Norah Fagan
Data Handlers Contact Details:	Academic Department of Palliative Medicine, Our Lady's Hospice and Care Services, Harold's Cross, Dublin 6W
Data Protection Officer's Identity:	Pat Pierce
Data Protection Officer's Contact Details:	ppierce@olh.ie; 01-4068725

You are being invited to take part in a research study to be carried out at St James' Hospital and Our Lady's Hospice and Care Services, Harold's Cross by Professor Andrew Davies.

Before you decide whether or not you wish to take part, you should read the information provided below carefully and, if you wish, discuss it with your family, friends or GP (doctor). Take time to ask questions – do not feel rushed and do not feel under pressure to make a quick decision.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you. This process is known as 'Informed Consent'.

You do not have to take part in this study. If you decide not to take part it will not affect your future medical care.

You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt out. You do not have to give us a reason. If you do opt out, rest assured it will not affect the quality of treatment you get in the future. If you wish to opt out, please contact Dr Niamh Cleary (ncleary@olh.ie) who will be able to organise this for you.

PART 1 – THE STUDY

Why is this study being done?

Oral (or mouth) symptoms are common in older patients who live with frailty. We know that frailty describes someone's overall resilience and how this relates to their chances of recovery following a health problem. A questionnaire called the Oral Symptom Assessment Scale (or OSAS) was designed to look at mouth symptoms in patients who had an advanced cancer. These symptoms may overlap with patients who have frailty. This research study is taking place to find out if the OSAS will be a suitable questionnaire that can be used in older patients who live with frailty.

Why am I being asked to take part?

You have been invited to participate in this study because you are a patient at Our Lady's Hospice and Care Services, Harold's Cross, Dublin or St James' Hospital, Dublin. It is hoped that your participation in the study will inform our assessment of oral (mouth) symptoms and contribute to how we ask about these symptoms in the future.

Do I have to take part? What happens if I say no? Can I withdraw?

Participation in this study is **voluntary**. You do not have to take part in this study. If you decide not to take part it will not affect your future medical care. You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt out. You do not have to give us a reason. If you do opt out, rest assured it will not affect the quality of treatment you get in the future. If you wish to opt out, please contact Dr Niamh Cleary (ncleary@olh.ie) who will be able to organise this for you.

How will the study be carried out?

You will be asked by our researcher about the presence or absence of 21 mouth symptoms in the past week. If present, you will be asked about how bothersome each symptom is for you as well as the severity and frequency. You can also name any three additional mouth symptoms that are not listed. You will also be asked about the questionnaire itself to provide feedback. It will take approximately 10-15 minutes to complete both.

The study is taking place over a period of 6 months. 250 patients will be participating in the study.

Your identity will remain confidential. A study number will identify you. Your name will not be published or disclosed to anyone. The research team will collect information from you or your medical record including your age, sex, medical background, and medications. This information will be kept private.

What will happen to me if I agree to take part?

You will meet with a researcher in either the Robert Mayne Day Centre in St. James' Hospital or in Our Lady's Hospice and Care Services at Harold's Cross who will conduct a 'one-off' interview with you. You will be asked about the presence or absence of 21 mouth symptoms in the past week. If present, you will be asked about how bothersome each symptom is for you as well as the severity and frequency. You can also name any additional mouth symptoms that are not listed. You will also be asked about the questionnaire itself to provide feedback. It will take approximately 10-15 minutes to complete both.

The study is taking place over a period of 6 months.

The research team will collect information from you or your medical record including your age, gender, medical background and medications. This information will be kept private.

Are there any benefits to me or others if I take part in the study?

You will not benefit directly from taking part in this study, but the information obtained may contribute to improving the assessment, diagnosis and management of mouth symptoms. The ultimate goal of this study is to improve quality of life for those who suffer with mouth symptoms.

Are there any risks to me or others if I take part in the study?

There are no risks involved in participating in the study.

What will happen if something goes wrong when I'm taking part in the study?

In the event of an abnormality being discovered and you consent e.g., dry mouth your doctor will then be informed so that appropriate steps can be taken to improve this for you.

Will I be told the outcome of the study?

You will not be told about the outcome of the study.

The results of the research will be disseminated in relevant medical journals and medical conferences.

PART 2 – DATA PROTECTION

What information about me (personal data) will be used as part of this study? Will my medical records be accessed?

The research team will collect information from you or your medical record including:

- Age
- Sex
- Medical background
- Clinical frailty score
- Medications

We will be using your personal information in our research to help us study if there are any associations of the information collected with the mouth symptoms you may report.

What will happen my personal data?

Your data will be processed only as is necessary to achieve the outcome of the study and not in any way which may cause damage or distress. Processing of your personal data will comply with the General Data Protection Regulation and the Data Protection Act 2018.

Your results from the OSAS questionnaire and feedback will be uploaded to a password-protected Excel spreadsheet. Only those listed as the principal investigator and co-investigators will have access to the research drive where the password-protected spreadsheet will be.

Your consent form and data collection sheets will be stored securely in the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Services, Harold's Cross for five years following the end of the study period before being destroyed. You have the right to withdraw consent to your personal data being used in this research project. You will be able to do this by contacting Dr Niamh Cleary at 01-406 8700.

Your personal data will not leave the State.

Who will access and use my personal data as part of this study?

The Principal Investigator and co-investigators will have access to your personal data. Your personal data will only be used for the purpose of this research study. Any potential data breaches will be reported immediately to the Data Protection Officer, and where required, to the Data Protection Commission.

Will my personal data be kept confidential? How will my data be kept safe?

The information about you will be kept private and confidential. Your personal data will only be used for the purpose of this research study.

You will not receive the results of this research study. The results of this study will be disseminated at relevant medical conferences and published in relevant medical journals.

No presentation or publication in relation to the study could identify you. No information will be kept for use in future research studies.

Your results from the OSAS questionnaire and feedback will be uploaded to a password-protected Excel spreadsheet. Only those listed as the principal investigator and co-investigators will have access to the research drive where the password-protected spreadsheet will be.

Your consent form and data collection sheets will be stored securely in the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Services, Harold's Cross for five years following the end of the study period before being destroyed.

What is the lawful basis to use my personal data?

As per the European General Data Protection Regulation (GDPR), the lawful basis for using your personal information is for scientific research (Article 9(2) (j)) in the public interest (Article 6(1)(e)).

What are my rights?

You have rights under Data Protection Legislation. These rights include:

- The right to access your data and to request a copy of it.
- The right to restrict or object to processing of your data.
- The right to object to any further processing of the information we hold about you (except where it is de-identified).
- The right to have inaccurate information about you corrected or deleted.
- The right to receive your data in a portable format and to have it transferred to another data controller.
- The right to deletion of your data.
- The right to object to automated processing including profiling.
- You have the right under data protection legislation to lodge a complaint with the Data Protection Commissioner in Ireland if you have concerns that we have infringed data protection legislation while processing your data.

By law, you can exercise these rights in relation to your personal data unless the request would make it very difficult to conduct the research. You can exercise these rights by contacting your study doctor (Dr Niamh Cleary, 01-406 8700) or The Data Protection Officer Ms Pat Pierce, Our Lady's Hospice & Care Services, Dublin 6W. Email: ppierce@olh.ie. Phone: 01-4068725.

PART 3 – COSTS, FUNDING & APPROVAL

Will it cost me anything if I agree to take part?

There is no payment or expenses for taking part in this research.

Who is funding this study? Will the results study be used for commercial purposes?

This research is being organised by the Academic Department of Palliative Medicine at Our Lady's Hospice and Care Services. There is no commercial or pharmaceutical sponsorship of this research. This research is being conducted as part of an academic qualification in collaboration with Trinity College Dublin.

Has this study been approved by a research ethics committee?

St James's Hospital / Tallaght University Hospital Joint Research and Ethics Committee has reviewed and approved this study (researchethics@tuh.ie)
The date ethical approval was given by the committee was:

PART 4 – FUTURE RESEARCH

Will my personal data and/or biological material be used in future studies?

Your data will not be used for future research.

PART 5 – FURTHER INFORMATION

Where can I get further information?

If you have any further questions about the study or if you want to opt out of the study, you can rest assured it will not affect the quality of treatment you get in the future.

If you need any further information now or at any time in the future, please contact:

- Principal Investigator: Professor Andrew Davies, Academic Department of Palliative Medicine, Our Lady's Hospice & Care Services; 01-4986235.
- Data Protection Officer: Ms Pat Pierce, Our Lady's Hospice & Care Services; 01-4068725

What happens if I wish to make a complaint?

If you wish to make a complaint, please contact Dr Niamh Cleary (ncleary@olh.ie or 01 406 8700)

Will I be contacted again?

You will not be contacted again.

We wish to thank you for taking the time to consider participating in this study.

APPENDIX 12: DATA COLLECTION SHEET/CASE REPORT FORM.

Study number:

Study Date:

Sex: Male ☐ Female ☐

Age:

CFS:

CIR-G:

Medications - Please list

APPENDIX 13: CIRS-G SCORING GUIDANCE.

Heart	No problem (0) Remote MI (> five years ago)/occasional angina treated with prn meds (1) CHF compensated with meds/daily anti-angina meds/left ventricular hypertrophy/atrial fibrillation/bundle branch block/daily antiarrhythmic drugs (2) Previous MI within five years/abnormal stress test/status post percutaneous coronary angioplasty or coronary artery bypass graft surgery (3) Marked activity restriction secondary to cardiac status (i.e., unstable angina or intractable congestive heart failure)(4)
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Vascular	No problem (0) Hypertension compensated with salt restriction and weight loss/serum cholesterol > 200 mg/dl (1) Daily antihypertensive meds/one symptom of atherosclerotic disease (angina, claudication, bruit, amaurosis fugax, absent pedal pulses)/aortic aneurysm < 4 cm (2) Two or more symptoms of atherosclerosis [see above] (3) Previous surgery for vascular problem/aortic aneurysm > 4 cm (4)
Haematopoietic	No problem (0) Haemoglobin: females > 10 < 12, males > 12 < 14/anaemia of chronic disease (1) Haemoglobin: females > 8g/dL < 10g/dL, males > 10g/dL < 12g/dL/anaemia secondary to iron, vitamin B12, or folate deficiency or chronic renal failure/total white blood cell count > 2000 but < 4000 (2) Haemoglobin: females < 8g/dL, males < 10g/dL/total WBC < 2000 (3) Any leukaemia, any lymphoma (4)
Respiratory	No problem (0) Recurrent episodes of acute bronchitis/currently treated asthma with prn inhalers/cigarette smoker > 10 but < 20 pack years (1) X-ray evidence of COPD/requires daily theophylline or inhalers/treated for pneumonia two or more times in the past five years/smoked 21-40 pack years (2) Limited ambulation secondary to limited respiratory capacity/requires oral steroids for lung disease/smoked > 40 pack years (3) Requires supplemental Oxygen/at least one episode of respiratory failure requiring assisted ventilation/any lung cancer (4)

Eyes, ears, nose, throat, and larynx	No problem (0) Corrected vision 20/40;/chronic sinusitis/mild hearing loss (1) Corrected vision 20/60 or reads newsprint with difficulty/requires hearing aid/chronic sinonasal complaints requiring medication/requires medication for vertigo (2) Partially blind (requires an escort to venture out)/unable to read newsprint/conversational hearing still impaired with hearing aid (3) Functional blindness/functional deafness/laryngectomy/requires surgical intervention for vertigo (4)
Upper GI	No problem (0) Hiatal hernia/heartburn complaints treated with prn meds (1) Needs daily H2 blocker or antacid/documentated gastric or duodenal ulcer within five years (2) Active ulcer/guaiac positive stools/any swallowing disorder or dysphagia (3) Gastric cancer/history of perforated ulcer/melena or haematochezia from UGI source (4)
Lower GI	No problem (0) Constipation managed with prn meds/active haemorrhoids/status post hernia repair (1) Requires daily bulk laxatives or stool softeners/diverticulosis/untreated hernia (2) Bowel impaction in the past year/daily use of stimulant laxatives or enemas (3) Haematochezia from lower GI source, currently impacted, diverticulitis flare up/status post bowel obstruction/bowel carcinoma (4)

Liver, pancreas and biliary	No problem (0) History of hepatitis > five years ago/cholecystectomy(1) Mildly elevated LFT's (up to 150% of normal)/hepatitis within five years/cholelithiasis/daily or heavy alcohol use within five years (2) Elevated bilirubin (total > 2mg/dL)/marked elevation of LFTs (> 150% of normal)/requires supplemental pancreatic enzymes for digestion (3) Biliary obstruction/any biliary tree carcinoma/cholecystitis/pancreatitis/active hepatitis (4)
Renal	No problem (0) Kidney stone passage within the past 10 years or asymptomatic kidney stone/ pyelonephritis within five years (1) Serum creatinine > 1.5mg/dL but < 3.0mg/dL without diuretic or antihypertensive medication (2) Serum creatinine > 3.0mg/dL or serum creatinine > 1.5mg/dL in conjunction with diuretic, antihypertensive, or bicarbonate therapy/current pyelonephritis (3) Requires dialysis/renal carcinoma (4)
Genitourinary	No problem (0) Stress incontinence/hysterectomy/BPH without urinary symptoms (1) Abnormal pap smear/frequent UTI's (three or more in past year)/urinary incontinence (non-stress) in females/BPH with hesitancy or frequency/current UTI/any urinary diversion procedure/status post TURP (2) Prostate cancer in situ (i.e., found incidentally during TURP)/vaginal bleeding/cervical carcinoma in situ/haematuria/status post urosepsis in past year (3) Acute urinary retention/any GU carcinoma except as above (4)

Musculoskeletal and skin	No problem (0) Uses prn meds for arthritis or has mildly limited ADLs from joint pathology/excised non-melanotic skin cancers/skin infections requiring antibiotics within a year (1) Daily antiarthritic meds or use of assistive devices or moderate limitation in ADLs/daily meds for chronic skin conditions/melanoma without metastasis (2) Severely impaired ADLs secondary to arthritis/requires steroids for arthritic condition/vertebral compression fractures from osteoporosis (3) Wheelchair bound/severe joint deformity or severely impaired usage/osteomyelitis/any bone or muscle carcinoma/metastatic melanoma (4)
Neurologic	No problem (0) Frequent headaches requiring prn meds without interference with daily activities/a history of TIA phenomena (at least one). Requires daily meds for chronic headaches or headaches that regularly interfere with daily activities/status post CVA without significant residual/neurodegenerative disease (Parkinson's, MS, ALS, etc) - mild severity (2) Status post CVA with mild residual dysfunction/any CNS neurosurgical procedure/neurodegenerative disease - moderate severity (3) Status post CVA with residual functional hemiparesis or aphasia/neurodegenerative disease-severe (4)
Endocrine and breast	No problem (0) Diabetes mellitus compensated with diet/obesity: BMI > 30/requires thyroid hormone replacement (1) Diabetes mellitus requiring insulin or oral agents/fibrocystic breast disease (2) Any electrolyte disturbance requiring hospital treatment/morbid obesity BMI > 45 (3) Brittle or poorly controlled diabetes mellitus or diabetic coma in the past year/requires adrenal hormone replacement/adrenal, thyroid or breast carcinoma (4)

Psychiatric illness	No problem(0) Minor psychiatric condition or history thereof. Specifically: previous outpatient mental health treatment during a crisis/outpatient treatment for depression > 10 years ago/current usage of minor tranquilizers for episodic anxiety (occasional usage)/mild early dementia (MMSE > 25 < 28) (1) A history of Major Depression (by DSM) within the past 10 years (treated or untreated)/mild dementia (MMSE 20-25)/any previous psychiatric hospitalization/any psychotic episode substance abuse history > 10 years ago (2) Currently meets DSM criteria for major depression or two or more episodes of major depression in the past 10 years/moderate dementia (MMSE 15-20)/current usage of daily antianxiety medication/currently meets DSM criteria for substance abuse or dependence/requires daily antipsychotic medication (3) Current mental illness requiring psychiatric hospitalization, institutionalization, or intensive outpatient management, e.g., patients with severe or suicidal depression, acute psychosis or psychotic decompensation, severe agitation from dementia, severe substance abuse etc./Severe dementia (MMSE < 15) (4)
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APPENDIX 14: PUBLICATION: THE ORAL SYMPTOM ASSESSMENT (OSAS): CRITERION VALIDATION WITH THE EORTC QLQ-OH15 AND RELIABILITY TESTING.

Supportive Care in Cancer (2023) 31:647
https://doi.org/10.1007/s00520-023-08118-2

RESEARCH



The Oral Symptom Assessment Scale (OSAS): criterion validation with the EORTC QLQ-OH15 and reliability testing

Niamh Cleary¹ · Suzanne Guerin² · Norah Fagan³ · Andrew Davies^{1,3,4}

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Abstract

Purpose The aim of this study was to investigate the criterion validity and reliability of the Oral Symptom Assessment Scale (OSAS) in patients with advanced cancer receiving specialist palliative care.

Methods To examine criterion validity, participants completed the OSAS, EORTC QLQ-C30 and EORTC QLQ-OH15. Twenty-four hours later participants repeated the OSAS to investigate test–retest reliability.

Results 54 participants were recruited (median age 70; range: 35–93 years). 51 complete datasets were obtained. Cohen's kappa test was used to evaluate the agreement for the presence / absence of symptoms on the OSAS on the first and second days (test–retest reliability). This analysis showed values of moderate and higher for agreement for all symptoms. All kappa values were statistically significant. The test–retest reliability for symptom severity, frequency and distress was assessed using Intraclass Correlation Coefficient. Spearman's rank correlation coefficients were used to evaluate agreement between similar questions on the OSAS from day one and the EORTC QLQ-OH15 also on day one to examine criterion validity.

Conclusion This study supports the validity of the OSAS, and provides evidence for the reliability of this novel oral symptom assessment tool, in patients with advanced cancer. Further research is needed to corroborate the findings of this study.

Trial registration CancerTrials.gov registry registration no.: PM202166

Keywords Oral care · Oral health · Neoplasms · Palliative care

Introduction

Oral symptoms are common in patients with advanced cancer [1], and are often associated with significant distress / “bothersomeness” and a negative impact on quality of life [2]. However, many generic symptom assessment tools contain no or only a very limited number of oral symptoms [3]. For example, the commonly-employed Memorial Symptom Assessment Scale / MSAS [4], which consists of 32 symptoms (26 physical, six psychological), includes only four oral symptoms, i.e., “dry mouth”, “change in the way food tastes”, “difficulty swallowing”, and “mouth sores”.

A recent scoping review identified a dearth of validated oral symptom assessment tools in patients with advanced cancer [5]. The review highlighted the Oral Symptom Assessment Scale (OSAS), which was specifically developed to assess oral symptoms in this cohort of patients [2]. The OSAS is a patient-rated tool, which asks about twenty oral symptoms. Patients are asked about the presence of each symptom in the preceding week, and (if present) to rate how often the symptom was experienced (i.e., “rarely”, “occasionally”, “frequently”, “almost constantly”), how severe it was (i.e., “slight”, “moderate”, “severe”, “very severe”), and how distressing or bothersome it was (i.e., “not at all”, “a little bit”, “somewhat”, “quite a bit”, “very much”). Patients are also asked about the presence of any other oral symptoms.

The OSAS has undergone a degree of validation during its development, including content validity, and an initial observational study in patients with advanced cancer that established criterion validity [2]. However, it has not previously undergone any reliability testing, including test–retest reliability. The aim of this study was to carry out further testing of the psychometric properties of the original OSAS (see supplementary

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material), with the objectives being to assess its reliability, and to further assess its criterion validity using a cancer-related oral quality of life instrument (the EORTC QLQ-OH15) [6]. The EORTC QLQ-OH15 was developed for patients with cancer, but not specifically for patients with advanced cancer.

Methods

This prospective observational study was conducted at Our Lady's Hospice and Care Services (Dublin, Ireland). The study was sponsored by Our Lady's Hospice and Care Services, and received ethical approval from the St Vincent's University Hospital Ethics Committee (RS21-044). The study was registered on ClinicalTrials.gov (reference number: PM202166).

Participants were recruited from inpatients at the Hospice. All patients that met the study criteria were eligible for entry into the study. The inclusion criteria were: (1) advanced cancer (as defined by the National Cancer Institute in USA) [7]; (2) age ≥ 18 years old; (3) able to understand and speak English; (4) able to provide written consent; and (5) in a 'stable' palliative care phase [8]. The exclusion criteria were: (1) unable to provide written consent; (2) unable to complete the study assessments; and (3) in an 'unstable', 'deteriorating' or 'terminal' palliative care phase [8].

Informed consent was obtained prior to entry into the study. The study was undertaken on two consecutive days in order to assess the reliability of the OSAS. This time scale was chosen due to the clinical instability of this cohort of patients, and is supported by a systematic review of validation studies in patients with advanced cancer [9]. On the first day, demographic (age, sex) and other relevant information (cancer diagnosis, ECOG performance status) were collected, and the participants were asked to complete the OSAS, the EORTC QLQ-C30, and the EORTC QLQ-OH15 (see below): on the second day the participants were asked to complete the OSAS again. The time taken to complete the questionnaires was recorded.

The EORTC QLQ-C30 is a health-related quality of life (HRQoL) measurement instrument, which has been extensively validated (and utilised) in patients with cancer [10]. It is 30-item tool and contains five functional scales, three symptom scales, six single items, and a global health status/quality of life scale. The EORTC QLQ-OH15 is a 15-item tool, and patients are asked to rate the "extent" to which the fifteen symptoms or problems have been experienced in the past week [6]. It contains an eight-item oral health quality of life scale, three single items (i.e. sticky saliva, mouth soreness, sensitivity to food/drink), and two two-item scales: the first scale relates to the use (yes/no) and problems with dentures, whilst the second scale relates to the reception (yes/no) and satisfaction of information received about dental or mouth problems. The EORTC QLQ-OH15 is the oral health module

of the EORTC QLQ-C30, and as such it must be completed in conjunction with the EORTC QLQ-C30. Permission was granted to use the EORTC QLQ-OH15 in this study (Permission reference ID: 74963).

Statistical analysis

The estimation method [11] for sample size calculation for intraclass correlation coefficient was used to determine the sample size for this study. An expected reliability of 0.8 with a precision of ± 0.1 was determined through review of the relevant literature [9], and from researcher experience (based on confidence level: 95%; number of repetitions per subject(k): 2; expected dropout rate: 20%). A sample size of 51 complete datasets was determined based on this calculation method. Three participants did not complete both days so recruitment continued until 51 completed tests were obtained.

IBM®SPSS® Statistics (Version: 28.0.1.1(14)) software was used to undertake the statistical analysis. The OSAS responses were scored as follows for the statistical analysis: if a symptom is not present it is assigned a score of zero. If present, the frequency was scored as "rarely" (= 1), "occasionally" (= 2), "frequently" (= 3), "almost constantly" (= 4); the severity was scored as "slight" (= 1), "moderate" (= 2), "severe" (= 3), "very severe" (= 4); and the level of distress / bothersomeness was scored as "not at all" (= 0.8), "a little bit" (= 1.6), "somewhat" (= 2.4), "quite a bit" (= 3.2), "very much" (= 4). Similarly, the EORTC QLQ-OH15 "extent" experienced responses were scored as follows: "not at all" (= 1), "a little bit" (= 2), "quite a bit" (= 3), "very much" (= 4).

Reliability testing: Cohen's kappa test was used to evaluate the agreement for the presence / absence of symptoms on the OSAS on the first and second days. Intraclass correlation coefficient (ICC) analysis was used to evaluate the agreement for the frequency, severity, and degree of distress / bothersomeness of symptoms on the first and second days. The evaluation of ICC in this study was based on a single-rating (type), absolute agreement (definition), two-way mixed effects model (model) [12]. Concurrent validity testing: Spearman's rank correlation coefficients were used to evaluate agreement between similar questions on the OSAS from day one and the EORTC QLQ-OH15 (also from day one).

Results

Fifty-four patients were recruited, and 51 completed both assessments. The reasons for the three patients not completing the second assessment were one patient transitioned into the 'deteriorating' phase and two patients declined. Table 1 shows the characteristics of the recruited patients.

Fifty three patients (98.1%) reported at least one oral symptom on the OSAS, and the median number of oral

Table 1 Characteristics of participants

Characteristic	Number of participants (n = 54)
Age	
Median (range)	70 years (35–93 years)
Gender	
Female	26 (48.1%)
Male	28 (51.9%)
Cancer diagnosis	
Breast	6 (11.1%)
Gastrointestinal	13 (24.1%)
Gynaecological	1 (1.9%)
Haematological	3 (5.6%)
Head and neck	4 (7.4%)
Lung	12 (22.2%)
Neurological	2 (3.7%)
Skin	1 (1.9%)
Urological	11 (20.4%)
Primary of unknown origin	1 (1.9%)
ECOG performance status (self-reported)	
0	0 (0%)
1	4 (7.4%)
2	23 (42.6%)
3	26 (48.1%)
4	1 (1.9%)

symptoms was four (range 1–12). Table 2 shows the prevalence of oral symptoms and the level of distress associated with these symptoms. Dry mouth (xerostomia) was the most common symptom (77.8%), with 57.1% reporting that it occurred “frequently” or “almost constantly”, 83.4% reporting that it was “moderate”, “severe” or “very severe”, and 40.5% reporting that the distress it caused was “quite a bit” or “very much”. Tables demonstrating the frequency and severity of these symptoms can be found in the online supplemental resources. The median time to complete the OSAS was 5.15 min (range 2.24–14.35 min).

Table 3 shows the extent of the oral symptoms / problems experienced by the patients on the EORTC QLQ-OH15. The data from the EORTC QLQ-C30 is reported in the supplementary material. 75.9% reported “a little”, “quite a bit” or “very much” dry mouth. This is similar to the OSAS data (77.8% reported the presence of dry mouth). 14 patients reported problems with ill-fitting dentures however only 2 patients reported “denture fitting problems” on the OSAS. The reason for this significant difference is unclear. Table 4 shows the correlations between the scores derived from the EORTC QLQ-OH15 and the scores derived from the OSAS for the seven analogous questions. There was a very strong correlation between the extent of “soreness in your mouth” experienced on

Table 2 Amount of distress caused by oral symptoms (OSAS data)

Symptom	Number patients (n = 54)	Amount of distress / Bothersomeness				
		Not at all	A little bit	Somewhat	Quite a bit	Very much
Dry mouth	42 (77.8%)	6 (14.3%)	12 (28.6%)	7 (16.7%)	12 (28.6%)	5 (11.9%)
Mouth discomfort/pain	17 (31.5%)	2 (11.8%)	2 (11.8%)	6 (35.3%)	3 (17.6%)	4 (23.5%)
Lip discomfort	24 (44.4%)	7 (29.2%)	6 (25%)	6 (25%)	3 (12.5%)	2 (8.3%)
Cracking of lips	15 (27.8%)	4 (26.7%)	4 (26.7%)	2 (13.3%)	4 (26.7%)	1 (6.7%)
Cracking of corner of mouth	14 (25.9%)	3 (21.4%)	3 (21.4%)	3 (21.4%)	5 (35.7%)	0 (0%)
Taste disturbance	21 (38.9%)	3 (14.3%)	7 (33.3%)	3 (14.3%)	5 (23.8%)	3 (14.3%)
Difficulty chewing	18 (33.3%)	2 (11.1%)	3 (16.7%)	1 (5.6%)	7 (38.9%)	5 (27.8%)
Difficulty swallowing	15 (27.8%)	3 (20%)	2 (13.3%)	4 (26.7%)	2 (13.3%)	4 (26.7%)
Difficulty speaking	17 (31.5%)	1 (5.9%)	8 (47.1%)	2 (11.8%)	4 (23.5%)	2 (11.8%)
“Dirty mouth”	25 (46.3%)	1 (4%)	8 (32%)	6 (24%)	4 (16%)	6 (24%)
Coating of tongue	17 (31.5%)	5 (29.4%)	3 (17.6%)	2 (11.8%)	3 (17.6%)	4 (23.5%)
Bad breath	7 (13%)	2 (28.6%)	1 (14.3%)	0 (0%)	3 (42.9%)	1 (14.3%)
Toothache / pain in teeth	5 (9.3%)	0 (0%)	1 (20%)	1 (20%)	3 (60%)	0 (0%)
Sensitivity of teeth	6 (11.1%)	0 (0%)	3 (50%)	2 (33.3%)	1 (16.7%)	0 (0%)
Jagged teeth	12 (22.2%)	5 (41.7%)	3 (25%)	1 (8.3%)	2 (16.7%)	1 (8.3%)
Denture fitting problems	2 (3.7%)	0 (0%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)
Bleeding from mouth	1 (1.9%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Burning sensation in mouth	7 (13%)	3 (42.9%)	1 (14.3%)	2 (28.6%)	0 (0%)	1 (14.3%)
Altered sensation in mouth	3 (5.6%)	1 (33.3%)	0 (0%)	1 (33.3%)	1 (33.3%)	0 (0%)
Ulcers in mouth	3 (5.6%)	1 (33.3%)	0 (0%)	1 (33.3%)	0 (0%)	1 (33.3%)

Table 3 “Extent” oral symptoms experienced (EORTC QLQ-OH15 data)

Symptom	“Extent to which you have experienced”			
	Not at all	A little	Quite a bit	Very much
Have you had pain in your gums?	46 (85.2%)	4 (7.4%)	4 (7.4%)	0 (0%)
Have you had problems with bleeding gums?	52 (96.3%)	2 (3.7%)	0 (0%)	0 (0%)
Have you had lip sores?	44 (81.5%)	5 (9.3%)	2 (3.7%)	3 (5.6%)
Have you had problems with your teeth?	48 (88.9%)	2 (3.7%)	2 (3.7%)	2 (3.7%)
Have you had soreness in your mouth?	37 (68.5%)	10 (18.5%)	4 (7.4%)	3 (5.6%)
Have you had sores in the corners of your mouth?	44 (81.5%)	4 (7.4%)	2 (3.7%)	4 (7.4%)
Have you had a dry mouth?	13 (24.1%)	12 (22.2%)	10 (18.5%)	19 (35.2%)
Have you had sticky saliva?	29 (53.7%)	9 (16.7%)	9 (16.7%)	7 (13%)
Has your mouth been sensitive to food and drink?	31 (57.4%)	9 (16.7%)	7 (13%)	7 (13%)
Have food and drink tasted different than usual?	34 (63%)	8 (14.8%)	5 (9.3%)	7 (13%)
Have you had problems with eating solid foods?	23 (42.6%)	12 (22.2%)	7 (13%)	12 (22.2%)
Have you had problems with an ill-fitting denture? (<i>n</i> = 14)	11 (78.6%)	0 (0%)	0 (0%)	3 (21.4%)

the EORTC QLQ-OH15 and the frequency of “mouth discomfort / pain” on the OSAS (with a strong correlation with the distress caused, but a weak correlation with the severity). Similarly, there was a strong correlation between the extent “dry mouth” experienced on the EORTC QLQ-OH15 and the frequency of “dry mouth” on the OSAS (with a moderate correlation with the distress caused and the severity). It was not possible to determine any correlation for denture fitting problems, or bleeding from the mouth, due to limited number of patients with these oral problems.

Table 5 shows the data relating to test–retest reliability of the OSAS. Difficulty chewing showed almost perfect agreement, whilst 12 other symptoms showed substantial agreement, and six symptoms showed moderate agreement. It was not possible to assess bleeding from the mouth due to limited number of patients with this symptom (*n* = 1). Ulcers in mouth and denture fitting problems showed excellent reliability in the bothersomeness domain: two other symptoms showed excellent reliability, six good reliability, six moderate reliability, and four poor reliability (with no values calculable for two problems due to limited number of patients with these symptoms).

Table 4 Correlation between responses to analogous questions on the EORTC QLQ-OH15 and OSAS

EORTC symptom / problem	OSAS symptom			
	Prevalence	Frequency	Severity	Amount of distress / bothersomeness
‘Have you had a dry mouth?’	“Dry mouth” (<i>n</i> = 42)	$r_s = 0.643$ (<i>p</i> = < 0.001)	$r_s = 0.522$ (<i>p</i> = < 0.001)	$r_s = 0.481$ (<i>p</i> = 0.001)
‘Have you had soreness in your mouth?’	“Mouth discomfort/pain” (<i>n</i> = 17)	$r_s = 0.830$ (<i>p</i> = < 0.001)	$r_s = 0.294$ (<i>p</i> = 0.251)	$r_s = 0.689$ (<i>p</i> = 0.002)
‘Have you had lip sores?’	“Lip discomfort” (<i>n</i> = 24)	$r_s = 0.590$ (<i>p</i> = 0.002)	$r_s = 0.447$ (<i>p</i> = 0.028)	$r_s = 0.378$ (<i>p</i> = 0.068)
‘Have you had lip sores?’	“Cracking of lips” (<i>n</i> = 15)	$r_s = 0.534$ (<i>p</i> = 0.040)	$r_s = 0.642$ (<i>p</i> = 0.010)	$r_s = 0.056$ (<i>p</i> = 0.842)
‘Have you had sores in the corners of your mouth?’	“Cracking of corner of mouth” (<i>n</i> = 14)	$r_s = 0.585$ (<i>p</i> = 0.028)	$r_s = 0.304$ (<i>p</i> = 0.291)	$r_s = 0.652$ (<i>p</i> = 0.012)
‘Have food and drink tasted different than usual?’	“Taste disturbance” (<i>n</i> = 21)	$r_s = 0.312$ (<i>p</i> = 0.169)	$r_s = 0.411$ (<i>p</i> = 0.064)	$r_s = 0.528$ (<i>p</i> = 0.014)
‘Have you had problems eating solid foods?’	“Difficulty chewing” (<i>n</i> = 18)	$r_s = 0.311$ (<i>p</i> = 0.209)	$r_s = 0.214$ (<i>p</i> = 0.394)	$r_s = 0.287$ (<i>p</i> = 0.248)

r_s spearman’s rank correlation coefficient

Spearman’s Rank Correlation Coefficient (r_s) of 0.00–0.19 is considered “very weak”, 0.20–0.39 is “weak”, 0.40–0.59 is “moderate”, 0.60–0.79 is “strong”, and 0.80–1.0 is “very strong” [13]

Table 5 Test–retest reliability of OSAS

Symptom	Cohen's Kappa (κ)	Intraclass correlation coefficient (ICC)		
		Presence [51]	Frequency	Severity
Dry mouth (n = 35)	$\kappa = 0.564$ ($p = < 0.001$)	ICC = 0.425 [95% CI: 0.113–0.661]	ICC = 0.503 [95% CI: 0.203–0.715]	ICC = 0.279 [95% CI: -0.064–0.560]
Mouth discomfort/pain (n = 13)	$\kappa = 0.647$ ($p = < 0.001$)	ICC = 0.576 [95% CI: 0.069–0.848]	ICC = 0.276 [95% CI: -0.214–0.688]	ICC = 0.536 [95% CI: 0.046–0.827]
Lip discomfort (n = 16)	$\kappa = 0.598$ ($p = < 0.001$)	ICC = 0.791 [95% CI: 0.508–0.921]	ICC = 0.127 [95% CI: -0.412–0.583]	ICC = 0.242 [95% CI: -0.242–0.651]
Cracking of lips (n = 11)	$\kappa = 0.622$ ($p = < 0.001$)	ICC = 0.739 [95% CI: 0.265–0.923]	ICC = 0.185 [96% CI: -0.271–0.651]	ICC = 0.713 [95% CI: 0.210–0.915]
Cracking of corner of mouth (n = 11)	$\kappa = 0.622$ ($p = < 0.001$)	ICC = 0.704 [95% CI: 0.192–0.912]	ICC = 0.294 [95% CI: -0.378–0.749]	ICC = 0.638 [95% CI: 0.094–0.888]
Taste disturbance (n = 14)	$\kappa = 0.620$ ($p = < 0.001$)	ICC = 0.684 [95% CI: 0.260–0.887]	ICC = 0.387 [95% CI: -0.182–0.755]	ICC = 0.604 [95% CI: 0.159–0.851]
Difficulty chewing (n = 17)	$\kappa = 0.914$ ($p = < 0.001$)	ICC = 0.509 [95% CI: 0.068–0.787]	ICC = 0.509 [95% CI: 0.078–0.786]	ICC = 0.233 [95% CI: -0.206–0.618]
Difficulty swallowing (n = 11)	$\kappa = 0.705$ ($p = < 0.001$)	ICC = 0.543 [95% CI: -0.070–0.854]	ICC = 0.882 [95% CI: 0.627–0.967]	ICC = 0.751 [95% CI: 0.291–0.927]
Difficulty speaking (n = 10)	$\kappa = 0.528$ ($p = < 0.001$)	ICC = 0.591 [95% CI: -0.027–0.880]	ICC = 0.679 [95% CI: 0.144–0.909]	ICC = 0.897 [95% CI: 0.649–0.973]
“Dirty mouth” (n = 16)	$\kappa = 0.559$ ($p = < 0.001$)	ICC = 0.368 [95% CI: -0.081–0.711]	ICC = 0.363 [95% CI: -0.164–0.723]	ICC = 0.739 [95% CI: 0.410–0.900]
Coating of tongue (n = 14)	$\kappa = 0.735$ ($p = < 0.001$)	ICC = 0.307 [95% CI: -0.267–0.713]	ICC = 0.761 [95% CI: 0.407–0.916]	ICC = 0.888 [95% CI: 0.693–0.962]
Bad breath (n = 6)	$\kappa = 0.766$ ($p = < 0.001$)	ICC = 0.898 [95% CI: 0.513–0.985]	ICC = 0.706 [95% CI: -0.019–0.952]	ICC = 0.536 [95% CI: -0.295–0.917]
Toothache/pain in teeth (n = 4)	$\kappa = 0.778$ ($p = < 0.001$)	ICC = 0.889 [95% CI: 0.260–0.992]	ICC = 0.250 [95% CI: -0.363–0.907]	ICC = -0.235 [95% CI: -1.598–0.864]
Sensitivity of teeth (n = 5)	$\kappa = 0.670$ ($p = < 0.001$)	ICC = 0.806 [95% CI: -0.019–0.978]	ICC = 0.000 [95% CI: -1.272–0.843]	ICC = 0.824 [95% CI: 0.040–0.980]
Jagged teeth (n = 8)	$\kappa = 0.652$ ($p = < 0.001$)	ICC = 0.234 [95% CI: -0.551–0.783]	ICC = 0.887 [95% CI: 0.527–0.976]	ICC = 0.767 [95% CI: 0.263–0.947]
Denture fitting problems (n = 2)	$\kappa = 0.790$ ($p = < 0.001$)	ICC = 0.000 [95% CI: -0.997–0.997]	ICC = 0.000 [95% CI: -0.997–0.997]	ICC = 1 [95% CI: -]
Burning sensation in mouth (n = 3)	$\kappa = 0.558$ ($p = < 0.001$)	ICC = 1 [95% CI: -]	ICC = 0.833 [95% CI: -0.100–0.995]	ICC = 0.783 [95% CI: -0.154–0.993]
Altered sensation in mouth (n = 2)	$\kappa = 0.646$ ($p = < 0.001$)	ICC = 0.800 [95% CI: -0.631–1]	ICC = -4.00 [95% CI: -9.000–0.967]	*Part of the scale showed zero vari- ance
Ulcers in mouth (n = 2)	$\kappa = 0.541$ ($p = < 0.001$)	ICC = 0.000 [95% CI: -0.997–0.997]	ICC = 0.000 [95% CI: -0.111–0.985]	ICC = 1 [95% CI: -]

Cohen's kappa values of 0.41–0.60 are considered “moderate”, 0.61–0.80 are considered “substantial”, and 0.81–1.0 are considered “almost perfect” [14, 15]

ICC values < 0.5 are considered to indicate “poor” reliability, values between 0.5–0.75 “moderate” reliability, values between 0.75–0.9 “good” reliability, and values > 0.9 “excellent” reliability

Discussion

A recent scoping review of the literature identified a lack of validated oral symptom assessment tools in patients with advanced cancer [6]. Thus, there is no gold standard to compare against the OSAS. The EORTC QLQ-OH15 is an adjunct to the EORTC QLQ-C30, and was developed to assess the impact of oral health problems on quality of life

in patients with cancer (but not specifically patients with advanced cancer). However, the EORTC QLQ-OH15 has been extensively validated, and so we decided to use this tool to further validate the OSAS.

The validity of an instrument is the degree to which it measures what it claims to measure [16]. Criterion (or concurrent) validity demonstrates evidence of the extent “to which scores of the instrument are related to a criterion

measure” [16]. The study data suggests at least moderate agreement between analogous questions on the OSAS and the EORTC QLQ-OH15. There was a weak correlation between the questions “difficulty chewing” (OSAS) and “problems eating solid foods” (EORTC QLQ-OH15), and this undoubtedly reflects that “problems eating solid foods” is often related to other oral symptoms, e.g. dry mouth, mouth discomfort. Indeed, the correlation between the EORTC QLQ-OH15 and the OSAS varied across the various domains, and there was no obvious pattern to the variation. Thus, the correlation was strongest with frequency for dry mouth, but strongest with bothersomeness for taste disturbance.

The EORTC QLQ-OH15 states: “Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week” (with the options being “not at all”, “a little”, “quite a bit”, and “very much”). However, it is unclear what is the concrete meaning of “the extent” of the symptoms experienced and there appears to be no guidance within this tool (or indeed the other EORTC tools) about the intended meaning of the phrasing “extent” i.e. does it refer to the amount of distress or the severity of the symptom, or a combination of both. The OSAS in contrast is easy to interpret and in particular attention should be given to distressing symptoms, since this domain is most closely linked to health-related quality of life [4].

The reliability of an instrument is the extent to which it yields scores that are stable over time in “respondents who are assumed not to have changed” [16]. The test–retest results for the presence of symptoms were good, with one symptom having “almost perfect” agreement, 12 symptoms having “substantial” agreement, and six symptoms having “moderate” agreement. However, the test–retest results for the symptom domains (i.e. frequency, severity, and amount of distress / bothersomeness) were not quite as good. Nevertheless, in terms of amount of distress / bothersomeness, two symptoms showed “excellent” reliability, six showed “good” reliability, and four “moderate” reliability. It should be noted that the analysis was looking for absolute agreement, whilst many of the responses differed by a single category / point between the two test periods (e.g. a symptom’s severity rated as moderate on one day, and severe on another day).

The OSAS was modelled on the Memorial Symptom Assessment Scale [4], and importantly assesses the amount of distress or bothersomeness of the relevant oral symptoms. The latter is important since this is the domain most closely linked to quality of life [17]. Indeed, these are the symptoms that should be prioritised by healthcare professionals. However, it is important to stress that some oral problems may be asymptomatic (initially), and so the OSAS should always be accompanied by a thorough clinical (oral) examination. For

example, oral candidosis is frequently asymptomatic, even when the infection is widespread.

Conclusion

This study supports the validity of the OSAS, and provides evidence for the reliability of this novel oral symptom assessment tool, in patients with advanced cancer. Further research is needed to corroborate the findings of this study.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00520-023-08118-2>.

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Data availability All relevant generated data are presented within the manuscript or the supplementary material.

Declarations

Ethics approval This study received ethical approval from the St Vincent’s University Hospital Ethics Committee (RS21-044) and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish Consent to publish has been received from all participants in the study.

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APPENDIX 15: PUBLICATION: ORAL SYMPTOM ASSESSMENT TOOLS IN PATIENTS WITH ADVANCED CANCER: A SCOPING REVIEW.

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ORIGINAL ARTICLE



Oral symptom assessment tools in patients with advanced cancer: a scoping review

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Abstract

Purpose Oral symptoms are common in patients with advanced cancer. The aim of this scoping review was to identify oral symptom assessment tools that have been specifically utilised in patients with “advanced cancer”.

Methods The review was conducted/reported according to international guidelines for undertaking scoping reviews. PubMed, Embase, and CINAHL were searched for articles involving adult patients with advanced cancer, which involved assessment of ≥ 2 oral symptoms, and which involved patients with > 1 type of cancer.

Results The review identified four validated symptom assessment scales, including one cancer-specific quality of life scale (EORTC QLQ OH-15), one generic tool for assessing the “social impact” of specific oral problems (OHIP), one cancer-specific generic symptom assessment scale (MSAS), and one cancer-specific oral symptom assessment scale (OSAS).

Conclusion Symptom assessment tools can facilitate good symptom control in clinical practice, and are an integral component of clinical research. The review identified four validated symptom assessment scales that could be utilised to assess oral symptoms in patients with advanced cancer.

Keywords Oral care · Oral health · Neoplasms · Palliative care · Symptom assessment

Introduction

One of the main aspects of palliative care is the management of “pain and other distressing symptoms” [1]. Patients with advanced cancer experience a range of different symptoms, including a variety of different oral symptoms [2]. Thus, Davies et al. [3] reported that 97.5% of participants in their multicentre study experienced at least one oral symptom, and that the median number of oral symptoms experienced was five (range 1–18). Moreover, many of these oral symptoms had a high frequency and a high intensity, and were associated with significant distress/“bothersomeness” (and negative impact on quality of life). For example, 79.6% of participants experienced xerostomia/dry mouth, and this

was the third most common symptom overall (after “lack of energy” and “feeling drowsy”) [3].

Investigators have identified discrepancies between the recorded prevalence of oral symptoms and the true (higher) prevalence of these symptoms in patients with advanced cancer [4]. The reasons for the latter are unclear. Healthcare professionals may not enquire about a symptom if (a) they perceive the symptom to be uncommon; (b) they perceive the symptom to be unimportant; (c) they perceive there is no treatment for the symptom; and/or (d) time does not permit. Similarly, patients may not volunteer a symptom if (a) they perceive the symptom to be inevitable; (b) they perceive there is no treatment for the symptom; (c) they sense that healthcare professionals perceive the symptom to be unimportant; and/or (d) other symptoms predominate.

Symptom assessment tools can facilitate good clinical practice by improving the thoroughness of the assessment (and re-assessment) of common symptoms. Furthermore, validated symptom assessment tools are essential to undertaking robust research studies. However, many generic symptom assessment scales contain no oral symptoms (e.g., Edmonton Symptom Assessment Scale/ESAS [5]), or only a limited number of oral symptoms (e.g., Memorial Symptom

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Assessment Scale/MSAS [6]). For example, the MSAS, which consists of 32 symptoms (26 physical, 6 psychological), includes only four oral symptoms, i.e. “dry mouth”, “change in the way food tastes”, “difficulty swallowing”, and “mouth sores”. Interestingly, the Norwegian version of ESAS does include xerostomia, as this is one of the “10 common symptoms of advanced cancer” [7].

The aim of this scoping review was to identify/describe oral symptom assessment tools that have been specifically utilised in patients with “advanced cancer” [8], and particularly in cancer patients receiving symptom-oriented treatment (i.e. palliative care).

Methods

The function of a scoping review is to identify the available evidence rather than to produce critically appraised answers to research questions [9, 10]. The Arksey and O'Malley methodological framework [11], which has been enhanced/developed by Levac et al. [12] and the Joanna Briggs Institute [13], was used as a framework to conduct this scoping review. The PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist was used as a guide in reporting this scoping review [14].

Study eligibility criteria

We used the Population, Intervention, Comparator/control, Outcome and Study design (PICOS) framework to identify relevant research studies [15]. Eligible studies included adult patients with advanced cancer (as defined by the National Cancer Institute/NCI, USA): “cancer that is unlikely to be cured or controlled with treatment” [8]. Studies involving patient-rated oral symptom assessment tools, as well as quality of life (QoL) instruments that contain oral symptom items, were included. However, studies involving assessment of a single oral symptom (e.g., xerostomia), or a single cancer site (e.g., head and neck cancer), were not included. Observational and experimental studies were included. Perspective, commentary or opinion articles without original data were excluded.

Search strategy

A comprehensive search of three electronic databases including PubMed, Embase, and CINAHL was conducted from inception to 11 June 2021. The literature review was adapted to meet the requirements of each database searched with guidance from a health sciences librarian. The search was limited to English language articles. Reference lists of all eligible full texts were hand searched for other relevant articles. In addition, handsearching of reference lists of relevant

chapters in academic textbooks was undertaken to ensure a comprehensive search of the literature was conducted.

Data management and synthesis

The EndNote 20™ (Clarivate) bibliographic software was used to store the records retrieved from all the literature searches. This software enables duplicates to be removed. We then used the Covidence software to screen these records. Two reviewers (NC, OM) independently screened the titles and abstracts using the PICOS criteria. Where an abstract was unavailable, the paper was included in the full text review process. If there was any conflict between the two reviewers, a third reviewer was available to determine inclusion. The same two reviewers independently reviewed the full texts, and extracted the relevant information using a review-specific proforma. Again, if there was any conflict between the two reviewers, a third reviewer was available to determine inclusion.

Results

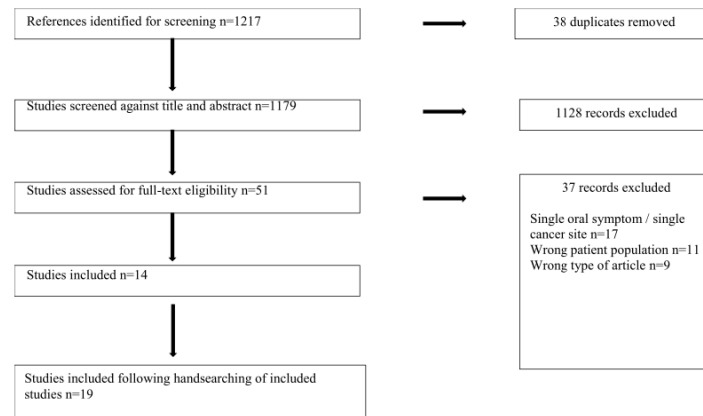
Search results

The search strategy identified 1179 unique references (Fig. 1). Fourteen papers were included in the full data extraction. One reference was a conference abstract and the authors confirmed that this was the same study as an included article. Five further articles were included following handsearching of the included full text articles. No further articles were included following handsearching of relevant chapters in academic textbooks.

Symptoms assessed

The number of oral symptoms assessed in each study varied from two [22, 23] to 20 [3, 36]. Xerostomia (“dry mouth”) was universally assessed, which is unsurprising as studies in patients with advanced cancer demonstrate a very high prevalence (i.e. 82–83.5%) [3, 36, 37]. Other commonly assessed symptoms included oral discomfort (18/18 studies), taste disturbance (15/18 studies), and denture problems (8/18 studies) (see Table 1).

It should be noted that the wording of the questions differed amongst the oral assessment tools: for example, taste disturbance was variously described as “altered taste”, “sour taste”, “disturbance of taste”, “taste disturbance(s)”, “unpleasant or altered taste sensation”, “bad or altered taste”, “change in the way food tastes”, “taste change”, “food and drink tasted different from usual”, and “dysgeusia” (although unclear as to the term used with the participants) [35].

Fig. 1 Study flow

Davies et al. [3] assessed 20 oral symptoms, many of which were not included in other studies (e.g. “sensitivity of teeth”, “altered sensation in mouth”, “burning sensation in mouth”, “bleeding from mouth”), and all of which were present in $\geq 7.5\%$ of participants. Moreover, Davies et al. [3] identified a number of so-called oral symptom “clusters” in this cohort of patients, i.e. symptoms that frequently co-existed.

Dimensions assessed

Many of the (generally older) studies simply assessed the presence or absence of specific oral symptoms [7, 16–19, 23]. However, many of the (generally newer) studies assessed one or more dimensions, including frequency [3, 24, 27, 31, 36], intensity/severity [3, 21, 22, 24, 25, 27, 30, 31, 35, 36], level of distress or bothersomeness [3, 24, 36], level of limitation [30], and relative importance [22].

Symptom time frames

Many of the studies did not specify the time frames used in the questions. Of the studies that did specify a time frame, this varied from “in the previous 24 h” [31], to “during the past week” [3, 26, 34, 36]. Nevertheless, some studies appear to have used longer time frames based upon the results reported (e.g., up to 1 year [22]).

Discussion

As highlighted, oral symptoms are common in patients with advanced cancer. Furthermore, these symptoms are often frequent in occurrence, moderate to severe in

intensity, and cause significant levels of distress (and so have a negative impact on quality of life). However, observational studies suggest that oral problems are not well-managed in this group of patients [38]. The reasons for the latter are several, and include inadequate assessment (including non-identification of oral symptoms/problems), inappropriate treatment, and inadequate re-assessment.

Symptom assessment tools can improve clinical practice through the improved/earlier identification of troublesome “orphan” symptoms (i.e. symptoms not usually reported or assessed) [39]. The “ideal” symptom assessment tool should be valid, reliable, relevant (for the population/specific scenario), comprehensive (for the specific scenario), multidimensional, and easy to administer/complete [40]. Symptom assessment tools also have a role in research, in both observational studies, and in interventional studies (as a means of demonstrating improvements in symptom control).

Currently, there is no consensus on the number of symptoms that should be included in symptom assessment tools. Longer (more comprehensive) symptom assessment tools may be more suited to research settings, whilst shorter assessment tools may be preferable for clinical practice due to related issues of patient burden, and inadequate completion.

Symptom assessment tools that only ask about the presence (or absence) of a symptom, or are limited to the assessment of a single dimension (e.g. frequency), risk under-estimating, and equally over-estimating, the importance of certain symptoms. For example, although a symptom may be frequent in nature, it may not cause significant distress (and so may not require any intervention). It should be noted that the level of distress of a symptom is

Table 1 Summary of data extraction

Reference	Study type	Number of oral symptoms assessed	Symptoms assessed	Symptom dimensions assessed	Time frame	Symptom assessment tool
Pople et al., 1986 [16]	Observational	3	"Dry mouth"; "altered taste"; "sore mouth"	Present/absent	Not described (but assessments performed on day 1, day 3, and day 5 after admission)	Non validated questionnaire
Clarke et al., 1987 [17]	Observational	5	"Xerostomia"; "glossodynia"; "painful gums"; "dysphagia"; "sour taste"	Present/absent	Not described	Non validated questionnaire
Aldred et al., 1991 [18]	Observational	6	"Disturbance of taste"; "dysphagia"; "oral soreness"; "dryness of the mouth"; "difficulty in wearing dentures"; "any other miscellaneous problems"	Present/absent	Not described	Non validated questionnaire
Jobbins et al., 1992 [19]	Observational	5	"Xerostomia"; "denture problems"; "taste disturbance"; "swallowing difficulty"; "oral soreness"	Present/absent	Not described	Non validated questionnaire
Sweeney et al., 1997 [20]	Interventional – clinical trial in patients with xerostomia	7	"Oral dryness during the day"; "dryness at night"; "soreness of the mouth"; "unpleasant or altered taste sensation"; "difficulty talking"; "difficulty eating"; "denture problems"	Present/absent Visual analogue scales used to assess response (no details provided)	Not described	Non validated questionnaire
Sweeney et al., 1998 [21]	Observational	7	"Dry mouth during the day"; "dry mouth at night"; "soreness of the mouth"; "bad or altered taste"; "difficulty talking"; "difficulty eating"; "problems with dentures"	Present/absent "Grading"—visual analogue scale 0–6 (no problem-severe problem)	Not described	Non validated questionnaire

Table 1 (continued)

Reference	Study type	Number of oral symptoms assessed	Symptoms assessed	Symptom dimensions assessed	Time frame	Symptom assessment tool
Oneschuk et al., 2020 [22]	Observational	2	"Mouth pain"; "mouth dryness"	Presence/absence Intensity—numerical rating scale 0–10 (low–high) "Importance" (relative to other symptoms/problems)—not important, slight importance, some importance, moderate importance, considerable importance, very important, great importance	Not described (but symptoms reported present from 1 day to > 1 year)	Non validated questionnaire
Milligan et al., 2001 [23]	Interventional – oral care regimen	2	"Oral pain"; "oral dryness"	Presence/absence	Not described (but assessments performed on day 1, and day 7)	Non validated questionnaire
Davies et al., 2001 [24]	Observational	4 ("standard" symptoms) 3 ("additional" symptoms)	"Dry mouth"; "difficulty swallowing"; "mouth sores"; "change in the way food tastes" "Oral discomfort"; "difficulty chewing"; "difficulty speaking"	Presence/absence Frequency—rarely, occasionally, frequently, almost constantly Intensity—slight, moderate, severe, very severe Amount of distress caused—not at all, a little bit, somewhat, quite a bit, very much	Previous week	Validated questionnaire (with additional questions)—Memorial Symptom Assessment Scale/MSAS [6]
Alt-Epping et al., 2012 [25]	Observational	5	"Dry mouth"; "taste disturbances"; "dysphagia"; "halitosis"; "pain of the oral cavity"	Presence/absence Intensity—numerical rating scale 0–10 (low–high)	Not described	Non validated questionnaire
Wilberg et al., 2012 [7]	Observational	5	"Oral discomfort"; "xerostomia"; "taste disturbances"; "problems eating"; "dental health"	Presence/absence	Not described (but xerostomia reported present for > 3 months)	Non validated questionnaire

Table 1 (continued)

Reference	Study type	Number of oral symptoms assessed	Symptoms assessed	Symptom dimensions assessed	Time frame	Symptom assessment tool
Hjermstad et al., 2012 [26]	Observational	14	"Pain in gums"; "bleeding gums"; "lip sores"; "problems with teeth"; "sore mouth"; "sores in mouth corners"; "dry mouth"; "sticky saliva"; "sensitive mouth"; "taste change"; "problems with solid food"; "trouble enjoying meals"; "worn dentures"; "ill-fitting dentures"	Presence/absence "Extent to which you have experienced these symptoms"—not at all, a little, quite a bit, very much	Previous week	Development study—EORTC QLQ-OH17
Fischer et al., 2014 [27]	Observational	3 main symptoms (with extra questions about related oral symptoms)	"Xerostomia" (with extra question about dry lips); "orofacial pain" (separate questions about intraoral and facial pain, with extra question about mouth sores); "taste change"	Presence/absence Frequency—Likert scale 0–4 (never-always) Severity (xerostomia, orofacial pain)—numerical rating scale 0–10 (low–high)	Not described	Non validated questionnaire (Oral Problem Scale)—based upon questions from other tools, including Oral Health Impact Profile/OHIP [28], and Oral Symptom and Function Scale [29]
Mercadante et al., 2015 [30]	Observational	3	"Limitation on nutrition or hydration" (due to mucositis); "dry mouth"; "dysphagia"	Presence/absence Mucositis intensity—no limitation, mucositis partially preventing nutrition or hydration, mucositis severely limiting nutrition or hydration, mucositis completely preventing nutrition or hydration Dry mouth/dysphagia intensity—numerical rating scale 0–10 (low–high)	Not described	Non validated questionnaire

Table 1 (continued)

Reference	Study type	Number of oral symptoms assessed	Symptoms assessed	Symptom dimensions assessed	Time frame	Symptom assessment tool
Nikles et al., 2015 [31]	Interventional – clinical trial in patients with xerostomia	3 generic symptoms 4 symptoms from Xerostomia Inventory (see final column) ? number symptoms from OHIP-49 (see final column)	“Dry mouth”; “difficulty in swallowing”; “altered taste” “Mouth feels dry”; “difficulty eating dry food”; “difficulties swallowing certain foods”; “lips feel dry” Symptoms different for different versions	Presence/absence Severity—numerical rating scale 0–10 (low–high), and summated score from Xerostomia Inventory (see below) Frequency—never, hardly ever, occasionally, fairly often, very often Frequency—scales different for different versions (see final column)	Previous 24 h Not described Not described	Non validated questionnaire—patients were also asked to complete Xerostomia Inventory/XI [32], and OHIP [28]. The XI is a validated single symptom assessment tool. The OHIP is a validated assessment tool that measures “the social impact of oral disorders”. The protocol paper states that the OHIP-14 (14 questions) would be used [33] but the main paper suggests that the OHIP-49 (49 questions) was used [31]
Hjermstad et al., 2016 [34]	Observational	12	“Pain in your gums”; “problems with bleeding gums”; “lip sores”; “problems with your teeth”; “soreness in your mouth”; “sores in the corners of your mouth”; “dry mouth”; “sticky saliva”; “mouth been sensitive to food and drink”; “food and drink tasted different than usual”; “problems eating solid foods”; “problems with an ill-fitting denture”	Presence/absence “Extent to which you have experienced these symptoms”—not at all, a little, quite a bit, very much	Previous week	Validation study—EORTC QLQ-OH17 (leading to EORTC QLQ-OH15)
Magnani et al., 2019 [35]	Interventional – oral care regimen	3	“Xerostomia/dry mouth”; “dysgeusia”; “orofacial pain”	Presence/absence Intensity—numerical rating scale 0–10 (low–high)	Not described (but assessments performed on day 1, and day 3)	Non validated questionnaire

Table 1 (continued)

Reference	Study type	Number of oral symptoms assessed	Symptoms assessed	Symptom dimensions assessed	Time frame	Symptom assessment tool
Davies et al., 2021 [3, 36]	Observational	20 (with option to report additional oral symptoms)	“Dry mouth”; “mouth discomfort/pain”; “lip discomfort”; “cracking of lips”; “cracking of corner of mouth”; “taste disturbance”; “difficulty chewing”; “difficulty swallowing”; “difficulty speaking”; “‘dirty’ mouth”; “coating of tongue”; “bad breath”; “toothache/pain in teeth”; “sensitivity of teeth”; “jagged teeth”; “denture fitting problems”; “bleeding from mouth”; “burning sensation in mouth”; “altered sensation in mouth”; “ulcers in mouth”	Presence/absence Frequency—rarely, occasionally, frequently, almost constantly Intensity—slight, moderate, severe, very severe Amount of distress caused—not at all, a little bit, somewhat, quite a bit, very much	Previous week	Oral Symptom Assessment Scale/OSAS Initial validation of OSAS undertaken as part of this study

often a very good indicator of its impact on the person's quality of life (although frequency, and especially intensity/severity, is also important) [40].

Many of the included studies used study-specific questionnaires, which had not been validated, although some contained elements from other validated assessment tools (see Table 1). Validated tools included the MSAS [24], the EORTC QLQ-OH17 [26], the EORTC QLQ-OH15 [34], and the OSAS [3, 36]. One study used the OHIP [31], although related results were not presented (and it was unclear which version was used). Of note, another study used selected elements from the OHIP [27].

The MSAS is a 32-item multidimensional generic symptom assessment scale, which has been extensively validated in cancer patients [6]. It contains four oral symptoms (i.e. “dry mouth”, “difficulty swallowing”, “mouth sores” and “change in the way food tastes”). The MSAS also provides blank spaces for the patient to add additional symptoms not mentioned within the tool. Davies et al. [24] supplemented the MSAS with three further oral symptoms (“oral discomfort”, “difficulty chewing” and “difficulty speaking”). The MSAS involves patients rating the frequency, severity, and distress caused by each of the physical symptoms.

The EORTC QLQ oral health module is a validated quality of life instrument, which includes a number of oral symptoms. It was initially developed as the EORTC QLQ OH-17 (a 17-item tool) [26], but was subsequently refined to the EORTC QLQ-15 (a 15-item tool) [34]. This oral health module must be completed alongside the core EORTC QLQ C-30 instrument. The EORTC QLQ-15 assesses 12 oral symptoms with three further items pertaining to the wearing of dentures, and information received about dental or mouth problems.

The OSAS is a novel 20-item multidimensional oral symptom assessment tool, which has undergone initial validation in patients with advanced cancer (and is currently undergoing further validation in this group of patients) [3, 36]. The OSAS was modelled on the MSAS. The symptoms assessed are shown in Table 1, and it also provides blank spaces for the patient to add any additional oral symptoms not mentioned within the tool. The OSAS involves patients rating the frequency, severity, and distress caused by each of the oral symptoms.

Conclusion

Symptom assessment tools can facilitate good symptom control in clinical practice, and are an integral component of clinical research. This scoping review identified four validated symptom assessment scales that could be utilised

to assess oral symptoms in patients with advanced cancer, including one cancer-specific quality of life scale (EORTC QLQ OH-15), one generic tool for assessing the “social impact” of specific oral problems (OHIP), one cancer-specific generic symptom assessment scale (MSAS), and one cancer-specific oral symptom assessment scale (OSAS).

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Author contribution The conception and design of this scoping review were formulated by NC. Material collection was conducted by NC. NC and OM contributed to the article review process. NC and AD contributed to the data collection and synthesis. The first draft of the manuscript was written by NC and AD commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Ethics approval This is a scoping review. Ethics approval was not required.

Consent to participate Not applicable.

Consent for publication No applicable.

Competing interests The authors declare no competing interests.

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