



The Oral Management of Oncology Patients Requiring Radiotherapy, Chemotherapy and / or Bone Marrow Transplantation

Clinical Guidelines

Updated 2018

The Royal College of Surgeons of England / The British Society for Disability and Oral Health

CONTENTS

GUIDE	LINE	DEVELOPMENT GROUP	3		
INTRO	DUC	TION	4		
AIM O	F TH	E GUIDELINE	6		
TARG	ET G	ROUP	6		
HOW ⁻	TO U	SE THESE GUIDELINES	6		
ORAL	MAN	IAGEMENT - OVERVIEW	7		
1.Path	ways	of Care	7		
1.1 Pre	e-trea	ntment Assessment	7		
	1.2 A	cute Phase of Cancer Therapy	7		
	1.3 D	ischarge Following Acute Phase of Cancer Therapy	7		
2. Prev	venti	ve and Clinical Regimen	8		
	2.1.	Prior to cancer therapy	8		
	2.2.	During cancer therapy	11		
	2.3	Following cancer therapy	13		
ORAL	MAN	IAGEMENT - EXPLANATORY NOTES	17		
1. Path	nway	s of Care	17		
	1.1 P	re-treatment Assessment	17		
	1.2	Acute Phase of Cancer Therapy	18		
	1.3	Discharge Following Acute Phase of Cancer Therapy	19		
2 Prev	entiv	e and Clinical Regimen	20		
	2.1.	Prior to cancer therapy	27		
	2.2	During cancer therapy	29		
	2.3	Following cancer therapy	35		
REFERENCES					
Table	1: N u	rsing Oral Care Guidelines	66		
Table	2: Ac	ute Changes during Therapy	69		
Table	3: C h	ronic Changes Following Therapy	73		
Table	4: Ma	nagement Guidelines Relative to Invasive Dental Procedures	74		
Appen	dix 1	: Example of Search Strategy used for mucositis / pain	76		
Appen	dix 2	: Referral for Oral Health Care Screening	77		
Appendix 3: Practical Oral Care:78					
Appendix 4: Oral Assessment Guide80					
Annendix 5: Patient Information Leaflet (i)-(ii)					

GUIDELINE DEVELOPMENT GROUP

The following colleagues were involved in the original publication of the Guideline in 1997 and / or earlier updates in 2004 and 2012:

- Jeremy Shaw

- Monty Duggal

Janice FiskeTom Nisbet

- Francesca Soldani

- Mary Burke

Navdeep Kumar

- Debbie Lewis

- Tracey Kinsella

- Amanda O'Donnell

- Rebecca John

- Anthony Brooke

This 2018 updated Clinical Guideline aims to update the evidence base for its recommendations. It has involved stakeholder involvement from specialists in Special Care Dentistry, Restorative Dentistry, Paediatric Dentistry, Oral Surgery, and Tutor for Hygienists / Therapists. The British Society of Disability and Oral Health Research Group have also reviewed and approved the document for publication.

Navdeep Kumar	Chair of the Working Party Consultant / Honorary Senior Lecturer in Special Care Dentistry	University College London Hospitals NHS Foundation Trust
Mary Burke	Consultant in Special Care Dentistry	Guy's and St Thomas' NHS Foundation Trust
Anthony Brooke	Consultant in Special Care Dentistry	University Hospitals Bristol NHS Foundation Trust
Fabia Chan	Assistant Clinical Director / Specialist in Special Care Dentistry	Assistant Clinical Director, Kent Community Health NHS Foundation Trust
Shabnum Ali	Specialist in Special Care Dentistry	University Hospitals Bristol NHS Foundation Trust
Janine Doughty	Academic Clinical Fellow in Special Care Dentistry	University College London Hospitals NHS Foundation Trust
Hana Cho	Academic Clinical Fellow in Special Care Dentistry	University College London Hospitals NHS Foundation Trust
Stewart Barclay	Consultant in Restorative Dentistry	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Lorna McCaul	Consultant / Honorary Clinical Senior Lecturer in Restorative Dentistry	Glasgow Dental Hospital and School
Jose Rodriguez	Specialty Trainee in Restorative Dentistry	University College London Hospitals NHS Foundation Trust
Elizabeth Bower	Tutor Dentist – Eastman Dental Hospital Education Centre	University College London Hospitals NHS Foundation Trust
Nikki Tanna	Consultant in Oral Surgery	University College London Hospitals NHS Foundation Trust
Edmund Bailey	Senior Lecturer / Honorary Consultant in Oral Surgery	Barts and The London School of Medicine and Dentistry
Adele Johnson	Consultant in Paediatric Dentistry	University College London Hospitals NHS Foundation Trust
Joana Monteiro	Consultant in Paediatric Dentistry	University College London Hospitals NHS Foundation Trust

INTRODUCTION

Cancer Statistics

Cancer is one of the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases in 2012 (Ferlay *et al.*, 2015). The number of new cases is expected to rise by about 70% over the next 2 decades. Cancer is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. Globally, nearly 1 in 6 deaths is due to cancer, although in low- and middle-income countries, this figure increases to 70% of deaths.

Tobacco use is the most important risk factor for cancer and is responsible for approximately 22% of cancer deaths (GBD Collaborators, 2016). Cancer causing infections, such as hepatitis and human papilloma virus (HPV), are responsible for up to 25% of cancer cases in low- and middle-income countries (Plummer *et al.*, 2016). In 2015, more than 90% of high-income countries reported treatment services are available compared to less than 30% of low-income countries.

In the United Kingdom, there were over 357,000 new cases of cancer in 2014. This equates to 980 cases diagnosed every day, with one person diagnosed every two minutes with cancer (Cancer Research UK, 2017). In 2014, there were 181,000 cases of males and 176,000 cases of females diagnosed with cancer. Since the early 1990s, incidence rates for all cancers combined have increased by 12% in the UK. The increase is more pronounced in females (16%), than in males (4%). Almost half of cancers are diagnosed at a late stage in England (2014) and Northern Ireland (2010-2014). Incidence rates for all cancers combined are projected to rise by 2% in the UK between 2014 and 2035, to 742 cases per 100,000 people by 2035.

Conversely, the outlook following treatment for malignant disease, has improved in the last two decades since the 1995 Calman-Hine report which outlined radical reform of the UK's cancer services with the aim of improving outcomes and reducing inequalities in NHS cancer care (Department of Health, 1995). Its main recommendation was to concentrate care into the hands of site-specialist, multi-disciplinary teams – dental care is an essential component of these teams.

Importance of Integrated Oral Care

Complications in the oral cavity commonly arise as a result of malignancy and/or the undesirable effects of its treatment (Brennan *et al.*, 2010) (Shaw *et al.*, 2000). The prevalence, extent, severity and longevity of the complications depend on the regime of cancer therapy regime and its intensity (National Cancer Institute, 2016).

Complications may include profound functional and sensory changes to the oral mucosa, in addition to an increased susceptibility to dental caries and periodontal disease (National

Cancer Institute, 2016) (Sroussi *et al.*, 2017). These may impact directly on cancer therapy resulting in the need to pause treatment, but also have a significant impact on the longevity and quality of life during and after cancer therapy (Gandhi *et al.*, 2017).

Adults with malignant disease, in common with the general population will increasingly keep their natural teeth to a greater age but they are likely to have more untreated dental disease. Children with cancer may also have untreated dental caries and, since many are under five years of age, a significant proportion may not have previously had a dental examination (Rosales *et al.*, 2009).

Following major head and neck surgery, around 78% of patients have been reported to experience severe difficulties with mastication, which may have implications for normal social adaptation. At least one third of head and neck survivors had moderate and severe level of distress. Seventy-four percent reported at least one unmet need, the most common being oral and eating problems (Kraaijenga *et al.*, 2015) (Wells *et al.*, 2015) (Wilberg *et al.*, 2014) (Kamstra *et al.*, 2013) (Roe *et al.*, 2012). Haemato-oncology patients equally experience poorer quality of life when measured using the parameters of oral functional limitation, physical pain and physical disability (Tinoco-Araujo *et al.*, 2015) (Mays *et al.*, 2013). These difficulties can be improved by carefully planned oral and dental assessment, early intervention and reconstruction (Butterworth *et al.*, 2016).

In summary, dentists are increasingly likely to find that they have children and adults in their care who may present before or after cancer treatment requiring dental assessment and / or urgent dental care. The patient's oral care and function are important contributors to post-treatment social adaptation and life quality (Kolokythas, 2010) (Shavi *et al.*, 2015) (Thani and Bumb, 2014). Appropriate preventive regimens, timely oral care and improved dental services can minimise complications and improve quality of life (Bennadi and Reddy, 2013).

These guidelines provide an overview of the current recommendations in relation to dental care for all patients undergoing cancer therapy. The reader is advised to also review complimentary guidelines specific for patients receiving surgical and non-Surgical treatment for Head and Neck Cancer produced by Restorative Dentistry UK in 2016 (RD-UK, 2016).

Dr. Navdeep Kumar Chair of the Guideline Development / Update Group

AIM OF THE GUIDELINE

To improve the quality of life for patients with malignant disease, who are receiving cancer therapy that has implications for oral comfort and function, by promoting consistent, evidence-based high standards of oral care through a co-ordinated team approach.

TARGET GROUP

Cancer therapy that may result in oral complications includes:

- Chemotherapy
- Radiotherapy to the head and neck
- Surgery to the head and neck
- Bone marrow transplantation involves chemotherapy +/- total body irradiation

HOW TO USE THESE GUIDELINES

These guidelines provide an overview of the oral management of both children and adults receiving radiotherapy, chemotherapy, surgery or a combination of these modalities.

The recommendations must be seen as a contribution to total patient care and as such should always be implemented in conjunction with the care priorities agreed with the oncology team.

An **Overview** of the recommendations with regards to oral management is summarised at the beginning of the document. This is followed by an **Explanatory Notes** section that provides the reader with further information where available.

A list of **References** accessed to support the recommendations is provided. There are also **Tables**, **Appendices** and a template for a **Patient Information Leaflet** at the end of the document.

REFERENCES / SEARCH STRATEGY

The search strategy used by the authors involved a review of the literature. Agreed search terms from the following databases were used to identify publications relevant to this cohort of patients:

- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Health Technology Assessment (HTA) database
- MEDLINE
- EMBASE
- NHS Evidence > Filter > Guidelines

An example of the search strategy used for mucositis in included in Appendix 1. The Oxford Centre for Evidence-based Medicine Level of Evidence (2009) was used to grade the level of evidence. The GRADE (Grading of Recommendations Assessment, Development and Evaluation) method was used to systematically assess the strengths and limitations of the evidence base.

ORAL MANAGEMENT - OVERVIEW

1. Pathways of Care

A clear pathway of care is necessary to prevent or minimise oral complications. It is recognised that not all cancer centres have a linked multi-disciplinary dental team and hygienist support. However the pathway outlined represents the evidence-based ideal pathway to ensure optimal outcomes.

1.1 Pre-treatment Assessment

- **1.1.1** Every relevant oncology protocol should include an early pre-treatment oral assessment.
- **1.1.2** A permanent member of the oncology team is responsible for arranging the oral assessment using a standardised referral form (Appendix 2).
- **1.1.3** A designated permanent member of dental team is responsible for organising oral care.
- **1.1.4** Dentally, the cancer patient will require multi-specialty, multidisciplinary and collaborative care approach to achieve best oral outcomes and an efficiently delivered oral care pathway.

1.2 Acute Phase of Cancer Therapy

- **1.2.1** The oncology team must include a trained dental professional who is responsible for the patients' oral care.
- **1.2.2** The dental hygienist is responsible to the designated member of dental team.
- **1.2.3** The designated member of dental team is responsible for arranging or carrying out any urgent dental treatment required.
- **1.2.4** Nursing guidelines for oral assessment and routine oral care should be followed (Appendices 3-4, Table 1).

1.3 Discharge Following Acute Phase of Cancer Therapy

- **1.3.1** The oncology patient discharge protocol includes a procedure for ensuring continuing oral care.
- **1.3.2** The designated member of dental team is responsible for organising and monitoring appropriate continuation of oral care.
- **1.3.3** Following the receipt of a bone marrow transplant and subsequent discharge home from hospital, children are reviewed to continually monitor the oral condition.
- **1.3.4** There is an agreed patient-specific minimum period of oral health monitoring post-treatment.
- **1.3.5** Children are monitored during their period of growth and development.

2. Preventive and Clinical Regimen

2.1. PRIOR TO CANCER THERAPY

2.1.1. Importance of Integrated Care:

Oral care should be seen as a contribution to total patient care and implemented in conjunction with the care priorities agreed with the oncology team (Shaw *et al.*, 2000).

2.1.2. Oral / Dental Assessment:

Prior to commencement of cancer therapy, an oral / dental assessment including radiographs, must be undertaken (Elad *et al.*, 2015). The specific aims are to:

- Identify existing oral disease and potential risk of oral disease.
- Remove infectious dental / oral foci before the start of cancer therapy.
- Prepare the patient for expected side effects of cancer therapy.
- Establish an adequate standard of oral hygiene to meet the increasing challenges during cancer therapy.
- Develop a plan for maintaining oral hygiene, providing preventive care, completing oral rehabilitation and follow-up.
- Establish the necessary multidisciplinary collaboration within the cancer centre to reduce / alleviate oral symptoms and sequelae before, during and after cancer therapy.

Each centre should have a multidisciplinary team to accomplish these goals; the exact methods used may vary between cancer centres (Schiødt and Hermund, 2002). Specific recommendations apply to the assessment of paediatric patients (Public Health England, 2017) (Abdullah, 2014) (SDCEP, 2010).

2.1.3. Advice Regarding Potential Side-Effects:

Chemotherapy and radiotherapy can cause adverse short- and long-term oral side effects (Butterworth *et al.*, 2016). Realistic simple preventive advice should be given, emphasising its value in maintaining oral comfort during therapy and reducing complications (Tables 2-3; Appendix 5 – Patient Information Leaflet)

2.1.4. Oral Hygiene instructions:

Detailed oral hygiene instruction is provided.

2.1.5. Dietary Advice:

It is recommended that dietary advice is given in liaison with the dietitian and presented with the emphasis upon ensuring oral comfort during therapy.

2.1.6. Chlorhexidine:

If gingival disease is diagnosed, oral hygiene practices can be supplemented with the use of an alcohol-free chlorhexidine mouthwash or dental gel.

2.1.7. Periodontal treatment:

Professional debridement of plaque and calculus deposits should be undertaken to stabilise periodontal disease.

2.1.8. Dental caries:

Where possible carious teeth should be definitively restored or stabilised with appropriate restorations.

2.1.9. Removal of trauma:

All sharp teeth and restorations are suitably adjusted and polished.

2.1.10. Impressions:

Impressions of the mouth are taken for study casts to construct applicator trays and, where appropriate, for intra-oral radiation stents and obturator planning.

2.1.11. Dentures / obturators:

The patient is counselled about denture wear during cancer therapy. If a removable prosthesis is worn, it is important to ensure that it is clean and well adapted to the tissue. The patient should be instructed not to wear the prosthesis during cancer therapy, if possible; or at least, not to wear it at night (National Institute of Dental and Craniofacial Research, 2015).

2.1.12. Dental Extractions:

Wherever possible, teeth with a dubious prognosis are removed no less than

ten days prior to commencement of cancer therapy (Clayman, 1997).

2.1.13. Antibiotic prophylaxis / haematological support:

Antibiotic prophylaxis prior to invasive oral procedure may be warranted in the context of neutropenia (neutrophils less than 2000/mm3) although liaison with the oncologist should take place and clinical judgement exercised. Haematological support may also be required (Table 4).

2.1.14. Orthodontics:

Orthodontic treatment should be discontinued and fixed appliances removed (Sheller and Williams, 1996).

KEY RECOMMENDATION

Wherever possible, teeth with a dubious prognosis are removed no less than ten days prior to commencement of cancer therapy (Weak recommendation, very low quality evidence).

2.2. DURING CANCER THERAPY

2.2.1. Hygienist Support:

The patient should receive appropriate support from a dental hygienist or therapist.

2.2.2. Oral / Denture Hygiene:

A high standard of oral hygiene is encouraged, including denture hygiene.

2.2.3. Antibacterial Mouthwash:

The use of an alcohol-free chlorhexidine mouthwash is recommended if toothbrushing is likely to be inadequate for plaque removal; it can be used in addition or as a short-term alternative to tooth brushing.

2.2.4. Dental Caries Risk:

Those patients receiving radiotherapy to the head and neck region, or total body irradiation prior to bone marrow transplantation are at higher risk of dental caries and should receive dietary advice and fluoride preparations appropriate to their age (Hong *et al.*, 2010) (Gawade *et al.*, 2015) (Gupta *et al.*, 2015).

2.2.5. Viral Infections:

Children and adults receiving bone marrow transplants often receive aciclovir as a prophylaxis if there is a high risk of viral infections. This is usually prescribed by the oncology team (Sanderr *et al.*, 2015) (Ullmann *et al.*, 2016).

2.2.6. Fungal Infections:

Antifungal medication is used following detection of oral candida (Pappas *et al.*, 2016). For children, this may be used routinely as a prophylaxis in some cancer centres.

2.2.7. Mucositis:

Regular assessment of the mouth should be undertaken to record the presence and severity of mucositis. Every effort is made to reduce the severity and control oral discomfort.

2.2.8. Xerostomia:

Every effort is made to reduce the effect of the xerostomia for quality of life and prevention of oral disease.

2.2.9. Dentures / Obturators:

Patients are advised that removable prostheses may become difficult to wear and may need to be left out. If there is any discomfort they should be examined by a member of the dental team and adjusted to ensure they are atraumatic.

2.2.10. Foam swabs / Oral Cleanser / Gauze:

If the mouth is too painful for cleaning with a soft toothbrush, the tissues can be cleaned with oral sponges, an oral cleanser stick (e.g. MC3), or gauze moistened with alcohol-free chlorhexidine mouthwash. Of note, some units have discontinued the use of oral sponges due to the risk of inhalation if the sponge becomes detached.

2.2.11. Dietary Advice:

Certain food, drinks and mouthwashes, which irritate the oral mucosa, should be avoided to maintain oral comfort.

2.2.12. Dental Treatment:

Elective dental treatment is avoided wherever possible during cancer therapy.

2.2.13. Obturators:

If the patient is having surgical resection to the maxilla / mid-face, obturators can be planned and fitted peri-operatively.

KEY RECOMMENDATION

Those patients receiving radiotherapy to the head and neck region, or total body irradiation prior to bone marrow transplantation are at higher risk of dental caries and should receive dietary advice and fluoride preparations appropriate to their age. (Strong recommendation, very low quality of evidence).

2.3 FOLLOWING CANCER THERAPY

2.3.1 Monitoring:

Susceptibility to dental disease can be lifelong following cancer therapy therefore patients must be monitored closely.

2.3.2 Dental Caries Risk:

The risk of dental caries following cancer therapy will depend on the type of treatment the patient has received, and changes in oral health-related behaviours as a consequence of the treatment. Individualised oral health prevention and monitoring programme should be established for each patient, with frequent recall intervals based on the patient's oral disease risk assessment.

2.3.3 Gingival / Periodontal Risk:

Bone marrow transplant patients on ciclosporin may need more frequent hygienist support if gingival hyperplasia is a side effect. In the event of uncontrolled periodontal disease, vigorous treatment is initiated. This may involve identification of atypical pathogens.

2.3.4 Preventive Advice and Fluoride supplementation:

Dietary analysis and advice should aim to encourage a healthy balanced diet and reduce the amount and frequency of sugars and acids. Close liaison with the patient's dietitian is necessary. The dental hygienist should provide tailored oral hygiene support. The use of fluoride preparations is recommended.

2.3.5 Xerostomia:

Salivary stimulants and saliva replacement products are outlined in section 2.2.8 explanatory notes.

2.3.6 Smoking Cessation:

Smoking and alcohol cessation support should be ongoing. Support to stop the use of smokeless tobacco and betel quid should also continue.

2.3.7 Abnormal Blood counts:

Patients on maintenance chemotherapy or with persistent haemato-oncology

disease may need blood tests pre-operatively if invasive treatment is planned. Bleeding and infection risk may be of concern for invasive procedures and require close liaison with the oncology team.

2.3.8 Herpes Labialis:

Herpes labialis can be a chronic problem and requires timely management. Topical aciclovir may be effective.

2.3.9 Limited Mouth Opening:

The team should be vigilant that this is not due to a local recurrence, metastatic lesions in the head and neck region and / or a second malignant lesion. If this has been excluded, jaw exercises, stacked tongue spatulas and jaw opening devices can be used. Starting therapy early and compliance with exercises improves treatment outcome.

2.3.10 Growth and Development:

This should be closely monitored. Survivors of childhood cancer are at risk of dental developmental abnormalities. Microdontia, tooth agenesis and xerostomia may present as delayed side effects of cancer therapy. Early specialist involvement is essential to ensure good outcomes.

2.3.11 Orthodontics:

The decision to embark upon orthodontic treatment must be taken carefully. Challenges include increased dental caries susceptibility, root stunting, risk of osteonecrosis following orthodontic extractions in patients who have received anti-resorptive agents, and the inhibiting effect of bisphosphonates on orthodontic tooth movement.

2.3.12 Restorations:

Restorations are kept simple ensuring acceptable aesthetics and function.

2.3.13 Dental Extractions:

The risk of osteoradionecrosis and / or medication-related osteonecrosis of the jaw should be considered. Dental extractions should be avoided wherever possible in patients at risk of developing these complications. If essential, they must be performed with appropriate precautions.

2.3.14 Dentures:

Dentures should be avoided wherever possible. Removable prostheses are left out at night. Oral lubricants / artificial saliva may be applied to the fit surface of the denture to improve comfort and retention when xerostomia is present. Acidic saliva substitutes (e.g. Glandosane) should be used for edentate patients only. Antifungals are used if a candidal infection is diagnosed. These can be applied directly to the fit surface of the denture or incorporated into the soft lining. Microwave disinfection may also be used for maxillary complete dentures. Appliance wear is discontinued if the mouth becomes painful and advice must be sought.

2.3.15 Dental Implants:

Implant stabilisation of prostheses and obturators may be feasible in some patients.

2.3.16 Obturators:

Unlike dentures, obturators should not be left out at night for the six months following treatment. They must be reviewed regularly by the restorative dental team, as frequent attention with adjustment or remake may be required.

2.3.17 Osteoradionecrosis (ORN):

Establish the clinical diagnosis of ORN and its stage, ensuring that the bony changes are not due to malignancy. Following a diagnosis of ORN it is recommended that oral trauma is minimised, and a high standard of oral hygiene is established. Local measures are employed to relieve symptoms including topical / systemic analgesia. Therapeutic use of antioxidant medications may be of significant benefit in ORN lesions identified early. High dose systemic antibiotics are prescribed if there are symptoms of persistent infection. Localised surgical excision of exposed necrotic bone with primary mucosal closure may become necessary. In some cases, the use of hyperbaric oxygen therapy (HBOT) may be a beneficial adjunct to surgical interventions but should only be used as part of a clinical trial. In advanced chronic cases, the extent of involvement of bone necrosis must be established followed by radical ablative surgery to remove necrotic bone.

2.3.18 Medication related Osteonecrosis of the Jaw (MRONJ):

MRONJ, although relatively rare, can occur as a result of medications commonly used in the treatment of some cancers. Patients should receive verbal and written information of the risks. Various preventive and treatment strategies have been proposed but the evidence regarding their efficacy is currently poor (SDCEP, 2017).

2.3.19 Discharge:

The majority of patients can be discharged to the primary care dental team for long-term review. More frequent follow up is required.

KEY RECOMMENDATION

The risk of osteoradionecrosis and / or medication-related osteonecrosis of the jaw should be considered. Dental extractions should be avoided wherever possible in patients at risk of developing these complications. If essential, they must be performed with appropriate precautions. (Strong recommendation, moderate quality of evidence)

ORAL MANAGEMENT – EXPLANATORY NOTES

These explanatory notes refer to the paragraph numbers indicated in the Pathways of Care and the Preventive and Clinical Regimen (see above).

1. Pathways of Care

1.1 Pre-treatment Assessment

- 1.1.1 There is no universally accepted pre-cancer therapy dental protocol because of the lack of clinical trials evaluating the efficacy of a specific protocol.
 - Currently, many of the dental protocols proposed are related to specific cancers only, such as head and neck cancer where the mouth may receive significant irradiation (Nekhlyudov et al., 2017) (Butterworth et al., 2016) (Cocks et al., 2016) (Jawad et al., 2015) (Patel et al., 2015).
 - A systematic review of the literature revealed only limited articles on oral care protocols prior to cancer therapy (Hong *et al.*, 2018) (Hong *et al.*, 2010) (Epstein *et al.*, 2014).
 - While there are no universally accepted dental protocols, all papers emphasize the importance of optimisation of oral health prior to, during and post cancer therapy. Effective oral management can reduce interruption of cancer treatment and improve quality of life (Talwar et al., 2016) (Rathod et al., 2015) (Wells et al., 2015) (Shiraz et al., 2014) (Kelly, et al., 2013). Additionally, all authors emphasise the importance of good communication between the oncology multidisciplinary team and the dental team throughout the patient journey.
 - An appropriately experienced dental team is often required to perform dental care for oncology patients (Epstein *et al.*, 2009).
 - Time must be made available during the pre-treatment phase for a dental assessment and necessary emergency care, especially when radiotherapy is planned and for those where dental treatment may be contraindicated once oncology intervention commences (Butterworth *et al.*, 2016) (Epstein *et al.*, 2009) (Elad *et al.*, 2003) (Raut *et al.*, 2001).
 - Ideally, a comprehensive oral evaluation should take place as soon as practicable after cancer diagnosis to allow maximum time for dental treatment and subsequent healing.
 - In the case of patients with head and neck cancer, it is important to undertake the oral assessment when the cancer treatment plan is available. This will allow the dental team to be aware of areas in the mandible and maxilla may be involved in

surgery and / or radiotherapy.

It has been suggested that dental teams should assess the patient approximately one month before cancer treatment begins in order to allow urgent dental treatment to be arranged and to subsequently ensure adequate time for recovery from any required invasive dental procedures (see section 2.12) (Bos-den Braber et al., 2015) (Abdullah, 2014) (McCaul, 2012) (Shaw et al., 2000).

1.1.3 Designated dental member of staff:

- The member of dental staff responsible for organising oral care will need to ensure that dental treatment is provided rapidly, taking into consideration the patient's existing continuing care arrangements.
- Depending on the specialty availability and the urgency, treatment may be provided either within the hospital service, the community dental service or the general dental service (Jawad *et al.*, 2015).
- Where there is any doubt about rapid efficient treatment, or the patient's general health status dictates, dental care should be undertaken within the specialist centre.
- Medical consultation is indicated before invasive procedures (Tsuji *et al.*, 2015) (Yamagata *et al.*, 2011) (Yamagata *et al.*, 2006).

1.1.4 Multidisciplinary care:

- Dentally the cancer patient will require a multispecialty, multidisciplinary and collaborative care approach to achieve best oral outcomes and an efficient oral care pathway (Nekhlyudov *et al.*, 2017) (Epstein *et al.*,2014).

1.2 Acute phase of cancer therapy

1.2.2 Oral care:

Oral care must be seen as an integral part of patient care. A dental hygienist should be part of the team providing the patient's oral care during therapy (Michele and Lloid, 2016) (Ray-Chaudhuri *et al.*, 2013). However, dental hygienists may be difficult to recruit. In such circumstances, an appropriately trained member of nursing staff can undertake this role (Dempsey *et al.*, 2016) (Jawad *et al.*, 2015).

1.2.4 Nursing guidelines:

It is particularly important for specific nursing guidelines to be available and utilised for oral care in the period leading up to and following bone marrow transplantation. (Appendix 2).

1.3 Discharge Following Acute Phase of Cancer Therapy

1.3.1 Monitoring:

In the absence of recurrent disease oral health monitoring should at least be equivalent to the period of monitoring by the oncology team (Nekhlyudov *et al.*, 2017) (Roman *et al.*, 2016) (Majhail *et al.*, 2012). Recall should be three-monthly to start with and the period should be adjusted dependent on the patient risk factors (NICE, 2004). Patients with unstable oral health will require more frequent monitoring. In circumstances of stable oral health, monitoring should be agreed with the primary care dentist with an appropriate procedure for urgent re-referral. In the case of patients with head and neck cancer, they should be seen as soon as possible after completion of radiotherapy and the frequency of follow up in the immedaite post treatment phase will also depend on severity of side-effects.

1.3.2 Children who have received bone marrow transplants should have a strict follow-up for preventive oral care at three monthly intervals.

2 Preventive and Clinical Regimen

2.1. PRIOR TO CANCER THERAPY

2.1.1. Importance of Integrated Oral Care:

When presented with a diagnosis of cancer a patient will be unlikely to consider the oral implications as a high priority. However, it is important that patients and carers are counselled about oral care procedures, diet and the oral implications of the proposed treatment (Shaw et al., 2000).

2.1.2. Oral / Dental Assessment:

Adults:

- The pre-treatment evaluation should include a thorough examination of hard and soft tissues, as well as appropriate radiographs to detect possible sources of infection and pathology (Butterworth *et al.*, 2016) (Epstein *et al.*, 2014).
- Those patients who are to undergo surgery and / or radiotherapy to the jawbone, should be assessed by the restorative dentist who works with the surgeon in the multidisciplinary team (Butterworth *et al.*, 2016) (Michele and Lloid, 2016) (Abdullah, 2014) (McCaul, 2012) (Westbrook *et al.*, 2003).
- Often, there is insufficient time to provide complex dental care before cancer treatment commences.
- Oral problems that already exist, such as periodontitis, caries, failing restorative work (such as leaking crowns or fillings), and ill-fitting dentures may increase the risk of infection (Tomblyn *et al.*, 2009).
- Elimination of dental disease by judicious restorative dentistry, periodontal treatments and extraction of teeth with a questionable prognosis are important preventive strategies to avoid future dental extractions, an important risk factor for osteonecrosis of the jaw (Patel et al., 2015) (Ertas et al., 2014) (NICE, 2012) (Peterson et al., 2010) (Stoopler et al., 2007).
- Guidelines for dental extractions, endodontic management, and related interventions can be used as appropriate (SDCEP, 2017) (National Cancer Institute, 2016) (Stoopler *et al.*, 2007).
- The likelihood that a tooth will require extraction within the next few years must be assessed. Additionally, not all patients are well motivated, and in such cases, retaining teeth may lead to complications in the future (Patel et al., 2015) (Elad et al., 2003). This is particularly important for the patient

who may receive oral radiotherapy or high dose intravenous bisphosphonates for cancer treatment (Stoopler *et al.*, 2007).

- The advice needs to be set within the overall framework of care set by the oncologist and their support staff.

Children:

The following specific recommendations have been made (Public Health England, 2017) (Abdullah, 2014) (SDCEP, 2010):

Access to Dental Care

- All children diagnosed with cancer should have access to or preferably be registered with an NHS general dental practitioner, Community Dental Service or Hospital based Paediatric Dental Service.
- Registration should be maintained during and following cancer treatment
- The routine dental care provider in community or general dental practice should be notified of the cancer diagnosis and arrangements for care during cancer treatment as directed by the hospital dental team, in a shared care arrangement.
- For paediatric dental units working with a cancer centre, there should be a mechanism of notification for new patients.
- All children should undergo a dental assessment, including radiographs at the time of diagnosis, if possible before cancer treatment commences. If this is not possible it should be as soon as it is practically possible.
- If invasive dental treatment is required, this should be undertaken either by a consultant or a specialist in paediatric dentistry as appropriate.
- If there is no paediatric dental unit liaising with the cancer centre, there should be clear communication between the cancer centre and routine care provider.
- Appropriate training in oral assessment should be available for the oncology nurses within the cancer centre, ideally in collaboration with a member of the dental team.

2.1.3. Advice Regarding Potential Side-Effects:

Patient education is an integral part of the pre-treatment evaluation and should include a discussion of potential oral complications (Abdullah, 2014) (Mays *et al.*, 2013) (Westbrook *et al.*, 2003).

2.1.4. Oral Hygiene Instruction:

Adults:

- It is very important that the dental team impress on the patient that optimal oral hygiene during treatment, adequate nutrition, and avoiding tobacco and alcohol can prevent or minimise oral complications and reduce recurrence / further cancers (Brand *et al.*, 2009) (Goldman, 2006). Patients should understand that good oral care during cancer treatment contributes to its success (Michele and Lloid, 2016) (Critchlow *et al.*, 2014) (Epstein *et al.*, 2014).
- To ensure that the patient fully understands what is required, detailed instructions should be provided on specific oral care practices, such as how and when to brush and floss, how to recognise signs of complications, and other instructions appropriate for the individual.

Children:

- Oral hygiene advice should be given to children and parents prior to commencing cancer treatment and this should be provided both verbally and in writing.
- Oral hygiene advice should be given by a designated member of the dental team or, in the absence of a dentally trained individual, a member of the medical or nursing team who has received appropriate training.
- Advice should be to brush at least twice a day last thing at night and at least one other occasion.
- Children from 0 to 10 years should use fluoridated toothpaste containing 1350-1500ppm fluoride. Up to 6 years old children should use only a smear or pea sized amount of toothpaste.
- Reinforce the importance of spitting and not rinsing after toothbrushing.
- From 8 years of age and above, children should use a fluoride mouth rinse daily (0.05% NaF) at a different time to brushing.
- Children with active caries should use a prescribed 2800ppm fluoridated toothpaste (if 10 years or above) or prescribed 5000ppm fluoridated toothpaste (if 16 years old or above).
- The toothbrush should be for the sole use of the child and changed on a three-monthly basis, or when bristles splay, if earlier. A child's toothbrush should be changed following an oral infective episode.
- If the child has a sore mouth a soft brush with a small head should be used.

- Children need to be helped or supervised by an adult until at least 7 years of age; parents/carers should be instructed on how to brush their child's teeth.
- For babies without teeth, parents/carers should be instructed on how to clean the mouth with oral sponges if available. The sponge should be moistened with water. Some units have discontinued the use of oral sponges due to the risk of inhalation if the sponge becomes detached. In this situation, a soft brush or gauze may be used.
- For children where it is not possible to brush teeth, parents / carers should be instructed on how to clean the mouth with oral sponges / gauze, as a temporary measure. The sponge / gauze should be moistened with water or an antimicrobial agent such as diluted alcohol-free chlorhexidine may be used.
- Additional aids such as flossing may be advised for motivated parents / carers.
- The need to restrict sugary food and drink to meal times only 3-4 occasions in a day should be discussed in accordance with the dietitian's instructions.
- Give examples of sugar-free snacks, warn of hidden sugars in foods and highlight the high acid content of some drinks.
- If possible, sugar free medication should be considered, if available, in order to minimise cariogenic effects.

2.1.5. Dietary Advice:

- Since many children and some adults need a frequent high calorific intake during therapy, this usually translates into an increased and frequent intake of refined carbohydrate (sugar), which, if sustained, can lead to dental caries.
- It is important to ensure that dietary advice pre-cancer therapy does not conflict with the advice given by the dietician. The focus is on the patient maintaining their weight and receiving adequate nutrition.
- It may be possible to utilise alternative strategies such as the use of straws when consuming sweet drinks.
- Information at this stage must be supported by an appropriately designed information leaflet.

2.1.6. Chlorhexidine:

The use of an aqueous alcohol-free chlorhexidine mouthwash, dental gel or

spray will contribute to the treatment of gingival disease in combination with improved oral hygiene practices. Use either a mouthwash or dental gel twice daily for at least one week prior to commencing treatment. The following are appropriate:

- 10ml of 0.2% aqueous alcohol-free chlorhexidine gluconate mouthwash or dental gel
- 18ml of 0.12% aqueous chlorhexidine gluconate solution

In children chlorhexidine is rarely used unless toothbrushing cannot be performed. There is often poor compliance because of the taste.

2.1.7. Periodontal Treatment:

A thorough debridement of plaque and calculus should decrease gingival inflammation and has the potential to decrease the severity of oral mucositis (Saito *et al.*, 2014). The oncology team should be consulted where blood counts may be altered in relation to haemato-oncological disease.

2.1.8. Dental Decay:

Where time permits it is preferable to restore teeth with a permanent restorative material. When time is limited, glass ionomer cements or preferably resin modified glass ionomer cements make an effective provisional restoration.

2.1.9. Removal of Trauma:

Sharp teeth or restorations can be particularly uncomfortable during the period of mucositis. They can contribute to soft tissue damage, ulceration, mucositis and attendant discomfort. They should be appropriately adjusted.

2.1.10. Impressions:

- Impressions may be required for the construction of intraoral stents when radiotherapy is used for the treatment of head and neck cancers. Stents can be effective in decreasing doses to healthy structures and delaying the emergence of mucositis (Doi et al 2017)
- In cases with mandibular resection (and / or reconstruction) resulting in edentulous areas, it may be possible to restore with conventional full or partial dentures.
- Pre-operative decision making in conjunction with the surgeon can optimise

hard and soft tissue contours to aid prosthesis stability and retention.

- Study casts should be used for obturator planning in liaison with the surgical team.
- Where possible a maximal number of well-maintained natural teeth of reasonable prognosis should be retained to assist with support and retention.
- However, obturators will often require a combination of tissue and / or tooth-borne support and can also be retained by osseointegrated dental and / or zygomatic implants.
- If multiple casts are required, applicator trays can always be made on duplicate casts to avoid repeated impressions.
- The applicator trays are used for fluoride or chlorhexidine gel delivery later in the management process.

2.1.11. Dentures / Obturators:

- Dentures or obturators are uncomfortable during the period of mucositis.
- The patient may wish not to wear dentures during this time.
- Those who discontinue the use of their dentures often experience problems with denture stability when they return to them, probably as a result of adaptation loss. They should be counselled in advance so that they can make an informed choice and relatives can be prepared for any change in appearance.
- Obturators must be worn since wound contraction can occur within hours of removal. If painful, they must be examined by a member of the dental team.

2.1.12. Dental Extractions:

- The implications of any dental extractions subsequent to radiotherapy must be sensitively explained to the patient.
- Teeth in direct association with the tumour, in the direct path of the radiation beam, or teeth with doubtful prognosis (deep caries, deep periodontal pockets, non-vital teeth) should be extracted as soon as possible before radiotherapy and high dose intravenous bisphosphonate treatment (McCaul, 2012) (Stoopler et al., 2007) (SDCEP, 2017).
- It should be borne in mind that permanent teeth with non-symptomatic periapical lesions are rarely exacerbated by cancer therapy. Judgement needs to be made on overall prognosis.
- Children should have mobile and teeth of guestionable prognosis removed.

Pulp therapy in primary teeth is contra-indicated for immunocompromised children (Rodd *et al.*, 2006).

- Teeth should be removed with a minimum of trauma
- Primary closure has been advocated but the evidence supporting this approach is not conclusive (Elyas *et al.*, 2013).
- Ideally allow three weeks between dental extraction and commencement of radiotherapy, although this is not always practicable. This is to allow for maximal healing time (McCaul, 2012) (Stoopler et al., 2007).
- Some authors have proposed a minimum two weeks healing period and the patient should be reviewed to ensure mucosal healing (Butterworth et al., 2016) (Critchlow et al., 2014) (Yamagata et al., 2011) (Yamagata et al., 2006). Ten days should be considered a minimum period (Clayman, 1997).
- Where possible, children due to undergo an autologous stem cell transplant who are not compliant with dental treatment under local anaesthesia, may have any appropriate teeth removed at the time as their bone marrow harvest general anaesthetic.
- Patients are particularly at risk of ORN when tooth extractions are undertaken both immediately before and after radiotherapy.

2.1.13. Antibiotic Prophylaxis:

 Antibiotic prophylaxis regimens prior to invasive oral procedures in neutropaenic patients frequently use the current American Heart Association (AHA) protocol for infective endocarditis and oral procedures (Nishimura et al., 2017). It is important to discuss the proposed plan regarding antibiotics with the oncologist.

2.1.14. Orthodontics:

Children undergoing orthodontic therapy should have their orthodontic appliance removed and treatment discontinued until two years after completion of cancer therapy (Sheller and Williams, 1996).

2.2. DURING CANCER THERAPY

2.2.1. Hygienist / Nursing Support:

The period of mucositis is extremely unpleasant and close support from a dental hygienist or appropriately trained dental team member / general nurse is beneficial. The patient should be constantly reassured during this acute phase about the limited period of this side effect of treatment.

2.2.2. Oral / Denture Hygiene:

Normal daily toothbrushing by the patient, carer or parent, with a powered or manual medium brush should be undertaken, with supplemental use of floss or interdental brushes (Robinson *et al.*, 2005) (Public Health England, 2017).

- If brushing becomes very painful a soft brush (e.g. TePe Special Care Toothbrush) can be substituted, particularly for those patients receiving chemotherapy where their platelet levels are low.
- However, it should be noted that soft brushes are not as effective for plaque control and this is of particular concern for patients with head and neck cancer who may have profound changes in the oral cavity, including widespread mucositis and xerostomia. In these patients, a single tufted or children's toothbrush may be preferable.
- Normal toothbrushing should be resumed at the earliest opportunity

Dentures should be rinsed after meals and cleaned at least once daily by brushing with a toothbrush and soaked in chlorhexidine mouthwash overnight. An alternative is dilute sodium hypochlorite solution (Milton's diluted 1 in 80) provided there are no metal components. Dentures should not be worn at night.

2.2.3. Antibacterial Mouthwash

If brushing is difficult, for example after surgery, chlorhexidine mouthwash may be used in addition. It is an effective antibacterial and is available in concentrations 0.12-0.2% mouthwash. It is important to use the alcohol free preparations. 10ml should be rinsed round the mouth for 1 minute then spat out, twice daily. For children, it may be applied with gauze or sponges, as mouth rinsing may be difficult. Thirty minutes should be allowed between use of chlorhexidine and toothbrushing. The 0.2% concentration may be diluted 1:1 with water if it causes mucosal discomfort (SDCEP, 2016).

2.2.4. Dental Caries Risk:

The importance of preventing dental caries cannot be overemphasised. The need to maintain nutrition and body weight and difficulty with chewing often necessitates highly calorific and cariogenic food supplements (e.g. Fortisips by Nutricia). The following measures can be implemented to reduce the caries risk:

- The dental team should work with the dietitian team to keep the length of time these are used to a minimum, timing where possible limited to meal times and the mouth is rinsed after intake (Meurman and Gronroos, 2010).
- Sugar free medicines should be used wherever possible and discussed with the oncology team.
- Adults should use an alcohol-free fluoride mouth rinse at least once daily (0.05% NaF) at a different time from brushing. In addition, they should be prescribed 5,000ppm fluoride toothpaste for use twice daily and fluoride varnish (2.26% fluoride) should be applied twice a year (Public Health England, 2017).
- Children and young adults should have fluoride toothpaste, application of fluoride varnish and fissure sealants and fluoride mouthwashes appropriate to age (Public Health England, 2017) (SDCEP, 2016) (Kielbassa *et al.*, 2006). In addition, 2800ppm fluoride toothpaste can be prescribed for use twice daily in those aged 10 years and above.
- Fluoride gel application in custom made trays for ten minutes daily has been recommended but compliance is poor (Thariat *et al.*, 2012). This may be difficult for patients with trismus or after surgery and is not suitable for children.
- Further trials in this population are recommended before the widespread use of free calcium products (Tooth Mousse, GC) (Raphael and Blinkhorn, 2015).

2.2.5. Viral Infections:

Children and adults receiving bone marrow transplants often receive aciclovir as a prophylaxis if there is a high risk of viral infections. The facial and oral tissues may be sites of presentation of viral infections, such as those belonging to the herpes group. Anti-viral medication is usually prescribed by the oncology team (Ullmann *et al.*, 2016) (Sanderr *et al.*, 2015) (Glenny *et al.*, 2010).

2.2.6. Fungal infections:

There is increased risk of oral fungal infection in patients receiving

chemotherapy and / or radiotherapy (Lalla *et al.*, 2010). Antifungal medication should be used following detection of oral candida (Pappas *et al.*, 2016) (Lalla *et al.*, 2010). In some oncology centres, antifungal prophylaxis may be used routinely for children (Epstein *et al.*, 1996).

Topical agents may be preferred to systemic agents due to lower risk of side effects (Bensadoun *et al.*, 2011). However, there are inconsistent results of efficacy of topical agents and some oncology centres advise that systemic antifungal agents are preferable and each patient's risk should be identified before they are prescribed (Lalla *et al.*, 2010).

The following are recommended in adults:

- Nystatin oral suspension 100,000 units per ml four times daily for at least 7 days and 48 hours after resolution (Pappas et al., 2016) (Lalla, et al., 2010) (BNF, 2017). Pastilles are difficult to dissolve in a dry mouth. Compliance may be poor due to unpleasant taste (SDCEP, 2016) (Lalla et al., 2010). Ideally sugar-free preparations should be used as nystatin to avoid an increased risk of dental caries.
- Miconazole oral gel 24mg/ml 10ml applied four times daily continued for 48 hours after resolution is an alternative (SDCEP, 2016) (Bensadoun *et al.*, 2011).
- Systemic agents have more consistent efficacy and fluconazole is recommended for moderate or severe oropharyngeal candidiasis or unresponsive infection (Pappas *et al.*, 2016). The regime is 50mg capsules or suspension daily for seven to fourteen days.

Miconazole and fluconazole are contraindicated in patients taking warfarin or statins (BNF, 2017).

For children appropriate recommended doses should be used as per the British National Formulary (BNF, 2017).

Denture hygiene is very important if there is fungal infection; dentures should be cleaned with a toothbrush / nailbrush and soaked in chlorhexidine mouthwash or dilute sodium hypochlorite. Miconazole oral gel should be applied to the fit surface prior to re-insertion, provided it is not contraindicated (SDCEP, 2016) (De Sanctis *et al.*, 2016).

2.2.7. Mucositis:

The Oral Assessment Guide is the recommended tool to ensure the signs and symptoms of mucositis are observed and recorded (see Appendix 4 for a

modified version) (Eilers *et al., 1988*). It has been consistently judged to be user-friendly and appropriate for everyday clinical practice with adults and children, as well as a useful research tool (Gibson *et al.,* 2010).

Several interventions for prevention and management of mucositis have been found to have some benefit but there is no consensus of best protocol. There is limited evidence for their efficacy in children. The strength of evidence is variable and may be specific to cancer type and treatment (Riley *et al.*, 2015).

- The use of mucosal shields and intensity-modulated radiotherapy is to be encouraged since there is decreased severity of mucositis (Treister and Sonis, 2007).
- Intensive oral hygiene reduces mucositis (Treister and Sonis, 2007) (SIGN, 2006) (Stockman *et al.*, 2006).
- Poorly fitting dentures or sharp teeth may exacerbate symptoms and should be corrected (Treister and Sonis, 2007).
- Difflam (benzydamine hydrochloride) 0.15% mouthwash reduces the frequency and severity of mucositis and is recommended. A regime of 15ml four to eight times daily starting before radiotherapy and continuing during and for two to three weeks afterwards is recommended (Nicolatou-Galitis *et al.*, 2013).
- Chlorhexidine has not been shown effective and is not recommended for prevention or treatment of mucositis (Cardona et al., 2017) (McGuire et al., 2013).
- Oral cooling prior to chemotherapy is recommended where mucositis inducing chemotherapeutic agents are used (e.g. 5-FU) (Peterson et al., 2013).
- Patients receiving high dose chemotherapy or total body irradiation for stem cell transplantation are recommended intravenous keratinocyte growth factor-1 (palifermin) since there are promising effects on preventing mucositis. There is no benefit with palifermin taken as a mouthwash (Stockman et al., 2006) (Lucchese et al., 2016).
- There is insufficient evidence for intravenous amifostine for prevention of mucositis and this is not recommended (Nicolatou-Galitis *et al.*, 2013).
- A number of topical agents have been used. There is insufficient evidence for use of topical application of antimicrobial pastes or lozenges, prostaglandins, corticosteroids, sucralfate, allopurinol, acyclovir and these are not recommended (Stockman et al., 2006) (SIGN, 2006) (Saunders et al., 2013)
- Muso-adhesive oral rinses and gels have shown limited efficacy (Mugard,

Gelclair) (Allison et al., 2014) (Barber et al., 2007).

- Other palliative management recommended is 2% lidocaine mouthwash used prior to eating, fentanyl dermal patches, 2% morphine mouthrinse and systemic pain relief with morphine in severe cases (Treister and Sonis 2007) (Saunders *et al.*, 2013).
- Low level laser therapy may be beneficial for prevention in patients having radiotherapy alone (Migliorati *et al.*, 2013). It may also be of benefit in preventing oral mucositis in patients receiving hematopoietic stem cell transplantation conditioned with high-dose chemotherapy, with or without total body irradiation (Lalla *et al.*, 2014).
- Zinc supplements taken orally may reduce mucositis in radiotherapy and chemotherapy (Yarom et al., 2013).

2.2.8. Xerostomia:

A recent systematic review and meta-analysis has been undertaken to estimate the effectiveness of available interventions for radiotherapy-induced xerostomia and hyposalivation. Results from the meta-analysis, which included six studies, suggest that both cevimeline and pilocarpine can reduce xerostomia symptoms and increase salivary flow compared to placebo, although some aspects of the relevant effect size, duration of the benefit, and clinical meaningfulness remain unclear. It concluded that randomised trials of available treatment modalities have produced unclear results and offer little reliable guidance for clinicians to inform evidence-based therapy.

In view of the above, the recommendations below are based on the current best available evidence:

Flouride Supplementation:

- Xerostomia increases the risk of dental caries. Fluoride supplementation is recommended as outlined in section 2.2.4.

Lubrication of the soft tissues:

- Oral gel or lubricants (e.g. petroleum jelly based products (Vaseline) or emollients (Cetraben) are useful to coat and protect the lips and soft tissues.

Reducing damage to the salivary glands:

- Minimising the dose of radiotherapy to the parotid glands by IMRT is encouraged as has been shown to improve xerostomia-related quality of

- life (Jensen et al., 2010) (Zhang et al., 2015) (Nutting et al., 2011).
- Amifostine given with radiotherapy has been shown to protect the salivary glands, with patients experiencing minor benefits, but there are significant side effects and it is not routinely recommended (Jensen *et al.*, 2010) (Cancer Care Ontario, 2012).

Salivary stimulation:

- Pilocarpine is recommended after radiotherapy where some salivary function remains, provided there is no medical contraindication (Jensen *et al.*, 2010). However, one review found that only half of patients respond (Davies and Shorthose, 2007). The dose is 5-10mg orally taken three times a day (SIGN, 2006). Side effects can be problematic so dose should be kept to a minimum. It may take more than two months to reach maximum effect (Nieuw *et al.*, 2003). There is mixed evidence to recommend pilocarpine during radiotherapy, some studies have shown increase in unstimulated saliva flow up to 12 months afterwards (Jensen *et al.*, 2010) (Yang *et al.*, 2016).
- Stimulation by sugar free chewing gum may be recommended where there is some salivary function although there is a limited evidence base (Jensen *et al.*, 2010) (Kaae *et al.*, 2016). In addition, patients should be advised regarding the potential digestive side effects of xylitol, which include bloating, flatulence and diarrhoea.
- Acidic pastilles are to be use with caution as these may cause tooth erosion and sensitivity (e.g. Salivix (Provalia); SST (Medac).
- There is low quality evidence that acupuncture results in a small increase in saliva. Acupuncture has minimal side effects and clinical trials are recommended (Jensen *et al.*, 2010) (Furness *et al.*, 2013).

Saliva substitution:

- For many patients, saliva replacement is the only option. Many use frequent sips of water (ideally non-carbonated and without acidic flavouring). Substitutes may improve patient's perception of xerostomia.
- Saliva is difficult to replicate and there are several substitutes with little indication of which is most effective (Porter *et al.*, 2010).
- It is important to avoid the use of acidic saliva replacements in dentate patients (e.g. Glandosane).
- Similarly, consideration should be given as to whether the substitutes contain fluoride.

- It is recommended patients sample alternative therapies to assess which suits them best. Gels may have longer duration of benefit. It is important to note that some products contain animal derived ingredients which need to be considered in the context of religion and also allergies / intolerances. If a preparation without fluoride is used, a fluoride mouthwash should also be used daily in dentate patients The following are suggested:
 - Saliva orthana (ASPharma) (contains porcine mucin; contains fluoride)
 - Biotene Oral Balance Gel (GSK) (new formulation not acidic; contains milk, egg white)
 - BioXtra Gel (Molar) (Shahdad *et al.*, 2005) (contains milk, egg white; contains fluoride)

2.2.9. Dentures / Obturators:

If dentures are left out during the period of mucositis they should be cleaned and kept moist. If candidal infection has been diagnosed this should be treated

Obturators should not be discontinued. If painful a clinical examination and adjustment is indicated.

2.2.10. Foam swabs / Oral Cleanser / Gauze:

Foam swabs are not as effective as a toothbrush but there may be times, for example post-surgery or in advanced disease, when either foam swabs or gauze are necessary (Addems *et al.*, 1992). Oral cleanser sticks (e.g. MC3), may also be used. Use soaked in chlorhexidine three to four times daily. Care should be taken with oral care if patients are at risk of aspirating following surgery / radiotherapy. Patients should be sitting up and minimal amount of fluid used and aspiration should be available. Nursing staff should be trained in oral care and family and carers may be involved. Normal toothbrushing should be resumed as soon as possible.

2.2.11 Dietary Advice:

Avoidance of certain food, drinks and mouthwashes can help to prevent discomfort.

The following should be avoided:

- Hard food, spicy food, strongly flavoured toothpaste: these traumatise the tissues
- Alcohol (especially spirits), tobacco: these exacerbate xerostomia

- Fizzy drinks, acidic fruit and fruit drinks: these contribute to tooth surface loss and sensitivity, especially in the dry mouth where there is reduced saliva buffering.

2.2.12 Dental Treatment:

Dental treatment should be avoided during the period of cancer therapy because the mouth may be very sore and there is risk of systemic infection during the period of mucositis. If the patient is having chemotherapy the suppressive effect on the bone marrow may cause low platelets, low white cells and anaemia. Therefore, special care needs to be taken and timing of interventive dental treatment should be agreed with the haematologists or the oncology team. Pulp treatment of primary teeth is contra-indicated in immunocompromised patients (Rodd *et al.*, 2006). Extractions are always contraindicated after radiotherapy to the head and neck area, careful patient pre-treatment assessment and planning should avoid the need.

2.2.13. Obturators:

Maxillary / mid face defects can be rehabilitated using surgery and / or obturated using a prosthesis. Developments in surgical techniques have resulted in wider use of microvascular free tissue transfer to provide vascularised hard and soft tissue for reconstruction, commonly at the time of tumour resection. However, as an alternative to surgical reconstruction, defects can be obturated using a removable prosthesis. This may be more relevant for patients with increased surgical morbidity or risk, but other factors require to be assessed.

2.3. FOLLOWING CANCER THERAPY

2.3.1. Monitoring:

- All oncology patients should be monitored for local recurrence, metastatic lesions in the head and neck region (daSilva *et al.*, 2012), and a second malignant lesion (Morton *et al.*, 2014).
- Furthermore, susceptibility to dental disease can be lifelong following cancer therapy (Hong *et al.*, 2018) (Hong *et al.*, 2010) (Jensen *et al.*, 2010).
- It is the dental team's responsibility to ensure patients fully understand the long-term dental adverse effects that can follow treatment for malignant disease and emphasise good oral care and prevention (Gupta *et al.*, 2015).
- Individualised oral health prevention and monitoring programme should be established for each patient reflecting the treatment they have received, their particular needs and risk factors and the presence of active dental disease (Public Health England, 2017).
- Regular oral healthcare monitoring should be undertaken by a designated member of dental staff in close liaison with the dental hygienist/therapist. The recall interval is based on the patient's risk assessment but is likely to be no less frequent than three monthly, at least in the first instance (NICE, 2004).
- Good communication between the oncology team, the patient, and all members of the dental team is essential (Tremblay *et al.*, 2016).

2.3.2. Dental Caries Risk:

The risk of dental caries following cancer therapy will depend on the type of treatment the patient has received (Hong *et al.*, 2018) (Hong *et al.*, 2010). The following factors increase the risk of dental caries:

- Salivary hypofunction caused by damage to the salivary glands during radiotherapy, leading to xerostomia and a more cariogenic oral microflora (Gawade *et al.*, 2015).
- Patients choosing cariogenic foods and drinks due to altered taste (Bressan et al., 2016), mucositis (Riley et al., 2015), and difficulties with mastication and swallowing (Cousins et al., 2013).
- The prescription of a cariogenic diet and nutritional supplements by dieticians because of weight loss, malnutrition and difficulties with eating (Talwar *et al.*, 2016).
- Poor oral hygiene due to difficulties with toothbrushing/interdental aids as a result of limited oral opening (Gebre-Medhin *et al.*, 2016) (Macfarlane *et al.*,

- 2012), or reduced motivation secondary to psychosocial distress (Dunne *et al.*, 2017).
- The presence of enamel defects and dental hypoplasia secondary to radiotherapy and chemotherapy in childhood (Gawade *et al.*, 2015).

2.3.3. Gingival and Periodontal Risk:

- Bone marrow transplant patients on ciclosporin may need more frequent hygienist support to help maintain health in the presence of gingival hyperplasia (Aimetti *et al.*, 2008).
- Oral hygiene instructions, supra- and subgingival scaling, polishing, and gingival curettage should be carried out in the first instance with this having been found to reduce the need for gingivectomy (Kantarci *et al.*, 1999).
- Patients who have received radiation therapy to the head and neck region are at increased risk of progressive, uncontrolled periodontal tissue breakdown and/or ORN (Epstein and Stevenson-Moore, 2001).
- This is likely due to reduced repair capacity of the periodontium following direct irradiation with progressive widening of the periodontal ligament, destruction of the lamina dura and progressive loss of attachment having been reported (Epstein and Stevenson-Moore, 2001).
- Furthermore, the risk of periodontal infection is increased because of radiation-induced hyposalivation, the concomitant increased plaque accumulation, and the shift in oral microflora.
- There do not, however, appear to be any significant long-term changes to periodontal pathogens following head/neck radiation therapy (where treatment of the periodontium had included irrigation with chlorhexidine) (Al-Nawas and Grötz, 2006).
- Poor oral health status post-radiotherapy has been found to increase the risk of ORN (Katsura et al., 2008). As such any evidence of periodontal disease should be treated rigorously but nonetheless causing minimal damage to the adjacent structures; trauma to the soft tissues can also predispose to ORN (Kielbassa et al., 2006).

2.3.4. Preventive advice and fluoride supplementation:

Dietary analysis and advice should be undertaken at frequent intervals with an emphasis on reducing the amount and frequency of sugars and acids in the diet and encouraging a healthy balanced diet (Public Health England, 2017). The patient's diet is likely to change during the post-treatment period as their health improves, and ongoing advice and support for behaviour change is required (Public Health England, 2017).

- Close liaison with the dietician is needed throughout the post-treatment period (Talwar *et al.*, 2016). It is important to balance the need for good nutrition and weight gain against the risk of developing dental caries.
- Plaque and gingival scores, such as the Basic Periodontal Examination (BPE), should be regularly monitored by the dental hygienist/therapist looking after the patient. Oral hygiene advice should be individualised and tailored to the specific needs of the patient (Public Health England, 2017).
- The role of fluoride in the continuing prevention of dental caries is essential to the maintenance of oral health. Teeth should be brushed twice daily with a fluoridated toothpaste. Strong evidence shows that toothpastes containing higher concentrations of fluoride are more effective at controlling caries. It is clear that low fluoride toothpastes (those containing less than 1,000ppmF-) are ineffective at controlling caries. The following fluoride content of toothpaste is recommended for patients giving concern to the dentist (e.g. those with active caries, dry mouth and other predisposing factors which may be linked to cancer therapy) (Public Health England, 2017)
 - o Children 0-10 years old: 1350-1500ppm
 - Children aged 10-16 years old: 2800ppm
 - Adolescents / adults aged 16 years old and over: 2800ppm -5000ppm
- The professional application of fluoride varnish (2.26% NaF) has a caries inhibitory effect (Marinho *et al.*, 2013). Applications should be twice yearly or more frequently (Public Health England, 2017).
- A daily fluoride mouthwash can be advised to increase the amount of available fluoride (Marinho *et al.*, 2016). This is only recommended for children aged eight years and over and adults (Public Health England, 2017).
- There is insufficient evidence in children / adolescents without xerostomia to recommend the use of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) products such as Tooth Mousse® over fluoride products in the prevention and treatment of early carious lesions (Raphael and Blinkhorn, 2015). However, in patients with Head and Neck cancer who have xerostomia due to radiotherapy, there is depletion of calcium and phosphate in the saliva and hence these products may be of benefit, particularly as they are available in sweet flavours which may be better tolerated.
- There is also insufficient evidence to support the use of chlorhexidine

gluconate products to prevent dental caries (Walsh et al., 2015)

2.3.5. Xerostomia:

Salivary stimulants and saliva replacement products are outlined in section 2.2.8 explanatory notes

2.3.6. Smoking cessation:

Smoking cessation support should be ongoing and patients should be encouraged to reduce alcohol consumption (Hashibe *et al.*, 2009). Support to stop the use of smokeless tobacco and betel quid should also continue (Gupta and Johnson, 2014).

2.3.7. Abnormal blood counts

Patients on maintenance chemotherapy / a history of low blood profiles due to haemato-oncology disease, should have a full blood count performed within the 24-48 hours period prior to any proposed dental treatment that might result in bleeding/bacteraemia. The results of such blood tests should be discussed with the patient's medical team and appropriate precautions taken.

2.3.8 Herpes labialis

Herpes labialis can be a chronic problem. Topical aciclovir (5% cream applied five times daily for five to ten days, starting at first sign of attack) is effective (Arduino and Porter, 2006) (BNF, 2017).

2.3.9 Limited mouth opening:

- Despite better focused radiation dose and improved screening, progressive jaw stiffness and limitation of opening remains a common complication (Gebre-Medhin *et al.*, 2016). Reduction of mouth opening due to tumour recurrence should be excluded.
- In the event of limitation, physical therapy modalities e.g. passive and active stretching exercises, and the use of devices for stretching the muscles of mastication e.g. Therabite jaw motion rehabilitation system, Dynasplint Trismus System, and stacked tongue depressors, are the mainstay of treatment (Rapidis, et al., 2015).
- Evidence is conflicting, with one recent systematic review finding that no stretching technique was superior to others regarding either prevention or treatment of trismus (Kamstra *et al.*, 2013) and another suggesting that the use of a jaw-mobilising device yielded better results than no exercise in

- patients with radiotherapy-induced trismus (Scherpenhuizen et al., 2015).
- Starting therapy early and compliance with exercises were important factors in the success of treatment (Kamstra *et al.*, 2013).
- Other therapy modalities include drug therapy such as pentoxifylline to improve microcirculation and tissue oxygenation, although the evidence for this intervention is very weak (Chua *et al.*, 2001).
- Botulinum toxin injection can be used to reduce pain associated with trismus, although it does not improve mobility (Hartl *et al.*, 2008).
- Coronoidectomy can be considered to increase the range of motion (Bhrany *et al.*, 2007). Increasing levels of trismus should be investigated for potential local recurrence (Rapidis *et al.*, 2015).

2.3.10 Growth and Development:

- In children, general growth and development including facial growth and dental development should be closely monitored (SIGN, 2013).
- Survivors of childhood cancer who received radiotherapy, chemotherapy and total body irradiation with high-dose chemotherapy prior to stem cell transplant are all at an increased risk of dental developmental abnormalities including agenesis, microdontia, hypoplasia, root stunting and enamel defects, in addition to xerostomia (Pedersen *et al.*, 2012) (Cubukcu *et al.*, 2012) (Verterbacka *et al.*, 2012) (Hsieh *et al.*, 2011).
- The risk of dental abnormalities increases by younger age at treatment, higher doses of radiation and/or chemotherapeutic agents, and combined treatment (Gawade *et al.*, 2015).
- This has implications in future dental care for the restorative specialist.

2.3.11 Orthodontics:

- The decision to embark upon orthodontic treatment must to be taken carefully, and discussed with the patient's medical team in advance.
- Overall health, susceptibility to dental caries and response to oral health prevention regimes should be assessed (Wishney, 2017).
- Consideration must be given to the forces to be used and length of time that the patient will be in active orthodontic treatment. This is due to possible damage/effects that may have occurred previously to the roots of the teeth (Gawade *et al.*, 2015). When roots have either been damaged or not developed properly, orthodontic work can have detrimental effects on the root structure so the advantages and disadvantages of such treatment must be

explained carefully to the patient.

- The effects of antiresorptive agents should be considered carefully if orthodontic extractions are anticipated. The risk of medication-related osteonecrosis following dental extraction in patients who have received antiresorptive agents for cancer treatment is approximately 1% (range 0.2%-6.7%) (Dodson, 2015).
- Oral bisphosphonates have been shown to inhibit orthodontic tooth movement, prolong treatment time, and increase the odds of poor space closure and poor root parallelism in a small retrospective cohort study (Lotwala et al., 2012).
- There are currently no human studies examining the effects of intravenous bisphosphonates on orthodontic tooth movement. However the general consensus is to avoid orthodontic treatment when IV bisphosphonates are being administered and for a period after cessation.

2.3.12 Restorations:

- Where appropriate, a restorative material with fluoride release may be used.
- Of note, conventional glass ionomer restorations have been found to perform more poorly than resin modified glass ionomer, composite resin, and amalgam restorations in patients who have been treated with radiotherapy (Hong *et al.*, 2018).
- In those patients who have xerostomia related to radiation therapy, cervical caries is problematic and particularly so in those patients who fail to comply with preventive measures. Conservative restorative management of cavitated lesions is to be recommended in the first instance. Full / partial coverage crowns should be provided only when the patient can demonstrate good oral hygiene; caries can quickly progress around the margins of full / partial coverage crowns with the potential for eventual 'carious amputation' of the crown. Should a full coverage restoration be warranted, the margins should be subgingival (Chung and Sung, 2006).
- Routine restorative treatment must be delayed until the patient is in remission, when a careful study of the medical history should be made.
- Some children may have developed other medical complications as the result of cancer treatment (e.g. cardiomyopathy) with possible implications for their dental management.

2.3.13 Dental extractions:

- Where possible, extraction of teeth from irradiated sites should be avoided due to the risk of ORN (see section 2.3.17).

- Cancer patients who have received a bisphosphonate or other anti-resorptive drug therapy are also at increased risk of medication related osteonecrosis of the jaw (MRONJ) and dental extractions avoided (Ruggiero et al., 2006) (see section 2.3.18).
- There is currently no effective treatment for of ONJ and MRONJ and they can adversely affect the quality of life for patients.
- A systematic review has estimated the total incidence of ORN after tooth extraction in irradiated patients to be 7% (Nabil and Samman, 2011). When extractions were performed in conjunction with prophylactic HBOT, the incidence was 4% while extraction in conjunction with antibiotics gave an incidence of 6%.
- However, there is no clear evidence that HBOT reduces the chance of ORN following tooth extraction in an irradiated field. Its use may be considered in the context of clinical trials (NICE-NG36 2016).
- Although there is no conclusive evidence regarding pre-extraction antibiotic prophylaxis to prevent ORN, the general consensus would recommend antibiotic prophylaxis and continued antibiotics until completion of healing. Co-amoxiclav / amoxicillin (metronidazole in those allergic to penicillins) are generally the drugs of choice (Koga *et al.*, 2008) (Ruggiero *et al.*, 2006). Discussion with the oncology team is essential.
- Some studies recommend the use of alcohol free 0.2% chlorhexidine gluconate mouthwash prior to extractions and the use of low-adrenaline/adrenaline free local anaesthesia may also reduce the risk of ORN. (Koga *et al.*, 2008). The evidence regarding this approach is not clear.
- Any extractions completed should be performed with minimal trauma and, where possible, soft tissue primary closure obtained (Nabil and Samman, 2011).
- Patients are at particular risk of ORN when:
 - The total radiation dose exceeded 60Gy (Nabil and Samman, 2011) (Clayman, 1997).
 - The dose fraction was large with a high number of fractions.
 - There is local trauma as the result of a tooth extraction (especially mandibular extractions), uncontrolled periodontal disease or an ill-fitting prosthesis.
 - The person is immunodeficient.
 - The person is malnourished.
- Where there is a high risk of ORN and where it is clinically feasible, serious consideration to root canal therapy and restoration/crown amputation should be made (Kielbassa *et al.*, 2006) (Chung and Sung, 2006) (Ruggiero *et al.*, 2006)

- The risk of medication-related osteonecrosis (MRONJ) in patients who have received bisphosphonates and / or antiresorptive agents for cancer treatment should also be considered when dental extractions are being discussed (see section 2.3.18). Where possible, dental extractions should be avoided and, as in the case for risk of ORN, teeth stabilised with root canal treatment (SDCEP, 2017).

2.3.14 Dentures:

- Dentures should be avoided wherever possible. Appliances will contribute to plaque retention and oral disease, particularly when there is xerostomia.
- When dentures are essential to ensure good function following cancer treatment, their construction will aid the ability to chew solid food and, by extrapolation, promote social adaptation and weight gain.
- Removable prosthetic appliances should be removed and left out of the mouth overnight and subjected to a cleansing regimen involving careful brushing with household washing up liquid and warm water to remove all visible debris and immersion in a sodium hypochlorite if they have no metal parts (Milton's) solution (1% sodium hypochlorite in a 1:80 dilution). Chlorhexidine mouthwash can also be used.
- For those edentulous patients who have xerostomia, a suitable oral lubricant / artificial saliva solution or gel can be applied to the fit surface of their prosthesis prior to reinsertion; this may help to ameliorate xerostomia.
- Artificial salivas with an acidic base (e.g. Glandosane) should be avoided in dentate patients (Holliday *et al.*, 2015).
- Artificial saliva reservoirs, incorporated into complete or partial prostheses, have been shown to relieve xerostomia symptoms temporarily (Mendoza and Tomlinson, 2003).
- In the event of oral candidal infection, antifungals should be prescribed for at least two consecutive weeks:
- Miconazole varnish or gel applied to fit denture surface. This should be avoided if the patient is taking warfarin; the anticoagulant effect is enhanced by miconazole.
- Nystatin powder- 500,000-1000000 units per application of Viscogel can be incorporated into a denture soft lining material. The nystatin powder is added when the powder and liquid of the liner are mixed. The fungicidal activity of such modified lining materials reduces with time and as such requires to be changed on a regular basis e.g. between seven and fourteen days (Falah-Tafti et al., 2010) (Geerts et al., 2008).
- Tea tree oil (*M. Alternifolia*) mixed with the Coe Comfort tissue conditioner has an anti-fungal effect and could be used as an alternative therapy for denture stomatitis which is resistant to traditional therapies (Catalán *et al.*, 2008).
- Microwave disinfection of maxillary complete dentures has also been found to be effective (Neppelenbroek *et al.*, 2008).
- Miconazole / Fluconazole may be required for resistant infections but are

- contraindicated for patients on warfarin (BNF, 2017).
- Appliance wear should be discontinued if the mouth becomes painful and advice must be sought from the supervising consultant. Trauma from dentures has been implicated in an increased risk of MRONJ. Modification or replacement of dentures may be required to alleviate symptoms.

2.3.15 Dental Implants:

- Osseointegrated implants may facilitate effective oral rehabilitation following cancer treatment (including radiotherapy). They can be used to support fixed or removable prostheses.
- The provision of implants should take into consideration the patient's prognosis, published national guidelines on their use, and where relevant evidence regarding their use in head and neck oncology patients (Alani *et al.*, 2012) (Barber *et al.*, 2011).

Careful planning and appropriate patient selection are essential prior to any such intervention (RD-UK, 2016).

- Where full planning can be undertaken pre-operatively, placement of implants at the time of tumour resection may be beneficial for suitable patients where continuity of the mandible is either preserved or reconstructed, or for patients requiring significant maxillary defects to be obturated by way of a prosthesis.
- Where segmental resection with reconstruction of the mandible is undertaken, implant survival and usefulness may be improved by delayed placement after suitable prosthodontic planning.
- Where post-operative radiotherapy is part of the initial plan, primary implant placement may be preferred, although it may reduce time and opportunity for the planning of ideal implant location (Javed *et al.*, 2010).
- For most patients, placement of osseointegrated implants will be a consideration in response to ongoing problems with oral function after cancer treatment. Management at this time allows a full detailed assessment of the patient's prognosis, risk factors (smoking, alcohol, oral hygiene, radiotherapy fields and their impact) as well as consideration of other factors including residual anatomy, reconstructive tissue grafts (both bone and soft tissues), metal reconstruction frameworks, and overall oral function, including tongue mobility, mouth opening and swallowing function and airway protection. The use of computerised planning and surgical stents is advocated for optimal outcomes.
- While implants may be placed in irradiated bone, careful case assessment is necessary. Failure rates are higher than in non-irradiated bone and higher in the maxilla than in the mandible (Barber et al., 2011).

- Osteoradionecrosis is an acknowledged risk of implant placement in irradiated tissues.
- Failure is less likely with a radiation dose lower than 45Gy.
- It has been suggested that a delay of one to two years after irradiation for implant placement and a further 6 months delay for abutment connection reduces risk but further review of this is necessary (Dholam and Gurav, 2012).
- There may be an increased risk of implant failure in free flap bone that has been irradiated (Barrowman *et al.*, 2011).
- There is no good quality evidence for the use of hyperbaric oxygen for patients who require implant placement in irradiated bone (Esposito *et al.*, 2008).
- While zygomatic implants may be used to retain obturators as an alternative to free flaps, the efficacy of zygomatic implants in aiding maxillary obturation is not clear (Schmidt *et al.*, 2004).
- Implant-supported prostheses and complex conventional prostheses require long-term review by the restorative dentistry consultant.
- The placement of implants in patients who are being treated with intravenous high potency bisphosphonates for cancer, is not recommended due to the higher risk of MRONJ (SDCEP, 2017).

2.3.16. Obturators:

- Obturators should be reviewed regularly. They may require frequent attention with adjustment or remake.
- Obturators should not be left out at night for the six months following treatment and may be worn at night for longer dependent on patient comfort and function, e.g. breathing, and with the approval of and regular review by the treating restorative dentistry consultant.
- Where longer-term appliance wear is continued, prosthesis hygiene must be emphasised with patients and a daily period of cleansing of the prosthesis as above is mandatory.
- Maxillary / mid face defects can be rehabilitated using surgery and / or obturated using a prosthesis. Developments in surgical techniques have resulted in wider use of microvascular free tissue transfer to provide vascularised hard and soft tissue for reconstruction, commonly at the time of tumour resection. However, as an alternative to surgical reconstruction, defects can be obturated using a removable prosthesis. This may be more relevant for patients with increased surgical morbidity or risk, but other factors require to be assessed.
- The level of evidence available to support surgical reconstruction using free

flaps versus prosthetic obturation of maxillary and mid-face defects remains low.

- Maxillectomy is sufficiently uncommon that patient numbers for analysis remain low. While larger defects are increasingly surgically reconstructed this has an impact on both the feasibility of as well as an opportunity to assess the effectiveness of prosthetic obturation / reconstruction (Rogers et al., 2003) (Moreno et al., 2010)
- Other factors such as any surgical flap which has been used, the final dimensions and morphology of the defect and adjunctive (chemo) radiotherapy all affect success, as does the initial dental health status of the patient and previous prosthetic experience.
- The most significant predictor of obturator function is the size of the defect. Statistically better obturator function is associated with defects where resection of the soft palate is one third or less and resection of the hard palate is one quarter or less (Rogers *et al.*, 2003) (Kornblith *et al.*, 1996).
- Statistically significant higher obturator speech scores are achieved as the resection volume of soft palate decreases (Kornblith et al.,1996). However, whether obturation or free flap reconstruction of maxillary and mid-face defects provides better oral rehabilitation remains controversial.
- While patients may prefer to have a reconstruction, which brings a sense of more permanent replacement of the lost tissues rather than a defect that is always evident on removal of the obturator, the nature of the reconstruction may make prosthetic rehabilitation more problematic in the longer term.

2.3.17. Osteoradionecrosis:

- Osteoradionecrosis (ORN) of the jaws is one of the most severe and debilitating complications following radiation therapy for head and neck cancer patients in the proven absence of tumour, and may be a major complicating factor following surgery or trauma to a previously irradiated maxilla or more commonly mandible. Radiation-induced fibrosis, and reduction of fibroblastic activity in the irradiated area, produces atrophic tissue with damage to microvessels, resulting in vascular insufficiency which rather than infection contributes to bone death (Costa et al., 2016) (Nadella et al., 2015) (McLeod et al., 2010) (Lyons and Ghazali, 2008).
- Risk factors include the total radiation dose, modality of treatment, fraction size and dose rate, oral hygiene, timing of tooth extractions or other invasive procedures the continued use of tobacco and alcohol may further increase the incidence of ORN (Wang et al., 2017) (Maesschalck et al., 2016).
- This condition is characterised by deep-seated bone pain often with a purulent discharge that may include sequestrated bone and may result in significant

bone loss. If treated inadequately or left untreated it can be majorly debilitating and significantly impair quality of life (Rice *et al.*, 2015) (Silvestre-Rangil and Silvestre, 2011).

- Basic criteria for staging of ORN:
 - Stage 0: mucosal defects only; bone exposed
 - Stage I: radiological evidence of necrotic bone, dento-alveolar only
 - Stage II: positive radiographic findings above ID canal with denuded bone intraorally
 - Stage III: clinically exposed radionecrotic bone, verified by imaging techniques, along with skin fistulas and infection with addition of potential or actual pathological fracture. Radiological evidence of bone necrosis within the radiation field, where tumour recurrence has been excluded (Dhanda *et al.*, 2016) (Deshpande *et al.*, 2015) (Karagozoglu, *et al.*, 2014) (Shaw and Dhanda, 2011) (Notani, *et al.*, 2003) (Støre and Boysen, 2000).
- Strenuous efforts should be made to avoid ORN by careful oral health monitoring and ensuring prevention compliance, timely dental treatment and dealing promptly with oral trauma (Raguse *et al.*, 2016) (Butterworth *et al.*, 2016) (Chronopoulos *et al.*, 2015) (Kanatas *et al.*, 2002).
- Oral trauma can be reduced by implementation of a soft diet and adjustment or removal of any denture that could be contributing to trauma. Extractions are to be avoided where possible, particularly in the mandible (Wang *et al.*, 2017) (Beech *et al.*, 2017).
- The Antioxidant agent, pentoxifylline (PTX), facilitates microcirculation, and inhibits the inflammatory mechanisms, promotes fibroblast proliferation and the formation of extracellular matrix. Tocopherol (vitamin E) protects the cell membrane against peroxidation. A synergic effect has been observed between PTX and tocopherol in the treatment of ORN. These are accessible, well-tolerated and safe drugs at a suggested daily dosage of: PTX dose of 800mg/day and vitamin E 1000 IU/day. The evidence base for using these drugs is developing, and there is a lack of randomised controlled clinical trials supporting the use of these drugs. Any units using these drugs for the management or prevention of ORN should regularly audit their patient outcomes. (Patel et al., 2017) (NICE-NG36, 2016) (Patel et al. 2016) (Rice et al., 2015) (Robard et al., 2014) (McLeod et al., 2012) (Delanian et al., 2011) (Kahenasa et al., 2012).
- High dose antibiotic regimes should be instigated when symptomatic ORN is diagnosed and continued until a definitive treatment outcome or symptom relief is achieved. In more chronic cases the presence of Actinomycoses must be

considered as this will alter the dynamics of treatment protocols (Hall, 2008).

- The antibiotic of choice should be broad spectrum with a wide field of action such as amoxicillin with clavulanic acid; antibiotic prophylaxis prior to extraction or sequestrectomy should be given and continued until mucosal integrity has occurred (Hall, 2008). It is recommended that antibiotic treatment is initiated prior to surgery and continued through the surgical phase of ORN management, and post-surgery (Kanata et al., 2002).
- Localised disease control to remove sequestra and other debris from intra-oral defects in combination with adjunctive antibiotics is completed to gain pain relief. This treatment also facilitates sampling of material for culture and histopathology to establish both the non-malignant potential of diseased tissue and specificity and the sensitivity of microbial population to antimicrobial therapy (Shaw and Butterworth, 2011).
- There is a risk of serious complications developing after radiation cancer treatment due to late radiation tissue injury (LRTI).
- HBOT involves breathing oxygen under increased atmospheric pressure in a specially designed chamber. It is used as a treatment to improve oxygen supply to damaged tissue and stimulates healing. For patients with LRTI affecting tissues of the head, & neck, HBOT can be associated with improved outcome (Dieleman et al., 2017).
- However, there is no clear evidence that HBOT reduces the chance of ORN following tooth extraction in an irradiated field (only consider its use when involved with clinical trials (NICE-NG36, 2016).
- Indeed, there is an increased risk of tumour recurrence in patients who receive HBOT (Dieleman *et al.*, 2017) (Shaw and Dhanda, 2011).
- In advanced chronic cases, the extent of involvement of bone necrosis must be established. This can be via imaging cone bean CT r chemical markers, such as tetracycline to establish the healthy vital bone margins at surgery (Paultke et al., 2010). This is then followed by radical ablative surgery to remove all the necrotic bone and soft tissue, including hemi-mandibulectomy and reconstruction with either a pedical or microvascular free flap. These procedures aim to achieve closure of orocutaneous fistulae and restore function and aesthetics (NICE-NG36, 2016) (Rice et al., 2015) (Zaghi and Hendizadeh, 2014) (Gevorgyan et al., 2013) (Baumann et al., 2011).

2.3.18 Medication related osteonecrosis of jaw (MRONJ):

- MRONJ is an area of exposed bone in the jaw persisting for more than 8 weeks with no history of radiation therapy while having undergone a bisphosphonate or other anti-resorptive drug therapy. These medications are used in the management of some cancers, such as bone cancers,

- myeloma and metastases (Ruggiero et al., 2014).
- The incidence of MRONJ in adults when these medications are given in cancer patients has been reported as between 0.8% 12%, including spontaneous cases and those following invasive dental procedures. The risk of MRONJ following dental extraction in patients who have received antiresorptive agents for cancer treatment is approximately 1% (range 0.2%-6.7%) (Dodson, 2015).
- There is very little evidence on MRONJ in children following bisphosphonates, denosumab, or bevacizumab therapy (SDCEP, 2017) (Hernandez *et al.*, 2017) (Ngan *et al.*, 2013). Although no cases reports of MRONJ in children have been published to date, there is little knowledge on long-term effects.
- A staging system should be used to classify the extent of existing MRONJ. The
 most commonly used system has been described by the American association
 of Oral and Maxillofacial surgery (Ruggiero et al., 2014):
 - At Risk: No apparent necrotic bone in patients who have been treated with oral or intravenous bisphosphonates
 - Stage 0: No clinical evidence of necrotic bone but nonspecific clinical findings, radiographic changes, and symptoms
 - Stage 1: Exposed and necrotic bone or fistulas that probes to bone in patients who are asymptomatic and have no evidence of infection
 - Stage 2: Exposed and necrotic bone or fistulas that probes to bone associated with infection as evidenced by pain and erythema in the region of exposed bone with or without purulent drainage
 - Stage 3: Exposed and necrotic bone or a fistula that probes to bone in patients with pain, infection, and ≥ 1 of the following: exposed and necrotic bone extending beyond the region of alveolar bone (i.e. inferior border and ramus in mandible, maxillary sinus, and zygoma in maxilla) resulting in pathologic fracture, extraoral fistula, oral antral, or oral nasal communication, or osteolysis extending to inferior border of the mandible or sinus floor
- Suggested interventions for preventing MRONJ include antibiotics and / or antibacterial mouthwashes administered before and after dental extractions, insertion of plasma rich in growth factor (PRGF) into the dental socket post extraction and wound closure by primary or secondary intention. More frequent dental examinations, namely three monthly, have also been proposed (Beth-Tasdogan *et al.*, 2016).
- Suggested management for the treatment of MRONJ is stage specific and can be classified into non-surgical and surgical treatment.
- Non-surgical treatment options include: antiseptic treatment (chlorhexidine

mouthwash), antibiotics, drug treatment with teriparatide, pentoxifylline and α -tocopherol in combination with anti-microbial therapy, ozone therapy, hyperbaric oxygen, and low level laser therapy, platelet rich plasma have all been described.

- Surgical treatment options include: sequestrectomy, debridement, resection, immediate reconstruction and extraction of teeth within exposed necrotic bone. Autofluorescence-guided versus tetracycline fluorescence-guided bone surgery has also been described.
- The quality of evidence to support any of these approaches is currently is low or very low.

2.3.20 Discharge:

- For the majority of patients with radiation-induced side effects, discharge to the care of a primary care practitioner should be possible when the immediate post-treatment side effects have settled, diet modification has been addressed to reduce frequent intake of cariogenic food and drinks, consistently good oral hygiene is re-established and the use of topical fluoride products is comfortably tolerated. Where this is difficult to achieve, longer-term specialist support is advocated to minimise problems.
- However, even for patients discharged to primary care with good compliance and low initial evidence of pathology, the higher risk of caries and periodontal disease development and ORN will mean that they should have more frequent follow up than other patients in the primary care setting.
- Recall interval should be determined on an individual basis dependent on risk factors and the presence of active dental disease. Patients who persist with long-term energy-dense diets high in refined sugars and dietary supplements must be monitored closely for caries development (Public Health England, 2017)
- Life-long follow up for children is advised due to the late effects of cancer therapy.

REFERENCES

Abdullah, A. (2014). Protocol for dental treatment before bone marrow transplantation (BMT) in paediatric patients. *Pakistan Oral & Dental journal*, 34, 399-404. (3b)

Addems, A., Epstein, J., Damji, S., and Spinelli, J. (1992). The lack of efficacy of a foam brush in maintaining gingival health: a controlled study. *Spec Care Dentist,* 12, 103-106. (2b)

Aimetti, M., Romano, F., Marsico, A., and Navone, R. (2008). Non-surgical periodontal treatment of cyclosporin A-induced gingival overgrowth: immunohistochemical results. *Oral Dis*, 14, 244-250. (2b)

Alani, A., Bishop, K., Djemal, S. and Renton, T. (2012). Guidelines for Selecting Appropriate Patients to Receive Treatment with Dental Implants: Priorities for the NHS. 2012. Available at: https://www.rcseng.ac.uk/dental-faculties/fds/publications-guidelines/clinical-guidelines/ [accessed December 12, 2017].

Allison, R., Ambrad, A., Arshoun, Y., Carmel, R., Feldman, E., Finkelstein, S., Gandhavadi, R., Heron, D., Lane, S., Longo, J., Meakin, C., Papadopoulos, D., Pruitt, D., Steinbrenner, L., Taylor, M., Wisbeck, W., Yuh, G., Nowotnik, D. and Sonis, S. (2014). Multi-institutional, randomized, double-blind, placebo-controlled trial to assess the efficacy of a mucoadhesive hydrogel (MuGard) in mitigating oral mucositis symptoms in patients being treated with chemoradiation therapy for cancers of the head and neck." *Cancer*,120, 1433-1440. (1b)

Al-Nawas, B. and Grötz, K.(2006). Prospective study of the long term change of the oral flora after radiation therapy. *Support Care Cancer*,14, 291-296. (2b)

Arduino, P. and Porter, S. (2006). Oral and perioral herpes simplex virus type 1 (HSV-1) infection: review of its management. *Oral Dis*, 12, 254-70. (3b)

Barber, A., Butterworth, C. and Rogers, S. (2011). Systematic review of primary osseointegrated dental implants in head and neck oncology. *Br J Oral Maxillofac Surg*, 49, 29-36. (2a)

Barber, C., Powell, R., Ellis, A. and Hewett, J. (2007). Comparing pain control and ability to eat and drink with standard therapy vs Gelclair: a preliminary, double centre, randomised controlled trial on patients with radiotherapy-induced oral mucositis. *Support Cancer Care*, 15, 427-440. (1b)

Barrowman, R., Wilson, P. and Wiesenfield, D. (2011). Oral rehabilitation with dental implants after cancer treatment. *Aust Dent J*, 56, 160-165. (3b)

Baumann, D., Yu, P., Hanasono, M. and Skoracki, R. Free flap reconstruction of osteoradionecrosis of the mandible: a 10-year review and defect classification. *Head Neck*, 33, 800-807. (3b)

Beech, N., Porceddu, S. and Batstone, M. (2017). Radiotherapy-associated dental extractions and osteoradionecrosis. *Head Neck*, 39, 128-132. (3b)

Bennadi, D. and Reddy, C. (2013). Oral health related quality of life. *J Int Soc Prev Community Dent* 3 (2013): 1-6. (5)

Bensadoun, R., Patton, L., Lalla, R. and Epstein, J. (2011). Oropharyngeal candidiasis in head and neck cancer patients treated with radiation: update. *Support Care Cancer*, 19, 737-744. (5)

Beth-Tasdogan, N., Mayer, B., Hussein, H. and Zolk, O. (2016). Interventions for managing medication-related osteonecrosis of the jaw (MRONJ). *Cochrane Database of Syst Rev*, Issue11, CD012432. (1a)

Bhrany, A., Izzard, M., Wood, A., and Futran, N. (2007). Coronoidectomy for the treatment of trismus in head and neck cancer patients. *Laryngoscope*, 117, 1952-1956. (4)

BNF. British National Formulary, 74. www.BNF.org, 2017.

Bos-den Braber, J., Potting, C., Bronkhorst, E., Huysmans, M. and Blijlevens, N. (2015). Oral complaints and dental care of haematopoietic stem cell transplant patients: a qualitative survey of patients and their dentists. *Support Care Cancer*, 23, 13-19. (3b)

Brand, H., Bots, C. and Raber-Durlacher, J. (2009). Xerostomia and chronic oral complications among patients treated with haematopoietic stem cell transplantation. *Br Dent J*, 207, E17. (3b)

Brennan, M., Elting, L. and Spijkervet, F. (2010). Systematic reviews of oral complications from cancer therapies, Oral Care Study Group, MASCC/ISOO: methodology and quality literature. *Support Care Cancer*, 18, 979-984. (2a)

Bressan, V., Stevanin, S., Bianchi, M., Aleo, G., Bagnasco, A. and Sasso, L. (2016). The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: A systematic review. *Cancer Treat Rev*, 45, 105-19. (2a)

Butterworth, C., McCaul, L. and Barclay, C. (2016). Restorative dentistry and oral rehabilitation: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol*, S41-S44.

Cancer Care Ontario - Practice Guideline Report. (2012). The Role of Amifostine as a Radioprotectant in the Management of Patients with Squamous Cell Head and Neck Cancer. Available at: https://archive.cancercare.on.ca/common/pages/UserFile.aspx?fileId=34307 [Accessed December 12, 2017]. (2a)

Cancer Research UK. *Cancer Incidence Statistics*. (2017). Available at: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence [Accessed December 11, 2017].

Cardona, A., Balouch, A., Abdul, M., Sedghizadeh, P. and Enciso, R. (2017). Efficacy of chlorhexidine for the prevention and treatment of oral mucositis in cancer patients: a systematic review with meta-analyses. *J Oral Pathol Med*, 46, 680-688. (1a)

Catalán, A., Pacheco, J., Martínez, A. and Mondaca, M. (2008). In vitro and in vivo activity of Melaleuca alternifolia mixed with tissue conditioner on Candida albicans. *OralSurg Oral Med Oral Pathol Oral Radiol Endod*, 105, 327-332. (2b)

Chronopoulos, A., Zarra, T., Troltzsch, M., Mahaini, S., Ehrenfeld, M. and Otto, S. (2015). Osteoradionecrosis of the mandible: A ten year single-center retrospective study. *J Craniomaxillofac Surg*, 43, 837-846. (3b)

Chua, D., Lo, C., Yuen, J. and Foo, Y. (2001). A pilot study of pentoxifylline in the treatment of radiation-induced trismus. *Am J Clin Oncol*, 24, 366-369. *(2b)*

Chung, E. and Sung, E. (2006). Dental management of chemoradiation patients. *J Calif Dent Assoc*, 34, 735-742. (5)

Clayman, L. (1997). Clinical controversies in oral and maxillofacial surgery: Part two. Management of dental extractions in irradiated jaws: a protocol without hyperbaric oxygen. *J Oral Maxillofacial Surg*, 55, 275-281. *(5)*

Cocks, H., Ah-See, K., Capel, M. and Taylor, P. (2016). Palliative and supportive care in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol*, 130, S198-S207.

Costa, D., Costa, T., Netto, E., Joaquim, N., Ventura, I., Pratas, A., Winckler, P., Silva, I., Pinho, A., Sargento, I., Guerreiro, F. and Moreira, A. (2016). New perspectives on the conservative management of osteoradionecrosis of the mandible: A literature review. *Head Neck*, 38, 1708-1716. (5)

Cousins, N., MacAulay, F., Lang, H., MacGillivray, S. and Wells, M. (2013). A systematic review of interventions for eating and drinking problems following treatment for head and neck cancer suggests a need to look beyond swallowing and trismus. *Oral Oncology*, 49, 387-400. (2a)

Critchlow, S., Morgan, C. and Leung, T. (2014). The oral health status of pre-treatment head and neck cancer patients. *Br Dent J*, 216, E1. (3b)

Cubukcu, C., Sevinir, B. and Ercan, I. (2012). Distrubed dental development of permanent teeth in children with solid tumors and lymphomas. *Paediatr Blood Cancer*, 50, 80-84. (3b)

daSilva, S., Hier, M., Mlynarek, A., Kowalski, L. and Alaoui-Jamali, M. (2012). Recurrent oral cancer: current and emerging therapeutic approaches. *Front Pharmacol*, 30, 149. (5)

Davies, A. and Shorthose, K. (2007). Parasympathomimetic drugs for the treatment of salivary gland dysfunction due to radiotherapy. *Cochrane Database Syst Rev.* 18(3), CD003782. (1a)

De Sanctis, V., Boss, P., Sanguineti, G., Trippa, F., Ferrari, D. and Bacigalupo, A. (2016). Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements. *Crit Rev Oncol Hematol*, 100, 147-166. (2a)

Delanian, S., Chatel, C., Porcher, R., Depondt, J. and Lefaix, J. (2011). Complete restoration of refractory mandibular osteoradionecrosis by prolonged treatment with a pentoxifylline-tocopherol-clodronate combination (PENTOCLO): a phase II trial. *Int J Radiat Oncol Biol Phys*, 80, 832-839. (2b)

Dempsey, L., Orr, S., Lane, S. and Scott, A. (2016). The clinical nurse specialist's role in head and neck cancer care: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol*, 130, S212-S215.

Department of Health (1995). A Report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales. A Policy Framework for Commissioning Cancer Services – The Calman–Hine Report. Department of Health.

Deshpande, S., Thakur, M., Dholam, K., Mahajan, A., Arya, S. and Juvekar, S. (2015). Osteoradionecrosis of the mandible: through a radiologist's eyes. *Clin Radiol*, 70, 197-205. (5)

Dhanda, J., Pasquier, D., Newman, L. and Shaw, R. (2016). Current Concepts in Osteoradionecrosis. *Clin Oncol (R Coll Radiol)*, 28, 459-466. (5)

Dholam, K., and Gurav, S (2012). Dental implants in irradiated jaws: A literature review. *J Cancer Res Ther*, 9, S85-S93. (5)

Dieleman, F., Phan, T., van den Hoogen, F., Kaanders, J. and Merkx, M. (2017). The efficacy of hyperbaric oxygen therapy related to the clinical stage of osteoradionecrosis of the mandible." *Int J Oral Maxillofac Surg,* 46, 428-433. (3b)

Dodson, T. (2015). The frequency of medication-related osteonecrosis of the jaw and its associated risk factors. *Oral Maxillofacial Surg Clin N Am*, 27, 509-516. (2a)

Doi H, Tanooka M, Ishida T, Moridera K, Ichimiya K, Tarutani K, Kitajima K, Fujiwara M, Kishimoto H, Kamikonya N. (2017). Utility of intraoral stents in external beam radiotherapy for head and neck cancer. *Rep Pract Oncol Radiother*, 22, 310-318.

Dunne, S., Mooney, O., Coffey, L., Sharp, L., Desmond, D. and Timon, C. (2017). Psychological variables associated with quality of life following primary treatment for head and neck cancer: a systematic review of the literature from 2004 to 2015. *Psycho-Oncology*, 26, 149-160. (2a)

Eilers, J., Berger, A., and Peterson, M. (1988) Development, testing and application of the Oral Assessment Guide. *Oncology Nursing Forum*, 15, 325-330a.

Elad, S., Garfunkel, A., Or, R., Michaeli, E., Shapira, M. and Galili, D. (2003). Time limitations and the challenge of providing infection-preventing dental care to hematopoietic stem-cell transplantation patients. *Support Care Cancer*, 11, 674-677. (3b)

Elad, S., Raber-Durlacher, J., Brennan, M., Saunders, P., Mank, A., Zadik, Y., Quinn, B., Epstein, J., Blijlevens, N., Waltimo, T., Passweq, J., Correa, M., Dahllof, G., Garming-Legert, K., Logan, R., Rotting, C., Shapira, M., Soga, Y., Stringer, J., Stokman, M., Vokurka, S., Wallhult, E., Yarom, N. and Jensen, S. (2015). Basic oral care for hematology—oncology patients and hematopoietic stem cell transplantation recipients: a position paper from the joint task force of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISSO) and the European Society for Bone Marrow Transplantation (EBMT). Support Care Cancer, 23, 223-36.

Eliyas, S., Al-Khayatt, A., Porter, R. and Briggs, P. (2013). Dental extractions prior to radiotherapy to the jaws for reducing post-radiotherapy dental complications. *Cochrane Database of Syst Rev,* F28 (2): CD008857.

Epstein, J. and Stevenson-Moore, P. (2001). Periodontal disease and periodontal management in patients with cancer. *Oral Oncol*, 378, 613-619. (5)

Epstein, J., Ransier, A., Lunn, R., Chin, E., Jacobson, J., Le, N. and Reece, D. (1996). Prophylaxis of candidiasis in patients with leukemia and bone marrow transplants. *Oral Surg Oral Med Oral Pathol Endod*, 81, 291-296. *(2b)*

Epstein, J., Raber-Durlacher, J., Wilkins, A., Chavarria, M. and Myint, H. (2009) Advances in hematologic stem cell transplant: an update for oral health care providers. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 107, 301-3012. (5)

Epstein, J., Guneri, P. and Barasch, A. (2014). Appropriate and necessary oral care for people with cancer: guidance to obtain the right oral and dental care at the right time. *Support Care Cancer*, 22, 1981-1988. (5)

Ertas, E., Kurnaz, F., Zorba, Y., Kocyigit, I., Sisman, Y. and Kaynar, L. (2014). Comparison of chemotherapy and hematopoietic stem cell transplantation pre and postterm DMFT scores: a preliminary study. *Niger J Clin Pract*, 17, 32-37. (2b)

Esposito, M., Grusovin, M., Patel, S., Worthington, H., Coulthard, P. (2008). Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. *Cochrane Database of Syst Rev*, 23(1), CD003603. (1a)

Falah-Tafti, A., Jafari, A., Lotfi-Kamran, M., Fallahzadeh, H. and Hayan, R. (2010). A Comparison of the efficacy of Nystatin and Fluconazole Incorporated into Tissue Conditioner on the In Vitro Attachment and Colonization of Candida Albicans. *Dent Res J*, 7, 18-22. (2b)

Ferlay, J., Soerjomataram, I., dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D., Forman, D. and Bray, F. (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in. *Int J Cancer*, 136, E359-86.

Furness, S., Bryan, G., McMillan, R. and Worthington, H. (2013). Interventions for the management of dry mouth: non-pharmacological interventions. *Cochrane Database Syst Rev*, 30(8), CD009603. (1a)

Gandhi, K., Datta, G., Ahuja, S., Saxena, T. and Datta, A. (2017). Prevalence of Oral Complications occurring in a population of pediatric cancer patients receiving chemotherapy. *Int J Clin Paediatr Dent*, 10, 166-171. (3b)

Gawade, P., Hudson, M., Kaste, S. and Neglia, J. A (2015). Systematic Review of Dental Late Effects in Survivors of Childhood Cancer. *Paediatr Blood Cancer*, 61, 407-416. (3a)

GBD 2015 Risk Factors Collaborators. (2016). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*, 388, 1659-1724.

Gebre-Medhin, M., Haghanegi, M., Robért, L., Kjellén, E. and Nilsson, P. (2016). Dose-volume analysis of radiation-induced trismus in head and neck cancer patients." *Acta Oncologica*, 55, 1313-1317. (3b)

Geerts, G., Stuhlinger, M. and Basson, N (2008). Effect of an antifungal denture liner on the saliva yeast count in patients with denture stomatitis: a pilot study. *J Oral Rehabil*, 35, 664-649. (2b)

Gevorgyan, A., Wong, K., Poon, I., Blanas, N., Enepekides, D. and Higgins, K. (2013). Osteoradionecrosis of the mandible: a case series at a single institution. *J Otolaryngol Head Neck Surg*, 11, 42-46. (4)

Gibson, F., Auld, E., Bryan, G., Coulson, S., Craig, J. and Glenny, A. (2010). A systematic review of oral assessment instruments: what can we recommend to practitioners in children's and young people's cancer care?. *Cancer Nurs*, 33, E1-E19. (2a)

Glenny, A., Gibson, F., Auld, E., Coulson, S., Clarkson, J., Craig, J., Eden, O., Khalid, T., Worthington, H., Pizer, B. and Children's Cancer and Leukaemia Group (CCLG)/Paediatric Oncology Nurses Forum's (CCLG-PONF) Mouth Care Group. (2010). Children's Cancer and Leukaemia Group (CCLG)/Paediatric Oncology Nurses Forum's (CCLG-PONF) Mouth Care Group. The development of evidence-based guidelines on mouth care for children, teenagers and young adults treated for cancer. *Eur J Cancer*, 46, 1399-1412. (2a)

Goldman, K. (2006). Dental management of patients with bone marrow and solid organ transplantation." *Dent Clin North Am*, 50, 659-676. (5)

Gupta, B. and Johnson, N (2014). Systematic review and meta-analysis of association of smokeless tobacco and of betel quid without tobacco with incidence of oral cancer in South Asia and the Pacific. *PLoS One*, 9, e113385. (2a)

Gupta, N., Pal, M., Rawat, S. and Grewal, M. (2015). Radiation-induced dental caries, prevention and treatment - A systematic review. *Natl J Maxillofac Surg*, 6, 160-166. *(3a)*

Hall, V. (2008). Actinomyces--gathering evidence of human colonization and infection. *Anaerobe*, 14, 1-7. (5)

Hartl, D., Cohen, M., Julieron, M., Marandas, P., Janot, F. and Bourhis, J. (2008). Botulinum toxin for radiation-induced facial pain and trismus. *Otolaryngology – Head and Neck Surgery*, 138, 459-463. (2b)

Hashibe, M., Brennan, P., Chuang, S., Boccia, S., Castellsague, X. and Chen, C. (2009). Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiol Biomark Prev*, 18, 541–50. (3a)

Holliday, R., Barclay, S., Garnett, M. and Stacey, F. (2015). Acidic saliva substitutes. *Br Dent J*, 218, 438. (5)

Hong, C., Napeñas, J., Hodgson, B. and Stokman, M. (2010). A systematic review of dental disease in patients undergoing cancer therapy. *Support Care Cancer*,18, 1007-1021. (2a)

Hong, C., Hu, S., Haverman, T. Stokman, M., Napenas, J., Braber, J., Gerber, E., Geuke, M., Vardas, E., Waltimo, T., Jensen, S. and Saunders, D. (2018). A systematic review of dental disease management in cancer patients. *Support Care Cancer*, 26, 155-174. (2a)

- Hsieh, S., Hibbert, S., Shaw, P., Ahern, V. and Arora, M. (2011). Association of cyclophosphamide use with dental development defects and salivary gland dysfunction in recipients of childhood antineoplastic therapy. *Cancer*, 117, 2219-2227. (3b)
- Javed, F., Al-Hezaimi, K., Al-Rasheed, A., Almas, K. and Romanos, G. (2010). Implant survival rate after oral cancer therapy: a review. *Oral Oncol*, 46, 854-859. (2a)
- Jawad, H., Hodson, N. and Nixon, P. (2015). A review of dental treatment of head and neck cancer patients, before, during and after radiotherapy: part 1. *Br Dent J*, 218, 65-68. (5)
- Jensen, S., Pedersen, A., Vissink, A., Andersen, E. and Brown, C. (2010). A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: prevalence, severity and impact on quality of life. *Support Care Cancer, 18, 1039-1060.* (2a)
- Kaae, J., Stenfeldt, L. and Eriksen, J. (2016). Xerostomia after Radiotherapy for Oral and Oropharyngeal Cancer: Increasing Salivary Flow with Tasteless Sugar-free Chewing Gum. *Front Oncol*, 6, 111. (2a)
- Kahenasa, N., Sung, E., Nabili, V., Kelly, J., Garrett, N. and Nishimura, I. (2012). Resolution of pain and complete healing of mandibular osteoradionecrosis using pentoxifylline and tocopherol: a case report. *Oral Surg Oral Med Oral Pathol Oral Radio,I* 113, e18-23. (5)
- Kamstra, J., Roodenburg, J., Beurskens, C., Reintsema, H. and Dijkstra, P. (2013). TheraBite exercises to treat trismus secondary to head and neck cancer. *Support Care Cancer*, 21, 951-957. (3b)
- Kanatas, A., Rogers, S. and Martin, M. (2002). A practical guide for patients undergoing exodontia following radiother-apy to the oral cavity. *Dent Update*, 29, 498-503. *(5)*
- Kantarci, A., Cebeci, I., Tuncerm, O., Carin, M. and Firatli, E. (1999). Clinical effects of periodontal therapy on the severity of cyclosporin A-induced gingival hyperplasia. *J Periodontol*, 70, 587-593. (2b)
- Karagozoglu, K., Dekker, H., Rietveld, D., de Bree, R., Schulten, E., Kantola, S., Forouzanfar, T. and van der Wall, I. (2014). Proposal for a new staging system for osteoradionecrosis of the mandible. *Med Oral Patol Oral Cir Bucal*, 19, e433-437. (3b)
- Katsura, K., Sasai, K., Sato, K., Saito, M., Hoshina, H. and Hayashi, T. (2008). Relationship between oral health status and development of osteoradionecrosis of the mandible: a retrospective longitudinal study. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod*, 105, 731-738. (2b)
- Kelly, S., Jackson, J., Hickey, B. and Szallasi, F. (2013). Multidiscilinary clinic care improves adherence to best practice in head and neck cancer. *Am J Otolaryngol*, 34, 57-60. (3b)
- Kielbassa, A., Hinkelbein, W., Hellwig, E. and Meyer-Lückel, H. (2006). Radiation-related damage to dentition. *Lancet Oncol*, 7, 326-335. (5)

Koga, D., Salvajoli, J. and Alves, F. (2008). Dental extractions and radiotherapy in head and neck oncology: review of the literature. *Oral Dis*, 14, 40-44. (5)

Kolokythas, A. (2010). Long-Term Surgical Complications in the Oral Cancer Patient: a Comprehensive Review. Part II. *J Oral Maxillofac Res*, 1, e2. (5)

Kornblith, A., Zlotolow, I. and Gooen, J. (1996). Quality of life of maxillectomy patients using an obturator prosthesis. *Head & Neck*, 18, 323-334. (3b)

Kraaijenga, S., Oskam, I., van der Molen, L., Hamming-Vrieze, O., Hilgers, F. and van den Brekel, M. (2015). Evaluation of long term (10-years+) dysphagia and trismus in patients treated with concurrent chemo-radiotherapy for advanced head and neck cancer. *Oral Oncol*, 51, 787-794. (3b)

Lalla, R., Bowen, J., Barasch, A., Elting, L., Epstein, J., Keefe, D., McGuire, D., Migliorati, C., Nicolatou-Galitis, O., Peterson, D.E. and Raber-Durlacher, J.E. (2014). MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*, *120*, 1453-1461.

Lalla, R., Latortue, M., Hong, C., Ariyawardana, A. and D'Amato-Palumbo, S. (2010). A systematic review of oral fungal infections in patients receiving cancer therapy. *Support Care Cancer*, 18, 985-992. (2a)

Lotwala, R., Greenlee, G., Ott, S., Hall, S. and Huang, G. (2012). Bisphosphonates as a risk factor for adverse orthodontic outcomes: A retrospective cohort study. *Am J Orthod Dentofacial Orthop*, 142, 625-634. (2b)

Lucchese, A., Matarese, G., Ghislanzoni, L., Gastaldi, G., Manuelli, M. and Gherlone, E. (2016). Efficacy and effects of palifermin for the treatment of oral mucositis in patients affected by acute lymphoblastic leukemia. *Leuk Lymphoma*, 57, 820-827. (1b)

Lyons, A. and Ghazali, N. (2008). Osteoradionecrosis of the jaws: current understanding of its pathophysiology and treatment. *Br J Oral Maxillofac Surg*, 46, 653–660. *(5)*

Macfarlane, T., Wirth, T., Ranasinghe, S., Ah-See, K., Renny, N. and Hurman, D. (2012). Head and Neck Cancer Pain: Systematic Review of Prevalence and Associated Factors. *J Oral Maxillofac Res*, 3, e1. (2a)

Maesschalck, T., Dulquerov, N., Caparroti, F., Scolozzi, P., Picardi, C., Mach, N., Koutsouvelis, N. and Dulquerov, P. (2016). Comparison of the incidence of osteoradionecrosis with conventional radiotherapy and intensity-modulated radiotherapy. *Head Neck*, 38, 1695-1702. (2b)

Majhail, N., Rizzo, J., Lee, S., Aljurf, M., Atsuta, Y. and Bonfim, C. (2012). Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Hematol Oncol Stem Cell Ther*, 5, 1-30.

Marinho, V., Chong, L., Worthington, H. and Walsh, T. (2016). Fluoride mouthrinses for preventing dental caries in children and adolescents. *Cochrane Database of Syst Rev* 29(7), CD002283. (1a)

Marinho, V., Worthington, H., Walsh, T. and Clarkson, J. (2013). Fluoride varnishes for preventing dental caries in children and adolescents. Cochrane Database of Syst Rev, 11(7), CD002279. (1a)

Mays, J., Fassil, H., Edwards, D., Pavletic, S. and Bassim, C. (2013). Oral chronic graft-versus-host disease: current pathogenesis, therapy, and research. *Oral Dis*, 19, 327-346. (5)

McCaul, L. (2012). Oral and dental management for head and neck cancer patients treated by chemotherapy and radiotherapy. *Dent Update*, 39, 135-8, 140. (5)

McGuire, D., Fulton, J., Park, J., Brown, C., Correa, M., Eilers, J., Elad, S., Gibson, F., Oberle-Edwards, L., Bowen, J., Lalla, R., Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). (2013). Systematic review of basic oral care for the management of oral mucositis in cancer patients. *Support Cancer Care*, 21, 3165-3177. (3a)

McLeod, N., Bater, M. and Brennan, P. (2010). Management of patients at risk of osteoradionecrosis: results of survey of dentists and oral & maxillofacial surgery units in the United Kingdom, and suggestions for best practice. *Br J Oral Maxillofac Surg*, 48, 301-304. (3b)

McLeod, N., Pratt, C., Mellor, T. and Brennan, P. (2012). Pentoxifylline and tocopherol in the management of patients with osteoradionecrosis, the Portsmouth experience. *Br J Oral Maxillofac Surg*, 50, 41-44. (3b)

Mendoza, A., and Tomlinson, M. (2003). The split denture: a new technique for artificial saliva reservoirs in mandibular dentures. *Aust Dent J*, 48, 190-194. (5)

Mercadante V, Al Hamad A, Lodi G, Porter S, Fedele S. (2017) Oral Oncology 66, 64-74

Meurman, J., and Gronroos, L. (2010). Oral and dental health care of oral cancer patients: hyposalivation, caries and infections. *Oral Oncology*, 46, 464-467. (5)

Michele, C. and Lloid, E. (2016). Improving Outcomes for Transplant Patients: Contribution of a Dental Hygienist. *J Evidence Based Prac,* 16, 99-103. (5)

Migliorati, C., Hewson, I., Lalla, R., Antunes, H., Estilo, C. and Hodgson, B. (2013). Systematic review of laser and other light therapy for the management of oral mucositis in cancer patients. *Support Cancer Care*, 21, 333-341. (2a)

Moreno, M., Skoracki, R., Hanna, E. and Hanasono, M. (2010). Microvascular free flap reconstruction versus palatal obturation for maxillectomy defects. *Head Neck*, 32, 860-868. (2b)

Morton, L., Onel, K., Curtis, R., Hungate, E. and Armstrong, G. (2014). The rising incidence of second cancers: patterns of occurrence and identification of risk factors for children and adults. Educ Book. *Am Soc Clin Oncol*, 10, e57-67.

Nabil, S., and Samman, N. (2011). Incidence and prevention of osteoradionecrosis after dental extraction in irradiated patients: a systematic review. *Int J Oral Maxillofac Surg,* 40, 229-43. (3a)

Nadella, K., Kodali, R., Guttikonda, L. and Jonnalagadda, A. (2015). Osteoradionecrosis of the Jaws: Clinico-Therapeutic Management: A Literature Review and Update. *Journal of Maxillofacial & Oral Surgery*, 14, 891-901. (5)

National Cancer Institute. (2016). *PDQ® Supportive and Palliative Care Editorial Board. PDQ Oral Complications of Chemotherapy and Head/Neck Radiation.* National Cancer Institute. Available at: https://www.cancer.gov/about-cancer/treatment/side-effects/mouth-throat/oral-complications-hp-pdq [Accessed December 11, 2017].

National Institute of Dental and Craniofacial Research. (2015). *Oral Complications of Cancer Treatment: What the Dental Team Can Do.* Available at: https://www.nidcr.nih.gov/OralHealth/Topics/CancerTreatment/OralComplicationsCancerOral.htm [Accessed December 11, 2017].

Nekhlyudov, L., Lacchetti, C., Davies, N. and Garvey, T. (2017). Head and Neck Cancer Survivorship Care Guideline: American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the American Cancer Society Guideline. *J Clin Oncol*, 35, 1606-1621.

Neppelenbroek, K., Pavarina, A., Palomari-Spolidorio, D. and Sgavioli-Massucato, E. (2008). Effectiveness of microwave disinfection of complete dentures on the treatment of Candida-related denture stomatitis. *J Oral Rehabil*, 35, 836-846. (2b)

Ngan, K., Bowe, J. and Goodger, N. (2013). The risk of bisphosphonate-related osteonecrosis of the jaw in children. A case report and literature review. *Dental update*, 40, 733-738. (5)

NICE. (2004). *Dental checks: intervals between oral health reviews.* Available at: https://www.nice.org.uk/guidance/cg19 [Accessed December 11, 2017].

NHS Evidence Improving outcomes in head and neck cancers: Evidence Update (2012). Available at: file:///C:/Users/Anand/Downloads/Improving+outcomes+in+head+and+neck+cancer+Evidence+Update+May+2012%20(1).pdf [Accessed December 11, 2017].

NICE-NG36. (2016). Cancer of the upper aerodigestive tract. Available at: https://www.nice.org.uk/guidance/ng36/resources/cancer-of-the-upper-aerodigestive-tract-assessment-and-management-in-people-aged-16-and-over-pdf-1837395722437 [Accessed December 12, 2017].

Nicolatou-Galitis, O., Sarri, T., Bowen, J., Di Palm, M. and Kouloulias, V. (2013). Systematic review of anti-inflammatory agents for the management of oral mucositis in cancer patients. *Support Care Cancer*, 21, 3179-3189. (2a)

Nieuw Amerongen, A. and Veerman, E. (2003). Current therapies for xerostomia and salivary gland hypofunction associated with cancer therapies. Support Care Cancer, 11, 226-231. (5)

Nishimura, R., Otto, C., Bonow, R., Carabello, B., Erwin, J. and Fleisher, L. (2017). 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*, 135, e1159-e1195.

Notani, K., Yamazaki, T., Kitada, H., Sakakibara, N., Fukuda, H., Omori, K. and Nakamura, M. (2003). Management of mandibular osteoradionecrosis corresponding to the severity of osteoradionecrosis and the method of radiotherapy. *Head Neck*, 25, 181-186. (3b)

Nutting, C., Morden, J., Harrington, K., Urbano, T. and Bhide, S. (2011). Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial. *Lancet Oncol*, 12, 127-136. (1b)

Pappas, P., Kauffman, C., Andes, D. and Clancy, C. (2016). Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis*, 62, e1-e50.

Patel, V. and McGurk, M. (2017). Use of pentoxifylline and tocopherol in radiation-induced fibrosis and fibroatrophy. *Br J Oral Maxillofac Surg*, 55, 235-241. (5)

Patel, V., Kelleher, M., Sproat, C. and McGurk, M. (2015). New cancer therapies and jaw necrosis. *Br Dent J*, 219, 203-207. (5)

Patel, V., Gadiwalla, Y., Sassoon, I., Sproat, C., Kwok, J. and McGurk, M. (2016). Use of pentoxifylline and tocopherol in the management of osteoradionecrosis. *Br J Oral Maxillofac Surg*, 54, 342-345. (3b)

Paultke, C., Bauer, F., Bissinger, O. and Tischer, T. (2010). Tetracycline bone fluorescence: a valuable marker for osteoradionecrosis characterization and therapy. *J Oral Maxillofac Surg*, 68, 125-129. (4)

Pedersen, L., Clausen, N., Schroder, H., Schmidt, M. and Poulsen, S. (2012). Microdontia and hypodontia of premolars and permanent molars in childhood cancer survivors after chemotherapy. *Int J Paediatr Dent*, 22, 239-243. (3b)

Peterson, D., Ohrn, K., Bowen, J., Fliedner, M., Lees, J., Loprinzi, C., Mori, T., Osaguona, A., Weikel, D., Elad, S., Lalla, R., Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). (2013). Systematic review of oral cryotherapy for management of oral mucositis caused by cancer therapy. *Support Care Cancer*, 21, 327-332. (2a)

Peterson, D., Doerr, W., Hovan, A., Pinto, A., Saunders, D. and Elting, L. (2010). Osteoradionecrosis in cancer patients: the evidence base for treatment-dependent frequency, current management strategies, and future studies. *Support Care Cancer*, 18, 1089-1098. (2a)

Plummer, M., de Martel, C., Vignat, J., Ferlay, J., Bray, F. and Franceschi, S. (2016). Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Global Health*, 4, e609-616.

Porter, S., Fedele, S. and Habbab, K. (2010). Xerostomia in head and neck malignancy. *Oral Oncol*, 46, 460-463. (5)

Public Health England. (2017). Delivering better oral health: an evidence based toolkit for prevention.

Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/605266/Delivering_better_oral_health.pdf [Accessed December 11, 2017].

Raguse, J., Hossamo, J., Tinhofer, I. and Hoffmeister, B. (2016). Patient and treatment-related risk factors for osteoradionecrosis of the jaw in patients with head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 121, 215-221. (2b)

Raphael, S. and Blinkhorn, A. (2015). Is there a place for Tooth Mousse in the prevention and treatment of early dental caries? A systematic review. *BMC Oral Health*, 15, 113. (2a)

Rapidis, A., Dijkstra, P., Roodenburg, J., Rodrigo, J., Rinaldo., Strojan, P., Takes, R. and Ferlito, A. (2015). Trismus in patients with head and neck cancer: etiopathogenesis, diagnosis and management. *Clin Otolaryngology*, 40, 516-26. (5)

Rathod, S., Livergant, J., Klein, J., Witterick, I. and Ringash, J. (2015). A systematic review of quality of life in head and neck cancer treated with surgery with or without adjuvant treatment. *Oral Oncol*, 51, 888-900. (3a)

Raut, A., Huryn, J., Hwang, F. and Zlotolow, I. (2001). Sequelae and complications related to dental extractions in patients with hematologic malignancies and the impact on medical outcome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 92, 49-55. (3b)

Ray-Chaudhuri, A., Shah, K. and Porter, R. (2013). The oral management of patients who have received radiotherapy to the head and neck region. *Br Dent J*, 214, 387-393. (5)

RD-UK. (2016). Predicting and Managing Oral and Dental Complications of Surgical and Non-Surgical Treatment for Head and Neck Cancer. A Clinical Guideline. Available at: https://www.restdent.org.uk/uploads/RD-UK%20H%20and%20N%20guideline.pdf. [Accessed on 16 Feb 2018]

Rice, N., Polyzois, I., Ekanayake, K., Omer, O. and Stassen, L. (2015). The management of osteoradionecrosis of the jaws-a review. *Surgeon,* 13, 101-109. (5)

Riley, P., Glenny, A., Worthington, H., Littlewood, A., Clarkson, J. and McCabe, M. (2015). Interventions for preventing oral mucositis in patients with cancer receiving treatment: oral cryotherapy. *Cochrane Database of Syst Rev*, 23(12), CD011552. (1a)

Robard, L., Louis, M., Blanchard, D., Babin, E. and Delanian, S. (2014). Medical treatment of osteoradionecrosis of the mandible by PENTOCLO: preliminary results. *Eur Ann Otorhinolaryngol Head Neck Dis*, 131, 333-338. (3b)

Robinson, P., Deacon, S., Deery, C., Heanue, M., Walmsley, A., Worthington, H., Glenny, A. and Shaw, W. (2005). Manual versus powered toothbrushing for oral health. *Cochrane Database of Syst Rev*, 18(2), CD002281. *(1a)*

Rodd, H., Waterhouse, P., Fuks, A., Fayle, S., Moffat, M. (2006). Pulp therapy for primary molars. *Int J Paediatr Dent*, 16 Suppl,15-23. (3b)

Roe, J., Carding, P., Rhys-Evans, P., Newbold, K., Harrington, K. and Nutting, C. (2012). Assessment and management of dysphagia in patients with head and neck cancer who receive radiotherapy in the United Kingdom - a web-based survey. *Oral Oncol*, 48, 343-348. *(3b)*

Rogers, S., Lowe, D., Mcnally, D., Brown, J. and Vaughan, E. (2003). Health-related quality of life after maxillectomy: a comparison between prosthetic obturation and free flap. *J Oral Maxillofac Surg*, 61, 174-181. (3b)

Roman, B., Goldenberg, D. and Givi, B. (2016). AHNS Series--Do you know your guidelines? Guideline recommended follow-up and surveillance of head and neck cancer survivors. *Head Neck*, 38, 168-174.

Rosales, A., Esteves, S., Jorge, J., Almeida, O. and Lopes, M. (2009). Dental needs in Brazilian patients subjected to head and neck radiotherapy. *Brz Dent J*, 20, 74-77. (3b)

Ruggiero, S., Dodson, T., Fantasia, J., Goodday, R., Aghaloo, T., Mehrotra, B., O'Ryan, F. and American Association of Oral and Maxillofacial Surgeons. (2014). American Association of Oral and Maxillofacial Surgeons Position Paper on Medication-Related Osteonecrosis of the Jaw—2014 Update. *Journal of Oral and Maxillofacial Surgery*, 72, 1938-56.

Ruggiero, S., Gralow, J., Marx, R., Hoff, A., Schubert, M., Huryn, J., Toth, B., Damato, K. and Valero, V. (2006). Practical guidelines for the prevention, diagnosis, and treatment of osteonecrosis of the jaw in patients with cancer. *J Oncol Pract*, 2, 7-14.

Saito, H., Watanabe, Y., Sato, K., Ikawa, H., Yoshida, Y., Katakura, A., Takayama, S. and Sato, M. (2014). Effects of professional oral health care on reducing the risk of chemotherapy-induced oral mucositis. *Support Care Cancer*, 11, 2935-1940. (1b)

Sanderr, M., Hentrich, M., von Lilienfeld-Toal, M. and Massenkeil, G. (2015). Antiviral prophylaxis in patients with solid tumours and haematological malignancies--update of the Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society for Hematology and Medical Oncology (DGHO). *Ann Hematol*, 94, 2441-2450.

Saunders, D., Epstein, J., Elad, S., Allemano, J., Bossi, P. and van de Wetering, M. (2013). Systematic review of antimicrobials, mucosal coating agents, anesthetics, and analgesics for the management of oral mucositis in cancer patients. *Support Cancer Care* 21, 3191-3207. (2a)

Scherpenhuizen, A., van Waes, A., Janssen, L., Van Cann, E. and Stegeman, I. (2015). The effect of exercise therapy in head and neck cancer patients in the treatment of radiotherapy-induced trismus: A systematic review. *Oral Oncology*, 51, 745-750. (2a)

Schiødt, M., and Hermund, N. (2002). Management of oral disease prior to radiation therapy. *Support Care Cancer*, 10, 40-43. (5)

Schmidt, B., Pogrel, M., Young, C. and Sharma, A. (2004). Reconstruction of extensive maxillary defects using zygomaticus implants. *J Oral Maxil Surg*, 62, 82-89. (3b)

Scotish Intercollegiate Guidelines Network (SIGN). (2006). Diagnosis and management of head and neck cancer - SIGN 90. Available at: http://www.scottishdental.org/library/diagnosis-and-management-of-head-and-neck-cancer-sign-90/ [Accessed December 12, 2017].

Scottish Intercollegiate Guidelines Network (SIGN). (2013). Long term follow up of survivors of childhood cancer - SIGN 132. Available at: http://www.sign.ac.uk/assets/sign132.pdf [Accessed December 12, 2017].

Scottish Dental Clinical Effectiveness Programme. (2016). Drug Prescribing for Dentistry - Dental Clinical Guidance. Third Edition. Available at: http://www.sdcep.org.uk/wp-content/uploads/2016/03/SDCEP-Drug-Prescribing-for-Dentistry-3rd-edition.pdf [Accessed December 12, 2017].

Scottish Dental Clinical Effectiveness Programme. (2017). Oral Health Management of Patients at Risk of Medication- related Osteonecrosis of the Jaw - Dental Clinical Guidance. Available at: http://www.sdcep.org.uk/wp-content/uploads/2017/04/SDCEP-Oral-Health-Management-of-Patients-at-Risk-of-MRONJ-Guidance-full.pdf [Accessed 12 December 2017].

Scottish Dental Clinical Effectiveness Programme. (2010). Prevention and Management of Dental Caries in Children - Dental Clinical Guidance. Available at: http://www.sdcep.org.uk/wp-content/uploads/2013/03/SDCEP_PM_Dental_Caries_Full_Guidance1.pdf [Accessed December 11, 2017].

Shahdad, S., Taylor, C., Barclay, S., Steen, I. and Preshaw, P. (2005). Double-blind, crossover study of Biotene Oralbalance and BioXtra systems as salivary substitutes in patients with post-radiotherapy xerostomia. *European J Cancer Care*,14, 319-326. (1b)

Shavi, G., Thakur, B., Bhanbul, A., Jain, S., Singh, V. and Shukla, A. (2015). Oral Health Related Quality of Life in Patients of Head and Neck Cancer Attending Cancer Hospital of Bhopal City, India. *J Int Oral Health*, 7, 21-27. (3b)

Shaw, M., Kumar, N., Duggal, M., Fiske, J., Lewis, D., Kinsellam T. and Nisbet, T. (2000). Oral management of patients following oncology treatment. *Br J Oral Maxillofac Surg,* 38, 519-524. (5)

Shaw, R. and Butterworth, C. (2011). Hyperbaric oxygen in the management of late radiation injury to the head and neck. Part II: prevention. *Br J Oral Maxillofac Surg*, 49, 9-13. (5)

Shaw, R. and Dhanda, J. (2011). Hyperbaric oxygen in the management of late radiation injury to the head and neck. Part I: treatment. *Brit J Oral Maxillofac Surg*, 49, 2-8. (5)

Sheller, B. and Williams, B. (1996). Orthodontic management of patients with haematological malignancies. *Am J Orthod Dentofac Orthop*, 109, 575-80. (5)

Shiraz, F., Rahtz, E., Bhui, K., Hutchison, I. and Korszun, A. (2014). Quality of life, psychological wellbeing and treatment needs of trauma and head and neck cancer patients. *Br J Oral Maxillofac Surg*, 52, 513-517. (3b)

Silvestre-Rangil, J. and Silvestre, F. (2011). Clinico-therapeutic management of osteoradionecrosis: a literature review and update. *Med Oral Patol Oral Cir Bucal*, 16, e900-4. (5)

Sroussi, H., Epstein, J., Bensadoun, R., Saunders, D., Lalla, Migliorati, C., Heaivillin, N. and Zumsteg, Z. (2017). Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. *Cancer Med*, 6, 2918-2931. (5)

Støre, G. and Boysen, M. (2000). Mandibular osteoradionecrosis: clinical behaviour and diagnostic aspects. *Clin Otolaryngol Allied Sci*, 25, 378-384. (3b)

Stockman, M., Spijkervet, F., Boezen, H., Schouten, J. and Roodenburg, L. (2006). Prevention Intervention Possibilities in Radiotherapy- and Chemotherapy-induced Oral Mucositis: results of Meta-analyses. *J Dent Res*, 85, 690-700. (1a)

Stoopler, E., Vogl, D. and Stadtmauer, E. (2007). Medical management update: multiple myeloma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 103, 599-609. (5)

Talwar, B., Donnelly, R., Skelly, R. and Donaldson, M. (2016). Nutritional management in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol*, 130, S32-S40.

Thani, J. and Bumb, D. (2014). Impact of dental considerations on the quality of life of oral cancer patients. *Indian J Med Paediatr*, 35, 66-70. (3b)

Thariat, J., Ramus, L. and Darcourt, V. (2012). Compliance with fluoride custom trays in irradiated head and neck cancer patients. *Support Care Cancer*, 20, 1811-1814. (3b)

Tinoco-Araujo, J., Orti-Raduan, E., Santos, D., Colturato, V., Souza, M. and Mauad, M. (2015). Oral health-related quality of life before hematopoietic stem cell transplantation." *Clin Oral Investig,* 19, 2345-2349. (2b)

Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K. and Storek, J. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*, 15, 1143-238.

Treister, N. and Sonis, S. (2007). Mucositis: biology and management. *Otolaryngol Head Neck Surg*, 15, 123-129. (5)

Tremblay, D., Latreille, J., Bilodeau, K., Samson, A., Roy, L., L'Italien, M and Mimeault, C. (2016). Improving the Transition From Oncology to Primary Care Teams: A Case for Shared Leadership. *J Oncol Pract*, 12, 1012-1019. (5)

Tsuji, K., Shibuya, Y., Akashi, M., Furudoi, S., Yakushijin, K. and Kawamoto, S. (2015). Prospective Study of Dental Intervention for Hematopoietic Malignancy. *J Dent Res*, 94, 289-296. (2b)

Ullmann, A., Schmidt-Heiber, M., Bertz, H. and Heinz, W. (2016). Infectious diseases in allogeneic haematopoietic stem cell transplantation: prevention and prophylaxis strategy guidelines 2016. *An Hematol*, 95, 1435-1455.

Verterbacka, M., Ringden, O., Remberger, M., Huggare, J. and Dahllof, G. (2012). Disturbances in dental development and craniofacial growth in children treated with hematopoietic stem cell transplantation. *Orthod Craniofac Res*, 29, 21-29. (3b)

Walsh, T., Oliveira-Neto, J. and Moore, D. (2015). Chlorhexidine treatment for the prevention of dental caries in children and adolescents. *Cochrane Database of Syst Rev*, 13(4), CD008457. (1a)

Wang, T., Liu, C., Chao, T., Chen, T. and Hu, Y. (2017). Risk factors for and the role of dental extractions in osteoradionecrosis of the jaws: A national-based cohort study. *Head Neck*, 39, 1313-1321. (2b)

Wells, M., Cunningham, M., Lang, H. and Swartzman, S. (2015). Distress, concerns and unmet needs in survivors of head and neck cancer: a cross-sectional survey. *Eur J Cancer Care (Engl)*, 24, 748-760. (3b)

Westbrook, S., Paunovich, E. and Freytes, C. (2003). Adult hemopoietic stem cell transplantation. *J Am Dent Assoc*, 134, 1224-1231. (5)

Wilberg, P., Hjermstad, M., Ottesen, S. and Herlofson, B. (2014). Chemotherapy-associated oral sequelae in patients with cancers outside the head and neck region. *J Pain Symptom Manage*, 48, 1060-1069. (3b)

Wishney, M. (2017). Potential risks of orthodontic therapy: a critical review and conceptual framework. *Aust Dent J*, 62, 86-96. (5)

Yamagata, K., Onizawa, K., Yanagawa, T., Hasegawa, Y., Kojima, H. and Nagasawa, T. (2006). A prospective study to evaluate a new dental management protocol before hematopoietic stem cell transplantation. *Bone Marrow Transplant*, 38, 237-242. (3b)

Yamagata, K., Onizawa, K., Yanagawa, T., Takeuchi, Y., Hasegawa, Y. and Chiba, S. Prospective study establishing a management plan for impacted third molar in patients undergoing hematopoietic stem cell transplantation. *Oral Surg Oral Med Oral Pathol*, 111, 146-152. (3b)

Yang, W., Liao, G., Hakim, S., Ouyang, D., Ringash, J. and Su, Y. (2016). Is Pilocarpine Effective in Preventing Radiation-Induced Xerostomia? A Systematic Review and Meta-analysis. *Int J Radiat Oncol Biol Phys*, 94, 503-511. (1a)

Yarom, N. Ariyawardana, A., Hovan, A., Barasch, A., Jarvis, V., Jensen, S., Zadik, Y., Elad, S., Bowen, J., Lalla, R. and Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). (2013). Systematic review of natural agents for the management of oral mucositis in cancer patients. *Support Care Cancer*, 21, 3209-3221. (3a)

Zaghi, S., Danesh, J., Nabli, V. and Hendizadeh, L. (2014). Changing indications for maxillomandibular reconstruction with osseous free flaps: a 17-year experience with 620 consecutive ca-es at UCLA and the impact of oste. *Laryngoscope*, 124, 1329-1335. (2b)

Zhang, B., Mo, Z., Du, W., Wang, Y., Liu, L. and Wei, Y. (2015). Intensity-modulated radiation therapy versus 2D-RT or 3D-CRT for the treatment of nasopharyngeal carcinoma: A systematic review and meta-analysis. *Oral Oncol*, 51, 1041-1046. (2a)



TABLE 1: GENERAL NURSING ORAL CARE GUIDELINES

1. PRIOR TO CANCER THERAPY

Objective	Nursing Action			
Ensure all patients have been seen for a comprehensive assessment by a Dental Surgeon prior to cancer therapy	 For patients with head and neck cancer, patients should be identified for dental assessment at the multidisciplinary meeting and an assessment arranged For all other patients, complete the Oral Health Screening Chart and Referral (Appendix 2 and 4) and forward to dental team Liaise with the dental team to develop and implement an individual care plan 			
Advice on the oral side effects of treatment	 Provide written information on side effects of treatment (Appendix 5) Give support and encouragement 			
3. Preventive advice	 Dietary advice in liaison with the Dietitian Provide written information (Appendix 5) 			

^{*} Advise About Support Groups: Cancer BACUP: Changing Faces: Let's Face It; Macmillan Cancer Support



2. DURING CANCER THERAPY

Objective	Nursing Action
1. Maintenance of oral hygiene	 Provide advice and assistance where appropriate Follow Practical Oral Care (Appendix 3)
2. Inspection of the oral cavity should be carried out daily	 The Oral Assessment Guide (Appendix 4) should be completed daily and placed in the patient's individual care plan; contact the dental team for guidance prior to completion if required Document findings in the patient's individual care plan to monitor any changes Refer to the dental team when indicated
Monitor compliance in performing oral care	 Supervise and provide assistance; give instructions to carers where appropriate Give support and encouragement
4. Pain control	Give topical / systemic analgesia, as directed
5. Oral candidal infections (Thrush)	 Give topical / systemic antifungal agents, as prescribed If chlorhexidine gluconate mouthwash and nystatin suspension are prescribed, stagger their use by one hour
6. Manage xerostomia	 Give advice to help with a dry mouth Ensure recommended saliva substitute is prescribed and used when appropriate



3. AFTER CANCER THERAPY

Objective	Nursing Action		
Arrange follow-up visit to the dental team	 Provide the patient or carer with a contact telephone number Arrange an appointment To ensure follow up occurs when the patient is discharged, an oral care entry should be made in the summary notes / discharge letter 		
2. Reinforce preventive messages	 Provide equipment for home care where appropriate Ensure patient information leaflet has been provided to support the advice given 		



TABLE 2: ACUTE CHANGES DURING THERAPY

Acute Change	Explanatory Notes	Radiotherapy	Chemotherapy	BMT (Chemotherapy and Total Body Irradiation)
1. Mucositis	 Acute inflammation of the mucosa White/yellow fibrinous slough, often with ulceration Painful to speak/eat/swallow Portal for microbial entry Healing complete 2-3 weeks post-completion cancer therapy 	Onset 12-15 days after treatment commenced	 Onset usually one week after treatment commencement Ulceration often severe 	 Onset usually one week after treatment commencement Ulceration often severe
2. Blood Changes	 Anaemia Neutropenia Thrombocytopenia Present from commencement of cancer therapy until up to 4 weeks post therapy 		 Spontaneous gingival/mucosal bleeding Crusting of lips 	 Spontaneous gingival/mucosal bleeding Crusting of lips
3. Immuno- suppression	 Increases susceptibility to bacterial/candidal/viral disease Exacerbates pre-existing periodontal disease 		 Periapically involved teeth can become a medical emergency Acute herpetic gingivostomatitis and candida with systemic involvement in children 	Periapically involved teeth can become a medical emergency
4. Changes in Salivary Flow/Composition	 Saliva becomes thick, viscous, acidic Xerostomia results but is less common in children Onset within 14 hours of cancer therapy 	 Xerostomia can be prolonged Can last up to 2 years post therapy Often permanent 	Salivary flow usually returns to normal within 2 months	Salivary flow rarely returns to normal



Table 2 cont'd

Acute Change	Explanatory Notes	Radiotherapy	Chemotherapy	BMT (Chemotherapy and Total Body Irradiation)
5. Acute Ascending Sialadenitis	Can occur in children as a complication of xerostomia	Can occur in children as a complication of xerostomia	Can occur in children as a complication of xerostomia	Can occur in children as a complication of xerostomia
6. Loss of Taste (Dysguesia)	 Onset on treatment commencement Related to xerostomia and direct damage to taste buds Sense of taste often returns with an unpleasant interim period of altered taste Important to seek advice from dietitions as (1) the sense does not always return and (2) untreated dysgeusia can affect prognosis. 	Can be profound due to xerostomia	 Variable in relation to the cancer regime used A reduction in the number of taste buds in children has been implicated 	Combined effects of chemo and radiotherapy
7. Dysphagia	As a result of mucositis and xerostomia	Can be very severe due to severe ulceration	Can be very severe due to severe ulceration	Can be very severe due to severe ulceration
8. Changes in Oral Flora	 Due to reduced buffering action and antibacterial action of saliva Increase in cariogenic organisms within 2 weeks of cancer therapy Increased susceptibility to candidal/viral infections 	 Oral candidiasis more likely Implications for increased dental caries 	Oral Candidiasis: pseudomem- branous candidiasis with ulceration and perioral inflammation	 Oral candidiasis: severe with ulceration if persistent, indicative of systemic involvement Acute herpetic gingivostomatitis Cytomegalovirus and Varicella zoster virus infections



Table 2 contd.

Acute Change	Explanatory Notes	Radiotherapy	Chemotherapy	BMT (Chemotherapy and Total Body Irradiation)
9. Periodontal / Gingival Disease	Can be exacerbated by oral flora changes, mucositis, xerostomia and immunosuppression	Acute gingivitis	Acute gingivitisPericoronitis in childrenGingival hyperplasia in acute myeloblastic leukaemia	Acute gingivitisPericoronitis in children
10. Tooth Sensitivity	 Increased risk of toothwear observed due to bruxism + xerostomia Gingival recession may also contribute 	Xerostomia is an important contributor	May be due to pre- existing gingival recession	Xerostomia / gingival recession can contribute
11. Dental Pain	 Higher risk of dental decay May also be related to leukaemic infiltration of dental pulp tissue and direct jaw infiltration 	Higher dental caries risk due to xerostomia may result in dental abscesses	 Toothache -like pain related to vincristine administration Low white cell counts can cause chronic infections to become acute and cause pain 	Low white cell counts can cause chronic infections to become acute and cause pain
12. Trismus	Must exclude posterior invasion of carcinoma into pterygomasseteric muscles as a cause	May be caused by severe mucositis	 May be caused by severe mucositis Can occur in children Jaw pain may be related to vincristine administration 	May be caused by severe mucositis
13. Graft Versus Host Disease	Can occur in an acute form after bone marrow transplantation and be followed by a chronic form			Can occur in an acute form after bone marrow transplantation



TABLE 3: CHRONIC CHANGES FOLLOWING THERAPY

Chronic Change	Explanatory Notes	Radiotherapy	Chemotherapy	BMT (Chemotherapy and Total Body Irradiation)
1. Progressive endarteritis	 Occurs in irradiated bone, especially the mandible Can occur in muscle and cause trismus 3-6 months post therapy Uncommon in children 	Implications for dental extractions / surgery (see management guidelines)		Implications for dental extractions / surgery (see management guidelines)
2. Blood Changes	 Anaemia Neutropenia Thrombocytopenia Prolonged by maintenance chemotherapy 		Implications for dental treatment	Implications for dental treatment
3. Trismus	 Must exclude posterior invasion of carcinoma into pterygomasseteric muscles as a cause Predominantly due to fibrosis as a direct effect of radiotherapy, but also related to endarteritis 	Predominantly due to fibrosis as a direct effect of radiotherapy		
4. Prolonged Oral Flora Changes	Increase in cariogenic organisms and candida	 Increased susceptibility to dental caries Candidiasis more likely especially in denture wearers 	Viral infections and candidiasis more likely	 Increased susceptibility to dental caries Candidiasis more likely



Table 3 contd.

Chronic Change	Explanatory Notes	Radiotherapy	Chemotherapy	BMT (Chemotherapy and Total Body Irradiation)
5. Xerostomia	 May last up to 2 years post therapy It is often considered permanent although this can be subjective Predisposes to dental caries 	 More prolonged if parotid glands are in the irradiation field Salivary output can be maintained by ipsilateral parotid sparing during radiotherapy⁶⁹ 		
6. Tooth Erosion	Due to prolonged xerostomia, removing protective action of saliva	Linked to xerostomia		
7. Periodontal / Gingival Disease	 Can continue to be exacerbated by xerostomia and oral flora changes Gingival recession 	Rapid progression of periodontal disease	Maintenance chemotherapy may increase the risk	Rapid progression of periodontal disease can occur in children
8. Adrenal Suppression	Can occur as a result of corticosteroid therapy		Can occur as a result of corticosteroid therapy	Can occur as a result of corticosteroid therapy

TABLE 4: MANAGEMENT GUIDELINES RELATIVE TO INVASIVE DENTAL PROCEDURES

Medical Status	Guidelines Available	Comments
Patients with indwelling venous access lines (e.g., Hickman).	American Heart Association (AHA) prophylactic antibiotic recommendations: Low risk	There is no clear scientific proof detailing infectious risk for these lines following dental procedures.
Neutrophils		
Order FBC (full blood co	unt) with differential.	
>2,000/mm ³	AHA prophylactic antibiotic recommendations: No prophylactic antibiotics.	
1,000–2,000/mm ³	AHA prophylactic antibiotic recommendations:	Liaise with the oncologist
	Low risk.	Clinical judgment is critical. If infection is present or unclear, more aggressive antibiotic therapy may be indicated.
<1,000/mm ³	AHA prophylactic antibiotic recommendations: Amikacin 150mg/m² 1 h pre-surgery; ticarcillin 75 mg/kg IV ½ h pre-surgery. Repeat both 6 h	The antibiotic regimen suggested by AHA is not used widely in the U.K. where amoxicillin / clindamycin are more often used.
	postoperatively.	Liaise with the oncologist
		If organisms are known or suspected, appropriate adjustments should be based on sensitivities.

Table 4 contd.

Medical Status	Guidelines Available	Comments					
Platelets * Order platelet count and coagulation tests.							
>60,000/mm ³	National Cancer Institute guidelines (www.cancer.gov) No additional support needed.	Major surgery may require platelet supplementation					
30,000–60,000/mm ³	Platelet transfusions are optional for non-invasive treatment For surgical treatment (e.g., dental extractions), consider administering platelets preoperatively and 24 h later	Liaise with the oncologist Platelet requirements will also depend on the extent of the surgery required / need for block injections Utilise techniques to promote establishing and maintaining control of bleeding (i.e. sutures, pressure packs, minimise trauma).					
<30,000/mm ³	Platelets should be transfused 1 h before procedure Obtain an immediate post-infusion platelet count; transfuse regularly to maintain counts >30,000—40,000/mm³ until initial healing has occurred. In some instances, platelet counts >60,000/mm³ may be required.	In addition to the above, consider using haemostatic agents (i.e., microfibrillar collagen, topical thrombin). Tranexamic acid may help stabilise nondurable clots. Monitor sites carefully.					

^{*}Assumes that all other coagulation parameters are within normal limits and that platelet counts will be maintained at or above the specified level until initial stabilization/healing has occurred

APPENDIX 1: EXAMPLE OF SEARCH STRATEGY USED FOR MUCOSITIS / PAIN

PUBMED

SEARCH	SEARCH TERMS
#1	MESH TERM STOMATITIS OR STOMATITIS [TW] OR MUCOSITIS [TW] OR OROMUCOSITIS [TW]
#2	MESH TERM RADIOTHERAPY OR RADIOTHERAPY [TW] MESH TERM CHEMORADIOTHERAPY OR CHEMORADIOTHERAPY [TW] OR CHEMORADIATION [TW] MESH TERM RADIATION OR RADIATION [TW] OR CHEMORADIOTHERAPIES [TW] OR RADIOCHEMOTHERAPY [TW] OR RADIOCHEMOTHERAPIES [TW])
#3	PAIN [TW] OR SORENESS [TW] OR SORE [TW]



APPENDIX 2: REFERRAL FOR ORAL HEALTH CARE SCREENING

N.B. Please forward to the Dental Team prior to the commencement of Cancer Therapy Patient Name: Hospital no: Oncology D.O.B.: Consultant: Address: Inpatients: Ward / Location Ward telephone no: Date admitted: Telephone no: Duration of stay: 1. Diagnosis: 2. 3. 1. 4. **Past Medical History:** 2. 5. 6. 3. 1. 4. **Current Medication:** 2. 5. 3. 6. Treatment to date: 1. (including radiotherapy 2. dose, mask and 3. chemotherapy regime) Treatment proposed with 1. dates: (including radiotherapy 2. dose, mask and 3. chemotherapy regime) Tick as appropriate: **URGENT (Contact Dental Team by phone) ROUTINE** Name of referrer **Date**

Signature

Position

77

Contact number



APPENDIX 3: PRACTICAL ORAL CARE:

Care of the edentulous patient should start at step 5.

Oral Care	Notes
1. Tooth brushing	 Use a medium brush if possible, soft one if too sore Encourage or assist with gentle thorough brushing of teeth and gums at least twice daily Use a high fluoride toothpaste Spit out excess, do not rinse If toothbrushing has to be discontinued it should be resumed at the earliest opportunity Patients at risk of aspiration should have suction available and sit up
2. Aqueous alcohol free chlorhexidine gluconate mouthwash	 Recommended for short term use if tooth brushing is inadequate If toothbrushing is discontinued, use three to four times daily Thirty minutes should be allowed between use of chlorhexidine and tooth brushing Mouthwashes may need to be diluted for comfort, i.e. 10ml mouthwash to 10ml water, ensuring the whole diluted volume is used N.B. Stagger use of chlorhexidine mouthwash and nystatin antifungal agent - separate administration by at least one hour.
3. Fluoride mouthwash	 Fluoride should be used both during and after cancer therapy Use a high fluoride toothpaste when tooth brushing Use an alcohol free fluoride mouthwash daily as directed by the dental team Fluoride gel / varnish may be used, as directed by the dental team. Fluoride varnish or gel should not be used during acute episodes of mucositis
4. Pain relief mouthwashes / sprays	Benzydamine HCL mouthwash / spray may be of benefit if there is mucosal discomfort due to mucositis
5. Dietary advice	 Preventive advice to reduce the risk of dental decay should be given in liaison with a dietitian. Emphasis should be placed on adequate hydration and assist with healthy meal choices



Appendix 3 cont'd.

	Oral Care	Notes
6.	Gentle Swabbing of the Oral Tissues	 Where available, polygon/gauze swabs soaked in alcohol free chlorhexidine mouthwash may be used to gently clean the oral tissues If the above cannot be tolerated, the swabs may be soaked in 0.9% saline (N.B. no antibacterial effect)
7.	Moisten mouth and lips frequently	 Advise regular sips of water Oral Balance or similar gel may be applied to dry lips or mucosa, this can be particularly helpful at night Use recommended artificial saliva substitutes
7.	Swabs for candidal superinfection	 Regular swabs should be taken for detection of candida Topical / systemic antifungal agents should be prescribed following the diagnosis of candidaError! Reference source not found. Error! Reference source not found.
8.	Care of appliances	 After each meal / at least twice daily, dentures and obturators should be removed and meticulously cleaned with a tooth or denture brush It is advisable to do this over a basin of water to prevent damage if the appliance is dropped Rinse well before replacing in cleaned mouth Antifungal agents, as prescribed may be applied to the fit surface of the denture prior to reinsertion Remove all dentures at night and clean; soak in in chlorhexidine mouthwash overnight. An alternative is dilute sodium hypochlorite solution (Milton's diluted 1 in 80) provided there are no metal components If stored away from the patient they should be appropriately labelled
9.	Appliance wear	 Removable prostheses should be left out of the mouth if there is any evidence of ulceration Dentures should be removed at night Denture should be moistened with water or an appropriate saliva substitute before reinsertion Obturators should not be left out at night for the first 6 months. A specialist opinion should be sought if there is evidence of ulceration



APPENDIX 4: ORAL ASSESSMENT GUIDE

Please insert appointment number in relevant box based on your clinical examination of the patient. Contact the Dental Team for further advice on the management of patients with scores of 3.

PATIENT NAME:	METHOD OF	DATE AND SIGNATURE							
ASSESSMENT	ASSESSMENT	1	2	3	4	5	6	7	8
VOICE				•					
3 = Difficult/ painful speech 2 = Deeper/ raspy 1 = Normal	Converse with the patient. Listen to speech								
SWALLOW									
3 = Unable to swallow 2 = Painful 1 = Normal	Ask patient to swallow								
LIPS AND ANGLE OF MOUTH	IPS AND ANGLE OF MOUTH								
3 = Ulcerated / with or without bleeding 2 = Dry / cracked 1 = Normal	Observe and palpate the tissues								



APPENDIX 4: ORAL ASSESSMENT GUIDE CONTD.

ASSESSMENT	METHOD OF ASSESSMENT	1	2	3	4	5	6	7	8
TONGUE									
3 = Blistered / cracked 2 = Coated or loss of papillae 1 = Smooth, pink, moist	Observe the appearance of the tissues								
SALIVA									
3 = Absent 2 = Thick / ropy 1 = Watery	Insert tongue depressor and observe tongue, floor of mouth								
MUCOUS MEMBRANES/GINGIVA									
3 = Ulceration / bleeding - gentle pressure 2 = Candidal infection suspected - reddened/coated or white patches 1 = Pink and moist	Observe the appearance of the tissues								
ORAL CLEANSING COMPLIANCE									
3 = Unable to clean 2 = Cleans but needs help 1 = No difficulties	Observe tooth brushing / denture cleaning								

Adapted from Eilers, J., Berger, A and, Peterson, M. (1988). Development, testing and application of the Oral Assessment Guide. *Oncology Nursing Forum*,15(3), 325-330a. Copyright Host Defence Unit Great Ormond Street Hospital Trust.



Appendix 5: Patient Information Leaflet

Reproduced from the Royal College of Surgeons of England / The British Society for Disability and Oral Health Clinical Guidelines Updated 2018

Taking Care of Your Mouth during Radiotherapy or Chemotherapy

This leaflet gives you information on how to manage the possible side effects in the mouth due to radiotherapy and chemotherapy

Key points

- Radiotherapy and chemotherapy are treatments that are used to treat cancer.
- Radiotherapy to the head and neck and chemotherapy can cause side effects in the mouth.
- Your mouth needs to be as healthy as possible before the start of treatment to avoid problems later.
- Infected teeth and gums can be a risk during cancer treatment.
- You should have a thorough dental check-up and seek advice from a dentist before cancer treatment starts.
- If you have cancer of the head and neck, this is arranged by the oncology team when they plan your care.
- For other patients receiving cancer therapy, let your oncology team know if you don't have a dentist they may be able to arrange an appointment for you.
- Throughout your radiotherapy or chemotherapy your mouth needs careful monitoring by either a dental hygienist or an appropriately trained nurse.

How can my mouth be affected by cancer treatment?

- Not everyone will get changes in the mouth during cancer treatment
- About two weeks after the start of radiotherapy and chemotherapy you may notice changes
- The most common side effects include general soreness and mouth ulcers, dry mouth, altered
 / loss of taste and difficulty swallowing and eating.
- These generally improve a couple of weeks after cancer treatment is completed.

How can I help to reduce the impact of chemotherapy and radiotherapy on my mouth?

- Brush teeth twice daily using toothpaste, which contains fluoride to prevent dental decay.
- · Keep dentures clean and take them out at night.
- Sugary snacks and drinks can cause dental decay the dietician may need you to have these to keep your energy up. Discuss with the dentist how you can try and protect your teeth.
- Use a pain relieving mouthwash if your mouth is sore (ask you dentist / doctor for advice).
- Sip water if your mouth is dry avoid sipping sugary or acidic drinks or sucking sweets.

What else should I do?

- Stop smoking you can ask your doctor for help with this.
- Reduce alcohol consumption.
- Attend your dentist regularly and tell them about any problems that you are experiencing.
- Lifelong dental care is recommended

Possible side effect of treatment	Why does this happen during your cancer therapy?	What can I do? ✓	What should I avoid?
Sore mouth	 Radiotherapy and chemotherapy can make the lining of your mouth thin This can make your mouth, tongue and throat may become red and sore You may also get mouth ulcers It can become uncomfortable to eat, speak, swallow and brush your teeth. 	 ✓ Your dentist or doctor can recommend / give you a mouthwash to help with the soreness ✓ If there is thrush in your mouth, they can give you medication for this ✓ Use a brush with a small head to clean your teeth with a fluoride toothpaste ✓ If your blood counts are very low, a soft brush may be used for a limited period of time 	 χ Strongly flavoured toothpaste or mouthwash χ Hard food, spicy food and hot drinks χ Alcohol and tobacco
Dry Mouth	 Radiotherapy can damage the glands which produce saliva Saliva moistens the mouth and protects against tooth decay and tooth sensitivity. The dryness is worse during treatment but slowly improves. Saliva may not return completely 	 ✓ Sip water frequently. ✓ Try and chew sugar-free gum. ✓ Discuss saliva substitutes with the dentist / doctor ✓ Oral gel or lubricant (e.g. (Vaseline, Cetraben) are useful to coat and protect the lips and soft tissues. ✓ Follow the dietitian's advice regarding food and drink 	χ Fizzy drinks, diet drinks and fruit juice χ Sucking / chewing sweets
Altered / Loss of taste	 Radiotherapy and chemotherapy can affect your taste buds A dry mouth can also affect your taste Taste will return after cancer treatment is completed 	✓ Sip water regularly	χ Fizzy drinks, diet drinks and fruit juiceχ Sucking / chewing sweets

Possible side effect of treatment	Why does this happen during your cancer therapy?	What can I do? ✓	What should I avoid?
Difficulty swallowin g / eating	 Dryness and soreness of the mouth makes swallowing difficult This can reduce your enthusiasm for food and contribute to weight loss 	 ✓ Let your oncology team know if this occurs as they can monitor this and help ✓ Rinse your mouth with a pain relieving mouth wash before eating (the dentist / doctor can give you this) ✓ Sip water frequently ✓ Eat moist food / have water with food ✓ Eat high energy food such as pasta, bread, and potatoes ✓ Speak with your oncology team who can arrange for you to see a dietitian if you are losing weight 	χ Hard / dry food χ Acidic food
Difficulty Wearing Dentures	Lack of saliva and mouth soreness can make dentures difficult to wear.	 ✓ See your dentist if your dentures are painful ✓ Clean your dentures after each meal, at least twice daily 	χ Do not sleep with your dentures in your mouth

Useful Contacts for Additional Support

- 1. **The Mouth Cancer Foundation**, C/O Media Ambitions (Enterprises) Limited, 1 Victoria Parade, Sandycombe Road, Kew, Surrey, TW9 3NB, Phone: 02089402222, Email: info@mediaambitions.com
- 2. **Changing Faces,** The Squire Centre, 33-37 University Street, London WC1E 6JN, info@changingfaces.org.uk
- 3. **Macmillan Cancer Support Charity,** 89 Albert Embankment, Lambeth, SE1 7UQ, Phone: 0808 808 2020.
- 4. **BACP:** British Association of Counselling and Psychotherapy, 15 St John's Business Park, Lutterworth, LE17 4HB
- 5. **Let's Face It,** 1 Victoria Place, 90 Westgate Bay Avenue, Westgate on Sea, CT8 8NG, Tel: 01843491291
- 6. Maggie's Centres, https://www.maggiescentres.org/; Tel: 0300 123 1801