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**The oral health needs of children, adolescents and young adults after
cancer therapy for solid tumours.**

by

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SYNOPSIS

The survival rate of children with solid tumours is increasing. As a consequence the late effects of cancer therapy have become an important issue requiring further research. The oral health of an individual is central to their general health, level of nutrition and quality of life. This study therefore set out to investigate:

- Whether or not the effects of cancer therapy resulted in a reduced level of oral health during and after treatment.
- The need for dental input in comparison with the general population.
- If patients had knowledge of the effects of cancer therapy on the oral cavity.
- If the oral health care needs of patients differed according to tumour type and treatment regime undertaken.

The study group consisted of 120 patients aged 0-17 years, attending the solid tumour follow up clinic at Birmingham Children's Hospital from July 2006-February 2007. The complete study group was investigated and analysed, with stratification according to tumour diagnostic group and medical treatment regime. The results were compared with national data from the 2003 office of national statistics Child Dental Health Survey.

The study had two main parts. Part A included a dental examination, and part B included a questionnaire completed by the parent/guardian. Demographic information was collected about each subject, cancer diagnosis, date of diagnosis, type of cancer therapy and time since completion of therapy. Part A recorded the current oral health of each subject. Caries prevalence, enamel opacities and gingivitis were recorded. Part B utilised a questionnaire to assess the reported experience of the family regarding oral health care prior to, during and after cancer therapy. The parents/guardians perceived level of oral health input from the dental services and level of knowledge about the effects of cancer therapy on the oral cavity were also investigated.

The results of this study demonstrated that the neuroblastoma diagnostic group and the high dose chemotherapy with stem cell rescue (HDCSCR) therapy group had greater oral health needs compared to the remaining study group and

general population. The level of decay in the primary dentition was increased in the neuroblastoma and HDCSCR groups. Microdont teeth were found in children who had received chemotherapy under the age of 3.5 years. There was a statistically significant relationship between the age at receipt of chemotherapy and the presence of microdont teeth. Thirty seven percent of the study group reported problems involving the oral cavity during cancer therapy with 40% demonstrating limited knowledge of potential future oral health complications.

This study concludes that oral health input is important for all patients suffering from a solid tumour. The possible adverse sequelae on the oral cavity are significant and arise both during and after cancer therapy. Children receiving chemotherapy under the age of 3.5 years should be warned of the possibility of microdontia in the permanent dentition. Extra attention should be directed towards those with a neuroblastoma or who are receiving HDCSCR. Clinical protocols and care pathways should be created for the oral health care of those patients suffering from a solid tumour. Specific and separate care pathways for neuroblastoma patients and those patients receiving HDCSCR should also be considered.

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LIST OF ABBREVIATIONS.

BASCD	British Association for the Study of Community Dentistry.
BCH	Birmingham Children's Hospital.
BDH	Birmingham Dental Hospital.
BOP	Bleeding on probing.
BPE	Basic periodontal examination.
CCLG	Children's Cancer and Leukaemia Group.
CCRG	Childhood Cancer Research Group.
CDHS	Child Dental Health Survey.
CNS	Central nervous system.
CRF	Case Record File.
DMFT	Decayed, missing, filled permanent teeth.
dmft	Decayed, missing, filled deciduous teeth.
DNA	Deoxyribonucleic Acid.
FA	Fanconi's Anaemia.
FDI	World Dental Federation.
FIB	Fibromatosis.
HDCSCR	High Dose Chemotherapy and Stem Cell Rescue.
HEFCE	Higher Education Funding Council for England.
ICCC	International Classification of Childhood Cancer.
ICD	International Classification of Diseases.
LCH	Langerhans cell histiocytosis.
MYC-N	Myc myelocytomatosis viral related oncogene, neuroblastoma derived.
NCI	National Cancer Institute.
NCIC-ONS	National Cancer Intelligence Centre at the Office for National Statistics.
NICE	National Institute for Health and Clinical Excellence.
NRCT	National Registry of Childhood Tumours.
NS	Not significant.
NS-SEC	National Statistics Socio-Economic Classification.
ONS	Office for National Statistics.
PNET	Peripheral primitive neuroectodermal tumour.
PONF	Paediatric Oncology Nurses Forum.
R&D	Research and Development.
RNA	Ribonucleic acid.
RCSENG	Royal College of Surgeons of England
SBPCT	South Birmingham primary care trust.
SNS	Sympathetic nervous system.
UK	United Kingdom.
UKCCSG	United Kingdom Children's Cancer Study Group.
WAGR	Wilm's tumour, aniridia, genitourinary anomalies and mental retardation.
WHO	World Health Organisation.
WMRCTR	West Midlands Regional Children's Tumour Registry.

TABLE OF CONTENTS.

	Page Number
SYNOPSIS.	1
ACKNOWLEDGEMENTS.	3
LIST OF ABBREVIATIONS.	4
TABLE OF CONTENTS.	5
LIST OF TABLES.	10
LIST OF FIGURES.	11
1.0 INTRODUCTION, RELEVANT CURRENT LITERATURE, HYPOTHESES, AIMS AND OBJECTIVES.	12
1.1 INTRODUCTION.	12
1.2 CHILDHOOD CANCER AND CURRENT GUIDELINES.	14
1.3 STAGES OF DENTAL DEVELOPMENT.	17
1.3.1 Dental development.	17
1.3.2 Disorders of development.	19
1.4 CLASSIFICATION OF SOLID TUMOURS.	21
1.4.1 Common solid tumour categories.	23
1.5 EPIDEMIOLOGY OF SOLID TUMOURS.	23
1.5.1 Prevalence.	24
1.5.2 Age variance at diagnosis.	27
1.5.3 Trends.	27
1.5.4 Mortality.	27
1.5.5 Survival.	28
1.5.6 West Midlands data.	28
1.6 AETIOLOGY OF SOLID TUMOURS.	28
1.6.1 Genetics.	29
1.6.2 Infections.	29
1.7 SIDE EFFECTS OF TREATMENT WITH SPECIFIC REFERENCE TO THE ORAL SIDE EFFECTS.	30
1.7.1 Xerostomia.	32
1.7.2 Mucositis.	32
1.7.3 Fungal infections.	33
1.7.4 Herpes simplex virus.	33
1.7.5 Long term effects.	33
1.7.5.1 Dental caries.	33
1.7.5.2 Gingival health.	34
1.7.5.3 Enamel hypoplasia and discolourations.	35
1.7.5.4 Crown and root malformations.	35

1.7.5.5	Unerupted teeth.	36
1.7.5.6	Hypodontia.	37
1.7.5.7	Dental trauma.	37
1.7.5.8	Craniofacial growth.	37
1.7.6	Histology.	38
1.7.7	Summary of previous literature.	38
1.7.8	Overall conclusions.	40
1.8	TREATMENT REGIMES.	41
1.9	UK ORAL HEALTH EPIDEMIOLOGICAL SURVEYS.	50
1.9.1	Dental caries.	50
1.9.2	Enamel opacities.	51
1.10	RESEARCH TECHNIQUES.	51
1.10.1	Use of questionnaires.	51
1.11	OBJECTIVE, HYOPTHESES AND AIMS.	52
1.11.1	Objective.	52
1.11.2	Hypotheses.	52
1.11.3	Aims.	53
2.0	MATERIALS AND METHODS.	54
2.1	MATERIALS.	54
2.1.1	Dental examination (part A).	54
2.1.2	Questionnaire (part B).	54
2.2	METHODS.	55
2.2.1	Training of the examiner.	55
2.2.2	Selection of the study group.	55
2.2.3	Patients' personal details.	56
2.2.4	Patients' medical details.	57
2.2.5	Informed consent for the study group.	57
2.2.6	Control group.	57
2.2.7	Dental examination (part A).	58
2.2.7.1	Pilot dental examination (part A).	58
2.2.8	Development of the questionnaire (part B).	58
2.2.8.1	Pilot questionnaire study (part B).	59
2.2.9	Conduct of the study.	59
2.2.9.1	Location.	59
2.2.9.2	Data protection.	59
2.2.9.3	Study procedure.	59
2.2.9.4	Dental examination.	60
2.2.9.5	Repeat examinations.	64
2.2.9.6	Questionnaire completion.	64
2.2.10	Investigator interventions.	65
2.2.11	Review of the study.	65

2.2.12	Tabulation of the data.	65
2.2.13	Analysis of results.	66
2.2.13.1	Caries analysis.	66
2.2.13.2	Opacities analysis.	66
2.2.13.3	Questionnaire analysis.	67
2.2.13.4	Social class information.	67
3.0	RESULTS AND ANALYSIS.	69
3.1	RESULTS AND ANALYSIS DENTAL EXAMINATION (PART A).	69
3.1.1	Demographics of the study group.	69
3.1.1.1	Geographic distribution of the study group.	69
3.1.2	Composition of the study group.	70
3.1.2.1	The medical diagnosis of the group.	70
3.1.2.2	The age of the study group at diagnosis and dental examination.	71
3.1.2.3	Treatment regime the patient had experienced.	73
3.1.2.4	Type of chemotherapy received by the patient.	73
3.1.2.5	Time since therapy.	74
3.1.2.6	Composition of the sub-groups; post stratification.	76
3.1.3	Experience of dental caries.	78
3.1.3.1	Results by direct comparison with the 2003 Child Dental Health Survey.	79
3.1.3.2	Dental caries experience of treatment regime groups.	81
3.1.3.3	Dental caries experience of tumour diagnostic groups.	82
3.1.3.4	Summary of dental caries experience.	83
3.1.4	Enamel opacities.	83
3.1.4.1	Results for opacities by direct comparison with the Child Dental Health Survey 2003.	86
3.1.4.2	Opacities within each tumour group.	88
3.1.4.3	Opacities within each different treatment regime group.	89
3.1.4.4	Correlation between enamel opacities and the level of water fluoridation.	90
3.1.4.5	Summary of enamel opacities.	90
3.1.5	Gingival health.	91
3.1.5.1	Gingival health by comparison with the 2003 Child Dental Health Survey cohort.	92
3.1.5.2	Periodontal condition by diagnostic group.	94
3.1.5.3	Gingival health by treatment group.	95
3.1.5.4	Summary of gingival health.	95
3.1.6	Microdontia.	96
3.1.7	Traumatized teeth.	99
3.1.8	Fissure sealed teeth.	100
3.1.9	Summary of key findings.	102

3.2	RESULTS AND ANALYSIS QUESTIONNAIRE (PART B).	102
3.2.1	Social class of the study group.	102
3.2.2	Attitude.	105
3.2.3	Reported attendance.	106
3.2.3.1	Prior to cancer therapy.	107
3.2.3.2	During cancer therapy.	109
3.2.3.3	After cancer therapy.	111
3.2.4	General dental care.	113
3.2.5	Questionnaire comments.	114
3.2.5.1	Comments supporting an adequate level of dental care.	114
3.2.5.2	Comments revealing inadequate dental care.	115
3.2.5.2.1	Difficult access to care.	115
3.2.5.2.2	Inadequate information received.	115
3.2.5.2.3	Lack of confidence in the general dentist.	116
3.2.5.2.4	Orthodontic queries.	116
3.2.5.3	Miscellaneous comment.	116
4.0	DISCUSSION.	117
4.1	REVIEW AND CRITIQUE OF METHODOLOGY.	117
4.2	REVIEW OF DEMOGRAPHICS AND COMPOSITION OF THE GROUP.	118
4.2.1	Number of patients.	118
4.2.2	Geographical residence.	119
4.2.3	Social class.	119
4.2.4	Medical diagnosis.	120
4.2.5	Chemotherapy regime.	121
4.3	RATIONAL FOR CHOICE OF CONTROL DATA.	121
4.4	DENTAL CARIES.	121
4.5	ENAMEL OPACITIES.	124
4.6	GINGIVAL HEALTH.	126
4.7	MICRODONTIA.	128
4.8	TRAUMA.	130
4.9	FISSURE SEALANTS.	131
4.10	QUESTIONNAIRE.	131
4.10.1	The use of questionnaires.	131
4.10.2	Attitude towards oral health.	132
4.10.3	Reported attendance at the dentist.	132
4.10.3.1	Prior to cancer therapy.	134

4.10.3.2	During cancer therapy.	135
4.10.3.3	After cancer therapy.	135
4.10.4	Dental treatment required post cancer therapy.	136
4.10.5	General dental care and comments made.	137
5.0	CONCLUSIONS, OUTCOMES AND FUTURE RESEARCH.	138
5.1	CONCLUSIONS.	138
5.2	CLINICAL RECOMMENDATIONS.	139
5.3	FUTURE RESEARCH.	141
	REFERENCES.	143
	APPENDICES.	150
1	General information data collection sheet 1.	150
2	Dental charting, basic periodontal examination and gingival bleeding score data collection sheet 2.	151
3	Enamel opacities data collection sheet.	153
4	Parental letter explaining the study.	154
5	Parent information sheet.	155
6	Patient age 16+ information sheet.	159
7	Patient ages 13-15 information sheet.	163
8	Patient ages 8-12 information sheet.	167
9	Patient age under 8 information sheet.	170
10	Research project consent form.	171
11	Questionnaire.	172
12	Ethics approval.	176
13	SBPCT R&D approval.	179
14	BCH R&D approval.	181
15	BCH funding support.	182
16	Chi square test calculations.	183

LIST OF TABLES.

	Page Number
1.1 Timing of tooth development in both deciduous and permanent teeth.	20
1.2 International Classification of Childhood Cancer (ICCC).	21
1.3 Total number of childhood cancer cases for children under 15 years, registered in the UK 2000-2005.	25
1.4 Previous studies investigating the effects of cancer therapy on the developing dentition.	38
1.5 Classes of cytotoxic drug in common use in the UK to treat solid tumours in children.	43
1.6 Treatment and treatment regimes used in the UK over the past 14 years for the main groups of solid tumours affecting children.	46
3.1 Medical diagnoses of the study group.	70
3.2 Number, gender and age of the diagnostic stratifications.	76
3.3 Length of, and amount of time since chemotherapy in the diagnostic groups.	77
3.4 Number, gender and age of the treatment stratification groups.	77
3.5 Length of, and amount of time since chemotherapy in the treatment stratification groups.	78
3.6 DMFT, dmft of the study population.	78
3.7 Comparison of DMFT values for 8,12 and 15-year-olds within the study and national data (2003 CDHS).	80
3.8 Proportion of patients with opacities and type of opacity within the study group.	85
3.9 Extent of opacities within the study group.	85
3.10 Symmetry of opacities within the study group.	86
3.11 Extent of lesions on teeth within the Child Dental Health Survey and study data.	87
3.12 Opacities present within each tumour group.	88
3.13 Opacities present within each different treatment regime group.	89
3.14 Comparison between the occurrence of opacities and the level of fluoridation of the water supply.	90
3.15 Comparison between the type of enamel opacity and the level of water fluoridation.	90
3.16 Areas of gingivitis in the mouth for 15-year-olds.	93
3.17 Gingivitis by gender in 15-year-olds.	94
3.18 Gingival health of the different diagnostic groups.	94
3.19 Gingival health of the treatment groups.	95
3.20 Relationship between microdont teeth and age at which chemotherapy was received.	96
3.21 Details of microdont teeth within the study group.	97
3.22 Type of chemotherapy received by those with microdont teeth.	97
3.23 High dose chemotherapy and stem cell rescue group with and without microdont teeth.	98
3.24 Number of microdont teeth present in each group.	98
3.25 Number of microdont teeth within each diagnostic group.	99
3.26 Traumatized teeth illustrated within diagnostic groups.	99
3.27 Traumatized teeth present in each treatment group.	100
3.28 Number of fissure sealants placed per age group.	100
3.29 Number of fissured teeth within each treatment group.	101

LIST OF FIGURES.

	Page Number
1.1 Prevalence of childhood cancer in children under 15 registered in the UK 2000-2005 by tumour type.	26
3.1 Number of patients living in an area with fluoridated water n=120.	70
3.2 Age of patients at the time of diagnosis of cancer n=120.	72
3.3 Age of the patients within the study group at the time of dental examination n=120.	72
3.4 Length of time the patients were given chemotherapy for n=120.	73
3.5 Different chemotherapy regimes within the study group.	74
3.6 Amount of time elapsed since chemotherapy had finished.	75
3.7 Different dentitions of the study group n=120.	76
3.8 dmft values for patients who were 5 (n=9) and 8 years old (n=5) at the time of examination within the study group in comparison with the 2003 Child Dental Health Survey data.	79
3.9 Average DMFT, dmft values for each treatment group within the study data.	81
3.10 DMFT, dmft values of the different diagnostic groups within the study.	82
3.11 Pictures of diffuse lesions on the central incisor teeth (a+b).	84
3.12 a) Picture of demarcated lesions of the anterior teeth.	84
3.12 b) Demarcated lesion of the upper left central incisor.	84
3.13 Level of different types of enamel opacities within the study data, study 12-year-olds and the national data.	87
3.14 Proportion of those examined for gingivitis with gingivitis present and those with healthy gingivae.	91
3.15 Number of tooth sites affected by gingivitis for those patients affected by gingivitis.	92
3.16 The level of gingivitis in the study group, 15-year-old study group and the 2003 CDHS.	93
3.17 Percentage of patients with fissure sealants within each diagnostic group.	101
3.18 National statistics socio-economic classification (NS-SEC) categories of social class in the mothers and fathers of the study group.	103
3.19 Social class by occupation from the Registrar General's coding system (1980).	104
3.20 Age at which parents within the study group finished full time education.	105
3.21 Perceived level of importance of looking after the mouth and teeth using a visual analogue scale.	106
3.22 Frequency at which the parents and children of the study group attend the general dentist.	107
3.23 Did the families receive information regarding oral care before commencing cancer therapy?	108
3.24 Proportion of the study reported to have side effects within the oral cavity during cancer therapy.	109
3.25 Frequency of different oral complaints occurring within the affected group.	110
3.26 Proportion of the study group admitted into hospital for supportive medical/dental treatment during cancer therapy.	111
3.27 Type of dental treatment required post cancer therapy.	112
3.28 Location of the patients dental reviews and treatment appointments.	113
3.29 How parents felt about the level of dental care their child received.	114

1.0 INTRODUCTION, RELEVANT CURRENT LITERATURE, HYPOTHESES, AIMS AND OBJECTIVES.

1.1 INTRODUCTION.

Childhood cancer is fortunately rare with the UK incidence rates being in the range of 110-150 per million children per year. One in 500 children will be affected during the first 15 years of life (Stiller et al., 2004). There has been a large reduction in mortality due to early diagnosis and improved treatment regimes. By the year 2000, 1 in 900 adults aged 16-34 were survivors of childhood cancer (Stevens et al., 1998). Estimates from the Childhood Cancer Research Group, University of Oxford suggest there are now over 10,000 known adult survivors of childhood cancer in the UK (Stevens et al., 1998).

In 2005 The National Institute for Health and Clinical Excellence published a document; *Guidance on Cancer Services Improving outcomes in children and young people with Cancer* (NICE, 2005a). This evidence based document acknowledged that cancer treatment can result in acute oral problems such as mucositis and other viral, bacterial and fungal oral infections. Later in life, previous cancer treatment can cause structural anomalies of the developing dentition. The document identified that oncology patients often have inadequate dental input during their illness and are later often lost to dental follow up (NICE, 2005a). It proposed that:

- Special provision for urgent dental treatment should be available before any chemotherapy is commenced.
- Information on the effects of cancer therapy should be given to all cancer patients and their families.
- A named professional should be identified to co-ordinate oral health care throughout cancer therapy.
- During the transition to adult services and there should be clear protocols and referral routes for oral care (NICE, 2005a).

Further publications from The United Kingdom Children's Cancer Study Group (UKCCSG) and the Paediatric Oncology Nurses Forum (PONF) in February 2006 included evidence based guidelines about mouth care for children and young people with cancer (UKCCSG and PONF, 2006). These guidelines include suggestions regarding oral health care at diagnosis of cancer, during therapy and after acute cancer treatment has finished. In particular advice is given on prevention and treatment of oral mucositis, oral candidosis, xerostomia and herpes simplex virus infections. These have been based on available current evidence (UKCCSG and PONF, 2006).

LITERATURE REVIEW.

1.2 CHILDHOOD CANCER AND CURRENT GUIDELINES.

Children's cancers can be placed into three groups. These are leukaemias, central nervous system tumours and the so called 'solid tumours'. The present study focused on the solid tumour group which in this investigation also included children with Hodgkin's lymphoma and non-Hodgkin's lymphomas. This group was studied specifically as there is limited research in the literature to date with most of the research being focused on the leukaemias. Tumours are named according to their constituent cells. They include sarcomas (cancers arising from connective or supporting tissues such as muscle or bone), embryonal tumours (malignant counterparts of cells usually expressed during normal fetal development), carcinomas (malignant tumours originating from epithelial and glandular cells), and lymphomas (cancers of organs which produce and store cells of the lymphoid system for example lymph nodes), (NCI, 2005). In general, one third (32%) of childhood cancers will be leukaemia's, 10% lymphomas, 24% brain and spinal tumours and 15% embryonal tumours (such as: neuroblastoma, retinoblastoma, Wilm's tumour and hepatoblastoma). The remaining 19% comprise other types of cancer (Stiller et al., 2004).

Survival rates following treatment are increasing and, therefore, the late effects of childhood cancer are becoming increasingly important. Childhood cancer and its treatment can have a significant effect upon the physical, social and emotional well being of the child and thus their quality of life. Late effects include: endocrine damage resulting in growth disorders; pubertal failure or precocious puberty; inadequate bone mineralization; and discreet hormone deficiencies requiring replacement (Stevens et al., 1998, NICE, 2005a).

The oral health and therefore healthcare of these individuals has a significant impact upon their quality of life during their cancer therapy. If acute dental problems do arise they are difficult to manage. Many such problems are preventable if children are seen

by the dental team before commencing cancer therapy. Clarkson and Eden investigated the dental health of children with cancer. In a study of 60 children, 4-6 months post diagnosis, 21 required urgent dental treatment. In their conclusion the authors highlighted the need to improve the integration of dental services into the medical care pathways (Clarkson and Eden, 1998). Evidence regarding the effects of cancer therapy from the literature is weak and varied. Many studies demonstrate that patients who have received chemotherapy have disturbances in their dentitions (Duggal, 2003, Marec-Berard et al., 2005, Purdell-Lewis et al., 1988, Minicucci et al., 2003, Holtta et al., 2002, Nasman et al., 1997). Other studies have revealed the only significant effects to be small areas of enamel hypoplasia or opacities (Alpaslan et al., 1999, Nunn et al., 1991). There are a limited number of studies investigating the different solid tumour groups of patients, with much of the literature being based around patients with leukaemia.

In 2005 the National Institute for Health and Clinical Excellence (NICE) published Guidance on Cancer Services "*Improving outcomes in children and young people with Cancer*" (NICE, 2005a). This evidence based document acknowledged that cancer treatment can also result in acute oral problems such as mucositis and other viral, bacterial and fungal infections. Later in life historical cancer treatment can be associated with structural anomalies of the developing dentition. The document identified that oncology patients often have inadequate dental input during their illness and are later often lost to dental follow up despite the seriousness of their condition. The recommendations made by NICE (NICE, 2005a) were:

- to ensure special provision for emergency dental treatment is available prior to the commencement of chemotherapy,
- that information on the effects of cancer therapy should be given to all cancer patients and their families,
- that a named professional should be identified to co-ordinate care throughout cancer therapy and during the transition to adult services,
- to have clear protocols and referral routes for dental care.

The document also states there is very little good quality evidence on the effectiveness of treatments for oral infections and oral mucositis.

In February 2006 The United Kingdom Children's Cancer Study Group (UKCCSG) and the Paediatric Oncology Nurses Forum (PONF) produced evidence based guidelines about mouth care for children and young people with cancer (UKCCSG and PONF, 2006). This guideline covers oral care at the time of cancer diagnosis, oral hygiene at diagnosis and during cancer treatment, dental/oral care during and after cancer treatment, plus advice on the prevention and treatment of oral mucositis, oral candidosis, xerostomia and infections with the herpes simplex virus (UKCCSG and PONF, 2006). This advice was based on the current available evidence. The mucositis recommendations for treatment are, at best, based on evidence level B and include best practice (clinical expertise of the guideline group). The candidosis and xerostomia recommendations are based on evidence level D (case series and cross sectional studies) and herpes simplex advice is based on evidence levels ranging from A to D (UKCCSG and PONF, 2006).

Maintaining a good standard of oral health is important for all children. The UK Child Dental Health Survey 2003 (CDHS) found 43% of 5-year-olds and 57% of 8-year-olds had experienced obvious caries in primary teeth (Lader et al., 2005). In the permanent dentition 14% of 8-year-olds, 34% of 12-year-olds and 49% of 15-year-olds had experienced obvious caries (Pitts and Harker, 2005). With this knowledge on the state of children's general dental health, it highlights the importance of dental input before, during and after cancer therapy. The effects of cancer treatment are well known to be associated with oral complications (Cheng et al., 2002) and cause other generalised medical complications such as neutropenia and thrombocytopenia (Maguire and Welbury, 1996). Therefore, the management of any oral problem becomes more challenging in the presence of these additional risk factors.

The literature covering the effects of cancer therapy on the oral cavity is limited. Studies employ small sample sizes due to the nature of the disease and large numbers of confounding factors within the groups makes comparison between studies difficult. The majority of the literature is based on patients who have been treated for leukaemia with fewer studies on solid tumour patients.

1.3 STAGES OF DENTAL DEVELOPMENT.

The stage of dental development at the time of cancer diagnosis and subsequent surgery and chemotherapy is an important consideration. Cancer therapy is more likely to have a permanent effect during the early stages of tooth development. This section will therefore briefly explore the stages and timings of tooth development before exploring the available literature.

1.3.1 Dental development.

Dental development in humans begins in utero at 5-6 weeks and continues until the roots of the wisdom teeth are fully formed 20-25 years later. It is a prolonged process and can be affected by both external (trauma, radiation) and internal factors (chemotherapy, antibiotics, fever, metabolic disturbances, and genetic disturbances). The impact of cancer therapy upon dental development is likely to depend on the timing, severity and duration of the causative factor (Maguire and Welbury, 1996).

The first sign of tooth development is an epithelial thickening of the mandible and maxilla. The initiation of deciduous teeth begins during the second and third month in utero (RCSEng, 1998). Tooth development then occurs in 3 main stages. First “initiation” begins and tooth germs appear along an invagination of oral epithelium called the dental lamina. This is followed by “morphogenesis” where the shape of the tooth is determined. Finally, “histogenesis” begins, which is the process of differentiation of cells and the final dental tissues are formed (Berkovitz et al., 1992).

The tooth germ consists of the enamel organ which gives rise to the stellate reticulum, intermediate reticulum, inner enamel epithelium and outer enamel epithelium. The inner enamel epithelium then forms ameloblasts and enamel. The dental papillae subsequently create the odontoblasts and dentine and the dental follicle produces the periodontal ligament fibroblasts, cementoblasts and cementum, and the osteoblasts and alveolar bone. The development of a tooth germ into a fully

formed tooth involves complex interactions between the epithelium of the enamel organ and the mesenchyme of the dental papillae (Berkovitz et al., 1992).

Production of the mineralised tissues involves initial secretion of an organic matrix and then deposition of mineral within the matrix. The dentine matrix develops before the enamel matrix. In dentine, odontoblasts form a collagen matrix which is then mineralised. Enamel is formed by ameloblasts in a similar fashion to dentine. The organic material comprises a protein called amelogenin which is gradually removed as the mineral ions are added.

Root development starts when crown formation is complete and occurs by an apical growth of the root sheath of Hertwig. Root growth is usually two thirds complete on tooth eruption and continues after eruption of the tooth for up to 3 years (Berkovitz et al., 1992). During this time the supporting structures of the tooth also form. These consist of root cementum, alveolar bone, periodontal ligament and gingivae (RCSEng, 1998). The overall process from initiation to complete permanent tooth development takes at least 10 years (Beek, 1983).

1.3.2 Disorders of development.

Disorders in dental development can be due to abnormalities in the differentiation of the dental lamina and tooth germs resulting in differences in the number, size and form of teeth, or problems in the process of tooth development which results in structural deformities of a particular tooth depending on the time of the insult (RCSEng, 1998).

Individual tooth development is an extremely sensitive process and when disturbed can profoundly affect the individual developing tooth. Defects are described as “hypoplastic” or “hypocalcified”. A hypoplastic tooth means there is a disturbance in the normal prism patterns. A hypocalcified tooth is where the enamel is of normal thickness but is extremely soft and soon lost due to the forces of abrasion and erosion (RCSEng, 1998).

Throughout the whole tooth development process, disturbances can occur resulting in missing teeth, dental anomalies and poor root formation. These can arise due to both systemic or local insults. The literature to date is varied with regards to the effects of cancer therapy on the developing dentition. Effects thought to be attributed to chemotherapy include: arrested root development, enamel defects, discolorations, microdontia and agenesis (Oguz et al., 2004). The extent of disturbance is likely to depend on the stage of development of the teeth at the time of insult. Table 1.1 illustrates the timings of crown and root development for children’s teeth.

Table 1.1 Timing of tooth development in both deciduous and permanent teeth (Beek, 1983). All ages post full term delivery unless otherwise specified.

Tooth	Initial Calcification	Completion of crown	Eruption	Completion of root
Deciduous maxillary first molar	5 months in utero	6 months	12-16 months	2-2.5 years
Deciduous mandibular first molar	5 months in utero	6 months	12-16 months	2-2.5 years
Deciduous maxillary second molar	6 months in utero	10-12 months	1.75-2.5 years	3 years
Deciduous mandibular second molar	6 months in utero	10-12 months	1.75-2.5 years	3 years
Maxillary central incisor	3-4 months	4-5 years	7-8 years	10 years
Mandibular central incisor	3-4 months	4-5 years	6-7 years	9 years
Maxillary lateral incisor	10-12 months	4-5 years	8-9 years	11 years
Mandibular lateral incisor	3-4 months	4-5 years	7-8 years	10 years
Maxillary canine	4-5 months	6-7 years	11-12 years	13-15 years
Mandibular canine	4-5 months	6-7 years	9-10 years	12-14 years
Maxillary first premolar	1.5-1.8 years	5-6 years	10-11 years	12-13 years
Mandibular first premolar	1.75-2 years	5-6 years	10-12 years	12-13 years
Maxillary second premolar	2-2.5 years	6-7 years	10-12 years	12-14 years
Mandibular second premolar	2.25-2.5 years	6-7 years	11-12 years	13-14 years
Maxillary first molar	Birth or slightly before	2.5-3 years	6-7 years	9-10 years
Mandibular first molar	Birth or slightly before	2.5-3 years	6-7 years	9-10 years
Maxillary second molar	2.5-3 years	7-8 years	12-13 years	14-16 years
Mandibular second molar	2.5-3 years	7-8 years	12-13 years	14-16 years

1.4 CLASSIFICATION OF SOLID TUMOURS.

The National Cancer Intelligence Centre at the Office for National Statistics (NCIC-ONS) collates cancer registration data for Great Britain. All new cases of cancer each year are registered. The data is coded using the International Classification of Diseases system (ICD) version 10. This system uses a topographical description of the tumour site and allows detailed coding of adult tumours.

As childhood cancers are different to those in adult life they are classified by an alternative system. This classification system is called the International Classification of Childhood Cancer (ICCC) and is based on the histological characteristics of the tumour (Kramarova et al., 1996). The ICCC is illustrated in table 1.2.

Table 1.2 International Classification of Childhood Cancer (ICCC) (Kramarova et al., 1996).

I Leukemia	(a) Lymphoid Leukemia Excluding Acute Lymphoblastic Leukaemia (ALL)
	(b) Acute Leukemia Excluding Acute Myeloid Leukaemia (AML)
	(c) Chronic Myeloid Leukemia
	(d) Other Specified Leukemia's
	(e) Unspecified Leukemia's
II Lymphomas and Reticuloendothelial Neoplasms.	(a) Hodgkin's disease
	(b) Non-Hodgkin's lymphomas
	(c) Burkitt's lymphoma
	(d) Miscellaneous lymphoreticular neoplasms
	(e) Unspecified lymphomas
III Central Nervous System (CNS) and Miscellaneous Intracranial and Intraspinal Neoplasms	(a) Ependymoma
	(b) Astrocytoma
	(c) Primitive neuroectodermal tumours
	(d) Other gliomas
	(e) Miscellaneous intracranial and intraspinal neoplasms
	(f) Unspecified intracranial and intraspinal neoplasms

IV Sympathetic Nervous System Tumours	(a) Neuroblastoma and ganglioneuroblastoma
	(b) Other sympathetic nervous system tumours
V Retinoblastoma	
VI Renal Tumours	(a) Wilm's' tumour, rhabdoid and clear cell sarcoma
	(b) Renal carcinoma
	(c) Unspecified malignant renal tumours
VII Hepatic Tumours	(a) Hepatoblastoma
	(b) Hepatic carcinoma
	(c) Unspecified malignant hepatic tumours
VIII Malignant Bone Tumours	(a) Osteosarcoma
	(b) Chondrosarcoma
	(c) Ewing's sarcoma
	(d) Other specified malignant bone tumours
	(e) Unspecified malignant bone tumours
IX Soft-Tissue Sarcomas	(a) Rhabdomyosarcoma and embryonal sarcoma
	(b) Fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms
	(c) Kaposi's sarcoma
	(d) Other specified soft-tissue sarcomas
	(e) Unspecified soft-tissue sarcomas
X Germ-Cell, Trophoblastic and other Gonadal Neoplasms	(a) Intracranial and intraspinal germ-cell tumours
	(b) Other and unspecified non-gonadal germ-cell tumours
	(c) Gonadal germ-cell tumours
	(d) Gonadal carcinomas
	(e) Other and unspecified malignant gonadal tumours
XI Carcinomas and other Malignant Epithelial Neoplasms	(a) Adrenocortical carcinoma
	(b) Thyroid carcinoma
	(c) Nasopharyngeal carcinoma
	(d) Malignant melanoma
	(e) Skin carcinoma
	(f) Other and unspecified carcinomas
XII Other and Unspecified Malignant Neoplasms	(a) Other specified malignant tumours
	(b) Other unspecified malignant tumours

1.4.1 Common solid tumour categories.

- Brain and spinal tumours.
- Neuroblastomas.
- Retinoblastomas.
- Wilm's tumour.
- Hepatoblastoma.
- Lymphomas (Hodgkin's and non-Hodgkin's).
- Osteosarcoma.
- Ewing's Sarcoma.
- Rhabdomyosarcoma.
- Germ cell tumours.

1.5 EPIDEMIOLOGY OF SOLID TUMOURS.

Epidemiology literally means 'studies upon people'. It is a science concerned with the study of factors causing and influencing disease within a population (Farmer et al., 1996). Since 1962 children diagnosed with cancer in Great Britain should have been registered in a national data base. It should be noted however that at present registration of cancer cases is voluntary. The National Cancer Intelligence Centre at the Office for National Statistics (NCIC-ONS) collate cancer registration data for England, Scotland and Wales. The National Registry of Childhood Tumours (NRCT) in Oxford registers those cases in children under 15 years of age in the UK. The United Kingdom Children's Cancer Study Group (UK-CCSG) now renamed The Children's Cancer and Leukaemia group (CCLG) have also collected data of all registrations of childhood cancer for children under 15 years of age from 1977-2005.

1.5.1 Prevalence.

The prevalence of a disease is the number of existing cases of a particular disease in a given population at a given time or during a specified period (Farmer et al., 1996). Therefore the prevalence of specific childhood cancers is dependant upon both the incidence of the cancer and the rates of survival.

Cancers in children account for less than 1% of all cancers in industrialised countries (Stiller and Draper, 1998). The NRCT states between 1988-1997 the incidence of a childhood cancer was 133.7 per million (includes a small number of non-malignant diagnoses) (NICE, 2005a). The chance therefore of a child being diagnosed with cancer before the age of 15 is 1 in 500. This figure is derived from risks of about 1 in 1600 for leukaemia, 1 in 2200 for a brain or spinal tumour and 1 in 1100 for all other cancers combined (CCRG., 2004). Table 1.3 shows recent data from CCLG to show the number of cases of childhood cancer to be registered in the UK 2000-2005 (a six year period).

Table 1.3 Total number of childhood cancer cases for children under 15, registered in the UK 2000-2005 (CCLG, 2007c).

Cancer type	ICCC code	Number
Leukaemia	I	3002
Lymphomas	II	966
CNS	III	2131
SNS	IV	593
Retinoblastoma	V	240
Renal	VI	569
Hepatic	VII	116
Bone	VIII	388
Soft tissue sarcoma	IX	595
Germ-cell	X	273
Epithelial	XI	135
Other malignant	XII	17
Other non-malignant	LCH;FIB	810
Total		9835

CNS- central nervous system.

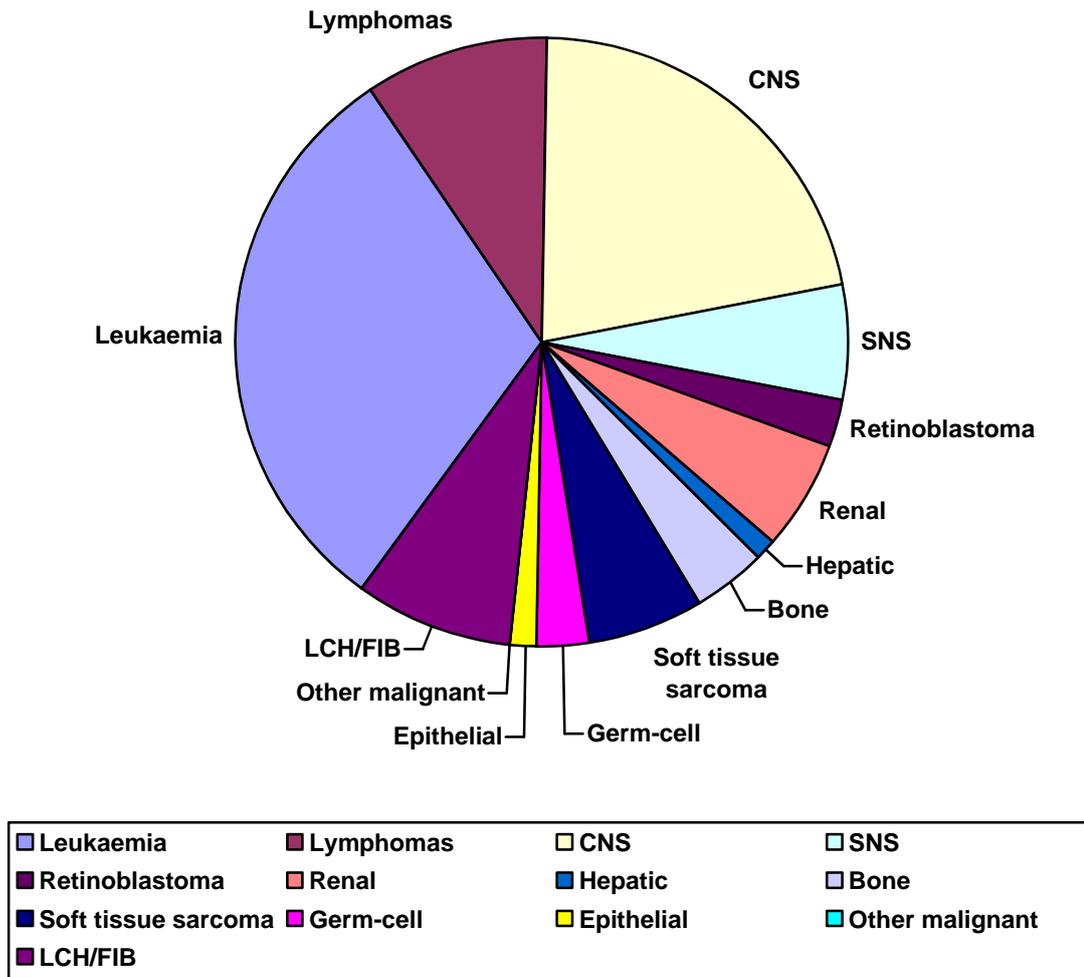
FIB- fibromatosis.

LCH- langerhans cell histiocytosis.

SNS- sympathetic nervous system.

Figure 1.1 Prevalence of childhood cancer in children under 15 registered in the UK 2000-2005 by tumour type (CCLG, 2007c).

The prevalence of childhood cancer in children under 15 in the UK 2000-2005 by tumour type.



Solid tumours in the UK therefore accounted for 6833 out of 9853 (69%) cases of cancer in children under 15 years old from 2000-2005 (CCLG, 2007c).

1.5.2 Age variance at diagnosis.

Childhood cancer has a peak incidence at around 5 years of age (Stiller and Draper, 1998). The lowest incidence was in the 8-10 year old group (Stiller, 2002). Cancer is more common in adolescents (aged 15-19 years) than in children aged 8-10 years. It is more common again in young adults (20-24 years) with an incidence here of 226 per million compared to 150-200 per million in the 15-19 age group (Stiller, 2002, Birch et al., 2002). The peak incidence of neuroblastoma, retinoblastoma and hepatoblastoma is under the age of 1 year. Wilm's tumour is most prevalent at 3 years of age. Osteosarcomas and Hodgkin's disease are uncommon under the age of 2 years but do increase in incidence beyond this age (NICE, 2005b).

1.5.3 Trends.

An increased incidence of childhood cancer has been reported in males (Cotterill et al., 2000, Birch et al., 2002). UK studies report a 1.2:1 M:F ratio in children aged 0-14 years (Parkin et al., 1998). As a whole, there has been a general increase in the incidence of childhood and adolescent cancer. This is especially significant for the 15-24 year old group (Birch et al., 2002). In the North West of England a linear increase in incidence of acute lymphoblastic leukaemia and Hodgkin's disease had been identified (Blair and Birch, 1994a). A similar study also in the north West of England showed an increased incidence of astrocytoma, medulloblastoma, neuroblastoma and non-skin epithelial tumours (Blair and Birch, 1994b).

1.5.4 Mortality.

Children aged 0-14 years with leukaemia are the group with the highest reported mortality rate because they are the group with the highest incidence of cancer. Figures obviously vary between groups depending on the nature of the tumour. For example, tumours of the sympathetic nervous system account for 12.3% of deaths but only contribute to 6.7% of new childhood cancer cases each year, whereas retinoblastoma accounts for 3.2% of new cases but only 0.8% of deaths demonstrating a more favourable survival rate (NICE, 2005a).

1.5.5 Survival.

Generally, survival rates from childhood cancer have increased over the past 30 years due to improved treatment regimes and are now as high as 70-75% (Gatta et al., 2002). Again the survival rate will vary according to the diagnosis. 100% survival rate is reported in thyroid carcinomas whereas neuroblastomas are reported at 55% and brain and spinal tumours at 43% (NICE, 2005a).

1.5.6 West Midlands data.

There are 5 specialist paediatric regional registries in England. These cover the North-Western, Northern, Yorkshire, West Midlands and South West regions. In 1984 a West Midlands Regional Children's Tumour Registry (WMRCTR) was established at Birmingham Children's Hospital (Muir et al., 1992).

In the West Midlands the distribution of childhood cancer is similar to the pattern in other developed countries. The most recent literature specific to the West Midlands states of the 1310 cases diagnosed between 1994-2003, 32% were leukaemias, 25% brain/CNS tumours, 10% lymphomas and 33% other solid tumours (Powell et al., 2004). The West Midlands group also showed a similar incidence between males and females and the age at diagnosis matched the national statistics (Powell et al., 2004).

1.6 AETIOLOGY OF SOLID TUMOURS.

The aetiology of childhood cancers remains largely unknown. It has been suggested by some authors that the aetiology and factors influencing disease progression in childhood cancers is different to those occurring in adults. For example tobacco and alcohol are known risk factors for oral squamous carcinoma in adults however this is also a disease that has increased in incidence among children worldwide in the last few decades. It is unknown why children, despite such a limited time of exposure to known carcinogenic risk factors experience similar cancerous lesions therefore

suggesting possible different disease processes (Llewellyn et al., 2001). For cancer to develop, tumour initiation and tumour progression must occur. The rate at which this occurs depends on changes in the cell and changes in the host. (Franks and Teich, 1997). The putative risk factors include genetics, infections, hormones and radiation (NICE, 2005a).

1.6.1 Genetics.

Around 5% of childhood malignancies are related to an inherited genetic tendency (NICE, 2005b). For example a somatic mutation in the retinoblastoma gene can cause an autosomal dominant inheritance of retinoblastoma with an 100% increase in the risk of osteosarcoma (Draper et al., 1992) and a somatic defect in the P53 tumour suppressor gene results in an increased risk of a number of sarcomas and carcinomas resulting in the Li-Fraumeni family cancer syndrome (Birch, 1994). Fanconi's anaemia (FA) is a rare autosomal recessively inherited condition involving defects in DNA repair. Subsequently patients suffer from congenital abnormalities and developmental abnormalities, progressive bone marrow failure and have a predisposition to cancer particularly acute myeloid leukaemia and solid tumours. (Franks and Teich, 1997, Rosenberg et al., 2003, Salum et al., 2006). There is a high incidence of oral squamous cell carcinoma in FA patients (Oksuzoglu and Yalcin, 2002, Lustig et al., 1995).

1.6.2 Infections.

Infections particularly by viruses are thought to play a role in the development of certain types of cancer. Associated with Epstein virus are Burkitt's lymphoma, Hodgkin's disease and nasopharyngeal carcinoma. Associated with human immunodeficiency virus and human herpes virus 8 is Kaposi's sarcoma. Hepatitis B virus is associated with liver carcinoma (CCRG, 2005).

The causes of childhood cancer are complex and probably multifactorial. Within the literature there are very few conclusive studies and it has been identified in many papers as an area which requires further investigation (Anderson, 2006).

1.7 SIDE EFFECTS OF TREATMENT WITH SPECIFIC REFERENCE TO THE ORAL SIDE EFFECTS.

The treatment of solid tumours usually involves surgery and chemotherapy and/or radiotherapy to the area affected. The aim of cancer therapy is obviously to destroy live but abnormal cells. Blood borne therapy will therefore, have an effect on all other living tissues and in particular rapidly dividing cells of the oral cavity.

Radiotherapy is used to destroy tumour cells that are reproducing at a rate higher than normal cells. Cell sensitivity to radiation depends on which part of the cell cycle they are at. The most susceptible cells are those in a state of increased mitotic activity in the cell cycle. The higher the dose of radiation the more cells are affected. The effects are cumulative and dependent on the dose. If the dose is high enough, the ameloblasts and odontoblasts will die regardless of the position of the cell cycle. This is the cause of tooth agenesis and arrested tooth development (Zarina and Nik-Hussein, 2005). Radiotherapy is targeted at a specific area of the body during cancer therapy. Away from the oral cavity, radiotherapy treatment does not cause effects within the oral cavity.

Chemotherapy also attempts to destroy tumour cells. It is toxic to actively proliferating cells by interfering with DNA synthesis and replication, RNA transcription and cytoplasmic transport mechanisms. Chemotherapeutic agents cause damage according to their dose and repetition of the agent. Odontoblasts and ameloblasts in susceptible phases of the cell cycle can be damaged easily. Cells in the non-proliferative stage should remain unaffected and continue to develop normally. This is different to radiotherapy where all cells in the path of the beam are destroyed. Chemotherapy is a systemic treatment and therefore the oral tissues are necessarily involved (Nasman et al., 1997, Zarina and Nik-Hussein, 2005).

Children are also often treated with adjunctive steroids. In the short term this can increase appetite, and therefore can cause more frequent acid attacks on the teeth. Long term steroids can reduce bone mineralization and may affect growth (Lai et al., 2000, Hoorweg-Nijman et al., 1999).

Oral side effects arise due to a direct effect of the chemotherapy drug on the oral mucosa and an indirect effect due to myelosuppression. Direct effects usually occur 7-14 days following therapy and indirect effects 12-14 days later and will commonly result in infection and haemorrhage (Chen et al., 2004). The oral mucosa is particularly susceptible due to the high cell turnover rate. Oral complications significantly affect the child's quality of life and when severe can interfere with treatment regimes or cause further complications such as septicaemia (Cheng et al., 2002).

Acute effects of chemotherapy include:

- Nausea.
- Vomiting.
- Malabsorption.
- Mucositis.
- Myelosuppression- thrombocytopenia, neutropenia, anaemia.
- Periodontal and soft tissue infections.
- Cytotoxic effects e.g. mucositis and reduced salivary gland function.
- Alopecia.
- Nutritional deficiencies.
- Neurological- trismus and jaw pain, weakness of the facial muscles. (Maguire and Welbury, 1996).

During cancer therapy children are often significantly unwell. A high calorie diet is usually required to maintain sufficient energy levels and to prevent significant weight loss (Doyle et al., 2006). These children are likely to receive a highly cariogenic diet during the time they are unwell. Frequent intakes of high calorie and sugary foods will be advocated increasing the number of daily acid attacks to the teeth, thus increasing

the caries risk (Cancer Research, 2007). Throughout this time the child will also be subject to many different medical investigations some of which are unpleasant. In the Birmingham Children's Hospital (BCH) unit children are given sweets and chocolates as a reward for cooperating with medical interventions thus increasing the caries risk further. A painful oral cavity may compromise the ability to provide adequate oral debridement. If plaque and debris are not removed there is increased risk of further ulceration, infection and dental caries (Kennedy and Diamond, 1997).

1.7.1 Xerostomia.

Chemotherapeutic drugs can alter the flow and composition of saliva. This is usually evident 7-10 days after chemotherapy (Chen et al., 2004). The effects result in taste disturbances, difficulty in chewing and swallowing, speech problems and oral discomfort, together with a significant effect on the patient's quality of life (UKCCSG and PONF, 2006). Patients experiencing xerostomia will also be at greater risk of oral infections such as candidosis and dental caries (UKCCSG and PONF, 2006, Epstein and Chow, 1999).

1.7.2 Mucositis.

This is inflammation and ulceration of the mucous membranes, and has been shown to occur in 30-75% of patients undergoing chemotherapy (Fulton et al., 2002, Dodd et al., 2000). Mucositis is known to be associated with a high morbidity and may often affect the patient's tolerance of treatment and therefore compromise their overall medical therapy. It can frequently result in hospital admission for fluid replacement and pain control and is known to increase the risk of septicaemia to up to four times that of a patient not suffering from mucositis (Cheng et al., 2002). Mucositis may also predispose the individual to other oral infections leading to systemic infections (UKCCSG and PONF, 2006, Dodd et al., 2000).

1.7.3 Fungal infection.

Oral fungal infections are commonly caused by candida albicans. This is a commensal organism which can cause infections of the mouth particularly during periods of host immunosuppression. Mucositis, xerostomia and poor oral hygiene can all contribute to the patient's risk of developing candidosis. The plaques present commonly on the buccal mucosa, dorsal tongue and palate. They are creamy white patches which are easily wiped off leaving an erythematous, eroded or ulcerated surface. The plaques can increase in number and size and may lead to further systemic infection (UKCCSG and PONF, 2006, Alberth et al., 2006).

1.7.4 Herpes simplex virus.

During cancer therapy, especially when immunocompromised, children may be more susceptible to infection with human herpes simplex virus (Ramphal et al., 2007). This can range from a cold sore type lesion to primary herpetic gingivostomatitis. There is a risk it can spread and develop into a systemic infection or that the vesicles become secondarily infected with bacteria (UKCCSG and PONF, 2006).

1.7.5 Long term effects.

1.7.5.1 Dental caries.

Radiation to the jaws is known to produce xerostomia and therefore render the individual more prone to caries (Franzel et al., 2006). The effects of chemotherapy regarding dental caries are largely unknown. Teeth could be more prone to decay as sweets are often given as rewards and diet and nutrition is more varied during treatment. There are several reports in the literature comparing the level of dental decay in patients who have received chemotherapy. Nunn et al (1991) looked at 52 children in remission from cancer and their siblings and found no difference in the level of decay between those who had experienced chemotherapy and their siblings in primary and secondary dentitions (Nunn et al., 1991). Alpaslan et al (1999) studied the dental disturbances of 30 survivors of childhood lymphoma and compared them

to 20 controls and also found no significant difference between the control and study group (Alpaslan et al., 1999). Maguire et al (1987) investigated 52 children and their siblings and found no difference in the level of dental decay between the 2 groups (Maguire et al., 1987). However a study concerning 52 children who had been treated for neuroblastoma found the primary dentition showed a greater caries rate than the national average but this was not the case for permanent teeth where caries prevalence was found to be the same as the general population. The patients with dental caries were found to have excessive carbohydrate intake and poor oral hygiene levels (Kaste et al., 1998). The largest amount of caries noted was in the Purdell-Lewis study (1988) where they found the study group had three times as many carious lesions as the control group (Purdell-Lewis et al., 1988). The studies described above utilising a control group used the same criteria for the examination of caries in the study group and control group allowing comparisons within the study (Maguire et al., 1987, Purdell-Lewis et al., 1988, Nunn et al., 1991, Alpaslan et al., 1999). However Kaste et al (1998) though referencing the index for caries used does not mention if this is the same index as used in the epidemiological data she draws comparison with (Kaste et al., 1998). Contrasts between studies are therefore difficult to draw as the same indices for caries diagnosis are not consistently used throughout the literature.

1.7.5.2 Gingival health.

In several studies no significant difference was found in the gingival health between the study group and the control groups (Alpaslan et al., 1999, Nunn et al., 1991, Maguire et al., 1987). Nunn et al (1991), Maguire et al (1987) and Alpaslan et al (1999) all used the Löe gingival index in their assessments to assess the gingival condition. This index records qualitative changes in the gingival soft tissue only and does not consider any periodontal changes (Loe, 1967). Maguire et al (1987) found no significant difference between the control and study group for gingival health but did find in both groups there was a significant correlation of gingivitis with age. The lowest scores being in the younger ages of both groups (Maguire et al., 1987).

1.7.5.3 Enamel hypoplasia and discolourations.

The prevalence of enamel hypoplasia and discolourations between control and study groups for those patients who had survived malignant disease was found to be increased in all studies but the significance of this varied. Alpaslan et al (1999) studied 30 children and found enamel hypoplasia's in 64 teeth in 14 patients and discolorations in 147 teeth in 17 patients. In the control group of 20 healthy volunteers 5 teeth in 3 volunteers exhibited enamel hypoplasia's and 4 teeth in 1 volunteer exhibited discolouration. The prevalence of enamel hypoplasia's and discolouration was significantly different between groups. In the report of the study it states the teeth were dried and enamel defects and discolourations were recorded. There is no indication of criteria used therefore making direct comparisons of this study with other studies unreliable (Alpaslan et al., 1999). Maguire et al (1987) and Nunn et al (1991) both used the Murray and Shaw method (Murray and Shaw, 1979) making direct comparisons between studies possible. The index consists of scores 1-7 and examines the occlusal, buccal and lingual surface of each tooth (Loe, 1967). Maguire et al (1987) found a higher prevalence of enamel opacities and hypoplasia in the study group but only in the maxillary teeth. The control group showed milder degrees of enamel opacities with the study group showing more horizontal lines and hypoplasia (Maguire et al., 1987). Nunn et al (1991) found more children in the study group had enamel opacities and hypoplasia but the overall difference between the study group and control (siblings) group was not significant. (Nunn et al., 1991).

1.7.5.4 Crown and root malformations.

Many studies have shown evidence of taurodontism, microdontia, thin roots and root constrictions (Nunn et al., 1991, Alpaslan et al., 1999, Maguire et al., 1987, Kaste et al., 1998). Maguire et al (1987) reported that in all cases where the radiographic findings showed failure of root development this could be attributed to a time when the child was receiving medical treatment for a malignancy. They found that treatment given during the first 3.5 years of life was most likely to affect the dental lamina and crown formation thus resulting in a small tooth (Maguire et al., 1987). Nunn et al (1991) found 16% of their study population to have thin roots (Nunn et al.,

1991). Alpaslan et al (1999) found there to have been root malformations on 23 teeth in 9 children out of a study group of 30 children, but found no microdontia or crown malformations. There was some evidence of premature apexification and therefore short roots, but this was not a significant difference (Alpaslan et al., 1999). Kaste et al (1998) found 71% of the study group of 52 patients had radiographic dental abnormalities, which included small roots, small teeth and hypoplasia (Kaste et al., 1998). A study looking at the effects of chemotherapy in Wilm's tumour patients also found 77% to have experienced dental anomalies comprising microdontia, excessive caries, root stunting, hypodontia and hypoplasia (Marec-Berard et al., 2005). Nasman et al (1997) found in their chemotherapy group there was a reduction in the mean root area of all teeth except the canines; the crown areas however did not seem to be affected (Nasman et al., 1997). Purdell-Lewis et al (1988) commented that the findings of different surveys cannot be compared due to different criteria used in diagnosing anomalies radiographically and the different ages of patients (Purdell-Lewis et al., 1988), a common problem seen throughout the available literature. Despite this there is general agreement in the literature that chemotherapy can have an effect on the crown and root malformation of teeth.

1.7.5.5 Unerupted teeth.

Purdell-Lewis et al (1988) found in a study of 45 children who had received chemotherapy for malignancies, that the test patients had fewer erupted teeth than the control group. At aged 7 years they had an average of 4 fewer teeth and by age 11 years they had 7 fewer teeth. The control in this paper was the national epidemiological studies of 2 towns in the Netherlands (n=300) using the same indices (Purdell-Lewis et al., 1988). Alpaslan et al (1999) reported that differences between study and control groups for unerupted teeth were not statistically significant but they did not explain the criteria used to define an unerupted tooth. Because the age range was 4-15 years and in many patients one would expect a number of unerupted teeth to be present anyway (Alpaslan et al., 1999).

1.7.5.6 Hypodontia.

Alpaslan et al (1999) again showed evidence in their study group that more children had missing teeth when compared with the controls; 48 teeth were missing in 12 children but, 38 of these were wisdom teeth and it was unclear in this study whether the younger children in whom one would not expect to see wisdom teeth were included or not (Alpaslan et al., 1999). Nunn et al (1991) found no difference in the two groups for hypodontia or supernumerary teeth (Nunn et al., 1991).

1.7.5.7 Dental trauma.

Patients treated for a childhood solid tumour are likely to have experienced several operations under general anaesthetic. As this will involve an intubation the patient may be at an increased risk of dental trauma. Previous studies have stated that dental trauma is a known complication of intubation and the most common cause of litigation against anaesthesiologists (Hoffmann et al., 2005, Givol et al., 2004, Owen and Waddell-Smith, 2000). The incidence of dental trauma has not been investigated before in relation to childhood cancer survivors.

1.7.5.8 Craniofacial growth.

Some studies reported disturbances in craniofacial growth and others did not. Alpaslan et al (1999) reported no differences in the study group and Michigan normal values for craniofacial growth (Alpaslan et al., 1999). Mouth opening and occlusion was also examined by Maguire et al (1987) who found no differences between the control and study groups (Maguire et al., 1987). Sonis et al (1990) identified study groups 1 and 2 (who had received chemotherapy only), to have no significant differences in mean cephalometric values compared with normal values (Sonis et al., 1990). Karsila-Tenovuo et al (2001) looked at disturbances in craniofacial morphology in children treated for solid tumours and concluded most deviations in craniofacial structures were in children treated for combined chemo and radio therapy and these differences were in the vertical plane. This is thought to be due to a reduction in cartilage mediated growth. Frequently however they were not clinically significant thus not requiring correction, or indeed statistically significant in nature (Karsila-Tenovuo et al., 2001).

1.7.6 Histology.

Maguire et al studied a group of 52 children. On examination 3 children from the study group required the removal of teeth, these teeth were subsequently histologically analysed. There was an increased prominence of incremental lines correlating with periods of intravenous therapy seen in ground tooth section. In 2 cases, the chemotherapy included a combination of drugs but the third utilised vincristine alone. The lines indicate a disturbance in dentinogenesis (Maguire et al., 1987). Vincristine had been shown to cause incremental lines in rat incisors previously (Stene and Koppang, 1976).

1.7.7 Summary of previous literature.

Summarised below in table 1.4 are the main findings from the main studies in the available literature investigating the effects on the dentition following malignant disease.

Table 1.4 Previous studies investigating the effects of cancer therapy on the developing dentition.

Authors, year + country	Study group + Disease type	Control group	Main findings
Alpaslan et al. 1999. Turkey.	30 children 4-15 years old with Hodgkins or non- Hodgkins disease.	20 healthy children 4-15 years.	Significant differences ($p < 0.5$) in the prevalence of enamel hypoplasias, discolourations and agenesis in the study group. Increased level of plaque in the study group. No differences for gingival index, dental caries, craniofacial growth and microdontia,

Authors, year + country	Study group + Disease type	Control group	Main findings
Kaste et al. 1998 America. (Memphis).	52 children 1.9- 19.3 years old with a neurolastoma.	Normal population but no details of methods.	Increase in dental abnormalities (71% with an abnormality). Including microdontia, caries of the primary dentition, hypodontia, root stunting and enamel hypoplasia.
Maguire et al. 1987. UK (Newcastle).	52 children 3-22 years old. 27 leukaemia, 25 solid tumours.	49 siblings ages 2-23 years.	Increased opacities and hypoplasia in the study group. Large number of radiographic abnormalities in the study group including failed root development, microdontia, hypoplasia and missing teeth. No significant differences in dental caries, gingivitis and oral hygiene, and mouth opening.
Nunn et al. 1991. UK. (Newcastle).	52 children 4.75-24.25 years. Childhood cancer (breakdown not specified).	41 siblings ages 3.4- 20.8 years.	Statistically significant radiographic evidence of enamel hypoplasia, taurodontism, microdontia, thin roots and root constrictions. Increased level of enamel opacities, enamel hypoplasia but not statistically significant. No significant differences in dental caries, and gingival health.
Purdell-Lewis et al. 1988. Netherlands.	45 children 7-13 years. Leukaemia and solid tumours.	National data.	Higher prevalence of dental caries and enamel opacities. Radiographic evidence of delayed tooth malformation, shortened malformed roots and smaller crown size. No difference in oral hygiene.

1.7.8 Overall conclusions.

The literature documenting the oral effects of cancer therapy is very variable and lacks consistency. The population being studied is small the amount of potential inconsistencies is high. The few studies that have investigated the oral effects of cancer therapy have been carried out over the past 20 years during which time there have been many changes and advances in medical technology. For example level of caries in the developed countries has fallen (Ferro et al., 2007, Hugoson et al., 2008, Downer et al., 2005), there have been advancements in medications and standardisation of cancer therapy protocols (CCLG, 2007a). The use of different indices between studies makes standards change between studies and therefore direct comparisons are often difficult to draw. The level of obvious decay is reported in some cases to be above the level in the general population whereas others show the caries level to be similar. Reports of the longer term effects on the teeth also vary. A number of studies however show consistent evidence of dental anomalies particularly hypoplasia, opacities, short thin roots and microdontia. With this level of information it is not possible to give consistent advice to parents/guardians and their families as to what oral events to expect or what to report following cancer therapy.

1.8 TREATMENT REGIMES FOR SOLID TUMOURS.

There are four main treatment modalities for childhood solid tumours. These are surgery, chemotherapy, radiotherapy and active observation.

Surgery is used to make the diagnosis, and may be curative itself if an excision biopsy is performed. An example would be orchidectomy for a stage I yolk sac tumour of the testicle. Definitive surgery to remove all, or the bulk of the tumour usually takes place after chemotherapy to reduce the bulk of the tumour.

Cytotoxic chemotherapy is a key component of treatment in many cases of childhood malignancy. It is usually used to shrink the primary tumour prior to surgery unless the tumour has been completely removed at diagnosis and has no features suggesting that it has spread. In the case of the non-Hodgkin's lymphomas chemotherapy alone may be curative without other treatment modalities. It is also usual to give chemotherapy after surgery. Chemotherapy may either clear metastatic tumour or make it small enough for surgery or radiotherapy to be considered.

Radiotherapy is used in a number of childhood solid tumours, particularly the Ewing's Sarcoma family of tumours (also known as peripheral primitive neuroectodermal tumours, or PNETs), rhabdomyosarcomas, neuroblastomas and Wilm's tumours. Radiotherapy is the use of beams of ionising radiation directed at sites of residual tumour visible on imaging such as a magnetic resonance scan, or directed at the tumour bed where there may be microscopic residual disease. Radiotherapy is given to precise anatomical areas and unless the oral cavity was involved in the radiation field there would be no effect on dental development.

The effects of radiotherapy on the oral cavity when in the primary radiation field are well documented in the literature. Radiotherapy will cause malformation and developmental arrest of the growing tooth germs, damage to the salivary glands with subsequent hyposalivation leading to radiation induced caries, trismus and the risk of developing osteoradionecrosis. (Guggenheimer et al., 1975, Vissink et al., 2003).

Some tumours may either remain stable in size or spontaneously reduce in size without any treatment. The most common solid tumour where this may happen is stage 4S neuroblastoma occurring in babies less than one year of age. In such cases 'treatment' may simply be active observation (Pinkerton et al., 2004).

More than 80% of children treated with solid tumours will require some form of cytotoxic chemotherapy. Children are treated according to the clinical trials and guidelines produced by the Children's Cancer and Leukaemia Group (CCLG). This was formed in January 2007 by the merger of the United Kingdom Children's Cancer Study Group and the Medical Research Council Childhood Leukaemia Working Party. Some of the clinical trials are international, but within the UK will be administered by the CCLG (CCLG, 2007b).

Treatment is given with combinations of cytotoxic drugs which have shown synergistic effects against the various tumour types. Conventional chemotherapy is usually given at intervals of 21 to 28 days to allow haematological recovery in between courses. Some regimes are more intense. For example children with high-risk neuroblastoma receive eight courses of chemotherapy given at 10 day intervals even if there is marrow suppression from the previous course of chemotherapy. Haematological toxicity in the form of low platelets and neutrophils is the usual dose limiting toxicity that prevents higher doses of chemotherapy being given. Episodes of fever in association with neutropenia are common after chemotherapy for childhood solid tumours. Less common, but potentially life-threatening, are episodes of septicaemia. The oral and gastrointestinal tract mucosa may be damaged directly by chemotherapy or secondarily infected by opportunistic organisms in the presence of neutropenia. Some chemotherapy drugs may be more likely to cause mucositis affecting the oral cavity. This particularly includes anthracyclines and high-dose methotrexate (Pinkerton et al., 2004).

High dose chemotherapy and autologous stem cell rescue is used for some solid tumours, particularly neuroblastoma. In this case the haematological dose limiting toxicity of chemotherapy is overcome by harvesting stem cells from the patient

(usually peripheral blood stem cells, occasionally bone marrow) and freezing and storing these. The patient is then given a high dose of chemotherapy that ablates the bone marrow and the stem cells are then reinfused intravenously. This is the same principle as a bone marrow transplant, but because the patient's own cells are used there is no risk of rejection of the cells. In UK practice over the past 20 years total body irradiation has not been used in patients with solid tumours undergoing autologous stem cell rescue, although it is used in patients who are having bone marrow transplants (Pinkerton et al., 2004).

Table 1.5 below shows the classes of cytotoxic drug in common use in the UK to treat solid tumours in children (Pinkerton et al., 2004, CCLG, 2007b).

Table 1.5

Drug	Notes regarding drug effects.
Alkylating agents	
Cyclophosphamide	Myelosuppressive and immunosuppressive.
Ifosphamide	Myelosuppressive and immunosuppressive. Some patients develop renal damage and in extreme cases hypophosphatemic rickets after prolonged treatment.
Chlorambucil	Myelosuppressive and immunosuppressive.
Melphalan	Myelosuppressive and immunosuppressive. Used in high dose in paediatric practice where it also causes mucositis and marrow ablation.
Busulphan	Myelosuppressive and immunosuppressive. Used in high-dose in combination with Melphalan where it causes mucositis and marrow ablation. May cause liver damage.

Platinum drugs	
Cisplatin	Some myelosuppression. Causes kidney and hearing damage. Patients may have permanently low serum magnesium due to a renal tubular leak.
Carboplatin	More myelosuppressive than cisplatin but effects on hearing and kidney function are less at conventional doses. May be used in high dose in combination with melphalan and etoposide to ablate bone marrow. Hearing and kidney damage more common in that setting especially if there is pre-existing damage.
Antimetabolites	
Methotrexate	In paediatric solid tumours methotrexate is usually used in high doses with folinic acid rescue. Mucositis is a very common side effect.
6-Mercaptopurine	Immunosuppressant. Affects bone marrow. Used for T-cell non-Hodgkin's lymphoma maintenance treatment as per treatment regimes for acute lymphoblastic leukaemia.
Cytosine arabinoside	Used in high doses in some non-Hodgkin's lymphomas. May cause mucositis.
Anthracyclines	
Doxorubicin	Principally used in sarcoma treatment as well as hepatoblastoma and Wilm's tumour. Also used in non-Hodgkin's lymphoma. Can cause mucositis and myelosuppression. Main late effect is cardiac damage which limits total exposure.

Epirubicin	Used up to 2004 for some cases of rhabdomyosarcoma. Causes less cardiac damage than doxorubicin, but does cause myelosuppression and mucositis.
Epipodophyllotoxins	
Etoposide	A topoisomerase II inhibitor used almost ubiquitously in childhood malignancy. Causes myelosuppression and in a small number of cases mucositis.
Vinca Alkaloids	
Vincristine	Relatively non myelotoxic and does not cause mucositis. Main dose limiting side effect is peripheral neuropathy or severe constipation.
Vinblastine	Slightly more myelosuppressive than vincristine, but no mucositis.
Other	
Actinomycin D	Antitumour antibiotic. Myelosuppressive and can cause acute liver damage. Not associated with mucositis.
Prednisolone	Steroid used in haematological malignancies where it has been shown to have a substantial anti-tumour effect.
Procarbazine	This is a cytostatic agent with weak monoamine oxidase inhibitor activity. The exact mechanism of action as an antimetabolic is not known. It is used in the treatment of Hodgkin's disease.

Alkylating agents (predominantly cyclophosphamide, ifosfamide and chlorambucil), platinum drugs (cisplatin and carboplatin) and anthracyclines (usually doxorubicin and epirubicin in this patient group) are the 3 main different chemotherapy groups used. The alkylating agents will cause profound bone marrow suppression and consequent neutropenia. Ifosfamide may cause renal tubular damage with leak of phosphate and in extreme cases hypophosphatemic rickets. Cisplatin may cause renal damage and leak of serum magnesium leading to chronic hypomagnesaemia. Carboplatin may have this effect to a lesser extent, but has more bone marrow toxicity. As well as causing bone marrow damage the anthracyclines may cause oral mucositis (Pinkerton et al., 2004).

Table 1.6 below gives an overview of current treatment, and for treatment regimes used in the UK over the past 14 years for the main groups of solid tumours affecting children (Pinkerton et al., 2004, CCLG, 2007b).

Table 1.6

Tumour	Notes regarding tumour management.
Renal tumours	
Wilm's tumour and clear cell sarcoma	<p>Usually diagnostic biopsy, pre-operative chemotherapy, surgery and then post operative chemotherapy stratified on the response to chemotherapy and extent of spread. Radiotherapy may be used to the lungs for pulmonary metastases or the renal bed if there was local spread.</p> <p>Treatment duration 8 weeks to 6 months depending on stage of disease (up to 12 months prior to 2001). Usual chemotherapy vincristine and actinomycin with adriamycin for advanced cases. Carboplatin, etoposide and cyclophosphamide may be used for resistant cases (rare).</p>

Soft tissue sarcomas	
Rhabdomyosarcoma	Usually diagnostic biopsy, pre-operative chemotherapy, surgery and then post operative chemotherapy stratified on the response to chemotherapy and extent of spread. Radiotherapy may be used to tumour bed if there is microscopic residual disease. Usual chemotherapy agents are ifosphamide, vincristine and actinomycin and sometimes adriamycin. Between 1995 and 2004 more advanced cases may also have received carboplatin, etoposide and epirubicin. Usual treatment duration 18 weeks to 30 weeks. HDCSCR used in a small number of more advanced cases.
PNET	See Ewing's sarcoma under bone tumours below.
Other soft tissue sarcomas	Management as per rhabdomyosarcoma. Tend to be more resistant to chemotherapy and local control may be more important. Usual chemotherapy agents ifosphamide, vincristine and actinomycin.
Lymphomas	
Hodgkin's Lymphoma	Usual management is with chemotherapy with radiotherapy in up to 20% as well. Treatment lasts from 8 weeks to 6 months. Chemotherapy has varied over time but usually includes vincristine or vinblastine, prednisolone, chlorambucil or cyclophosphamide, procarbazine, etoposide, adriamycin and in the past bleomycin. In case of recurrence high-dose chemotherapy and peripheral blood stem cell rescue may be used.

T-cell Non-Hodgkin's Lymphoma	Management is almost identical to acute lymphoblastic leukaemia (common and T-cell) with an intensive induction period over 6 months including anthracyclines and high-dose methotrexate followed by 18 months of maintenance chemotherapy.
B-cell Non-Hodgkin's Lymphoma / leukaemia	Management is with short pulses of intensive chemotherapy for up to 8 months. Treatment includes alkylating agents, anthracyclines and high-dose cytarabine and high-dose methotrexate. Highly myelosuppressive and associated with a lot of mucositis.
Anaplastic Large Cell lymphoma	Management similar to B-cell NHL.
Neuroblastoma	
High risk	Any tumour with amplification of the MYC-N oncogene, or stage III or IV disease in a child over one year of age. Intensive induction with 8 courses of chemotherapy in 70 days including cisplatin, carboplatin, cyclophosphamide and etoposide. Then surgery. Then high-dose chemotherapy with peripheral blood stem cell rescue (Melphalan alone before 2002, busulphan and melphalan or melphalan, carboplatin and etoposide since 2002). Then radiotherapy. Then treatment with high-dose retinoic acid (since 1999).
Intermediate risk (including infants less than 1 year)	Conventional chemotherapy cycled every 21 days. Included anthracyclines, cyclophosphamide, vincristine carboplatin and etoposide.
Stage 4S	Observation only unless the disease is causing life-threatening complications. Usually then responds to one or two courses of simple chemotherapy.

Bone tumours	
Osteosarcoma	<p>Pre-operative chemotherapy. Surgery to remove the tumour (usually endoprosthesis replacement, occasionally amputation). Then further post-operative chemotherapy. Total duration 6 to 8 months.</p> <p>Chemotherapy before 2002 was cisplatin and doxorubicin. Since 2002 chemotherapy also includes high-dose methotrexate. Ifosfamide and etoposide are also used where there is a poor response to initial chemotherapy. Treatment is frequently associated with severe mucositis.</p>
Ewing's Sarcoma	<p>Intensive induction treatment every 21 days with ifosfamide, vincristine, etoposide and doxorubicin for 6 courses. Then surgery \pm radiotherapy for local tumour control. Then 8 further course of chemotherapy with vincristine, actinomycin D and either cyclophosphamide or ifosfamide.</p>
Germ Cell Tumours	
Various subtypes	<p>For those extracranial germ cell tumours requiring chemotherapy the usual treatment is a 4 to 6 month course of carboplatin, etoposide and bleomycin.</p>
Liver tumours	
Hepatoblastoma	<p>Pre-operative chemotherapy with cisplatin or cisplatin and adriamycin. Surgical resection then further chemotherapy. Usual treatment duration about 6 months.</p>
Others	<p>Other primary liver tumours are usually managed surgically.</p>

1.9 ORAL HEALTH EPIDEMIOLOGICAL SURVEYS (UK).

The British Society for the Study of Community Dentistry (BASCD) in conjunction with the National Health Service have been coordinating a series of epidemiological surveys of caries prevalence in the UK since 1985/1986. Each year a different age group are investigated for caries experience rotating among 5, 12 and 14-year-olds. A sample of at least 250 children are chosen for each district and examined (BASCD, 2007). In conjunction with these epidemiological studies the Child Dental Health Survey (CDHS) is also conducted every 10 years. This started in England and Wales in 1973 and included the whole of the UK from 1983 onwards. The survey provides information on the dental health of children in the UK (aged 5, 8, 12 and 15), measures changes in oral health compared to other surveys and provides information on children's experiences of dental care and their oral hygiene. The CDHS specifically investigates obvious decay experience, tooth surface loss (since 1993 only), enamel opacities (since 1993 and only in 12-year-olds), accidental damage, periodontal condition, hygiene behaviour and attitudes to oral health, patterns of care and service use, impact of oral health, orthodontic condition and social factors in relation to oral health. The data collection occurs by examining subjects and using a posted parental questionnaire (Pendry et al., 2004). Each study has strict criteria to follow to ensure consistency across the country and enable valid comparisons between studies.

1.9.1 Dental Caries

The BASCD and CDHS have similar criteria for examination and coding systems for the diagnosis of dental caries but with slight differences. For example both studies examine the child in a supine position with a daray light placed 1 meter above the subject however, the CDHS specifically uses a table whereas the BASCD survey uses either a table or reclining sun lounger. In the diagnosis of caries the codes are similar except the CDHS 2003 splits code 2 (caries) and 4 (caries and restoration) into 2 categories depending on whether the caries is visually cavitated or not. BASCD describes decay as caries into dentine after visual inspection and does not

distinguish between cavitated or uncavitated lesions (BASCD, 1997, Pendry et al., 2004).

1.9.2 Enamel Opacities.

Measurement of enamel opacities was introduced into the CDHS in 1993 and were measured using the Developmental Defects of Enamel (DDE) Index (Clarkson and O'Mullane, 1989). Opacities and hypoplasia's of teeth can occur as a result of a local or systemic upset during the development and calcification of the tooth (Pindborg, 1982). As chemotherapy is a systemic treatment it is important to consider any role it has in enamel defects. As the DDE index is not specific for fluorosis symmetry is also observed to allow an estimation of whether the enamel defects can be attributed to the level of fluoride ingestion by the individual (Chadwick et al., 2006).

1.10 RESEARCH TECHNIQUES.

1.10.1 Use of questionnaires.

Questionnaires are a simple way of collecting a significant amount of information. They have to be carefully designed to be clear and specific. Leading and presuming questions should be avoided (Reid and Boore, 1987). A closed question involves participants indicating a given answer from a list of possible responses. Closed questions are quicker to complete and easier to analyse (Williams et al., 2004). Visual analogue scales can be used and consist of a line 10cm long with a stop at both ends. At each end are words descriptive of the maximal and minimal extremes of the dimension being measured (Revill et al., 1976). It has been shown that respondent error rates can be reduced by employing a horizontal line as apposed to a vertical line and by not defining points on the line (McCormack et al., 1988). Open questions allow the respondent to decide what level of detail and how to structure the answer. These questions can be difficult to analyse due to the variation of replies (Reid and Boore, 1987). Questionnaires should have clear instructions on use and be easy to read. A pilot version should be carried out first then again if amendments were required (Williams et al., 2004).

1.11 OBJECTIVE, HYPOTHESES AND AIMS.

1.11.1 Objective.

The project addressed the complete oral health needs of children who have experienced a solid tumour during childhood, a subject which was identified as an area where more research was needed (NICE, 2005a).

1.11.2 Hypotheses.

- Individuals who have been treated for solid tumours during childhood will have more dental complications in comparison with the general population.
- Individuals who have been treated for solid tumours during childhood will require a greater dental input in comparison with the general population.
- The oral health needs of individual groups of solid tumour oncology patients will differ according to the type of tumour and therefore the type of treatment regime both during and after treatment.
- These patients will have difficulty accessing satisfactory dental care from a general dental practitioner.
- These patients will have limited knowledge of possible future oral health complications.

1.11.3 Aims.

- To identify any patterns of dental care needed in children with solid tumours.
- To investigate if oral health care needs differ according to the specific tumour diagnosis or treatment.
- To ascertain if these patients and their parents/guardians understand the need for dental input.
- To assess their current dental care arrangements.
- To explore the need for specialist dental input before, during and/or after medical treatment.

2.0. MATERIALS AND METHODS.

2.1 MATERIALS.

2.1.1 Dental examination (part A).

Equipment:

Chair- sun lounger as used by the BASCD epidemiological studies.

Light- Daray light as used by the BASCD epidemiological studies.

Dental mirror.

WHO 621 C-Type probe. Plastic disposable probes were used with a marked force indicator ensuring a constant force of 20-25 grams. There was a 0.5mm spherical tip.

Banding was present from 3.5-5.5mm, additional marks were at 8.5mm and 11.5mm.

Cotton wool rolls.

Dividers and ruler.

Data collection sheets

Sheet 1- General information sheet (appendix 1).

Sheet 2- Dental charting sheet, BPE and bleeding score (appendix 2).

Sheet 3- Enamel opacities recording sheet (appendix 3).

Information sheets and consent form.

Parental letter explaining the study (appendix 4).

Parents information sheet (appendix 5).

Patient age 16 + information sheet (appendix 6).

Patient age 13-15 information sheet (appendix 7).

Patient age 8-12 information sheet (appendix 8).

Patient age under 8 information sheet (appendix 9).

Consent form (appendix 10).

2.1.2 Questionnaire (part B).

Paper questionnaires were used for collection of data (see Appendix 11 for details).

2.2 METHODS.

The study took place over 8 months from July 2006-February 2007. Ethical approval was obtained from Dudley Primary Care Trust Research Ethics Committee (appendix 12). The research and development departments of both South Birmingham Primary Care Trust (appendix 13) and the Birmingham Children's Hospital NHS Trust (appendix 14) also approved the research protocol and gave permission for the research to be carried out. Funding was awarded by the Birmingham Children's Hospital Research Foundation. (appendix 15).

2.2.1 Training of the examiner.

The primary investigator (Alison Hutton) was trained in the dental examination of caries by Mrs Pears, Senior Dental Officer, Birmingham Community Dental service, using the criteria of caries diagnosis as described by the British Association for the Study of Community Dentistry (BASCD, 2005). The primary investigator also worked through the 2003 dental health survey of children and young people computer training programme as required by the national examiners in the 2003 Child Dental Health Survey. This guidance is similar to the BASCD requirements for dental caries and gives further guidance on examination of gingival health and enamel opacities.

2.2.2 Selection of the study group.

There was a large geographical distribution because Birmingham Children's Hospital is a regional cancer centre covering more than 10% of the population of England and Wales. All children who were due to attend the solid tumour follow up clinic at Birmingham Children's Hospital between July 2006 and March 2007 had their previous clinic letters reviewed by the primary investigator and the clinic co-ordinator. Any children who had finished treatment and had received a course of chemotherapy as part of their cancer therapy were invited to take part in the study. Patients with tumours of the central nervous system were usually reviewed in a different clinic, but

a few who attended on an *ad hoc* basis were invited to take part in the study. When they reached 16 years of age patients were transferred to a transitional clinic at BCH prior to moving to adult services at the age of 18. The transitional clinic was held on a different day, so again apart from a few patients attending on an *ad hoc* basis most of the patients seen in the solid tumour follow-up clinic were 16 years of age or younger. The only exclusions were those children who had received radiotherapy to the head and neck area specifically. Relapsed patients were included and the total time of chemotherapy exposure was used for the calculations.

The patients were invited by a letter (appendix 4) and information sheet sent in the post a week before their expected appointment time (appendix 5). Upon arriving at the follow up clinic it was confirmed that they wished to participate in the oral health study by the clinic co-ordinator. There was an opportunity for the parent/guardian to reread the information sheet if they wished to do so and the appropriate aged information leaflets were available for the patients if requested.

2.2.3 Patients personal details.

The following personal details were ascertained from the children and their parent/guardian participating in the study:

- Hospital number- initially this was taken from the clinician's clinic sheet and confirmed by the family.
- Date of birth.
- Gender.
- Postcode.

2.2.4 Patients medical details.

The following details were collected from the medical records and confirmed by the families during the dental examination:

- Cancer diagnosis.
- Date of diagnosis of cancer.
- Treatment regime.
- Length of time chemotherapy treatment received.
- Time since cancer therapy finished.

2.2.5 Informed consent for the study group.

Informed consent (appendix 10) was obtained from the parents/guardians on agreeing to participate in the study. This could be withdrawn at any time by the parent or child without explanation throughout the study period. The informed consent process involved an explanatory letter through the post followed by the opportunity to ask further questions with any member of the research team (doctor, investigator, clinic co-ordinator and nurses) at the follow up clinic. Written consent was then obtained from every parent/guardian and the child if they wished to sign before the examination was started.

2.2.6 Control group.

Due to difficulties gaining access to schools and the request at the time of the study for positive consent, accessing a healthy age and sex matched population was not possible. The control used for this study was national data available in the public domain. This included the Child Dental Health Survey 2003 (CDHS) and the British Association for the Study of Community Dentistry (BASCD) epidemiological studies.

2.2.7 Dental examination (part A).

A dental charting, any enamel opacities, fissure sealed, microdont or traumatised teeth were recorded on specific data collection sheets. A basic periodontal examination and gingival bleeding score were recorded in patients with adult incisors and first molars providing they were fully erupted and there were no medical conditions predisposing them to infective endocarditis.

2.2.7.1 Pilot dental examination (part A).

After the first ten patients the results were reviewed by the investigator. Minor adjustments to the data collection forms were made to ease recording of information. These results were later included in the final analysis because the changes made were minimal.

2.2.8 Development of the questionnaire (part B).

A questionnaire was developed by the author for the parents/guardians to complete as the child was undergoing the oral assessment. The questionnaire involved closed ended questions of a tick box style to find out specific information, a visual analogue scale to give an indication of an opinion and an open ended question at the end, providing opportunity for comment. (appendix 12). Questions 2-5 were based on the CDHS questions to ascertain social class of the parents (O'Brien, 1994). Many of the questions had been taken from an internal audit regarding the provision of dental care for patients currently receiving cancer therapy which was previously carried out in the same unit by the primary investigator. Those questions had proven to be clear and easy for patients to understand.

2.2.8.1 Pilot questionnaire study (part B).

The questionnaire was initially piloted to 5 parents and the oncology patient support group members, any suggested modifications were made. It was then piloted on the first 10 patients recruited for the research and reviewed. These results were included in the final analysis as no further modifications were necessary.

2.2.9 Conduct of the study.

2.2.9.1 Location.

The study was carried out at Birmingham Children's Hospital in the oncology out patients department. The dental examination was performed in the oncology day case theatre which allowed adequate space for the patient and their accompanying adults.

2.2.9.2 Data protection.

Each subject was assigned their own case record folder (CRF) and code number therefore ensuring anonymity. Each CRF contained the general information sheet, data collection sheets and the questionnaire. The master codes and consent forms were locked in an office in the hospital to protect the patient's identity.

2.2.9.3 Study procedure.

When patients arrived at the clinic they were asked by the clinic co-ordinator if they wished to take part in the study. The families had previously received the letter through the post explaining the study and therefore had had time to think about whether they wished to take part. Both the parent/guardian and child were given the opportunity to ask any questions. On acceptance into the study patients were again given the opportunity to ask any questions and shown to the room where the research was being carried out. A consent form was completed by the parent/guardian. The child was also given the opportunity to sign the form if appropriate. If the child had permanent incisor teeth the dentist asked 'do you carry a medical card or has anyone ever advised you to pass on any information to a dentist?' This was the standard question used in the CDHS 2003 (Pendry et al.,

2004). This was then usually clarified to specifically ask if they suffered from a heart murmur, a heart condition or had received any heart surgery. The further clarification was used as many children do develop a heart murmur during therapy which later resolves. If the answer was yes then further clarification was sought from the medical notes to ascertain if antibiotic prophylaxis would be required. If it was thought antibiotic prophylaxis was required then the periodontal examination and gingival bleeding scores were not carried out for that patient. The questionnaire was then given to the parent/guardian to complete whilst the dental examination was being performed. Any queries about the questionnaire were therefore clarified as the form was being completed by the parent/guardian.

2.2.9.4 Dental examination.

Patients were asked to sit in the dental chair (sun lounger) which was then fully reclined bringing the patients into a supine position. Small children who could not sit alone were examined on their parents knee who were sitting in the sun lounger for the examination period. The Daray light was switched on and placed a metre above the mouth. These criteria are in accordance with the BASCD specifications for having a dental examination carried out (BASCD, 1997). The sun lounger was the same one that is used for the epidemiological studies for the West Midlands. The investigator used a chair without wheels to sit on behind the patients. The CDHS 2003 followed similar criteria except a flat table was used for the patient to lie on for the dental examination (Pendry et al., 2004).

The mouth was examined visually using only using a mouth mirror. A probe was used only to remove any debris on the surface of the tooth which impaired a direct view of the tooth. Each tooth and individual tooth surfaces were examined in a standard order (upper left, upper right, lower left, lower right, distal, occlusal, mesial, buccal and lingual) The teeth were not brushed beforehand. A tooth was deemed to be present if any part of it was observed. Surfaces that could not be fully examined, for example those with orthodontic bands, were recorded as “excluded” (Pendry et al., 2004, BASCD, 1997).

Decayed, missing, and filled teeth and surfaces were recorded on a dental examination chart. Orthodontic extractions were not included in the missing tooth data. The coding used was as follows:

0= sound
1= arrested caries
2= decayed
3= unrestorable
4= filled and decayed
5= filled with no decay
R= filled but needs replacing
6= extracted due to caries
7= extracted due to orthodontic reasons
8= unerupted
9= excluded
\$- sealant
N= sealant restoration
T= traumatised
C= crown/ advanced restoration
(BASCD, 1997)

Any obviously microdont teeth (in the primary investigators clinical opinion) were also recorded. A specific criteria was not used for this as there were none available but to be observed as microdont the teeth were at least under 50% of the expected size.

The basic periodontal examination (BPE) was carried out using a world health organisation 621 probe in children with all central incisors and first molar teeth who had not answered yes to the question regarding potential antibiotic prophylaxis. Scores of 0= healthy, 1= bleeding on probing, 2= calculus/possible restoration margin, 3= shallow pockets 4-5mm and 4= deeper pockets >5.5mm were used. All teeth were examined by placing the probe in the distal part of the sulcus and running the probe around the margin to the mesial surface on the buccal and lingual sides of each tooth. Teeth recorded for the BPE were the four first molars and central incisors in each quadrant only. All teeth were then examined for any areas of bleeding on probing which was recorded site by site (distal, buccal, mesial, lingual) on the data sheets where code 0= no bleeding from the gingival sulcus, code 1= bleeding from the gingival sulcus and code 9= assessment cannot be made. This method of recording the data allowed further analysis in accordance with the 2003 CDHS

criteria for measuring gingivitis as they do for 15-year-old patients (Pendry et al., 2004).

A subject was recorded as having gingivitis if there was a single site or more on any tooth (mesial, distal, buccal, lingual) which bled on probing. Gingival bleeding is a marker of gingivitis as defined in the Child Dental Health Survey 2003. The Child Dental Health Survey recorded gingivitis (as bleeding on probing) in 15-year-olds only. The criteria used included 6 teeth; the first molars in each quadrant and the upper right central incisor and the lower left central incisor. The upper teeth were recorded by looking at the mesial, distal and buccal surfaces only and the lower teeth had the distal, mesial and lingual surfaces recorded only. If there was bleeding in any of the specified sites the subject was considered to have evidence of gingivitis (Pendry et al., 2004).

When recording enamel opacities, if the surfaces of the teeth were obscured with plaque this was wiped away using a cotton wool roll. The teeth were examined whilst the patient was still in the sun lounger with the light on. The teeth examined were the upper eight front teeth (4321|1234) The labial (incisors and canines) or buccal (pre molars) surfaces were examined only. The criteria and descriptions are as below:

- *Normal*: Any single defect less than 1mm was classed as normal.
- *Demarcated opacity*: A defect involving an alteration in the translucency of the enamel, variable in degree. The defective enamel is of normal thickness with a smooth surface. It has a distinct and clear boundary with adjacent normal enamel and can be white, cream, yellow or brown in colour.
- *Diffuse opacity*: A defect involving an alteration in the translucency of the enamel, variable in degree. The defective enamel is normal in thickness and at eruption has a smooth surface and is white. It can have linear, patchy or confluent distribution but there is no clear boundary with the adjacent normal enamel.

Lines: Distinctive white lines of opacity which follow the lines of development of the teeth. Confluent adjacent lines may occur.

- *Patchy*: Irregular, cloudy areas of opacity lacking well defined margins.
- *Confluent*: Diffuse patchiness has merged into a chalky white area extending from mesial to distal margins which can cover the entire surface or be confined to a localised area of the tooth surface.
- *Hypoplasia*: A defect involving the surface of the enamel and associated with a reduced localised thickness of enamel. It can occur in the form of (a) pits; single or multiple, shallow or deep, scattered or in rows of pits arranged horizontally across the tooth surface. (b) grooves; single or multiple, narrow or wide (max 2mm) or partial or complete absence of enamel over a considerable area of dentine. Enamel of reduced thickness may be translucent or opaque.

TYPE OF DEFECT:

- Code 0- normal
- Code 1- demarcated opacity
- Code 2- diffuse opacity
- Code 3- hypoplasia
- Code 4- demarcated+ diffuse
- Code 5- demarcated +hypoplasia
- Code 6- diffuse+ hypoplasia
- Code 7- all 3 defects
- Code 8- other defects
- Code 9- Assessment cannot be made

EXTENT OF DEFECT:

- Code 0- normal
- Code 1- less than 1/3
- Code 2- at least 1/3-2/3
- Code 3- at least 2/3
- Code 9- assessment cannot be made

If more than two thirds of the tooth was decayed or fractured it was not used for recording in accordance with the 2003 CDHS regulations for recording enamel opacities (Pendry et al., 2004).

SYMMETRY OF DIFFUSE DEFECTS:

Code-0= no diffuse defects

Code 1= diffuse defects but not symmetrical

Code 2= diffuse defects symmetrical

(Pendry et al., 2004).

2.2.9.5 Repeat examinations.

Due to the limited staff available at the time of data collection the results could not be verified by another examiner at that dental visit. By the nature of the 'follow up' clinic patients were only attending every 6 months or yearly and therefore the investigator was unable to examine the patients on another separate occasion to improve validity of the results.

2.2.9.6 Questionnaire completion.

The questionnaire was always completed by the parent/guardian whilst the child was undergoing the dental examination. Any queries that arose were answered by the investigator or dental nurse. Non English speaking parents/guardians were always accompanied by an interpreter. The interpreter was present for both the medical and dental appointments that day. The questionnaire was collected at the end of the examination and placed in the CRF with the other data sheets.

2.2.10 Investigator interventions.

If any subject was identified to have a need for dental treatment the investigator informed the subject and their parent/guardian. If the subject had a dentist, the dentist was informed of the treatment need and the subject asked to make an appointment with the dentist. If the child was not registered with a dentist they were offered treatment by the Birmingham Children's Hospital dental team or referred to their nearest community dental clinic. The opportunity was given to all patients and their families to discuss any aspect of the study or their dental examination further at the end of the appointment.

2.2.11 Review of the study.

After a period of one month the study was reviewed by all authors. Minor changes were made to the practicalities running of the research data collection procedures during the clinic. These did not affect the analysis of results.

2.2.12 Tabulation of the data.

The results were tabulated in Microsoft XP Excel spreadsheets. The data was entered twice on separate occasions and then compared and corrected for any discrepancies before data analysis began. Any inconsistencies were highlighted and checked with the original data sheets.

Once all the data had been collected, the details of which chemotherapeutic agents had been used for each subject were added to the identification code by the research supervisor. This was done blind of any results. The details were then added to the main data sheet according to their subject number.

2.2.13 Analysis of results.

Analysis of the study group as a whole was undertaken initially. Separate spread sheets were then created of individual groups for analysis. These included separate sheets for those who were 5,8,12 and 15 years old on the day of examination, the tumour groups according to diagnosis and the groups according to type of chemotherapy regime received. The data analysis was largely descriptive given the small sample size and huge number of variables. Where appropriate a chi squared test and the Fishers exact test were used to investigate the relationship between two specific aspects. The Excel programme was used for the calculations

2.2.13.1 Caries analysis.

The experience of dental experience was described using the decayed, missing and filled tooth index (DMFT) (Klein et al., 1938). The 'DMFT' index is used for the secondary (adult) dentition. The 'dmft' index is used for teeth in the primary (deciduous). A child who was in the mixed dentition would therefore have had two separate values for both the DMFT (adult) and dmft (deciduous).

2.2.13.2 Opacities analysis.

The ingestion of fluoride either by water fluoridation or fluoride tablets is known to be associated with an increased incidence of enamel opacities (Wong et al., 2006, Cochran et al., 2004, Tabari et al., 2000). Because many of the study population live in fluoridated areas of the country this was investigated further. Therefore in the analysis of the opacities data references are made to the water supply and if it is fluoridated or not. This was identified from the postcode. It should be remembered the effect of fluoride on the dentition occurs at an age when the tooth is forming and calcifying only (Hong et al., 2006). For the purposes of the study it was assumed that the patient had lived at that post code all their life because more in depth analysis was beyond the scope of this thesis. In analysis of the results this assumption should be considered.

2.2.13.3 Questionnaire analysis.

In analysis of the questionnaire where the visual analogue scale was used, any tick, cross or circling of the word very 'important' was considered to be 10cm on the visual analogue scale.

2.2.13.4 Social class information.

The National Statistics Socio-Economic Classification (NS-SEC) was introduced in 2001 to replace the previous Registrar General's Social Class and Socioeconomic Grouping (1980). The new classification was derived after concern about the previous classification system having conceptual and operational deficiencies. These were first raised and reviewed in 1994. The new model is based on a wide conceptual model also used by many other countries. It is a hierarchical system and can be collapsed into several variables for use in policy modelling and research. The NS-SEC system includes 3 tiers of coding described as the eight category, five category and three category versions. The "never worked" and "long term unemployed" classification group can be added or removed from each version depending on the particular analysis required. It is described as being more flexible and has specific rules for the inclusion of un-employed people, provides improved classifications for women's employment positions and reflects current thinking by not splitting work into manual and non manual. It has been tested and validated (Rose and O'Reilly, 1998).

The new classification has 8 main categories:

- 1= Higher managerial and professional.
- 2= Lower managerial and professional.
- 3= Intermediate occupations.
- 4= Small employers and own account workers.
- 5= Lower supervisory and technical occupations.
- 6= Semi-routine occupations.
- 7= Routine occupations.
- 8= Never worked and long term unemployed.

(ONS, 2005, Pendry et al., 2004).

The coding used in the Children's Dental Health Survey 2003 is the modified three class version as above linking 1+2 as managerial and professional, 3+4 as intermediate and 5+6+7 as routine and manual with separate "never worked" and "long term unemployed" categories (Pendry et al., 2004). The data was analysed using both the NS-SEC and Registrar General's coding system.

3.0 RESULTS AND ANALYSIS.

3.1 RESULTS AND ANALYSIS DENTAL EXAMINATION (PART A).

3.1.1 Demographics of the study group.

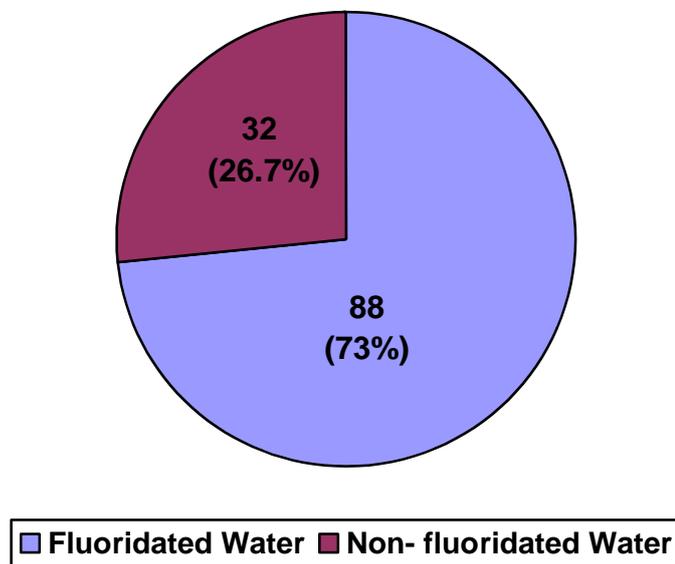
Out of the 125 patients who were invited to participate in the study 5 patients were not included. Of the 5 patients not participating 2 refused to consent, 1 family left before the examination forgetting to visit the dentist after their medical consultation, 1 could not co-operate for an examination due to behavioural difficulties and 1 had time constraints on the day preventing a dental examination. The study group therefore consisted of 120 patients (69 males and 51 females) attending the oncology follow up clinic between July 2006 and February 2007 at Birmingham Children's Hospital. All children selected had been previously diagnosed with a solid tumour and as part of their medical treatment had undergone a course of chemotherapy.

3.1.1.1 Geographic distribution of the study group.

Sixty six percent of the study patients were from the West Midlands (including Wolverhampton, Dudley, Walsall, Sandwell, City of Birmingham, Solihull, City of Coventry) and the remaining 34% from the surrounding areas (Warwickshire, Worcestershire, Staffordshire, Hertfordshire, Northamptonshire, Derbyshire, Shropshire, and Powys). All the above areas were supplied with water by either the Severn Trent Water Board or the South Staffordshire Water Board. The Severn Trent water is artificially fluoridated and the South Staffordshire water is not artificially fluoridated.

Figure 3.1

Number of patients living in an area with fluoridated water
n=120.



3.1.2 Composition of the study group.

3.1.2.1 The medical diagnosis of the group.

Table 3.1

Medical Diagnosis	Number (%)
Wilm's Tumour	29 (24.2)
Rhabdomyosarcoma	10 (8.3)
Hodgkin's Lymphoma	14 (11.7)
Non-Hodgkin's Lymphoma	10 (8.3)
Neuroblastoma	21 (17.5)
Other	36 (30.0)
Total	120

The other diagnoses were as follows (there being one of each diagnosis unless otherwise stated): hepatoblastoma (4), pineoblastoma, osteosarcoma (4), giant cell fibroblastoma, histiocytosis (2), Ewings sarcoma/ peripheral primitive neuroectodermal tumour (PNET), synovial sarcoma, Burkitt's lymphoma/leukaemia, germ cell tumour, fibrosarcoma, primitive neuroectodermal tumour, WAGR syndrome (Wilm's tumour, aniridia, genitourinary anomalies and mental retardation), retroperitoneal inflammatory myofibroblastic tumour, stage II sacrococcygeal yolk sac tumour, clear cell sarcoma (4), ganglioneuroblastoma (2), T-cell leukaemia and lymphoma, glioblastoma, optic chiasm glioma, hepatic sarcoma, medulloblastoma, synovial sarcoma, anaplastic large cell lymphoma, pleuropulmonary blastoma of hemi thorax.

3.1.2.2 The age of the study group at diagnosis and dental examination.

Figures 3.2 and 3.3 demonstrate the different ages of the study population at diagnosis of cancer and at the time of the dental examination. The diagnostic age group is positively skewed towards those below 5 years old. The age at examination is varied with peaks at 7, 13 and 15 years old.

Figure 3.2

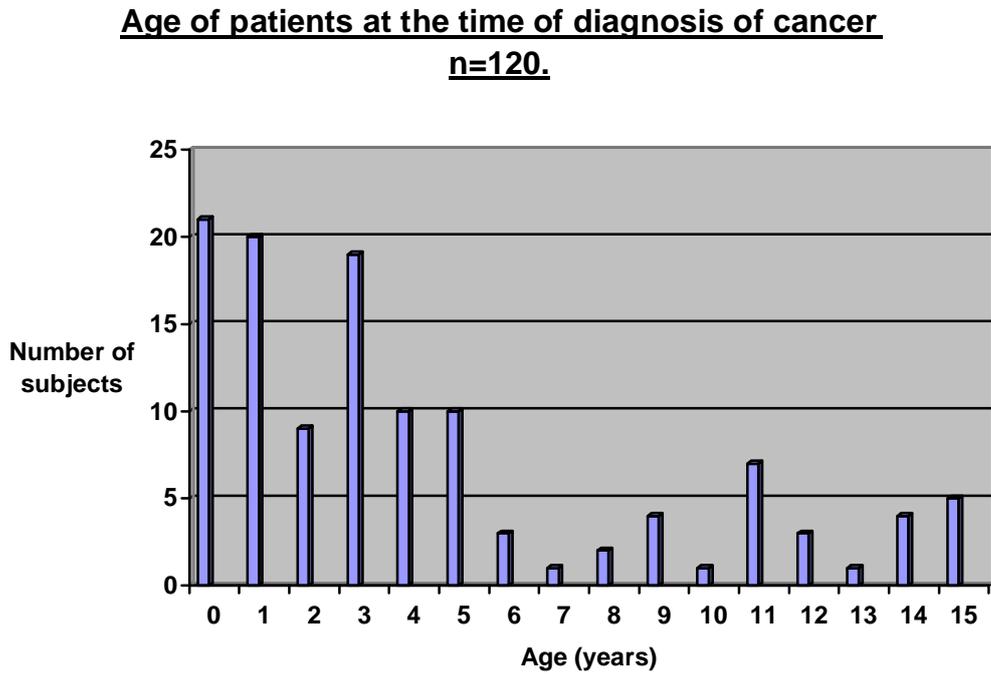
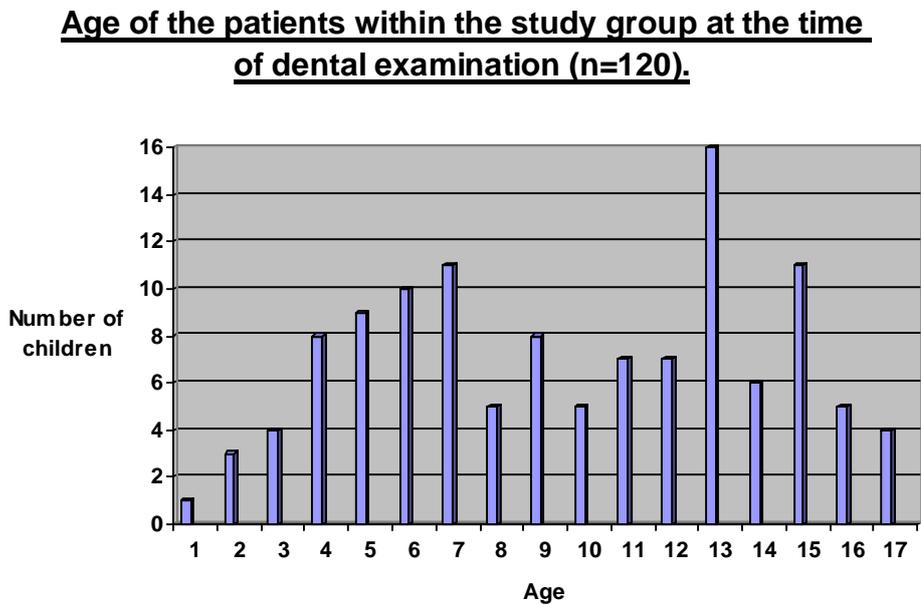


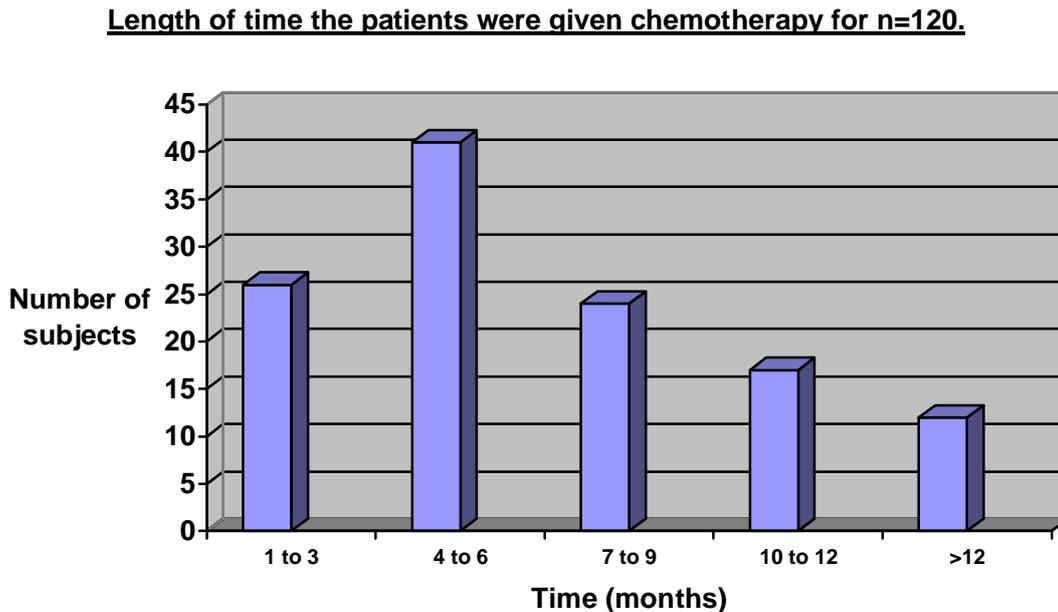
Figure 3.3



3.1.2.3 Treatment regime the patient had experienced.

All children must have experienced a course of chemotherapy to be included in the study. The length of time each child was subjected to chemotherapy varied within the study group. Figure 3.4 represents these different time periods.

Figure 3.4



The range in the length of time patients receive chemotherapy for was 1 month to 4.5 years, the mean was 8.19 months (S.D=7.39) the median was 6 months.

3.1.2.4 Type of chemotherapy received by the patient.

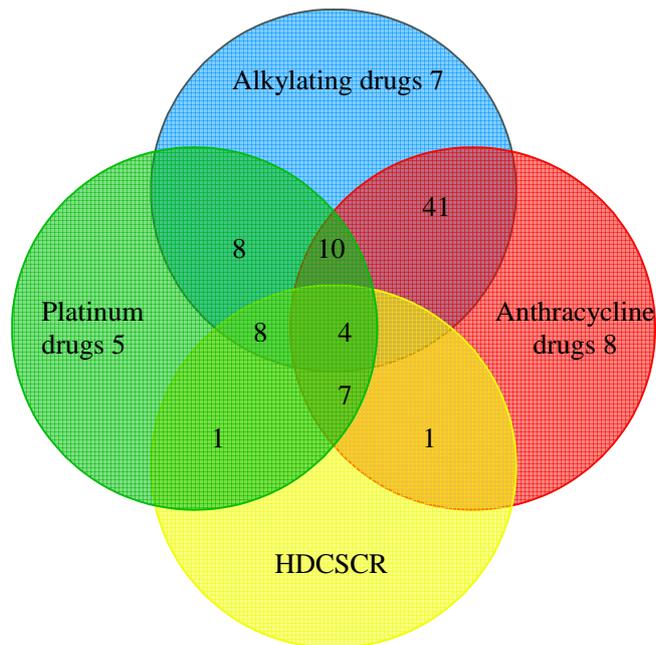
The study group received different forms and combinations of chemotherapy treatment. There were four main groups of agents used for the patients in the study.

These were:

- High dose chemotherapy with stem cell rescue (HDCSCR).
- Anthracycline drugs.
- Alkylating agents.
- Platinum drugs.

There were however, overlapping regimes as illustrated in the Venn diagram in figure 3.5.

Figure 3.5 Illustration of the different chemotherapy regimes within the study group.

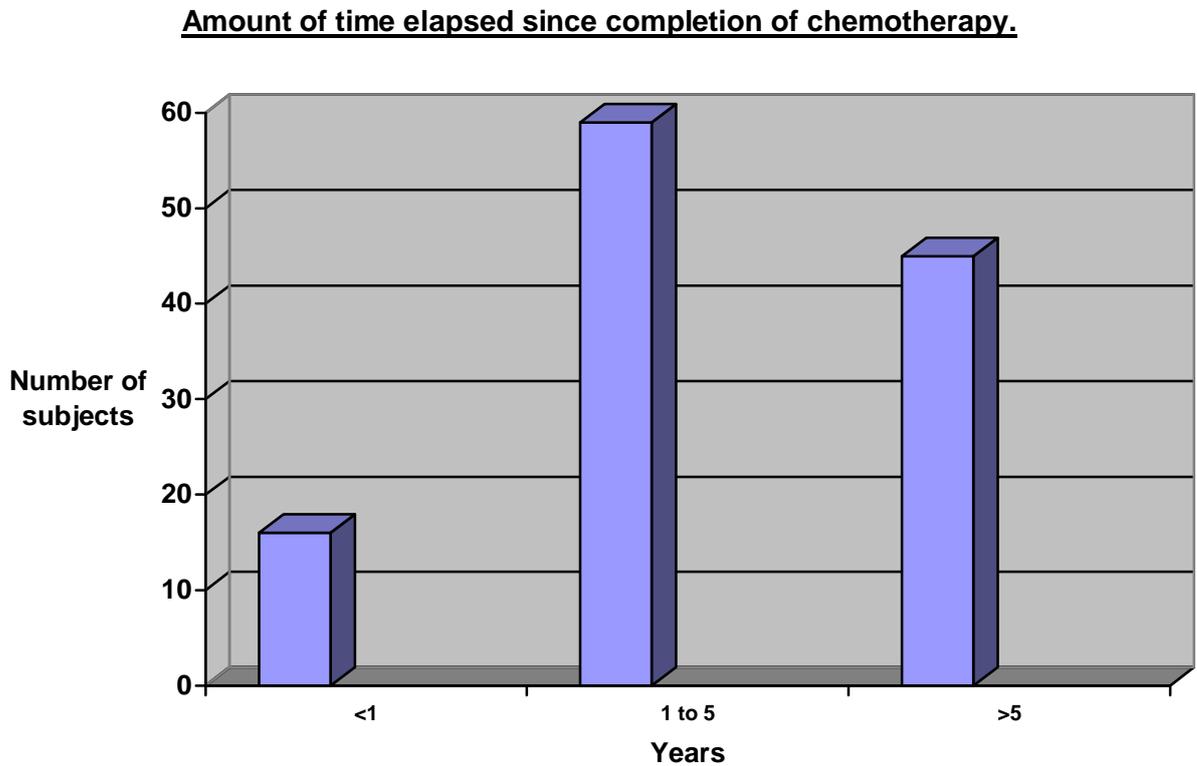


Given the multiple number of treatment regimes stratification into individual treatment groups was not possible because the therapeutic combinations were complex. The individuals not accounted for in the above diagram were given less toxic chemotherapeutic drug regimes.

3.1.2.5 Time since therapy.

The amount of time since the patients finished their active treatment and started attending the 'follow up' clinic was recorded and shown in figure 3.6. N=120, mean 51.97 (S.D 40.3) months.

Figure 3.6

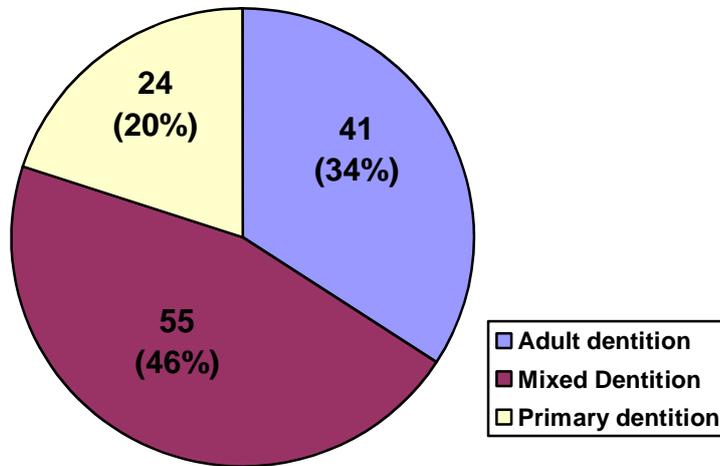


The follow up period varied from those who had recently finished chemotherapy treatment to those who had finished medical treatment 12-14 years previously. Those who had finished medical treatment more recently are monitored more frequently and therefore could account for the increased number of patients under the 5 year time period.

The study group was made up of children in the deciduous, mixed and adult dentition. Categories with the stages as illustrated in figure 3.7. Data were later grouped into age, medical diagnosis, and type of chemotherapy for further analysis.

Figure 3.7

Different dentitions of the study group n=120.



3.1.2.6 Composition of the sub-groups; post stratification.

The diagnostic and treatment groups are described below in tables 3.2-3.5.

Table 3.2. Number, gender and age of the diagnostic stratifications.

Group	Number of patients	Male/female	Mean age in years (age range).
Hodgkin's Lymphoma	14	13/1	12.9 (5-17)
Neuroblastoma	21	11/10	6.7 (1-15)
Non-Hodgkin's Lymphoma	10	8/2	12.5 (7-15)
Rhabdomyosarcoma	10	6/4	10.1 (4-15)
Wilm's tumour	29	15/14	7.8 (3-16)
Other	36	16/20	10.7 (1-17)

Table 3.3. Length of, and amount of time since, chemotherapy in the diagnostic groups.

Group	Mean time period of chemotherapy treatment in months (range).	Mean amount of time since completion of chemotherapy treatment in months (range).
Hodgkin's Lymphoma	6.2 (2-12)	40.1 (7-82)
Neuroblastoma	6.1 (1-18)	55.5 (8-177)
Non-Hodgkin's Lymphoma	6.8 (3-24)	67.1 (17-119)
Rhabdomyosarcoma	8.9 (3-24)	73.3 (29-151)
Wilm's tumour	7.8 (1-30)	58.1 (1-170)
Other	10.4 (1-54)	41.4 (1-130)

The smallest categories were the rhabdomyosarcoma and non-Hodgkin's lymphoma groups with the largest being the mixed tumour group. Data demonstrated a wide range of ages and treatment times within each group.

Table 3.4. Number, gender and age of the treatment stratification groups.

Group	Number of patients	Male/Female	Mean age in years (range)
HDCSCR	14	7/7	7.07 (1-15)
Alkylating agents and no HDCSCR	66	45/21	10.47 (1-17)
Anthracyclines and no HDCSCR	66	41/25	10.88 (3-17)
Platinum drugs and no HDCSCR	43	16/14	9.40 (2-17)

Table 3.5 Length of, and amount of time since completion of chemotherapy treatment in the treatment stratification groups.

Group	Mean time period of chemotherapy treatment in months (range)	Mean amount of time since completion of chemotherapy in months (range)
HDCSCR	6.04 (2.5-12)	58.93 (8-177)
Alkylating agents and no HDCSCR	8.35 (2-31)	46.45 (1-151)
Anthracyclines and no HDCSCR	8.96 (2-31)	48.88 (1-144)
Platinum drugs and no HDCSCR	8.52 (2-130)	49.47 (2-130)

3.1.3 Experience of dental caries.

The experience of dental caries was described using the codes as explained in the methodology. Overall 67 (55.8%) patients in the study population were caries free with the remaining 53 (44.2%) experiencing obvious decay at the time of the dental examination. Table 3.6 illustrates the mean DMFT, dmft of the study group indicating higher caries levels in the primary dentition.

Table 3.6 DMFT, dmft of the study population.

	Mean number of carious teeth +/- S.D.
DMFT	0.56 +/- 1.18
dmft	0.84 +/- 1.99

3.1.3.1 Results by direct comparison with the 2003 Child Dental Health Survey.

The 2003 Child Dental Health Survey investigated the caries experience of 5,8,12 and 15-year-olds. To allow direct comparisons the data for those age groups were analysed separately. It is important to remember the small sample sizes when interpreting the data and drawing conclusions from the data.

Figure 3.8 demonstrates the 8 year old study population has a higher dmft value by comparison with the CDHS 2003 (Pitts and Harker, 2005).

Figure 3.8

dmft values for patients who were 5 (n=9) and 8 years old (n=5) at the time of examination, within the study group by comparison with the 2003 Child Dental Health Survey (2003 CDHS) data.

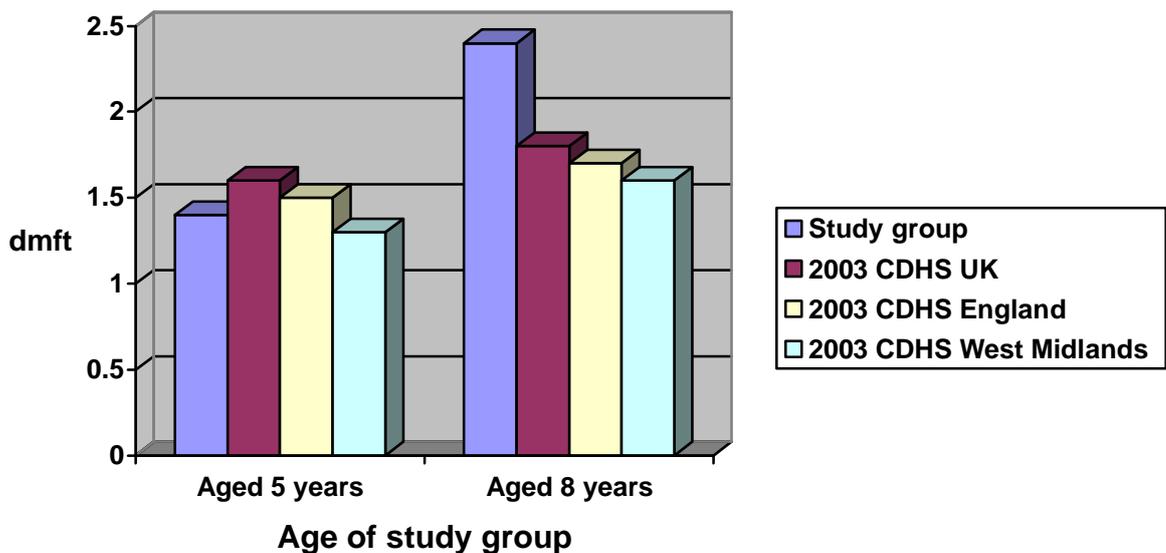


Table 3.7 compares the DMFT study data for 8,12 and 15-year-olds with the 2003 Child Dental Health Survey (Pitts and Harker, 2005).

Table 3.7 Comparison of DMFT values and percentage without any obvious caries experience for 8,12 and 15-year-olds with the study and national data (2003 CDHS) (Pitts and Harker, 2005).

	Obvious decay experience (mean no teeth)	Percentage without obvious caries experience (%)
8 yr study group (n=5)	0.2	80.0
8 yr UK 2003	0.3	86.0
8 yr England 2003	0.3	83.0
8 yr West Midlands 2003	0.3	83.0
12 yr study group (n=7)	0.3	85.7
12 yr UK 2003	1.1	66.0
12 yr England 2003	1.0	59.0
12 yr West Midlands 2003	0.9	61.0
15 yr study group (n=11)	2.0	72.7
15 yr UK 2003	2.0	51.0
15 yr England 2003	1.8	45.0
15 yr West Midlands 2003	1.9	47.0

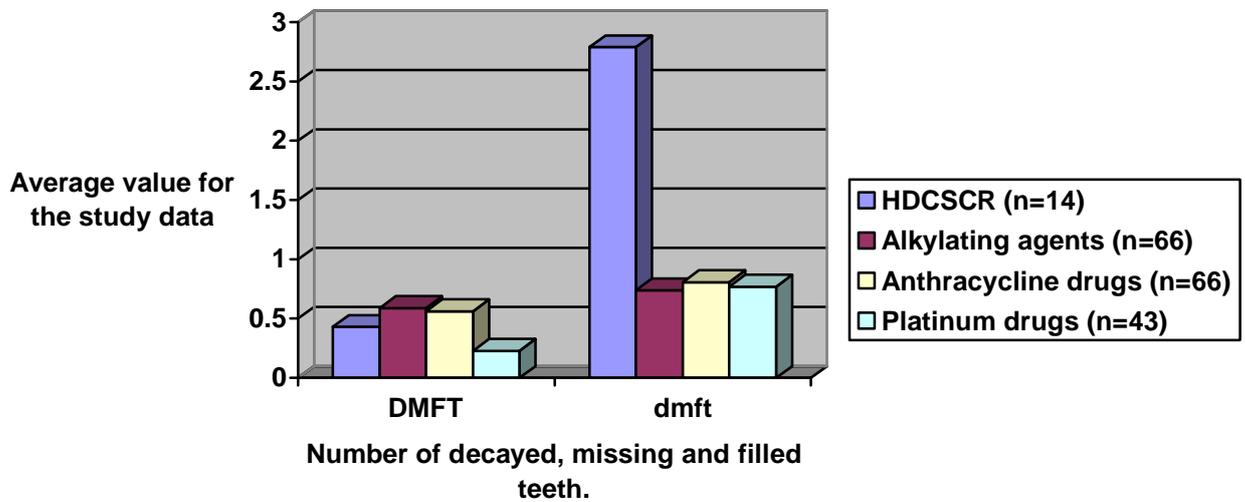
Despite there being low numbers in each group the figures show the only groups to be dissimilar to the Child Dental Health Survey group are the 8-year-old primary dentition data showing a higher dmft and the 12-year-old study group showing a lower DMFT. As the study groups are so small no definitive conclusions can be drawn.

3.1.3.2 Dental caries experience of treatment regime groups.

When the study data was stratified into medical chemotherapy treatment groups the results are represented in figure 3.9.

Figure 3.9

Average DMFT, dmft values for each treatment group within the study.



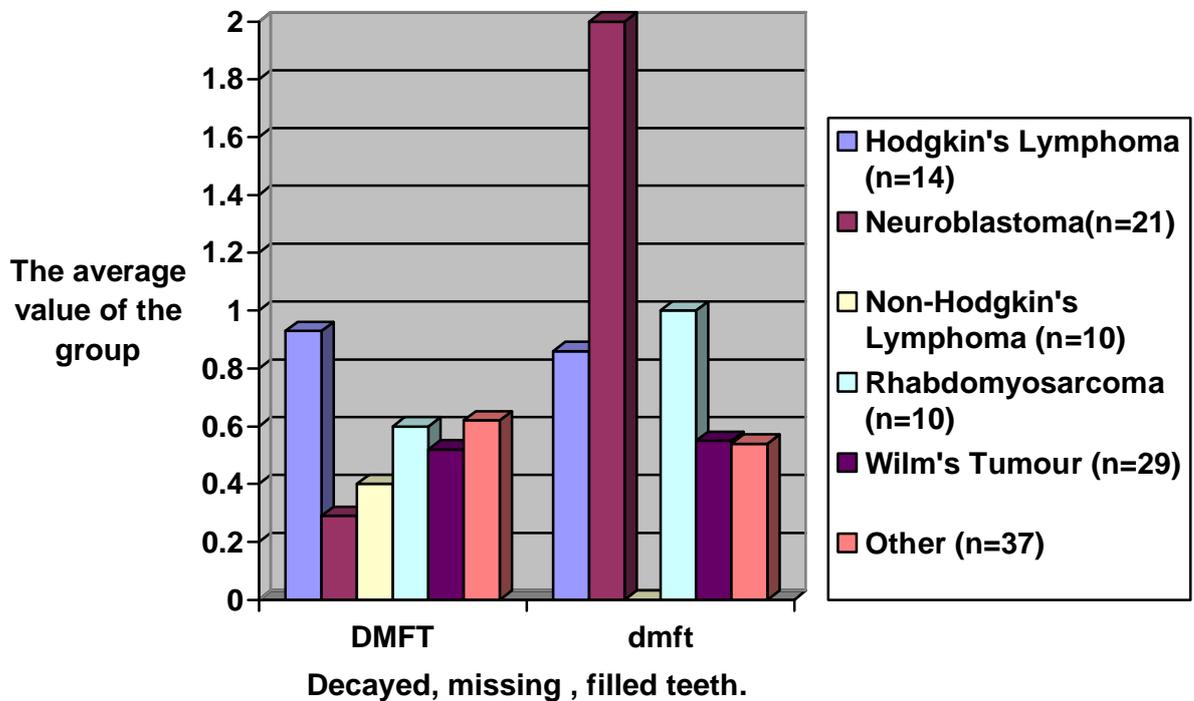
The high dose chemotherapy and stem cell rescue (HDCSCR) group demonstrated considerably higher dmft values by comparison with the other groups. This group comprised patients suffering mainly from neuroblastoma and were young at diagnosis. The DMFT values are similar between the different treatment groups.

3.1.3.3 Dental caries experience of the tumour diagnostic groups.

Figure 3.9 also illustrates differences in DMFT, dmft values within the different diagnostic groups.

Figure 3.10

DMFT, dmft values of the different diagnostic groups within the study.



The neuroblastoma group have the highest decay experience in the primary dentition, as shown by the number of teeth affected. The neuroblastoma group will have received more significant treatment as many are included in the HDCSCR treatment group (figure 3.9). The rhabdomyosarcoma group also show an increased level of decay experience in the primary dentition.

3.1.3.4 Summary of dental caries experience.

- 55.8% of the study group had no decay or treated decay present on examination.
- 42.2% of the study group had experienced decay in one or more teeth.
- 30.8% of the study group had untreated tooth decay in one or more teeth.
- 18.3% of the study group had untreated primary tooth decay in one or more teeth.
- 18.3% of the study group had untreated secondary tooth decay in one or more teeth.
- The neuroblastoma and HDCSCR group showed higher levels of primary dental caries by comparison with the other tumour diagnostic and treatment groups and the general population.

3.1.4 Enamel opacities.

Eighty patients had their dental enamel opacities recorded in the 8 upper anterior teeth (upper right 4,3,2,1 and upper left 4,3,2,1). Opacities were found in 50 (62.5%) patients from the study group.

Because not all patients had all 8 front teeth present at the time of examination, opacities were recorded in 145 teeth (27.9%) out of a possible 519 teeth which were erupted at the time of examination.

Figure 3.11 and 3.12 illustrates examples of “diffuse” and “demarcated” types of enamel opacities.

Figure 3.11 diffuse lesions on the central incisor teeth.

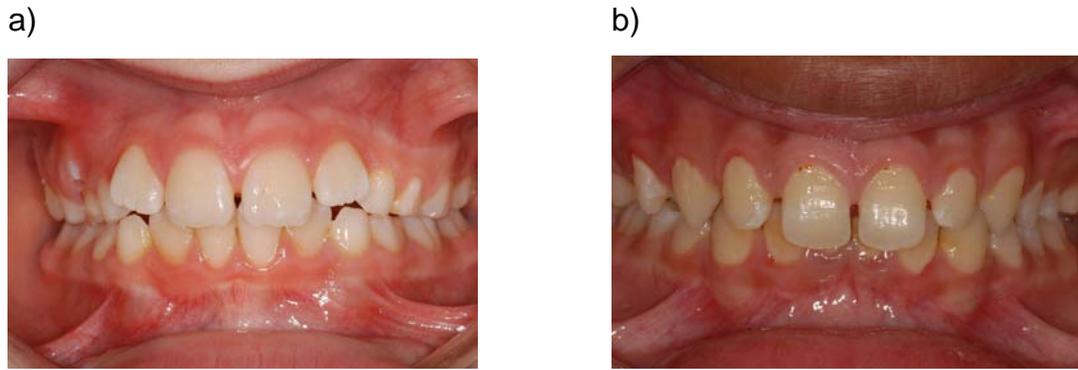
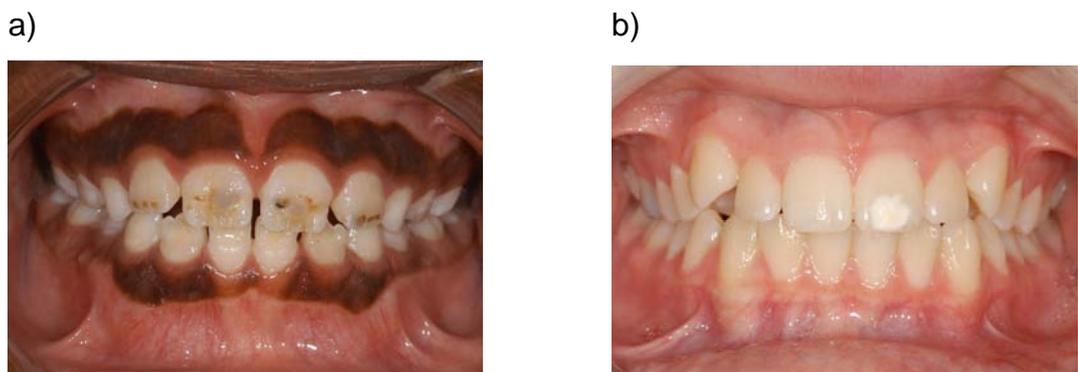


Figure 3.12 (a) A picture of demarcated lesions of the anterior teeth and (b) a demarcated lesion of the upper left central incisor.



The proportion of patients with opacities and the type of opacity within the study group are shown in table 3.8. It is worth noting some patients will have demonstrated more than one type of opacity on their front teeth.

Table 3.8 Proportion of patients with opacities and the type of opacity within the study group.

Opacity Code	Opacity type	Number of teeth with that code	Number of patients with that code (%) n=80
0	No opacity	372	50 (62.5)
1	Demarcated	16	12 (15.0)
2	Diffuse	120	42 (52.5)
3	Hypoplasia	0	0 (0.0)
4	Demarcated and diffuse	4	3 (3.8)
5	Demarcated and hypoplasia	3	3 (3.8)
8	Other defects	2	1 (1.3)
9	No assessment made	4	1 (1.3)

Table 3.9 Extent of opacities within the study group.

Opacity extent code	Extent	Number of teeth	Number of patients n=80 (%)
1	Less than 1/3	115	50 (62.5)
2	At least 1/3-2/3	23	15 (18.8)
3	At least 2/3	7	4 (5.0)
9	No assessment made	4	1 (1.3)

Table 3.10 Symmetry of opacities within the study group.

Opacity symmetry code	Symmetry of diffuse defects	Number of teeth	Number of patients n=80 (%)
1	Diffuse defects but not symmetrical	97	38 (47.5)
2	Diffuse defects symmetrical	27	13 (16.3)

3.1.4.1 Results for opacities by direct comparison with the 2003 Child Dental Health Survey.

In the Child Dental Health Survey only 12-year-olds were examined for enamel opacities. 35% in England had one or more opacity (Chadwick and Pendry, 2004). From the study data in 12 years olds, 3 (42.9% n=7) had an opacity. As opacities are stable and do not change over time this figure can also be compared with the whole study group percentage of 62.5% patients with an opacity on the front teeth.

Figure 3.13 shows enamel opacity results from the dental Health Survey in 12-year-olds (Chadwick and Pendry, 2004) compared with the 12-year-old study data and the study data as a group.

Figure 3.13

Level of different types of enamel opacities within the study data, study 12-year-olds and the national data.

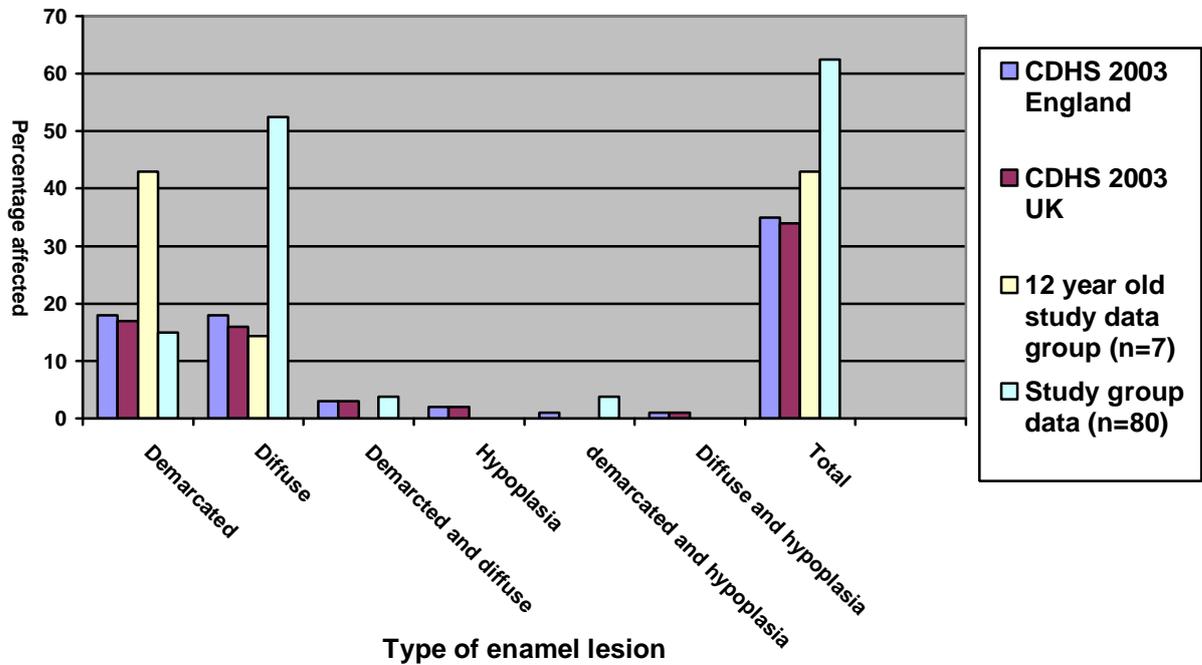


Table 3.11. Extent of lesions on teeth in the 2003 Child Dental Health Survey and the study data.

	Demarcated 2003 CDHS data (%)	Diffuse 2003 CDHS data (%)	Demarcated and diffuse 2003 CDHS data (%)	Demarcated study data number (%) (n=16)	Diffuse study data number (%) (n=120)	Demarcated and diffuse study data number (%) (n=4)
<1/3	92	59	32	12 (75.0)	96 (80.0)	4 (100)
1/3-2/3	6	28	54	3 (18.8)	20 (16.7)	0 (0.0)
>2/3	2	11	13	1 (6.3)	4 (3.3)	0 (0.0)

66% of diffuse lesions in the Child Dental Health Survey were symmetrical. 21.8% of the study group diffuse lesions were symmetrical.

Figure 3.13 and table 3.11 compare the study cohort as a population, the study 12-year-old group specifically and the national data from the 2003 CDHS. The 12-year-olds in the study group do show a higher level of demarcated lesions in comparison with the 2003 CDHS, however if the whole study population is considered the overall level of demarcated lesions are similar to the 2003 CDHS. The largest difference within the study population concerned the diffuse lesions. The study data do show an increased level.

3.1.4.2 Opacities present within each tumour group.

Table 3.12 Opacities present within each tumour group.

Group	Number of patients tested for opacities (number of teeth tested)	Number (%) of teeth observed with opacities	Of those with opacities number(%) of demarcated opacities	Of those with opacities observed number (%) of diffuse opacities	number (%) of other opacities
Hodgkin's Lymphoma	12 (92.0)	39 (42.0)	4 (10.3)	34 (87.1)	1 (2.6) demarcated and diffuse
Neuroblastoma	11 (58.0)	17 (29.3)	5 (29.4)	11 (64.7)	1 (5.9) demarcated and hypoplasia
Non-Hodgkin's Lymphoma	9 (62.0)	12 (19.4)	5 (42.0)	6 (50.0)	1 (8.3) demarcated and diffuse
Rhabdomyosarcoma	7 (41.0)	14 (35.9)	1 (6.7)	12 (80.0)	1 (6.7) demarcated and hypoplasia
Wilm's tumour	14 (80.0)	29 (36.2)	0 (0.0)	25 (86.2)	4 (13.8) demarcated and diffuse and other defects
Other	27 (184.0)	34 (17.7)	1 (2.9)	32 (94.1)	1 (2.9) demarcated and hypoplasia

3.1.4.3 Opacities present within each different treatment regime group.

Table 3.13 Opacities present within each different treatment regime group.

Group	Number of patients tested for opacities (number of teeth tested)	Number (%) teeth observed with opacities	Of those with opacities number (%) demarcated	Of those with opacities observed number (%) diffuse	Number (%) other opacities
HDCSCR	8 (42.0)	14 (33.3)	5 (35.7)	8 (57.1)	1 (7.1) demarcated + hypoplastic
Alkylating agents and no HDCSCR	47 (306.0)	89 (29.1)	11 (12.3)	73 (82.0)	9 (10.1) mixture of codes 4,5,8,9
Anthracyclines and no HDCSCR	53 (329.0)	91 (27.7)	0 (0.0)	76 (83.5)	5 (5.5) mixture of codes 4,5,8
Platinum drugs and no HDCSCR	20 (133.0)	21 (15.8)	0 (0.0)	21 (100.0)	0 (0.0)

Tables 3.12 and 3.13 demonstrate the level of opacities within each data analysis sub group. No significant trends were identified within the data.

3.1.4.4 Correlation between enamel opacities and the level of water fluoridation.

Table 3.14 Comparison between the occurrence of opacities and the level of fluoridation of the water supply.

	Fluoridated area	Non fluoridated area
Opacities	38 patients	12 patients
No Opacities	23 patients	8 patients

Table 3.15 Comparison between the type of enamel opacity and the level of water fluoridation.

	Fluoridated area	Non fluoridated area
demarcated opacities	8 patients	4 patients
diffuse opacities	33 patients	9 patients

Using Chi squared testing there were no significant differences between fluoridated and non-fluoridated areas with respect to enamel opacities (P=NS).

3.1.4.5 Summary of opacities.

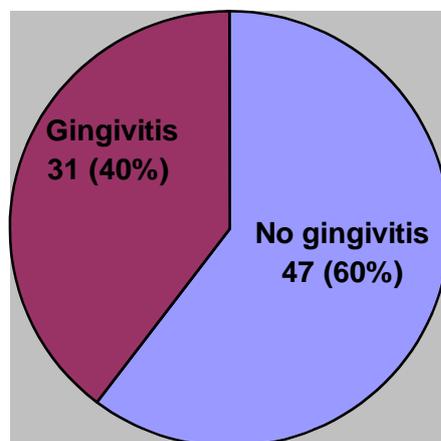
- Opacities were recorded in 62.5% of those tested from the study group.
- The commonest defect was a diffuse defect, shown in 52.5% of patients with an opacity. This was a higher incidence by comparison with the 2003 CDHS with 16.0% of opacities being diffuse defects.
- There were no significant differences between the diagnostic and treatment groups for prevalence of opacities.

3.1.5 Gingival health.

Gingival health was examined in 78 patients but was not assessed in those patients in the deciduous dentition and early mixed dentition (n=37) and those who were at risk of infective endocarditis (n=5).

Figure 3.14

Proportion of those examined for gingivitis with gingivitis present and those with healthy gingivae.



2.53%, of sites were affected by gingivitis, in the mouth overall (range 1 site to all sites).

Figure 3.15

Number of tooth sites affected by gingivitis for those subjects affected with gingivitis.

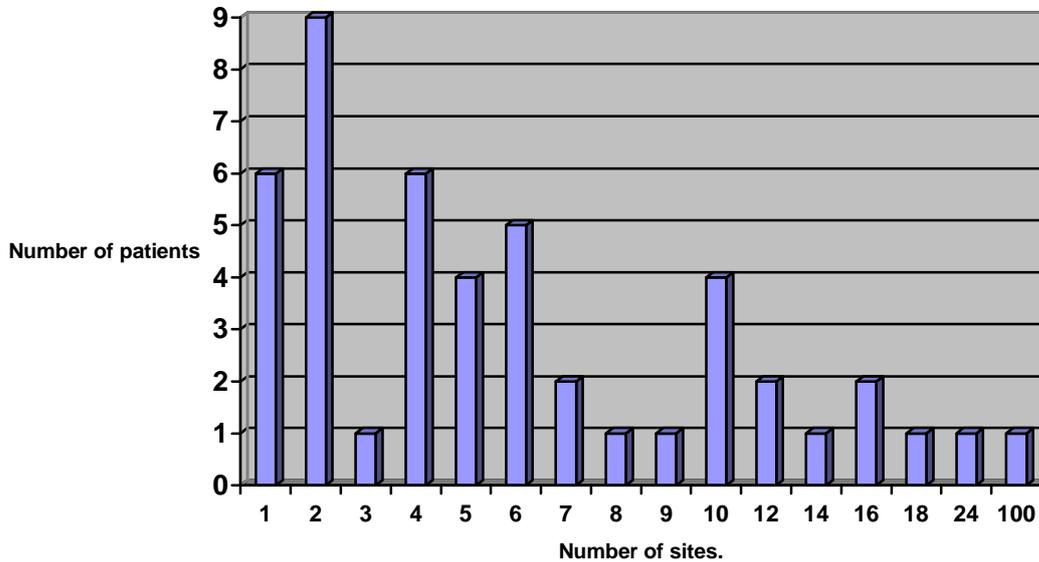


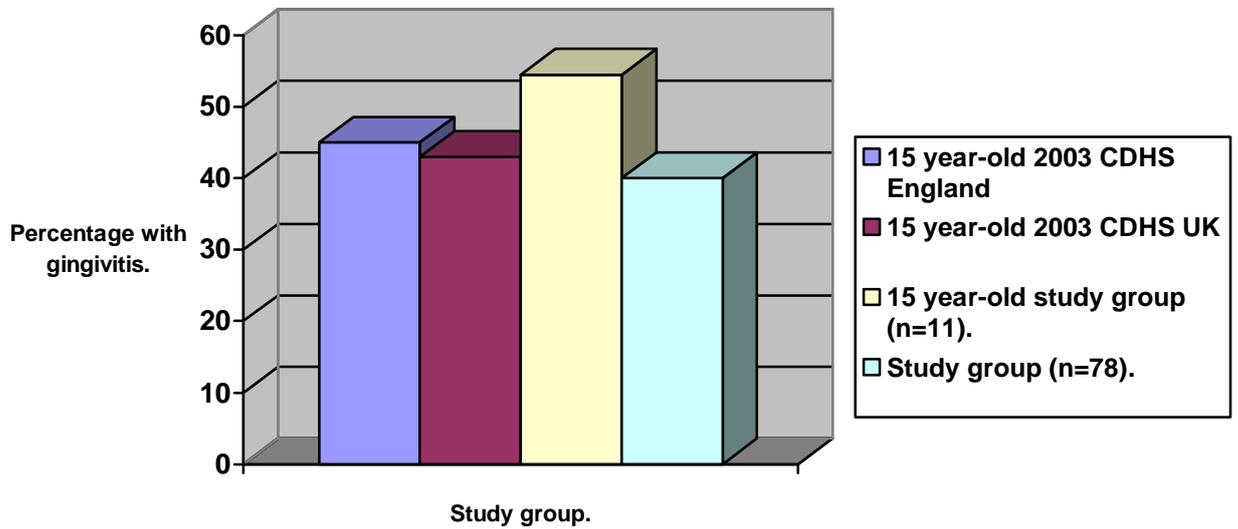
Figure 3.15 illustrated that the majority of patients (83.0%) had 1-10 sites in the mouth affected by gingivitis. No child was shown to have periodontal disease as all BPE scores were 0,1 or 2.

3.1.5.1 Gingival health by comparison with the 2003 Child Dental Health Survey cohort.

The 2003 CDHS found 45% of 15-year-olds in England to have evidence of gingivitis by assessment of bleeding on probing the gingivae (White and Lader, 2004). Of the study population of 15-year-olds, 6 (54.5% n=11) patients were found to have evidence of gingivitis. Figure 3.16 shows the number of patients with gingivitis in the study group and 15-year-olds and compares them to the England and UK 2003 CDHS data (White and Lader, 2004).

Figure 3.16

A graph to show the level of gingivitis in the study group, 15-year-old study group and the 2003 CDHS.



The specific teeth affected are illustrated in table 3.16.

Table 3.16 Areas of gingivitis in the mouth for 15-year-olds.

Percentage of 15-year-olds with gingivitis in the specified tooth							
	upper right 6	Upper right 1	Upper left 6	lower left 6	Lower left 1	lower right 6	any tooth
gingivitis n=11	18.2	27.3	18.2	18.2	18.2	18.2	54.5
2003 CDHS (UK)	15.0	13.0	15.0	21.0	13.0	23.0	43.0

The percentage of 15-year-olds with gingivitis stratified by gender in the study and general populations are illustrated in table 3.17.

Table 3.17 Gingivitis by gender in 15-year-olds.

	Percentage of boys (n=11)	Percentage of girls (n=11)
gingivitis (girls n=3, boys n=8)	62.5	33.3
2003 CDHS (UK)	39.0	46.0

More girls were found to have gingivitis than boys in the 2003 CDHS (White and Lader, 2004). The 2003 CDHS did recognise that this was the opposite of the findings when gingivitis was recorded by visual examination only. In the visual examination the gingivae were looked at and described as either healthy or not healthy (red inflammation present on the buccal or lingual surfaces of each tooth). The teeth were divided into sextants for this recording. When recorded in this manner 56% of male 15-year-olds had signs of gingivitis and 48% of female 15-year-olds had signs of gingivitis (White and Lader, 2004). Gingivitis was not recorded in this manner in this thesis. However more boys demonstrated gingivitis than girls.

3.1.5.2 Periodontal condition by diagnostic group.

Table 3.18 Gingival health of the different diagnostic groups. (BOP= bleeding on probing).

Group	Number of patients tested	Number of patients with BOP (%)	Average no. of sites BOP in those with BOP
Hodgkin's Lymphoma	12	7 (58.3)	8.14
Neuroblastoma	11	4 (36.4)	5.75
Non-Hodgkin's Lymphoma	10	8 (80.0)	5.12
Rhabdomyosarcoma	7	7 (100.0)	7.00
Wilm's tumour	11	5 (45.5)	5.80
Other	27	16 (59.2)	11.56

3.1.5.3 Gingival health by treatment group.

Table 3.19 Gingival health of the treatment groups. (BOP= bleeding on probing).

Group	Number of patients tested	Number of patients with BOP (%)	Average no. of sites BOP in those with BOP
HDCSCR	8	3 (37.5)	1.64
Alkylating agents and no HDCSCR	48	35 (72.9)	6.52
Anthracyclines and no HDCSCR	48	34 (70.8)	4.60
Platinum drugs and no HDCSCR	30	11 (36.7)	7.30

Tables 3.18 and 3.19 show no specific trends in any of the treatment and diagnostic groups. One patient's parent however did mention in the "comments" section that their child *"has major bleeding of his gums and they are so sore if we brush them they constantly bleed all day"* and another reported their child's *"teeth and gums bleed for no apparent reason and this started when the child began taking non steroidal anti inflammatory drugs as part of their cancer therapy."*

3.1.5.4 Summary of gingival health.

The gingival health of the study population was similar to that of the general population. The number of boys affected by gingivitis was higher than the number of girls. There were no obvious differences in gingival health within tumour diagnostic or treatment groups.

3.1.6 Microdontia.

There were 26 microdont teeth present in 9 patients from the study population. All these patients had received chemotherapy under the age of 3.5 years.

Table 3.20 Relationship between microdont teeth and age at which chemotherapy was received.

	number (%) with Microdontia	number (%) with No Microdontia
Chemotherapy given under 3.5 years old	9 (11.4)	70 (88.6)
Chemotherapy given over 3.5 years of age	0 (0.0)	41 (100.0)

Chi square analysis showed a significant $p=0.025$ ($p<0.05$) relationship between the age at which chemotherapy was received and the presence of microdont teeth. Using Fisher's exact test to account for the small numbers the relationship was still found to be significant $p=0.027$ ($p<0.05$) (appendix 16).

The group consisted of a mixture of tumour type rhabdomyosarcoma (2) neuroblastoma (3), hepatoblastoma, optic chiasm glioma, Wilm's tumour and Hodgkin's disease.

Table 3.21 Details of microdont teeth within the study group.

Tooth	Number of microdont teeth within the study group
Lower central incisor	2
Lower lateral incisor	2
Lower canine	2
Lower first pre-molar	5
Upper lateral incisor	3
Upper first pre-molar	5
Upper second pre-molar	4
Upper second molar	3

The type of treatment these children received was a mixture of chemotherapeutic agents as below in table 3.22.

Table 3.22 Type of chemotherapy received by those with microdont teeth.

Chemotherapy regime	Number of patients receiving that chemotherapy regime.
Anthracyclines	7
Alkylating agents	4
Platinum drugs	4
HDCSCR	3

One third of patients with microdont teeth had received HDCSCR. Table 3.23 shows the relationship between the HDCSCR group with and without microdont permanent teeth.

Table 3.23 Number of patients in the high dose chemotherapy and stem cell rescue group with and without microdont teeth.

	Microdontia	no microdontia
HDCSCR	3	11
no HDCSCR	6	35

Chi square analysis of the data in table 3.23 demonstrated no significant relationship. Further research using larger numbers would be required to draw any conclusions (appendix 16).

Of the treatment groups the HDCSCR group did show the largest proportion of microdont teeth (see table 3.24).

Table 3.24 Number of microdont teeth present in each group.

Group	Number of Microdont teeth	Number (%) patients with microdont teeth in each group
HDCSCR n=14	3	3 (20.0)
Alkylating agents and no HDCSCR n=66	10	3 (4.6)
Anthracyclines and no HDCSCR n=66	12	3 (4.5)
Platinum drugs and no HDCSCR n=43	12	2 (6.7)

Table 3.25 Number of microdont teeth within each diagnostic group.

Group	Number of Microdont teeth	Number of patients with microdont teeth (%) within each group
Hodgkin's Lymphoma n=14	0	0 (0.0)
Neuroblastoma n=21	3	3 (14.2)
Non-Hodgkin's Lymphoma n=10	4	1 (10.0)
Rhabdomyosarcoma n=10	6	2 (20.0)
Wilm's tumour n=29	1	1 (3.4)
Other n=36	12	2 (5.5)

Table 3.25 shows the rhabdomyosarcoma group to have the highest percentage of patients affected with microdont teeth. However the neuroblastoma group demonstrated the largest number of patients affected with microdont teeth, but proportionally it is a smaller percentage due to the larger sample size.

3.1.7 Traumatized teeth.

Thirty two incisor teeth were traumatized in 21 patients within the study group. Fifteen patients had incisors in the adult dentition and six were in the deciduous dentition. 14 (66.7%) patients were male and 7 were female (33.3%)

Table 3.26 Traumatized teeth illustrated within diagnostic groups.

Group	Number of traumatized teeth (TT)	Number of patients with TT (%)
Hodgkin's Lymphoma n=14	1	1 (7.0)
Neuroblastoma n=21	5	4 (19.0)
Non-Hodgkin's Lymphoma n=10	2	2 (20.0)
Rhabdomyosarcoma n=10	1	1 (10.0)
Wilm's tumour n=29	11	7 (24.1)
Other n=36	13	6 (16.7)

Table 3.27 Traumatized teeth present in each treatment group.

Group	Traumatized teeth (TT)	Number (%) Patients with TT
HDCSCR n=14	4	3 (20.0)
Alkylating agents and no HDCSCR n=66	16	11 (16.7)
Anthracyclines and no HDCSCR n=66	19	12 (18.2)
Platinum drugs and no HDCSCR n=43	8	4 (13.3)

The results have not been compared directly with the 2003 CDHS age groups because in the study population there are no affected 8-year-olds and only one affected 12 and 15-year-old and therefore the numbers are too small to draw comparisons. Table 3.26 and 3.27 show that the highest number of traumatized teeth were in the Wilm's tumour, the alkylating agents and anthracycline drug treatment groups. However these were also the largest groups. The largest proportion of trauma was seen within the HDCSCR group.

3.1.8 Fissure sealed teeth.

The study population included 32 sealed permanent teeth in 11 patients (9%, n=120). When the study data by age group is compared to the 2003 CDHS data for England and the UK the study population is found to have a lower level of fissure sealants (table 3.28).

Table 3.28 Number of fissure sealants placed per age group.

Age	2003 CDHS England fissured sealed permanent teeth %.	2003 UK fissured permanent teeth sealed teeth %.	Study data fissured permanent teeth sealed teeth. Number (%)
8	11	13	0 (0.0%)
12	22	25	1 (14.3 %)
15	28	30	3 (27.3 %)

Figure 3.17

Percentage of patients with fissure sealants within each diagnostic group.

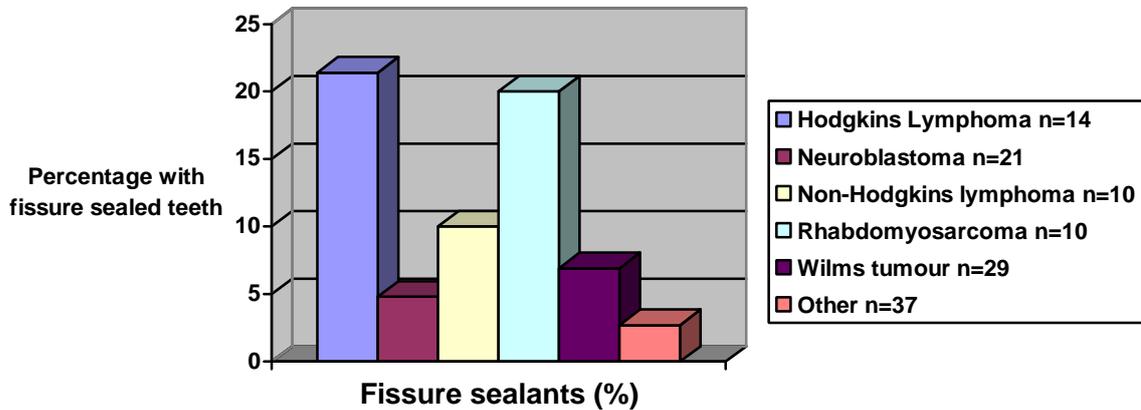


Figure 3.17 shows no trend in patients with fissure sealants within the diagnostic study groups. The “other” group shows the smallest proportion of patients with fissure sealants. Again table 3.29 does not identify any trends in fissure sealant placement within the treatment groups. However the study group did have a below average incidence of fissure sealants.

Table 3.29 Number of fissure sealed teeth within each treatment group.

Group	Fissure sealed teeth (FS)	Number (%) patients with FS
HDCSCR n=14	4	1 (6.6)
Alkylating agents and no HDCSCR n=66	20	6 (9.0)
Anthracyclines and no HDCSCR n=66	19	7 (10.6)
Platinum drugs and no HDCSCR n=43	1	1 (3.3)

3.1.9 Summary of key findings.

- The neuroblastoma and HDCSCR groups showed a higher level of primary dental decay compared with the general population and study population.
- All patients who had microdont teeth received chemotherapy under the age of three and a half years.
- The study group have a higher level of diffuse opacities by comparison with the general population.
- The prevalence of fissure sealants within the study population is decreased by comparison with the general population.

3.2 RESULTS AND ANALYSIS QUESTIONNAIRE (PART B).

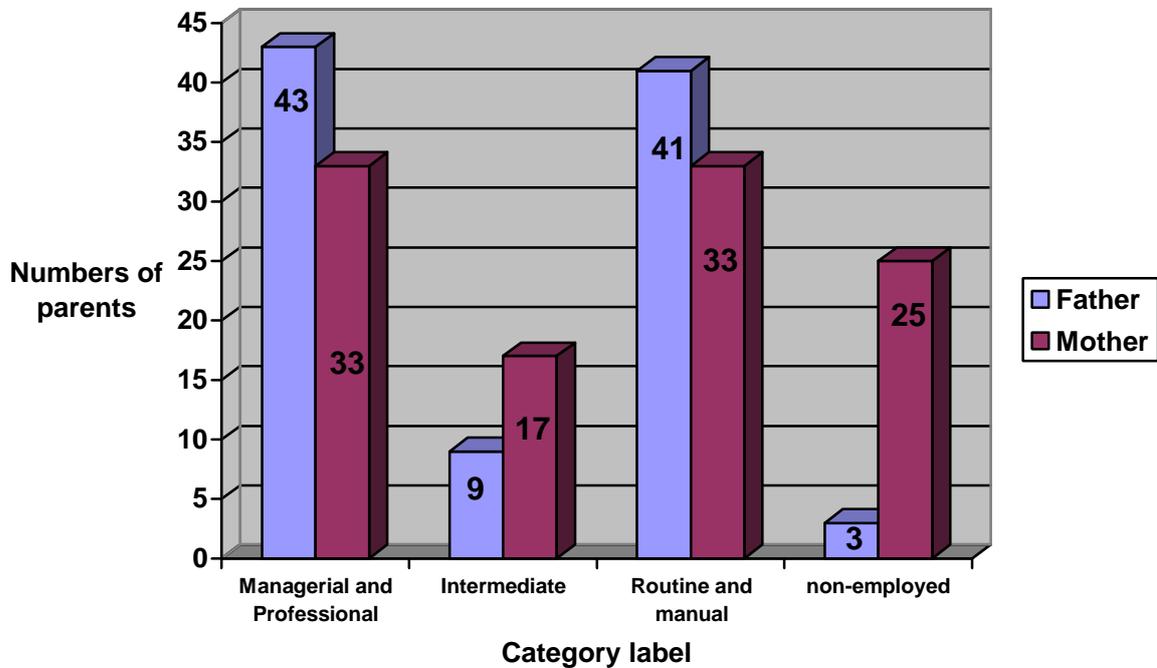
This section reports responses to the questionnaire in part B of the study. 120 questionnaires were part or fully completed by the parent/guardian of the patient.

3.2.1 Social class of the study group.

Questions 2-5 in the questionnaire were used to determine social class. Of 120 questionnaires (one per family), 108 answered questions relating to the maternal parents/guardians and 96 regarding the paternal parents/guardians. The results of those parents (96 fathers and 108 mothers) who answered the relevant question according to the NS-SEC system are shown in figure 3.18. The relationship of the parents/guardians to the child, and with each other was not investigated within the current study. It is not known if the 12 mothers who did not state the “father’s” occupation and school leaving age were single parents or if those who stated both the mother’s and father’s occupations were married or not.

Figure 3.18

The NS-SEC categories of social class in the mothers and fathers of the study group.



Using the Registrar General's social class coding system the main categories are described below:

I professional occupations.

II managerial and technical.

IIIN skilled-non-manual.

IIIM skilled manual.

IV partially skilled.

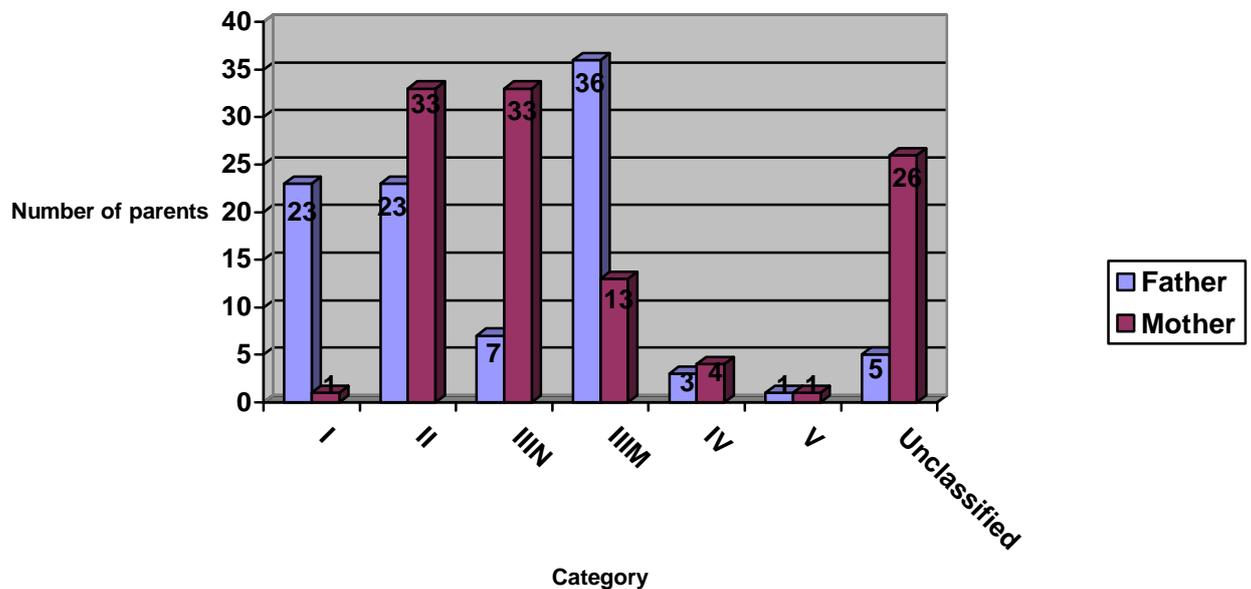
V unskilled.

(ONS, 1980)

The results using the Registrar General's coding system for those parents in the study population who answered the question alluding to social class are represented in figure 3.19.

Figure 3.19

The social class by occupation from the Registrar General's coding system (1980).

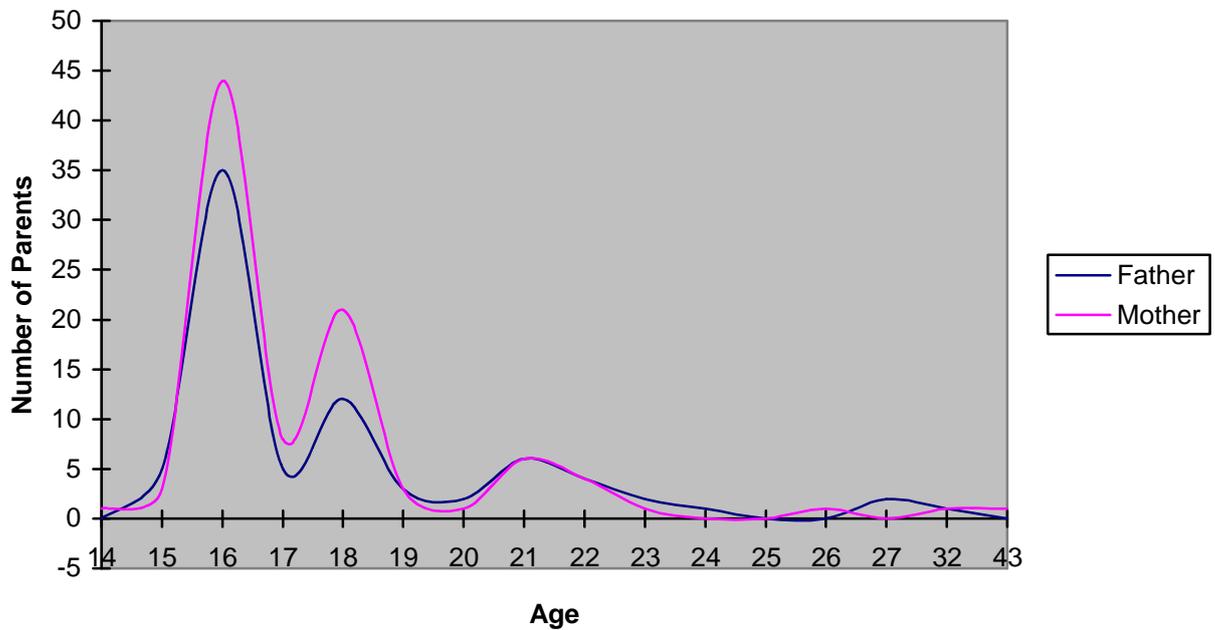


The results shown in figures 3.18 and 3.19 show a range of social backgrounds within the study group as would be expected in such a population.

Figure 3.20 illustrates the different ages of which the parents of the study group left full time education. This is a further way of mapping the socioeconomic status of individuals.

Figure 3.20

Age at which parents within the study group finished full time education.



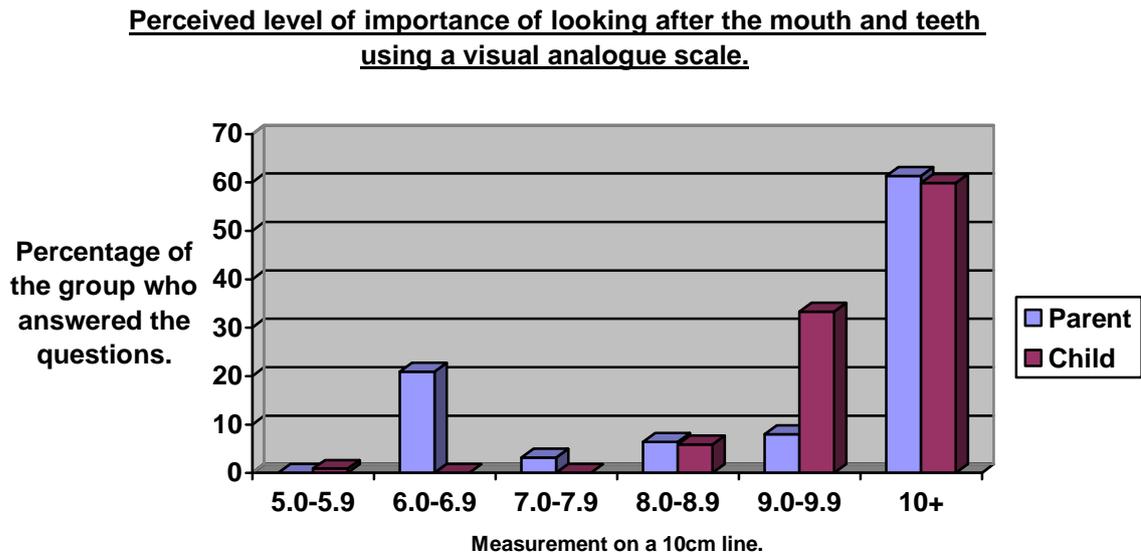
This graph shows three peak times when full time education was finished. These were at 16, 18, and 21 years of age. These ages would account for those finishing after O-levels or GCSE's, those after A-levels and those after a degree respectively. The older parents in the above graph have returned to education after a break.

3.2.2 Attitude.

Questions 1 and 7 of the questionnaire related to how important the parent answering the questionnaire felt looking after the mouth and teeth was. The first question concerned themselves and the second question concerned their child. A visual analogue scale was used for measurement of the perceived level of importance for both questions.

The first question (question 1) was answered by the parents in 62 cases (51.7%). When answering about the importance of oral health for their child (question 7) 117 (97.5%) parents answered the question. Figure 3.21 illustrates the results. The groups have been analysed in percentages to allow easier comparison.

Figure 3.21



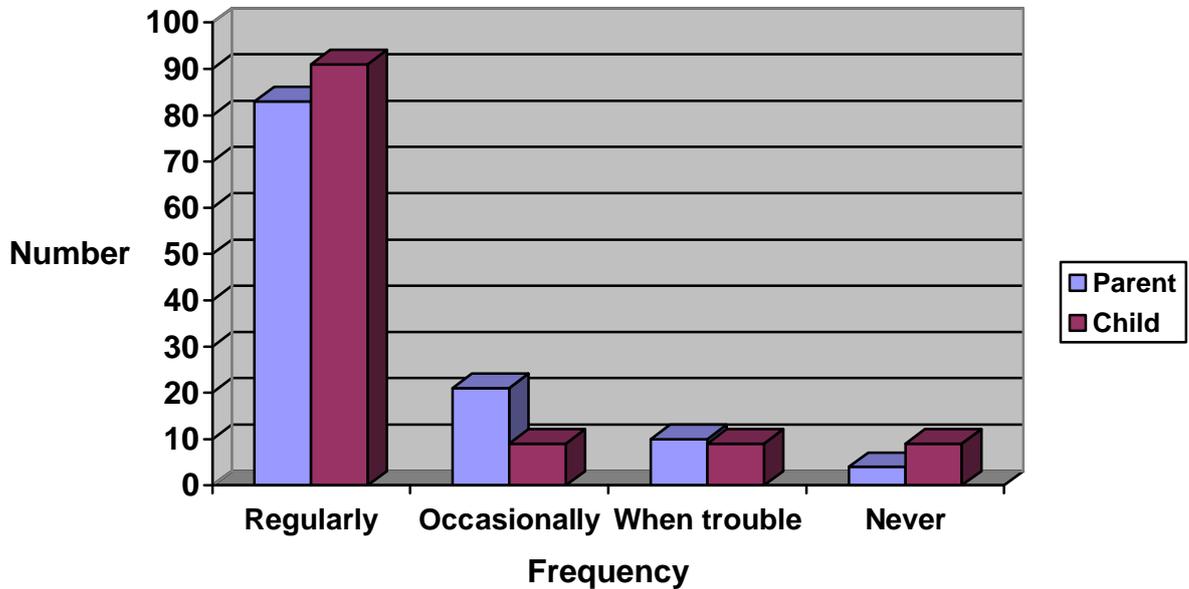
3.2.3 Reported attendance.

When asked about registration at a dental practice and how regularly the parent/guardian and child attended the results were the same for the child and parent/guardian (questions 6, 8 ,9).

Ninety nine (82.5%) parents reported their child to be registered with a general dental practitioner and 21 (17.5%) said they were not registered. The frequency of visits to a general dentist was described as below in figure 3.22.

Figure 3.22

Frequency at which the parents and children of the study group attend the dentist.



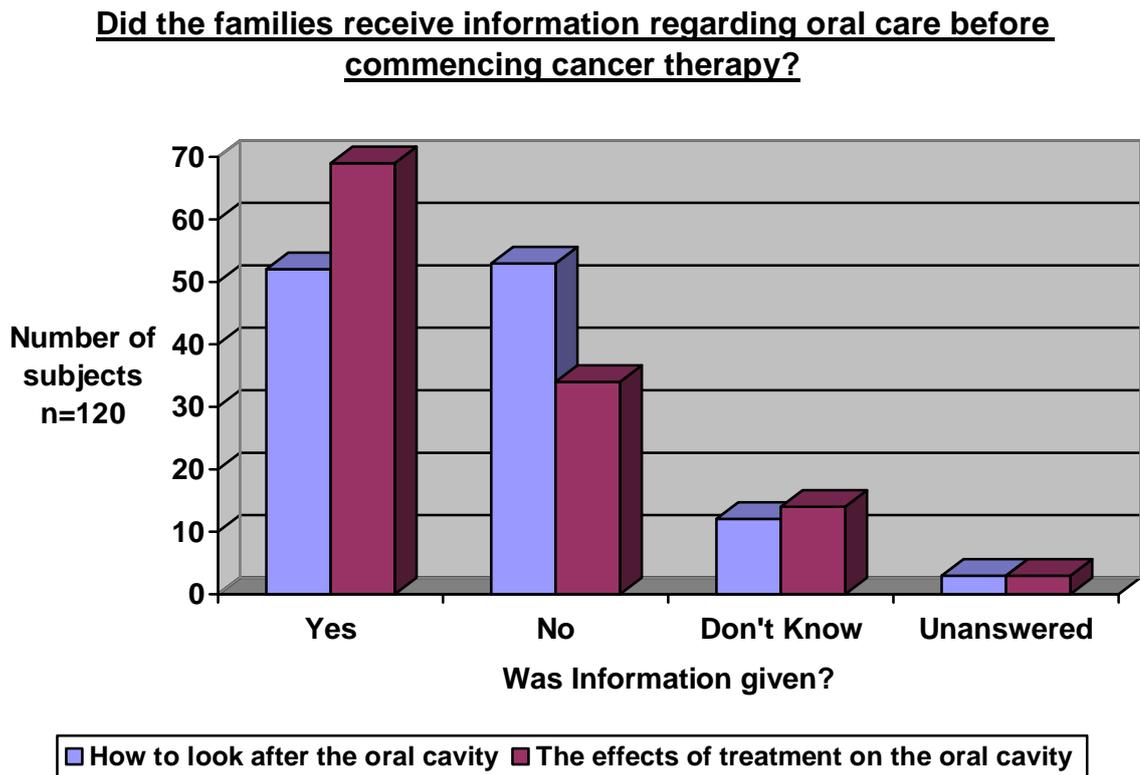
3.2.3.1 Prior to cancer therapy.

When asked if a dentist examined the teeth before cancer therapy started 14 (11.7%) said yes, 104 (86.7%) said no and 2 did not answer the question (question 10, 11). This question is subject to recall bias but despite this does show that most parents did not remember a dental review occurring as part of the preparation for commencing cancer therapy.

Of those who did recall a dental review before therapy, 1 stated that their child had been seen locally and 5 stated their children had been seen within a hospital setting. It should be noted here that this result suggests 18 (15.0%) were seen by a dentist before cancer therapy started rather than the previously quoted 14 (11.7%). However the results still demonstrate that only a minority of patients are being seen by a dentist before cancer therapy commences.

When enquiring what oral health advice has been received prior to starting cancer therapy; about how to look after the mouth and teeth during therapy, and the possible effects of cancer therapy on the mouth and teeth post therapy (questions 15,16) the response was as illustrated in figure 3.23.

Figure 3.23

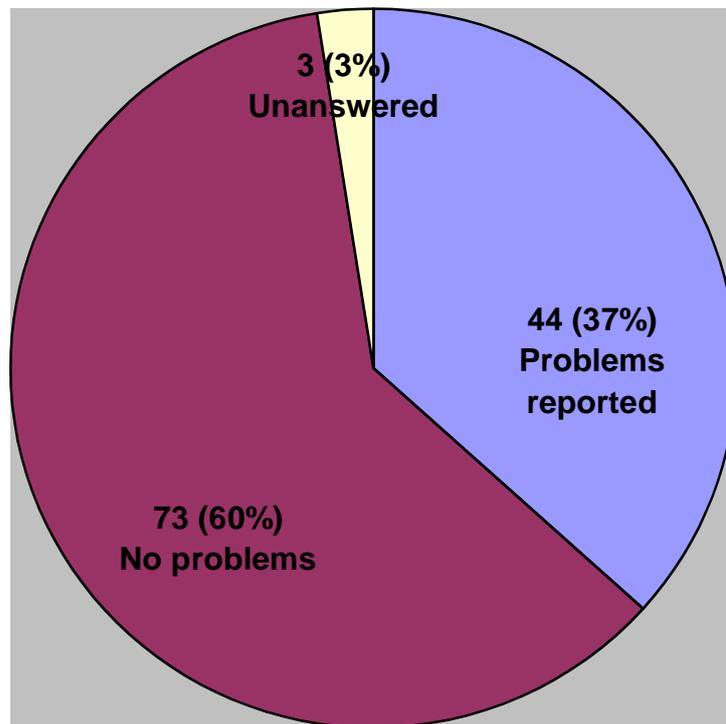


3.2.3.2 During cancer therapy.

Question 17, 18 and 19 explore any oral health issues that arose during cancer therapy. The number of patients who reported side effects within the oral cavity during cancer therapy was 44 (37.6% n=117).

Figure 3.24

The proportion of the study cohort reported to have side effects within the oral cavity during cancer therapy.

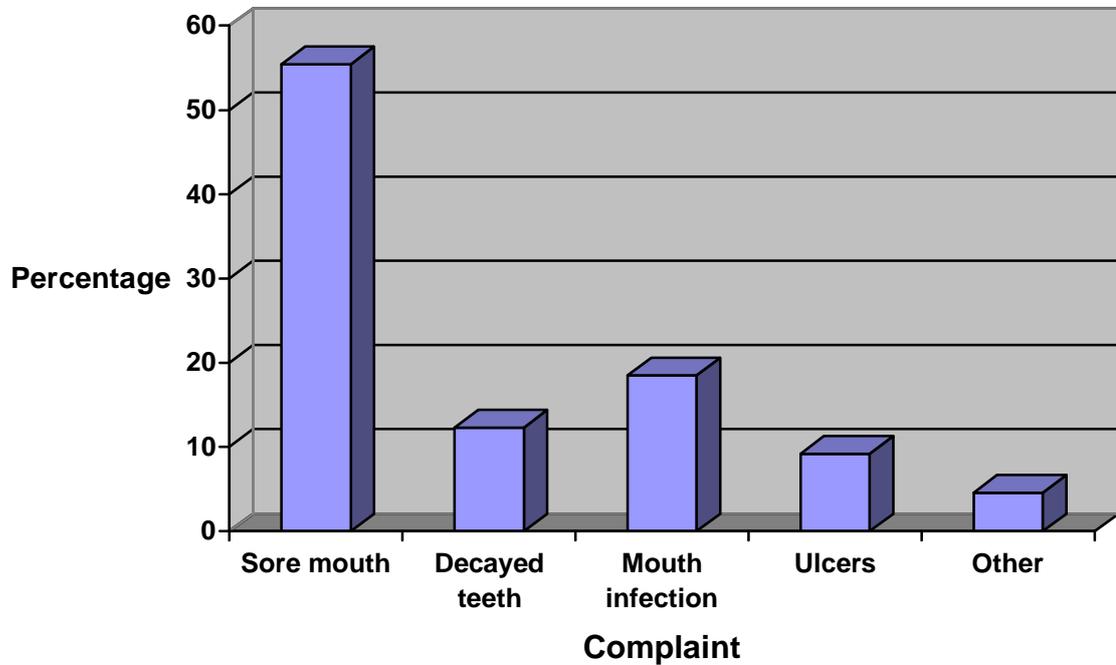


This pie chart shows that just over a third (37%) of patients can expect oral side effects when receiving treatment for a solid tumour. This emphasises the importance of preparing patients for the expected oral complications of cancer therapy.

The frequency of oral problems experienced by the patients are described in figure 3.25. The 'other' category in figure 3.25 includes mucositis, sore teeth and pain on swallowing.

Figure 3.25

Frequency of different oral complaints occurring within the affected group.



The severity of complaints was established by asking all parents if the child required admission to hospital for medical treatment regarding the oral complaint during cancer therapy. This methodology may leave minor symptoms under-represented.

Figure 3.26

Proportion of the study group admitted into hospital for supportive medical/dental treatment during cancer therapy.

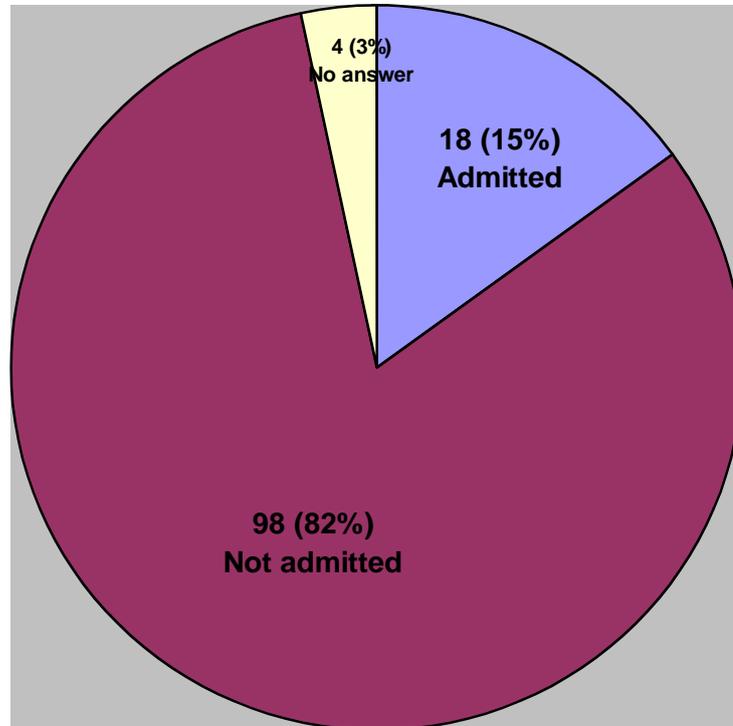


Figure 3.26 indicates 15% of the study population were admitted to hospital during their cancer therapy requiring medical intervention for oral problems. This illustrates the importance of prevention of oral disease where possible.

3.2.3.3 After cancer therapy.

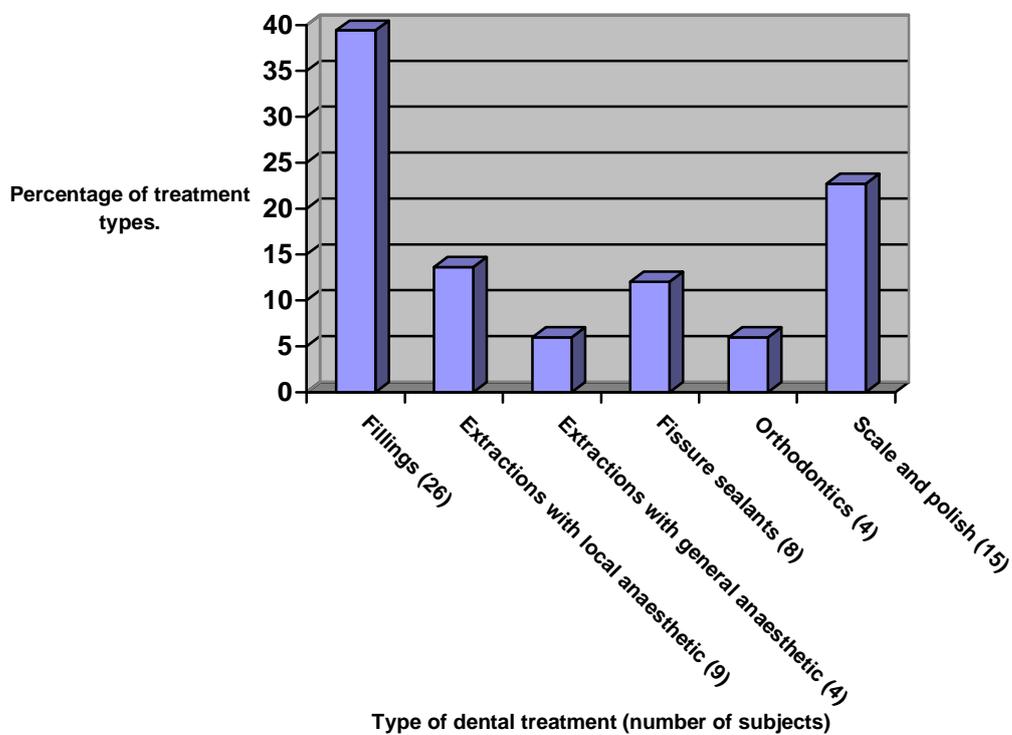
Parents were asked if they knew if the general dentist was still willing to see their child for reviews despite their medical diagnosis (question 14). Reassuringly 87 (72.5%, n=120) said their dentist was willing to review their child and only 3 (2.5%, n=120) gave a definite no.

Ninety nine (82.5%, n=120) had been seen by the dentist since medical treatment (question 12) had finished with the remainder not having been seen post cancer treatment. Of those seen the majority were seen within the general dental services (question 20,22).

The amount of dental treatment required since cancer therapy varied (question 21). Seventy six (63.8%, n=119) reported to have received some dental treatment and 43 (36.1%, n=119) had not received anything other than a simple dental examination. Of those who needed treatment, the type, and frequency of treatment required is described in figure 3.27.

Figure 3.27

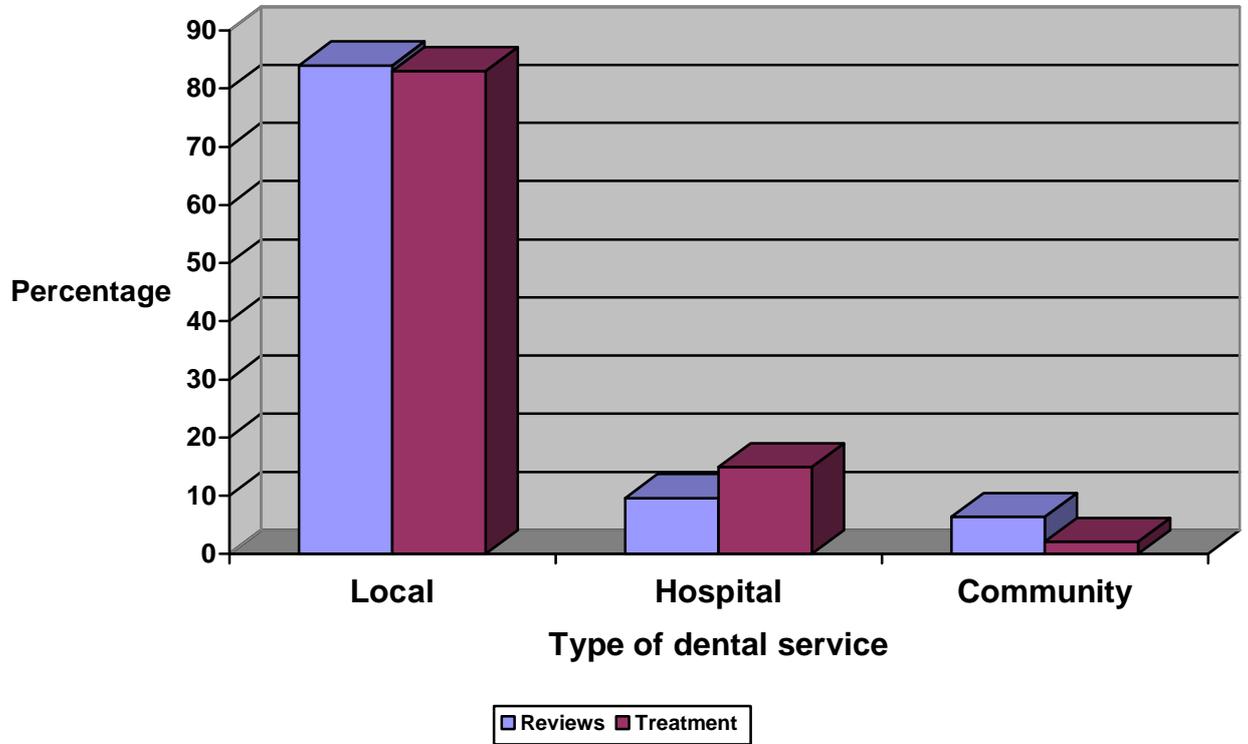
Type of dental treatment required post cancer therapy.



As with the dental reviews the required dental treatment is mainly carried out in the general dental service with only a small proportion requiring the hospital services. Figure 3.28 illustrates where dental care is sought within the study population.

Figure 3.28

Location of the patients dental review and treatment appointments.

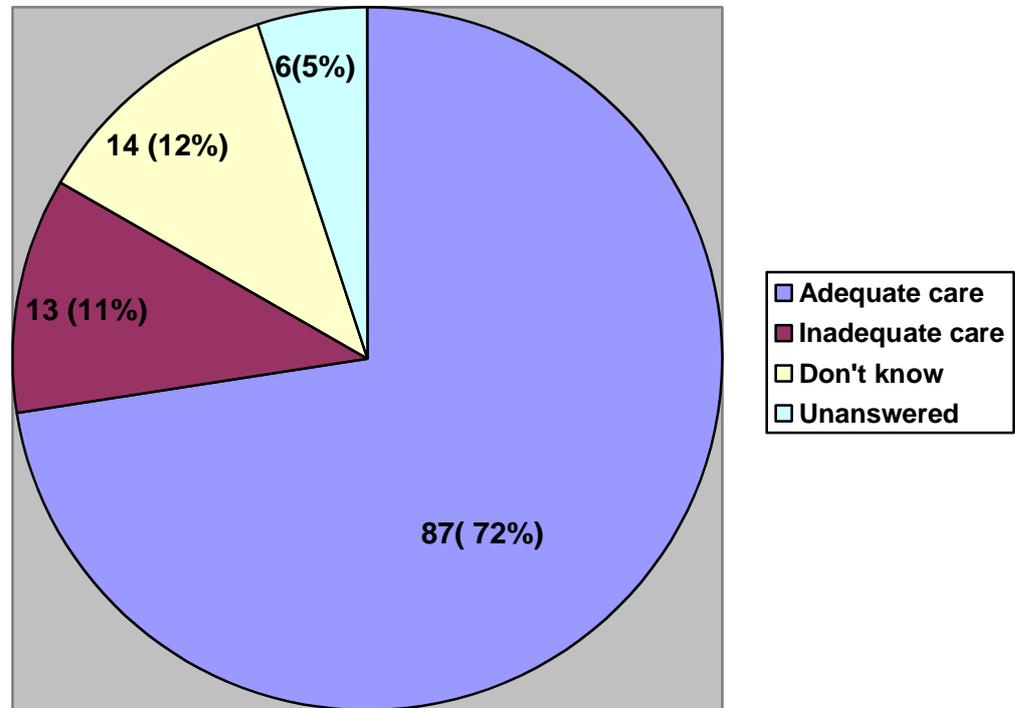


3.2.4 General dental care.

In general, parents were asked to comment on whether they felt their child had adequate dental care (question 23). The results are demonstrated in figure 3.29.

Figure 3.29

How parents felt about the level of dental care their child received.



The majority of parents felt they did receive adequate dental care. Remarks made in the 'comments' section occasionally supported this but there were other more worrying statements about the level of dental care accessed by the patients.

3.2.5 Questionnaire comments (question 24).

3.2.5.1 Comments supporting an adequate level of dental care.

'No comments because our dentist is good'.

'specialist dental care as child has autism.'

'The previous dentist appeared not to be interested in her illness, just in general dentistry but the practice has been taken over and we are due appointments within the next month.'

3.2.5.2 Comments revealing inadequate dental care.

3.2.5.2.1 Difficult to access care.

'2 abscesses during chemo -teeth extracted under local anaesthetic at BCH'

'I am having serious problems getting my child into a dental surgery due to the fact I am unemployed. I am very worried about his teeth.'

'it is very difficult to get appointments including check ups on time due to the size of the practice.'

'Dentist said not to take her for 6 months. We need to re register as they have gone mainly private.'

'waiting to see Birmingham Children's Hospital dentist after being referred from the dental hospital'

The statements above support a common complaint that it is becoming increasingly difficult to seek care at a general national health service (NHS) dental practice.

3.2.5.2.2 Inadequate information received.

'He was only 2 when diagnosed so we didn't worry about his teeth at the time. We hadn't started to visit the dentist but we were advised not to anyway.'

It is unlikely the oncology nurses would have advised a parent not to visit the dentist. The parents were however obviously given this information somewhere.

3.2.5.2.3 Lack of confidence in the general dentist.

'not sure if local dentist is aware that chemotherapy could have caused dental problems'

'dentist not sure how he would be with the anaesthetic.'

These statements suggest rightly or wrongly there is a lack of confidence by the parents in the general dental practitioners looking after these children.

3.2.5.2.4 Orthodontic queries.

'she has seen an orthodontist and she will need braces and removal of a few teeth. This obviously causes a problem unless the brace is not fixed due to the still having to have regular MRI scans (every 6 months)'

'She has been told she needs a brace but there is a 2 year waiting list'.

'concerns regarding milk teeth not dropping out with overcrowding and its making it hard to brush'

3.2.5.3 Miscellaneous comment.

'I was told during treatment about problems with teeth that may occur but as my daughter had a lot of ulcers/soreness during treatment, cleaning was very difficult and we have had a lot of dental problems since.'

4.0 DISCUSSION.

4.1 REVIEW AND CRITIQUE OF METHODOLOGY.

Given the time and resource constraints available to the investigator the study was carried out as effectively and efficiently as possible and with strict adherence to the methodology as described previously. Despite this several improvements as described below could have been included in the methodology to improve the validity of the results.

1. Sample size. Although a large sample size was used there were so many variables that formal conclusions were difficult to draw. Ideally each diagnostic group would have been larger and the treatments standardised therefore limiting the variables as much as possible. Similar data could have been collected between centres improving the sample sizes and therefore the power of any calculations. This would lead to more solid conclusions and also allow comparisons between centres.
2. Control group. Age and sex matched control groups with the same demographics would have been preferable as a control group. Using this method both groups could be compared against each other and then also to the 2003 CDHS perhaps making the conclusions more valid for this cohort of patients.
3. Conditions of examination. Where possible the conditions matched those of the 2003 CDHS. Ideally the enamel opacities would have been observed under natural light. The study took place in the only room available in the out patients department to the investigator at the time of the data collection. This room only had a small window high up. Therefore it was not practical to match this particular aspect.
4. Formal calibration of the primary investigator and another examiner. Despite being trained, an official calibration was not recorded for the primary investigator. If this had been carried out it would have improved the validity of the results. During the data collection period unfortunately, due to staff shortages no other dental examiners could be present at the time of the dental examination of the patients and it was not practicable to bring the patients to a further appointment for a second examination by the primary investigator.
5. The Questionnaire. The questionnaire data could have been further validated by cross examining the patient notes to verify answers, in particular the questions about

problems experienced during chemotherapy which are subject to recall bias. The questionnaire itself could have been validated.

6. Data analysis. Investigation of the enamel opacities should have looked into the postcode of the family from years 0-3. This would be when the tooth was at its most vulnerable developmentally. Further analysis of the caries level in fluoridated and non fluoridated areas would be interesting to assess the effect fluoride had on caries within this population. Cross matching the questionnaire data and examination data would have allowed a more in depth analysis of the population however these further investigations were beyond the scope of this thesis.

4.2 REVIEW OF DEMOGRAPHICS AND COMPOSITION OF THE GROUP.

4.2.1 Number of patients.

The study population had 1) all experienced a solid tumour during childhood, 2) been treated with chemotherapy as part of their treatment regime and 3) attended the Birmingham Children's Hospital (BCH) solid tumour follow up clinic. Children who had been treated with chemotherapy for brain tumours were included if they attended, but most of this group are seen in a clinic on a different day. Given the rare nature of childhood cancer all patients who met the three inclusion criteria above were included. This allowed a sufficient sample size, but did result numerous variables within the study population. This should be taken into account when interpreting the results. Considering the limited prevalence of solid tumours within the general population, despite the number of variables, this number of patients still represents one of the largest reported sample sizes. Other similar studies have been carried using smaller study groups (Holttta et al., 2005, Nunn et al., 1991, Maguire et al., 1987).

4.2.2 Geographical residence.

As Birmingham Children's Hospital is a regional cancer centre the large spread of patients over the West Midlands and surrounding counties would be expected. CCLG registrations of cancer for children aged under 15 (2000-2005) have not shown any particular area of the country to have higher solid tumour rates than others (CCLG, 2007c).

4.2.3 Social class.

The two different social class measurement scales are difficult to compare and draw any valid conclusions from as there are several differences between them. The NS-SEC coding system is designed to be more flexible when placing occupations into categories. Studies have shown there is an 87% level of continuity between the scales, (Rose and O'Reilly, 1998) therefore they cannot be directly compared with each other. Of the study population 18% preferred not to answer the questions alluding to social class but of those who did, using the national statistics socioeconomic classification, 44.8% of fathers and 30.5% of mothers were from managerial backgrounds, 9.4% of fathers and 15.7% of mothers from an intermediate background, 42.7% of fathers and 30.5% of mothers from routine and manual backgrounds and 3.1% of fathers and 23.1% of mothers were not employed. Both scales show a large spread of backgrounds within the study population as would be expected. This is also supported by the data alluding to socio-economic status by recording at what age the parents/guardians left full time education. The study population shows a variety of ages with decreasing value peaks at 16, 18 and 21 years (figure 3.20). The trend indicates fewer parents continued in full time education over time. These trends are supported by UK national statistics for the age at which students finish full time education. The number of children continuing in full time education is gradually increasing with 15% of 18-21-year-olds in full time education in 1988-1989 and 30% of 18-21-year-olds in full time education in 1993-1994 (HEFCE, 2001) but the pattern is still such that in the 2001 UK census 62% of 16-19-year-olds were still in full time education with 22% of 20-24-year-olds in full time education (ONS, 2004). This suggests there are more students finishing full time education at

16-18 by comparison with those completing higher education and finishing full time education at 21 years of age, within the general population. Thus the graph described in figure 3.20 is suggestive of a mixed social population within the study group similar to that of the general population within the UK. As the aetiology of childhood cancer is largely unknown it would be expected that the demographics of the study group reflect that of the average population.

4.2.4 Medical diagnosis.

The main diagnostic groups included Wilm's tumour, rhabdomyosarcoma, neuroblastoma and lymphomas. The relative proportions of medical diagnosis groups were as expected when based on the number and types of diagnoses of patients seen in the previous year and the prevalence of cancer types within the child population. These groups are also investigated by other authors. Näsman et al examined 24 children with a solid tumour of which 6 had Wilm's tumour, 6 had rhabdomyosarcoma, 3 neuroblastoma, and 9 other solid tumours (Nasman et al., 1997). Purdell-Lewis et al (1988) also observed 3 neuroblastoma, 6 Wilm's tumour and 5 rhabdomyosarcoma patients (Purdell-Lewis et al., 1988). Many of the other previous studies either clump together the solid tumour group (Karsila-Tenovuo et al., 2001, Maguire et al., 1987) or are more focused on one particular group. For example Kaste et al (1998) studied 52 neuroblastoma patients (Kaste et al., 1998). Hölta et al (2002) studied 18 neuroblastoma patients (Holta et al., 2002). Alpaslan et al (1999) studied 30 children with non-Hodgkin's and Hodgkin's disease (Alpaslan et al., 1999). There was a spread of age at examination from 0-17 years with peaks at 5-7, 13 and 15 years. This reflects the nature of cancer as a disease process affecting a large variety of children at different ages. Some trends are apparent: for example the neuroblastoma and Wilm's tumour group will include children diagnosed mainly under 5 years of age, as these tumours largely affect the younger age group. However the study groups do include children of all ages because they have been under follow up for varying periods of time.

4.2.5 Chemotherapy regime.

Analysis into the groups of high dose chemotherapy and stem cell rescue (HDCSCR), alkylating agents, anthracyclines and platinum drugs was performed as it was thought that these treatments would be more likely to affect the developing dentition. As seen in the Venn diagram, figure 3.5 there are some patients who have received more than one type of chemotherapy treatment regime. These individual groups were not analysed further due to the large number of different treatment regimes and the small patient numbers within the groups.

4.3 RATIONAL FOR CHOICE OF CONTROL DATA.

The Child Dental Health Survey 2003 (CDHS) was used to obtain control data. The CDHS was carried out in 2003 by dentists across the country on 5,8,12 and 15-year-olds. An appropriate age and sex, matched control group was unobtainable in the scope of this study. This was because there were no identifiable healthy populations accessible through the Birmingham Children's Hospital. The large variety of ages within the study group meant a control group would need to be made up from several sources and the time constraints of the research project precluded this. Previously school children have been used as a control group, it would however now be more difficult to obtain a sufficient sample size from this source as positive consent is likely to be required by the ethics boards to allow examination of the school children. The criteria used in this study were as close as possible to those used in the 2003 CDHS and the investigator carried out the same training in order to make the results as comparable as possible.

4.4 DENTAL CARIES.

Overall 42.2% of the study group had experienced decay in one or more teeth, 18.3% had untreated primary decay and 18.3% had untreated secondary decay. The figures for the level of untreated decay are interesting because they are similar for both the primary and the permanent dentitions. The 2003 CDHS from 1983-2003

reports that the number of restorations being placed in the primary dentition had declined in both 5 and 8-year-olds, but the proportion of filled permanent teeth had increased from 1983-2003 in 8, 12 and 15-year-olds. This data is calculated by measuring filled teeth as a percentage of obvious decay experience (Pitts and Harker, 2005). In the 2003 CDHS, 13% of 5-year-olds with obvious decay experience had filled teeth and 57% of 15-year-olds with obvious decay had filled teeth (Pitts and Harker, 2005). It is difficult to draw any comparisons with the above current study data because of the wide variety in age of the patients in the study group.

When comparing the study results with the 2003 CDHS directly by age groups, the only group which showed an increase in the level of decay was the primary dentition of 8-year-olds. The only group which showed a decreased level of decay was the 12-year-olds in the permanent dentition. The other groups were all very similar. Given the small size of the study groups within the current study data it is difficult to draw any firm conclusions.

The groups showing a high dental caries rate in the primary dentition included the HDCSCR group and the neuroblastoma group. These results are largely based on the same patients because all patients who received HDCSCR had a neuroblastoma except for one patient. Kaste et al (1998) reported on 52 patients over a 31 year period of patients being treated for neuroblastoma and also noted an increased level of decay in the primary teeth. The caries experience of the permanent teeth was the same as the general population (Kaste et al., 1998); a finding consistent within the current study. The increased decay rate could be attributed to the high level of systemic upset resulting from the cancer therapy. The chemotherapy the patients receive frequently results in the development of mucosal ulcerations and results in a sore mouth. During medical treatment the calorific intake for these children is important and it is often difficult to achieve an adequate level, hence these patients will be fed on high calorific diets which, by their nature, are likely to be cariogenic. Also they are likely to be receiving more medical interventions with sweets often given as rewards thus contributing to a cariogenic diet. The chemotherapy during this period may cause a xerostomia, altered salivary consistency and disturbance in

taste, and therefore perhaps contribute to an increase in susceptibility to dental caries during this time. Often for cancers of younger children, the treatment affects an age group where the primary teeth are present and who require parental assistance to effectively brush their teeth. In this group dental hygiene may be sub-optimal, especially in the presence of mucositis.

Apart from the above group, the caries experience of individuals in the study group does not seem to be above the level within the general population. This is shown by both the 2003 CDHS and The British Association for the Study of Community Dentistry (BASCD) epidemiological studies. The BASCD survey of 14-year-olds (2003) stated the mean DMFT over England and Wales to be 1.48 and the West Midlands is described as being below 1.24 (Pitts et al., 2004). The BASCD survey (2000) looking at 12-year-olds stated the DMFT to be 0.63 across the West Midlands (Pitts et al., 2001). When comparing the study population (mean DMFT 0.56 and mean dmft 0.84) with the epidemiological studies described above, the study population does not have a particularly high caries rate. Apart from the neuroblastoma and HDCSCR group, the study population actually shows a decrease in caries experience compared with the general UK population. This finding is consistent with other groups of cancer patients and is supported by Alsplan et al (1999), Maguire et al (1987), Nunn et al (1991) and Oguz et al (2004), but unsupported by Purdell Lewis et al (1988) who found the caries experience of the cancer group to be higher than the controls. He did however use a different method of caries diagnosis. Caries in his study was defined by the presence of a white spot lesion, a criteria which would not be designated as caries by the 2003 CDHS (Pendry et al., 2004). The control group in the Purdell-Lewis et al (1988) study were recent longitudinal epidemiological studies that are reported to have used the same caries diagnosis criteria (Purdell-Lewis et al., 1988). Pajari et al (1988) also found a higher caries incidence in their cancer group by comparison with the healthy control group when using the World Health Organisation 1977 criteria for caries diagnosis (Pajari et al., 1988).

4.5 ENAMEL OPACITIES.

Several different indices have been proposed to assess enamel opacities in teeth. The earliest index was by Murray and Shaw (Murray and Shaw, 1979). This included a 7 point index differentiating small white spots, larger white spots, coloured patches, horizontal lines, hypoplasia and possible early caries. A second index, called the defects of dental enamel index (DDE index) was introduced in 1981 by the general assembly of the world dental federation (FDI, 1982). This covered types of defect, the number of and demarcation of defects and the location of defects. This index was simplified and modified to include; normal, demarcated, diffuse and hypoplasia categories, also considering the extent of such lesions (Clarkson and O'Mullane, 1989). The criteria used in the study population were as close as possible to the 2003 CDHS to allow direct comparisons (Pendry et al., 2004). This index is based on the modified DDE index but included symmetry of diffuse lesions and codes accounting for the presence of, a mixture of lesions on a single tooth.

Of the study group tested 50 (62.5%, n=80) had enamel opacities present. The 2003 CDHS only recorded opacities in 12-year-olds. 35% of the 2003 CDHS 12-year-olds in England were reported to have enamel opacities (Chadwick et al., 2006). Of the 12-year-olds in the study population 3 (42.9% n=7) had enamel opacities. Due to the small sample size it is hard to draw any conclusions as none of the results were significantly different.

Within the study there were a large number of patients with diffuse defects, (42 (52.5% n=80)) when compared with the 16% in the 2003 CDHS national data for diffuse opacities. The 2003 CDHS report had as many demarcated (17%) lesions as diffuse (16%) lesions. This however was not a finding in the study population where the demarcated lesions were only noted in 12 (15% n=80) patients and diffuse lesions were noted in 42 (52.5%, n=80). The 2003 CDHS reported demarcated lesions to generally affect a smaller proportion of the tooth, with 92% being under 1/3. The current study supports this with 75% of demarcated lesions being under a third of the total tooth surface. Diffuse lesions are reported as being slightly more

widespread over the tooth surface, but still the majority in the 2003 CDHS (59%) are under a third of the tooth surface. The present study found 80% to be under a third and fewer of the diffuse defects (13, 25.5% n=51) were symmetrical across the midline by comparison with the 2003 CDHS results which found 65% of diffuse defects to be symmetrical (Chadwick and Pendry, 2004). Looking between the different sub-groups, there were no significant differences between them. The HDCSCR group did have the highest number (33.3% n=14) of patients with enamel opacities, but this was not significantly higher than the other groups. The study showed a large number of diffuse opacities to have been present in those patients living in a fluoridated area (38 patients in a fluoridated area compared with 12 patients with opacities not living in a fluoridated area); a known cause of opacities that could be related to the effects of fluoridation as opposed to chemotherapy. However it is difficult to draw any firm conclusions from this data because analysis was carried out using the present post code and assumes the patient has lived in a fluoridated all their lives which may not be the case. Further investigation of this was beyond the scope of the project.

Many of the other studies in the literature report cancer patients to have a higher incidence of enamel opacities and hypoplasias. Pajari et al (1988) studied 13 patients who had received chemotherapy, who lived in a non or low fluoridated area and had similar diagnoses to the patients the study population. He reported a significant increase in opacities per patient compared with the control group using the Developmental Defects of Enamel Index (DDE index). Pajari's study group had 100% with enamel opacities compared with the control group which had 86.5% with opacities. The results were not statistically significant. However, when they assessed the mean number of opacities per child, this was 10.4 in the cancer group and 3.4 in the control group showing a statistically significant difference in the level of opacities experienced (Pajari et al., 1988). Alpaslan et al (1999) who studied 30 lymphoma survivors also reported a significant difference between groups concerning opacities, with more in the cancer group when tested by comparison with the control group. Fourteen patients (64 teeth) showed hypoplasias and 17 patients (147 teeth) showed discolourations compared with the control group of 20 healthy patients, where 3

patients (5 teeth) showed hypoplasia's and one patient (4 teeth) showed discolourations. However, he did not explain the criteria used for this examination (Alpaslan et al., 1999). Maguire et al (1987) again found an increase in prevalence of enamel opacities (horizontal lines) and hypoplasia's using the index described by Murray and Shaw (1979) but only in the upper teeth (Maguire et al., 1987). Purdell Lewis et al (1988) found 80% of the test group to have experienced enamel opacities using the DDE index and compared the data to the country's national data which stated 43.3% as experiencing enamel opacities (Purdell-Lewis et al., 1988). Nunn et al (1991), another study carried out in a known fluoridated area showed an increase in hypoplasias in the study group (7% in the siblings and 19% of the test group) but all other enamel defects, i.e. white patches, coloured patches and white lines (tested according to Murray and Shaws method (Murray and Shaw, 1979) were not found to be significantly different to the sibling group (Nunn et al., 1991). Given the number of different indices described it is difficult to draw conclusions about enamel opacities. However, many of the studies mention enamel opacities as a significant finding within study populations. The cause of enamel opacities and hypoplasias has been attributed to many different factors, one of which could be chemotherapy. Other factors include fluoride, spikes of temperature during fever and infections, nutritional deficiencies and trauma (Welbury, 2004).

4.6 GINGIVAL HEALTH.

The recording of gingival health in research studies is carried out using many different indices. The criteria indicative of "gingivitis" can be measured using non-invasive, visual methods, invasive specific methods or both. The gingival index first described by Loë (1967) is hierarchical and includes both a visual assessment, recording redness, oedema and glazing, and bleeding on probing (Loe, 1967). An example of a non-invasive method would be the modified gingival index. This scores gingival redness by observing the gingival margin and papillae visually only. It is modified from the original gingival index described above and therefore does not include bleeding on pressure (Lobene et al., 1986). More specific methods include the Community Periodontal Index of Treatment Needs (CPITN) (Ainamo et al., 1982)

and indices of bleeding on probing, which have been shown to indicate gingival inflammation (Greenstein, 1984).

The current study recorded “gingivitis” by carrying out a basic periodontal examination on each patient (CPITN score) and then recording any sites of gingival bleeding on the mesial, distal, buccal and lingual aspect of each tooth. Any sites positive for bleeding indicated gingivitis. The 2003 Child Dental Health Survey recorded gingivitis (as bleeding on probing) in 15-year-olds only (White and Lader, 2004). The criteria used included 6 teeth; the first molars in each quadrant and the upper right central incisor and the lower left central incisor. The upper teeth were recorded by looking at the mesial, distal and buccal surfaces only and the lower teeth had the distal, mesial and lingual surfaces recorded only. If there was bleeding in any of the specified sites the subject was considered to have evidence of gingivitis (Pendry et al., 2004). The specific data to match the above criteria was extracted from the present study data to allow comparisons.

The gingival health of the study group when compared to the 2003 national data was slightly worse. Of the study population 54.5% showed signs of gingivitis (measured by bleeding on probing) compared to 43% of 15-year-olds in the UK. The current study also found more boys (62.5 %) to experience gingivitis compared with girls (33.3%). This finding is supported by Taani and Alhaija (2003) who investigated gingival health among 12-14-year-olds. They found that boys tend to have increased plaque levels and show poorer compliance with oral health measures (Taani and Alhaija, 2003). This is inconsistent with the 2003 CDHS results which reported more girls at 15 (46%) to be affected by gingivitis than boys (39%). However the 2003 CDHS did report that this finding was inconsistent with earlier findings in the study, when gingivitis was measured by looking at the mouth in sextants and marking where gingival inflammation was visually present. The other studies in the literature report to have found no difference in gingivitis and the oral hygiene levels of test and control groups. This was also the finding of both Maguire et al (1987) and Alsplan et al (1999); there were no studies supporting a difference. Despite these findings, bleeding gums are a concern to parents during cancer therapy as described by the

parental statements in the comments section. Such findings can exacerbate parental anxiety over a child's general health at a difficult time. Oral health education and improved preventative care may therefore reduce the level of anxiety felt by the parents and should be an important area for education, as part of the pre-treatment work up.

4.7 MICRODONTIA.

Microdontia was found in 9 of the study group patients. The most significant factor noted regarding microdont teeth, was that all patients who had a microdont tooth within the study population had received chemotherapy before the age of 3.5 years. When this relationship was investigated further it was found to be statistically significant, $p=0.03$. Maguire et al assessed the level of microdontia from radiographs by measuring crown size and found that within the solid tumour group 16.2% ($n=37$) had microdontia in the upper arch and 2.7% ($n=37$) in the lower arch. This however was not a test carried out in the sibling control group and therefore has no control comparisons. It is interesting to note that as with the study population, all children presenting with microdont teeth in the Maguire study received their chemotherapy treatment under the age of 3.5 years (Maguire et al., 1987).

The highest percentage of microdont teeth in the study data were found in the HDCSCR group (20%), whereas the other study groups with microdont teeth present were; alkylating agents (4.6%), anthracyclines (4.5%) and platinum drugs (6.7%). This finding would be consistent with the type of medical treatment, as it is more likely to affect the developing germ cells in the developing dentition. However, the results of the Chi squared test on the relationship between the HDCSCR treatment regime and microdont teeth was not statistically significant.

Because there is no current validated index classifying what a microdont tooth is, it is difficult to draw definitive conclusions and comparisons between studies. There are no epidemiological studies assessing microdontia in the UK population, but the paper by Holtta et al (2004) describes the Japanese population as having a prevalence of

1.9% microdontia when measured by taking casts of the teeth. Hawaiian studies show the prevalence to be higher at 3.1% (Holtta et al., 2004).

The most recent study investigating microdont teeth in this field is by Holtta et al (2004) (Holtta et al., 2004). They studied 55 patients who had received high dose chemotherapy under the age of 10 years and found microdontia in 44% of the study population against 2% in the control group. The control was the national epidemiological study data showing the Finish population to have a 2% incidence of microdontia. The investigators did acknowledge that the assessment of microdont was based on a subjective visual recording. If the investigators felt the size of the crown was at least 50% smaller than that of a 'normally sized tooth' it was labelled as microdont. They found the most commonly affected teeth to be first premolars (46%) followed by second premolars (26%) and second molars (23%) (Holtta et al., 2004). These results are consistent with the findings of the current study population in that the first premolar (38.5%) was the most commonly affected tooth.

Microdontia is described as a common finding in other similar studies, but again the criteria for what a microdont tooth is, are not clear between studies. Holtta et al (2002) looked at a group of 18 neuroblastoma survivors. These were split into two groups, those who had received total body irradiation (tbi) and those who had not; all had received high dose chemotherapy. They found 80% and 87.5% of the tbi and non-tbi groups respectively to be affected by microdontia. The difference between the two groups was not significant but the group as a whole did show significant microdontia levels. Alpaslan et al (1999) reported to have found no microdontia in either the lymphoma or control group (Alpaslan et al., 1999). Kaste et al (1998) studied microdontia from radiographs in their neuroblastoma study and reported 38% to have experienced microdontia. Again there was no control with this study and therefore the results are difficult to interpret (Kaste et al., 1998). Oguz et al (2004) investigating the non-Hodgkin's lymphoma group (n= 36) with an age and sex matched control group (n= 36), assessed microdontia from radiographs and found 3% of the test group to be affected by microdontia and 0% of the control group to be affected (Oguz et al., 2004). The literature therefore supports the finding of

microdontia in children who have received chemotherapy particularly those who had received chemotherapy at a young age, when the tooth germs are still developing.

From this data only limited observations can be drawn due to the small sample size. Microdontia and the presumed association with chemotherapy is well supported by several studies. However no studies actually define 'microdontia.' The teeth recorded in the current study as microdents had an obviously smaller crown size than the expected size of the tooth in the investigator's opinion. Many studies mention microdontia when analysing dental radiographs from patients who have received chemotherapy but none define the term. This is an area that requires a consensus opinion and diagnostic guidelines to establish consistency of reporting in future studies.

There are no epidemiological studies reporting the prevalence of microdontia in the UK population available in the literature. Comparisons can therefore only be made with other similar studies (Alpaslan et al., 1999, Holtta et al., 2004). As mentioned above this is difficult due to a lack of case definitions.

4.8 TRAUMA.

Dental trauma was experienced by 21 (17.5%, n=120) patients in the study group. As with national data the current study shows an increase in the prevalence of trauma in boys (66.7%) when compared with girls (33.3%). National data for 15-year-olds in England show 17% of boys and 10% of girls to have experienced dental trauma (Chadwick and Pendry, 2004). This is most likely due to boys being more boisterous and participating in contact sports activities than girls. There were no differences between the patient and treatment groups of the present study. These results suggest, despite possibly having more endotracheal intubations under general anaesthetic than the "average" child the patients within the current study group did not experience an increased level of dental trauma.

4.9 FISSURE SEALANTS.

Fissure sealants have been shown to protect the occlusal surfaces of teeth against caries (McCune et al., 1979). A recent Cochrane review investigating the use of fissure sealants concluded fissure sealants are a recommended method of preventing occlusal caries in molar teeth. However the application of sealants should be based on the prevalence of caries in the individual and the local population (Ahovuo-Saloranta et al., 2004). A further Cochrane review investigating the use of fissure sealants versus fluoride applications concluded the application of fissure sealants to be superior to the application of fluoride varnish, but again the use of each should be based on the individuals concerned and local population needs (Hiiri et al., 2006). The level of fissure sealants in the study population is low by comparison with national data. Nine percent of the study population had fissure sealants compared with between 13-15% of 8, 12 and 15-year-olds in the 2003 CDHS. This is possibly due to the fact that the caries rate is lower in the West Midlands and some dentists feel the need for fissure sealants in the Midlands area is reduced by comparison with elsewhere in the UK. However, what was concerning was that none of the patients in the neuroblastoma group and only 1 subject in the HDCSCR group received fissure sealants, when these are the two groups which would benefit the most from such a preventative technique.

4.10 QUESTIONNAIRE.

4.10.1 The use of questionnaires.

The questions were designed so as not to employ leading questions however the analysis of the results still has to take into account any bias. For example, the study group were asked to complete the questionnaire at the dental visit and so knew the investigator was a dentist which have could have led the person filling in the questionnaire to provide more favourable answers to 'please' the investigator. Also the questionnaire did require some recollection of information about when the child was initially diagnosed and initial treatment and therefore could be subject to recall bias.

4.10.2 Attitude towards oral health.

The study group did appear to perceive oral health to be important according to the questionnaire answers. Most parents/guardians answered favourably when considering the importance of oral health care in their child. 116 (99.1% n=117) crossed the line above 8cm and 70 (59.8% n=117) crossed at 10cm. One parent did cross the line at 5cm, but by the nature of the scale it is not certain quite how this parent actually felt about the oral health care of their child. It just gives an indication that they would not place oral health care at maximum importance. Fewer parents/guardians answered questions about themselves. Of the 62 parents who answered about their perception of the importance of oral health care for themselves 62 (100%) crossed the line above 6cm with 61.3% (38) crossing the line at 10 cm, indicating maximum importance. The parents may have been reluctant to answer the question about themselves as they felt it was not important because the investigations were mainly about their child, or perhaps it was not noticed due to the position of the question on the paper. It should be remembered that, these answers will be subject to bias with parents perhaps answering more favourably than their day to day practice would support.

4.10.3 Reported attendance at the dentist.

Of the parents who answered the question about how often they visit the dentist, 83 (69.2%, n=118) reported to visit regularly, 21 (17.8%, n=118) reported to visit occasionally, 10 (8.5%, n=118) when in trouble and 4 (3.4%, n=118) never visited the dentist.

When answering about their child's dental visits again 118 patients answered the question; 99 (82.5%, n=118) reported to be registered with a dentist; 91 (77.1%, n=118) reported to visit regularly; 9 (7.6%, n=118) reported to visit occasionally with the same proportion visiting only when having trouble or never. The CDHS has shown over the years that there is a positive correlation between the mother's dental

attendance pattern and the child's (Morris et al., 2004). Thus if the parents are regular attenders the child is likely to be so. This theory was supported by the current data.

The study data when compared with the national data from the same question asked in the 2003 CDHS does show similar responses (question 6). 2003 CDHS results show 82-88% 5-15-year-olds reported to visit regularly, 8-14% occasionally and 3-5% when in trouble. From the 2003 CDHS data those who had never visited the dentist were 7% of 5-year-olds and 1% of 15-year-olds (Morris et al., 2004). This does indicate that the study group had a high level of patients who had never attended the dentist. There was one 5-year-old, two 9-year-olds and 4 teenagers who had never been to the dentist. Given the nature of the disease the patients had experienced and the tumour's medical treatment, these figures, though within a small sample size, are disappointing. The findings of the study do emphasise the importance of receiving some dental input within this particular group of patients.

It is interesting to note that in April 2005, before this study's data collection phase began, the National Health Service (NHS) general dental services within England changed their structure. Instead of being paid on a fee per item basis the services have moved towards "salaries" for general dentists. The system for patients also changed and now patients are no longer officially registered with a specific dental practice, but anyone who attends requesting a dental review and course of dental treatment should be accepted, provided that dentist has not exceeded his NHS contract value for that year. This change is poorly understood by the general population at the present time. However future research may be unable to ask the question about registration at the general dental practice, because it will no longer be a valid measure. It would be interesting to research the impact of the new system within such population groups. Already, as shown in the comments section, several remarks were made expressing concerns over access to a national health service dentist, mentioning their dentist had "gone private" or the practice was so busy that it was difficult to obtain review appointments.

4.10.3.1 Prior to cancer therapy.

Before starting cancer therapy only 14 (11.8% n=118) reported to have specifically seen the dentist, the remainder answered “no” (104, 88.2% n=118). When asked where they were seen, 18 parents answered the question of which 13 were seen locally and 5 by a hospital dentist. These figures are below the ideal. The UKCCSG/PONF mouth care guidelines (UKCCSG and PONF, 2006) now suggest every patient should be specifically screened by a dentist before starting cancer therapy in an attempt to prevent any unnecessary dental complications during cancer treatment. Often during this time the child is immunosuppressed and any treatment of dental disease becomes more complicated. The seriousness of complications is highlighted by the study data stating 40% of those patients who did experience problems with the oral cavity did require hospital admission. It may be useful from a protocol, to include a hospital dental review on the same day that all the other pre-treatment medical tests are carried out. This would identify problems and allow arrangements to be made to address any pre-existing dental disease before chemotherapy was due to start.

Information on how to look after the mouth and teeth during cancer therapy was reported to have been given in 52 cases (44.1% n=118), 12 (10.2% n=118) did not know and 53 (44.9%, n=118) specifically claimed they did not receive any information. The possible long term sequelae are reported to have been discussed in 69 (59.0% n=117) cases, with 34 (28.8%, n=117) specifically saying no discussion occurred and 14 (12.0%, n=117) having not remembered if this was discussed or not. One parent did mention in the comments section they felt “*more information at the time of treatment verbally*” would help. These questions are both subject to recall bias. More recently the level of general information given to patients on the diagnosis of cancer has improved. However, upon the diagnosis of cancer so much information will be given to the families regarding the medical treatment required and its late effects on the whole body, it is possible the oral effects are forgotten (or over looked) as other effects seem more significant. It may be helpful to develop a leaflet to give to parents for future reference once the cancer therapy has started. Despite having no teeth this information should also be given to the parents of very young children. The

comment *'he was only 2 when diagnosed so we didn't worry about his teeth at the time. We hadn't started to visit the dentist but we were advised not to anyway'* highlights how at least one family felt this issue was unimportant at such a young age yet this is the age where the developing dentition is most vulnerable and the families should be warned of potential issues during treatment and the potential late effects.

4.10.3.2 During cancer therapy.

Forty four (37.6% n=117) parents did report problems with their child's mouth during cancer therapy. The most frequently reported problem was a sore mouth (36, 55.4% n=65) followed by 12 (18.5%, n=65) complaining of a mouth infection, 8 (12.3%, n=65) dental decay and 9 (13.8%, n=65) other complaints including ulcers, mucositis, sore teeth or difficulty swallowing. Of these 18 (40% n=65) required hospital admission. Those requiring hospital admission often require supportive therapy for oral pain control and provision of fluids due to a sore mouth and inability to swallow. Mucositis is difficult to predict and cannot be easily prevented. It has been shown to occur in 30-75% of patients undergoing chemotherapy (Fulton et al., 2002, Dodd et al., 2000). More accurate incidences of mucositis, xerostomia and taste disturbance during chemotherapy for solid tumours are difficult to find in the literature and would be worth exploring further, however this was beyond the scope of this thesis. It is difficult to fully assess the impact of pre-existing dental disease during the time chemotherapy is undertaken. In the comments section of the questionnaire, one parent did write it was necessary for their child to have two teeth removed due to dental abscesses whilst mid-chemotherapy. This acute scenario could probably have been avoided if a dental review had been carried out before the chemotherapy commenced.

4.10.3.3 After cancer therapy.

Since medical treatment finished 99 patients (83.2%, n=119) reported to have seen a dentist and the majority (79, 67.0%, n=118) had seen a local dentist. When considering the results of this question it should be remembered the question was potentially subject to recall bias and also may have been more favourably answered to 'please' the investigator as it was being completed at the time of the dental

examination. According to the results most patients are still being seen within the general dental services. This is supported by the fact that 87 (73.7%, n=118) general dentists would happily see their child despite the medical treatment and condition and only 3 (2.5%, n= 118) specifically saying “no” to treating the patient. Provided the patients are accessing oral health care and their general dentist is managing any problems adequately, no specialist input would be required. If necessary the general dentist can refer the child to the hospital service for an opinion or treatment if required. What was more worrying was that 21 (17.5%, n=120) patients had not sought any dental care after the treatment for their cancer. This number may be slightly inflated due to the fact that 8 patients had finished their therapy within the previous 6 months. Taking this into account along with the potentially more favourable results there were still at least 13 patients who should have received a dental review and had not.

4.10.4 Dental treatment required post cancer therapy.

Since cancer therapy finished, 63.9% (76 out of 119) reported to have had dental treatment carried out. This data is subject to recall bias and may not be factually accurate. Parents could have mis-interpreted the dentists explanation of treatment carried out or simply have forgotten exactly what happened. Of this group 26 (39.3%, n=66) had required fillings, 9 (13.6%) extractions under local anaesthetic, 4 (6%) extractions under general anaesthetic and 4 (6%) were undergoing orthodontic treatment. This treatment was provided by the local dentist in 39 (33.3% n=117) cases and in hospital for 7 cases (6.0%). These findings show that the majority of care is still being received within the general dental services despite the medical history, therefore suggesting that some patients who are able to seek care within the general dental services do receive adequate care. With changes to NHS dentistry this may change.

4.10.5 General dental care and comments made.

In general 87 (76.3%, n=114) felt they did have adequate access to dental care, 13 (11.4%, n=114) felt they did not have adequate care and 14 (12.3%,n=114) did not know if they had adequate dental care. These findings suggest 27 (23.7%, n=114) of the study population were not receiving, in their parents opinion, adequate dental care. It would be interesting if interviews of these patients and their parents were carried out, to ascertain why they felt this way and whether or not there was a real need for arrangements to be made for these children to be reviewed within the hospital system. Despite the figure of 76.3% who felt they did have adequate access to dental care there were several comments to the contrary. The comment '*2 abscesses during chemo- teeth extracted under local anaesthetic at BCH*' highlights the need for a dental review before commencing chemotherapy and potential inadequate dental care being received. If a screening examination had taken place it would have been likely that these teeth would have been identified and extracted or restored before chemotherapy started, therefore not causing further complications during the period of chemotherapy. Active disease was noted in during the examination in 30.8% of the study population, and upon questioning some of the families had no readily available dental care and were therefore referred or seen at BCH. In further studies it would be interesting to cross match the dental examination with the questionnaire answers to investigate how many of these patients had recorded in question 23, to have felt they did have adequate dental care.

When considering the overall results, it is important to note the answers given on all the questionnaires are likely to be slightly in favour of good oral health practices. This was because the parents/guardians knew the investigator was a dentist and were therefore more likely to write favourable answers, some of the questions were also subject to recall bias as it may have been some time since the event occurred.

5.0 CONCLUSIONS, OUTCOMES AND FUTURE RESEARCH.

5.1 CONCLUSIONS.

1. The study group of solid tumour patients did not have significantly more dental complications in comparison with the general population.
2. The study group did require a greater dental input in comparison with the general population particularly during chemotherapy treatment.
3. The oral health needs of individual groups of solid tumour oncology patients did differ according to the type of tumour and treatment regime. The oral health needs of the neuroblastoma patient group and those patients receiving high dose chemotherapy with stem cell rescue (HDCSCR) were increased when compared to the remaining study and general population. These groups require a greater dental input with more emphasis on prevention techniques such as fissure sealants, oral health care regimes and long term dental follow up to address the likely dental anomalies occurring.
4. In general the study patients did not have difficulty in accessing dental care at the present time. Though in some cases this was not perceived to be satisfactory care.
5. There was a varied level of knowledge of oral health care implications in parents following their child's cancer therapy.
6. Children receiving chemotherapy under the ages of 3.5 years appear more likely to have one or more microdont teeth in the adult dentition by comparison with those who are older when they receive their chemotherapy.

CLINICAL RECOMMENDATIONS.

Clear protocols and care pathways should be created for the solid tumour patients regarding oral health care upon diagnosis, during chemotherapy and after chemotherapy.

It is recommended that a dental examination is carried out for all patients before commencing chemotherapy and regular follow up is continued throughout the therapy and the teenage years. If the child does have a family dentist, the dental reviews can be carried out within the general dental services, but should the level of care not suffice, the hospital dental specialities team should provide oral health care for this group of patients. Information sheets should be designed for general dental practitioner's to explain the short term and long term oral health problems these patients may be facing and what oral health interventions are recommended before, during and after cancer therapy.

With the recent re-structuring of NHS dentistry and the unknown outcome of such changes it may be advisable to provide hospital surveillance for those patients being reviewed within the general dental services. If patients are found to have difficulties in accessing care, oral health log books could be designed such that for children who change general dental practitioners frequently all of the relevant medical and dental information would be readily accessible to each different practitioner. These books would be held by the parents/guardians of the child (similar to the way the 'red book' for young children is used for general health records) and therefore ease the transition among different dental practitioner's, record what interventions had been required in the past and facilitate hospital surveillance ensuring adequate oral health care for patients.

Urgent care should be available to these patients through the hospital, particularly if dental treatment is required to achieve a healthy mouth before the patient starts chemotherapy.

Training should be available for the oncology team regarding the effects of cancer therapy on the dentition, signs and symptoms of oral disease and where and how to seek further advice when it is required. Regular updates and training of new members of the oncology team should be regularly provided by the dental team within the community and hospital environments.

Verbal and written information should be provided about the effects of chemotherapy on the oral cavity and the teeth. This should cover the oral health side effects during chemotherapy and also cover long term effects such as microdontia and other dental anomalies. Different information leaflets should be designed explaining the above information aimed at children of different ages and their parents/guardians. The information should be available in different languages and approval for the use of the symbol of clarity (a crystal) sought from the Plain English Campaign.

Greater dental input is required for the neuroblastoma and HDCSCR group with development of separate protocols for these patients. Of all the oncology patients this group are most likely to benefit from a dental screening appointment by a dental specialist pre-treatment as the consequences of sepsis are significantly detrimental to their health. They are the group which need most help with prevention and reinforcement of prevention with support for the parents on oral health care. They are also likely to need the most dental intervention in the future due to the increased possibility of dental anomalies. It should perhaps be suggested this group are seen by a specialist paediatric dentist and fissure sealants are provided as a preventative measure in all cases.

5.3 FUTURE RESEARCH.

To enable the collection of reliable epidemiological data that records the level of microdont teeth within the general population and specific study population groups further research into microdont teeth is required. A consensus of opinion on the definition of a “microdont tooth” should be sought with a proposed scale of measurement. The development of such an index would allow comparable data between studies researching similar subjects to be calculated. This is important for subject areas such as the current study, where obtaining large numbers of subjects is difficult due to the rare nature of the disease.

Further long term follow up studies of neuroblastoma and HDCSCR patients would be beneficial to investigate the oral health effects of chemotherapy treatment further. These patients have been shown in the current study to be the most “at risk” patients for long term oral health side effects of their treatment. There are few studies investigating the long term health outcomes for these patients because previously many patients died as a result of their disease however with newer treatment regimes the survival rate has significantly improved.

Research into the frequency of oral health problems during the chemotherapy phase of solid tumour cancer treatment would also help our understanding of the short term oral side effects of chemotherapy. Investigating the exact number of patients requiring supportive therapy from the hospital during therapy and the incidence of mucositis, xerostomia, taste disturbance would help in the preparation of the patients for chemotherapy. Further trials of how best to treat these side effects are also required as also mentioned by the recent Cochrane review on oral mucositis (Worthington et al., 2005).

During the planning and data collection phases of this research study the general dental services in England were restructured. Instead of a general dentist looking after a cohort of the general public and being paid on a “fee per item” basis, they have moved to obtaining a contract with the local health authority. This enables the

dentist to undertake so many units of dental activity a year for which they are paid a salary. The provision of out of hours care is no longer the responsibility of the dentist and the patient is no longer “registered” with that dentist. If therefore the dentist has fulfilled the contracted units of required dental activity before the end of the contract period they can no longer see further patients under the National Health Service regulations until a new contract begins. The effects concerning the provision of oral health care following the change in structure of the general dental services to the general population and in particular this group of patients should be reviewed and investigated again.

The dental examination and questionnaire results could be crossed matched to allow a more in depth analysis of the current or future populations. The data collection might be expanded to include patients such as those with central nervous system tumours and those with leukaemia. This would enable a larger study population and possibly highlight further differences in oral health between different types of cancer. Multi centre trials would also be beneficial to increase the overall numbers of patients and the diagnostic group numbers.

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APPENDIX 1.

Data collection sheet 1.

Identification code:

Hospital number:

Date today:

Date of birth:

Gender:

Postcode:

Diagnosis:

Date of diagnosis:

Treatment regime:

Chemotherapy	<input type="checkbox"/>	Chemotherapy and Radiotherapy	<input type="checkbox"/>
Radiotherapy	<input type="checkbox"/>	Observation	<input type="checkbox"/>

Length of chemotherapy treatment:

Date started the follow up clinic:

APPENDIX 2.

Data Collection sheet 2

Identification code:

Dental Examination:

- Teeth Present
- DMFT

1,7	6	5	4	3	2	1	E	D	C	B	A		A	B	C	D	E	1	2	3	4	5	6	2,7
												D												
												O												
												M												
												B												
												L												
												D												
												O												
												M												
												B												
												L												
4,7	6	5	4	3	2	1	E	D	C	B	A		A	B	C	D	E	1	2	3	4	5	6	3,7

Codes:

- 0= sound
- 1= arrested caries
- 2= decayed
- 3= unrestorable
- 4= filled and decayed
- 5= filled with no decay
- R= filled but needs replacing
- 6= extracted due to caries
- 7= extracted due to orthodontic reasons
- 8= unerupted
- 9= excluded
- \$- sealant
- N= sealant restoration
- T= traumatised
- C= crown/ advanced restoration

Data collection sheet 2
 Identification code.....

BPE score:

Tooth	1,6	1,1	2,1	2,6
Code				
Tooth	4,6	4,1	3,1	3,6
Code				

Scores: 0=healthy
 1= bleeding on probing
 2= calculus
 3= shallow pockets 4-5mm
 4= deep pockets 6mm+
 *= furcation or recession of 7mm+

7-11 years only use codes 0,1,2
 12-16 full coding but above teeth used only
 >16 full BPE

If above 16 years
 Use table below for adult BPE scoring.

Periodontal Health

1,7	6	5	4	3	2	1	E	D	C	B	A		A	B	C	D	E	1	2	3	4	5	6	2,7
												D												
												O												
												M												
												B												
												L												
												D												
												O												
												M												
												B												
												L												
4,7	6	5	4	3	2	1	E	D	C	B	A		A	B	C	D	E	1	2	3	4	5	6	3,7

Code 0= no bleeding from the gingival sulcus.
 Code 1= bleeding from the gingival sulcus.
 Code 9= assessment cannot be made.

APPENDIX 3.

Identification code.....

Opacities

Consent for photo: yes/no
(please circle)

Tooth	1,4	1,3	1,2	1,1	2,1	2,2	2,3	2,4
Type of defect								
Extent of defect								
Symmetry								

TYPE OF DEFECT:

- Code 0- normal
- Code 1- demarcated opacity
- Code 2- diffuse opacity
- Code 3- hypoplasia
- Code 4- demarcated + diffuse
- Code 5- demarcated +hypoplasia
- Code 6- diffuse+ hypoplasia
- Code 7- all 3 defects
- Code 8- other defects
- Code 9- Assessment cannot be made

EXTENT OF DEFECT:

- Code 0- normal
- Code 1- less than 1/3
- Code 2- at least 1/3-2/3
- Code 3- at least 2/3
- Code 9- assessment cannot be made

If more than 2/3 is decayed fractured it should not be examined

Symmetry of defect:

- Code-0= no diffuse defects
- Code 1= diffuse defects but not symmetrical
- Code 2= diffuse defects symmetrical

APPENDIX 4

Version 3.0. 03/12/05

Dear Parent/Guardian,

I am writing to you to inform you about some research that is currently being carried out at Birmingham Children's Hospital on patients who attend the late effects clinic and wish to participate.

We are looking into the short term and the long term effects of cancer treatment on children and young adults' teeth and mouth.

Your child is being invited to take part at their next follow up clinic appointment. This is on a purely voluntary basis and will not affect the medical care he/she receives it will however increase the amount of time you spent at the hospital.

Please read the enclosed information leaflet regarding the study and consider whether you wish your child to take part. By taking part your child will help improve our knowledge about the dental health of children with cancer and enable us to improve services appropriately. Any questions or queries can be answered at your appointment.

Thanking you in anticipation

Yours Sincerely

Alison Hutton
Specialist Registrar in Paediatric Dentistry
[address]
[phone number]

APPENDIX 5

Version 5.0 03/12/05

Patient Information Sheet for Parents/Guardians Group 1.

Study Title:

The Dental Needs of Children Undergoing Cancer Treatment for Solid Tumours.

Invitation to Participate

You and your child are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

It is known that children who have, or have been treated for leukaemia have more dental problems than children who have not. There is less evidence available for children who have been treated for solid tumours. This project aims to examine a cross section of children who are under follow-up for the treatment of solid tumours at Birmingham Children's Hospital to identify what dental problems they have and assess whether they have access to adequate dental care.

1. What is the purpose of the study?

Research in children with leukaemia has identified that sometimes children have increased need for dental care during and after treatment. Less research has been carried out in children with solid tumours. Potentially there may be an increased risk of problems for the teeth and mouth even after treatment has finished. Some studies of adult survivors of childhood cancer have commented that individuals find it difficult to access dental care.

Preventing dental disease will help to improve overall health. The effects of treatment for their malignancy on the development of the teeth and function of oral tissue will be assessed in children taking part in the study.

This survey aims to look at the dental health of a cross section of children treated for solid tumours of childhood who are attending the follow-up clinic at Birmingham Children's Hospital. It will also record the extent of input that children are receiving from their own dentist or community dental services.

2. Why has my child been chosen to take part in the study?

Your child has received treatment for a solid tumour of childhood and is attending the follow up clinic in the oncology department at Birmingham Children's Hospital.

3. Do they have to take part?

No. It is up to you and your child to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

4. What will happen to my child if he/she takes part?

If your child chooses to take part they will see a dentist for a dental examination taking approximately 10mins. If he/she is over 7 years old a photograph will be taken of the front teeth and they will be asked to have an x-ray of the teeth in the dental hospital. You will be asked to fill out a short questionnaire about your child's current dental treatment.

5. What do I have to do?

When you attend the clinic for a regular follow-up appointment your child once you have read this information sheet again you will be asked to sign a consent form if you agree for your child to take part. Your child will then also be seen by the dentist and you will be asked to fill out a short questionnaire. If your child is over 7 years old a photograph will be taken of your child's teeth and you will be asked if you would be willing to attend the dental hospital (which is next door to the Children's Hospital) for an X-ray of the teeth.

6. What are the alternatives?

If you do not wish to take part in the study your child can continue to receive their usual care from their own dentist or community dental services.

7. What are the side-effects of any treatment received when taking part?

This study is an examination only. There is no treatment involved. If the dentist considers that your child does require treatment they will inform your child's dentist or community dental service, or if necessary refer your child to the dental clinic at Birmingham Children's Hospital.

8. What are the disadvantages and risks of taking part?

The only disadvantage is extending your clinic visit for the time required for the examination, to complete the questionnaire and to have the X-ray of the teeth. Your child will be exposed to some radiation when we take the x-ray. This is a very small dose of radiation equivalent to 2 days of background radiation from being outdoors.

9. What are the possible benefits of taking part?

If early dental disease is discovered it will be possible to treat this before symptoms such as toothache develop.

10. What if new information becomes available?

It is unlikely that new information relevant to this study will become available while it is in progress.

11. What happens when the research study stops?

Your dentist or community dental services will be informed of the results of the examination and the X-ray. If you do not have a dentist advice about how to obtain dental services will be given.

12. What if something goes wrong?

There is no treatment involved in this study.

13. Will my child taking part in this study be kept confidential?

Yes. All information about your child will be kept anonymous. The results will be published in a scientific paper, but there is no way that any individual could be identified from the information that is given. The photograph of your child's teeth will be kept confidentially and used for research. In the event that we wished to publish the photograph of your child's teeth or the X-ray of your child's teeth for illustration in any scientific paper we would approach you for consent to do that at the time.

14. What will happen to the results of the research study?

The results will be analysed and published in a scientific paper.

15. Who is organising and funding the research?

The research is organised and funded between the oncology and dental departments of Birmingham Children's Hospital and the Paedodontics department at the Birmingham Dental Hospital.

16. Whom do I contact for further information?

If you have any questions please contact [details]

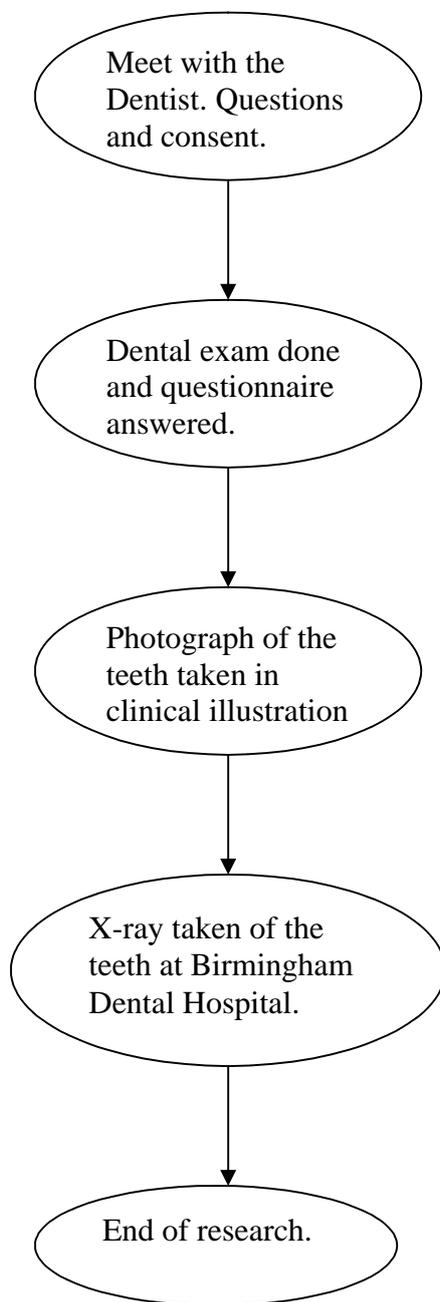
17. What if I have any concerns?

If you have any concerns or questions about the study you could contact [details]

Thank you for taking time to read this information.

Flow diagram of proposed study

2/11/05



APPENDIX 6

Version 5.0 14/12/05

Patient Information Sheet for adolescents 16+

Study Title:

The Dental Needs of Children Undergoing Cancer Treatment for Solid Tumours.

Invitation to Participate

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

It is known that children who have, or have been treated for leukaemia have more dental problems than children who have not. There is less evidence available for children who have been treated for solid tumours. This project aims to examine a cross section of children who are under follow-up for the treatment of solid tumours at Birmingham Children's Hospital to identify what dental problems they have and assess whether they have access to adequate dental care.

1. What is the purpose of the study?

Research in children with leukaemia has identified that sometimes children have increased need for dental care during and after treatment. Less research has been carried out in children with solid tumours. Potentially there may be an increased risk of problems for the teeth and mouth even after treatment has finished. Some studies of adult survivors of childhood cancer have commented that individuals find it difficult to access dental care.

Preventing dental disease will help to improve overall health. The effects of treatment for their malignancy on the development of the teeth and function of oral tissue will be assessed in children taking part in the study.

This survey aims to look at the dental health of a cross section of children treated for solid tumours of childhood who are attending the follow-up clinic at Birmingham Children's Hospital. It will also record the extent of input that children are receiving from their own dentist or community dental services.

2. Why have I been chosen to take part in the study?

You have received treatment for a solid tumour of childhood and are attending the follow up clinic in the oncology department at Birmingham Children's Hospital.

3. Do I have to take part?

No. It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

4. What will happen to me if I take part?

If you choose to take part you will see a dentist for a dental examination taking approximately 10mins. A photograph will be taken of the front teeth and you will be asked to have an x-ray of the teeth in the dental hospital. Your parent/guardian will be asked to fill out a short questionnaire about your current dental treatment.

5. What do I have to do?

When you attend the clinic for a regular follow-up appointment once you have read this information sheet again you will be asked to sign a consent form if you agree for your child to take part. You will then also be seen by the dentist and your parent/guardian will be asked to fill out a short questionnaire. A photograph will be taken of your front teeth and you will be asked if you would be willing to attend the dental hospital (which is next door to the Children's Hospital) for an X-ray of the teeth.

6. What are the alternatives?

If you do not wish to take part in the study you can continue to receive your usual care from your own dentist or community dental services.

7. What are the side-effects of any treatment received when taking part?

This study is an examination only. There is no treatment involved. If the dentist considers that you require dental treatment they will inform your dentist or community dental service, or if necessary refer you to the dental clinic at Birmingham Children's Hospital.

8. What are the disadvantages and risks of taking part?

The only disadvantage is extending your clinic visit for the time required for the examination, to complete the questionnaire and to have the X-ray of the teeth. You will be exposed to some radiation when we take the x-ray. This is a very small dose of radiation equivalent to about 2 days of background.

9. What are the possible benefits of taking part?

If early dental disease is discovered it will be possible to treat this before symptoms such as toothache develop.

10. What if new information becomes available?

It is unlikely that new information relevant to this study will become available while it is in progress.

11. What happens when the research study stops?

Your dentist or community dental services will be informed of the results of the examination and the X-ray. If you do not have a dentist advice about how to obtain dental services will be given.

12. What if something goes wrong?

There is no treatment involved in this study.

13. Will my taking part in this study be kept confidential?

Yes. All information about you will be kept anonymous. The results will be published in a scientific paper, but there is no way that any individual could be identified from the information that is given. The photograph of you teeth will be kept confidentially and used for research. In the event that we wished to publish the photograph of your teeth or the X-ray of your teeth for illustration in any scientific paper we would approach you for consent to do that at the time.

14. What will happen to the results of the research study?

The results will be analysed and published in a scientific paper.

15. Who is organising and funding the research?

The research is organised and funded between the oncology and dental departments of Birmingham Children's Hospital and the Paedodontics department at the Birmingham Dental Hospital.

16. Whom do I contact for further information?

If you have any questions please contact [details]

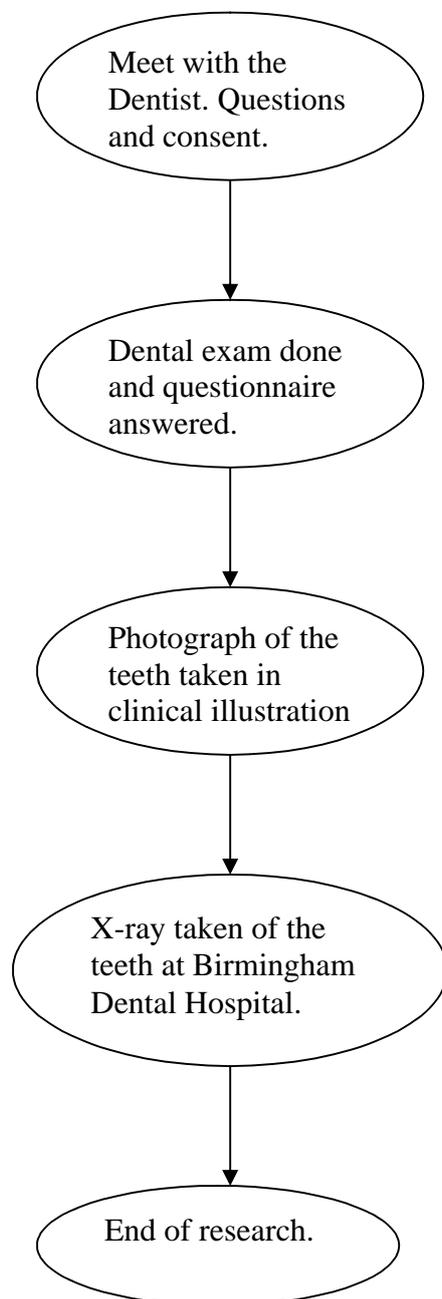
17. What if I have any concerns?

If you have any concerns or questions about the study you could contact [details]

Thank you for taking time to read this information.

Flow diagram of proposed study

2/11/05



APPENDIX 7

Version 4.0
03/12/05

Patient Information Sheet 13-15 yrs Group 1.

Study Title:

The Dental Needs of Children Undergoing Cancer Treatment for Solid Tumours.

You are being invited to take part in a research study. It is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish take part.

It is known that children who have, or have been treated for leukaemia have more dental problems than children who have not. There is less evidence available for children who have been treated for solid tumours. This project aims to examine children who are under follow-up for the treatment of solid tumours at Birmingham Children's Hospital to identify what dental problems they have and assess whether they have access to adequate dental care.

1. What is the purpose of the study?

Research in children with leukaemia has identified that sometimes children have increased need for dental care during and after treatment. Less research has been carried out in children with solid tumours. Potentially there may be an increased risk of problems for the teeth and mouth even after treatment has finished. Some studies of adult survivors of childhood cancer have commented that individuals find it difficult to access dental care.

Preventing dental disease will help to improve overall health. The effects of treatment for the tumour on the development of the dentition and function of oral tissue will be assessed.

This survey aims to look at the dental health of a cross section of children treated for solid tumours of childhood who are attending the follow-up clinic at Birmingham Children's Hospital. It will also record the extent of input that children are receiving from their own dentist or community dental services.

2. Why have I been chosen?

You have received treatment for a solid tumour of childhood and are attending the follow-up clinic in the oncology department at Birmingham Children's Hospital.

3. Do I have to take part?

No. It is up to you to decide whether or not you take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

4. What will happen to me if I take part?

You will see a dentist in the oncology clinic for a dental examination taking approximately 10 minutes, a photograph will be taken of your front teeth only and you will be asked to have an x-ray of the teeth in the dental hospital. Your parent/guardian will be asked to fill out a questionnaire about your current dental treatment.

5. What do I have to do?

When you attend the clinic for your regular follow-up appointment if you agree and your parent/guardian has signed a consent form you will also be seen by the dentist and your parent/guardian will be asked to fill out a short questionnaire. A photograph will be taken of your front teeth and you will be asked if you would be willing to attend the dental hospital (which is next door to the Children's Hospital) for an X-ray of the teeth.

6. What are the alternatives?

If you do not wish to take part in the study you can continue to receive your usual care from your own dentist or community dental services.

7. What are the side-effects of any treatment received when taking part?

This study is an examination only. There is no treatment involved. If the dentist considers that you do require treatment they will inform your dentist or community dental service, or if necessary refer you to the dental clinic at Birmingham Children's Hospital.

8. What are the disadvantages and risks of taking part?

The only disadvantage is extending your clinic visit for the time required for the examination, for your parent to complete the questionnaire and to have the X-ray of the teeth. You will be exposed to some radiation when we take the x-ray. This is a very small dose of radiation equivalent to 2 days of background radiation from outdoors.

9. What are the possible benefits of taking part?

If early dental disease is discovered it will be possible to treat this before symptoms such as toothache develop.

10. What if new information becomes available?

It is unlikely that new information relevant to this study will become available while it is in progress.

11. What happens when the research study stops?

Your dentist or community dental services will be informed of the results of the examination and the X-ray. If you do not have a dentist advice about how to obtain dental services will be given.

12. What if something goes wrong?

There is no treatment involved in this study.

13. Will my taking part in this study be kept confidential?

Yes. All information about you will be kept anonymous. The results will be published in a scientific paper, but there is no way that any individual could be identified from the information that is given. The photograph of your teeth will be kept confidentially and used for research. In the event that we wished to publish the photograph of you teeth or the X-ray of you teeth for illustration in any scientific paper we would approach you for consent to do that at the time.

14. What will happen to the results of the research study?

The results will be analysed and published in a scientific paper.

15. Who is organising and funding the research?

The research is organised and funded between the oncology and dental departments of Birmingham Children's Hospital and the Periodontics department at the Birmingham Dental Hospital.

16. Whom do I contact for further information?

If you have any questions please contact [details]

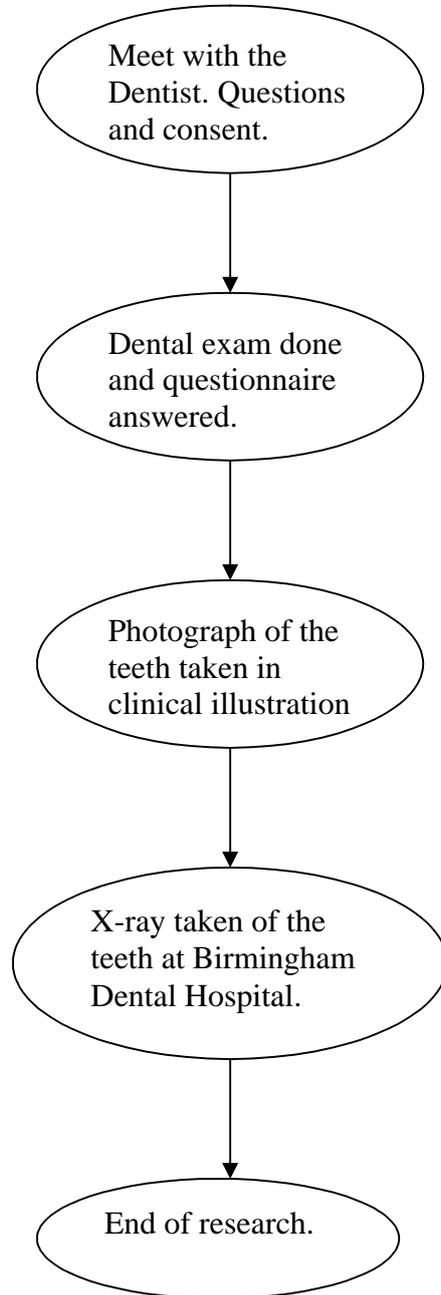
17. What if I have any concerns?

If you have any concerns or questions about the study you could contact [details]

Thank you for taking time to read this information.

Flow diagram of proposed study

2/11/05



APPENDIX 8

Version 4.0
03/12/05

Patient Information Sheet 8-12 yrs Group 1.

You are being invited to take part in a research study. Think about whether or not you wish take part. Ask us or your parent or guardian if there is anything you do not understand.

1. Why are we doing a study?

Dentists have found patients who have had cancer as a child sometimes do not have dental treatment before, during and after their illness. The treatment you have received for the cancer can sometimes make your mouth sore during treatment and can occasionally affect the developing teeth.

We want to find out if this is true. Then we can make dental services better where they are needed.

2. Why have I been chosen to take part in the study?

You have been chosen to take part because you have had treatment for cancer during childhood.

3. Do I have to take part?

No it is your choice.

4. What will happen to me if I take part?

If you choose to take part you will see a dentist for a dental check up taking approximately 10mins, a photograph will then be taken of your front teeth in the medical illustration department and then you will then be required to go to the dental hospital for an x-ray of the teeth. Your parent/guardian will be asked to fill out a questionnaire regarding your dental experiences

5. What are the possible disadvantages and risks of taking part?

You will have to give up some of your time to allow the dental examinations to take place. You will be exposed to a very small amount of radiation when we take the x-ray.

6. What are the possible benefits of taking part?

You will help us find out if chemotherapy treatment does have an effect on your teeth. This may help us with treatment of our patients in the future by identifying any problems you have experienced.

You will be told if any dental treatment is needed and advised on where to seek treatment if you do not already have a dentist.

7. Will my taking part in this study be kept confidential?

Yes.

8. Whom do I contact for further information?

If you have any questions please contact [details]

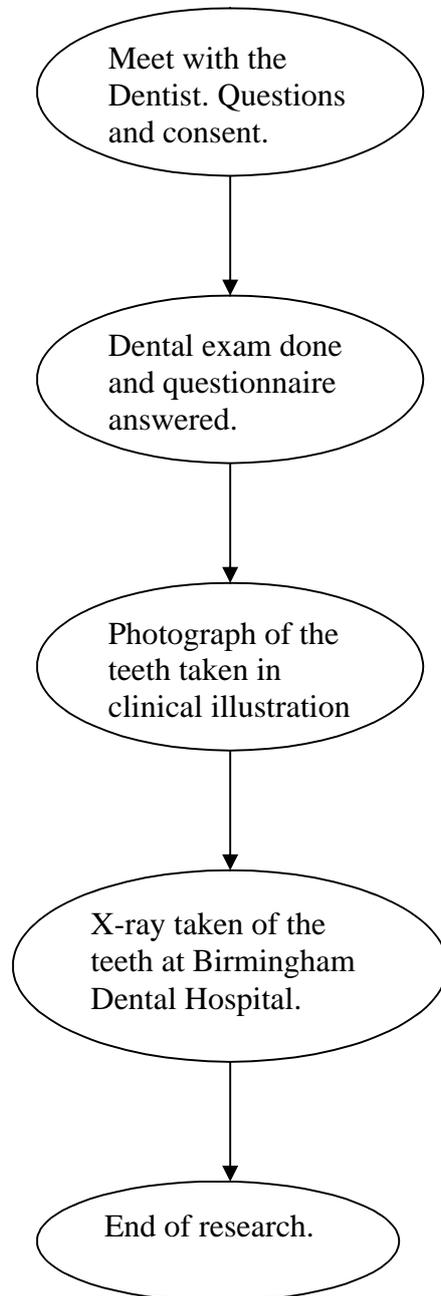
9. What if I have any concerns?

If you have any concerns or questions about the study you could contact [details]

Thank you for taking time to read this information.

Flow diagram of what will happen.

2/11/05



APPENDIX 9

Version 2.0
03/12/05

Patient Information Sheet under 8 yrs Group 1.

You are being invited to take part in a special study.

This means some dentists and doctors are seeing if the treatment you have had for your illness has had any affect on your teeth so far.

They are doing this because they are not really sure if it does or not. If it does the information they get will help other boys and girls with the same illness as you.

If you do want to help you will have to sit in the chair and let the dentist look at your teeth.

If you don't want to take part its ok no-one will mind.

Contact for Further Information

If you have any questions please contact [details]

APPENDIX 10

Patient identification number:

Version 2.0 03/12/05

Research project consent form

Title:

The dental needs of children, adolescents and young adults undergoing cancer treatment for solid tumours.

Researcher: Alison Hutton

I confirm the nature and purpose of this study has been explained to me by reading the patient information leaflet. Any further questions have been answered.	
--	--

I agree for my child to participate in the study and understand that I or my child may withdraw at any time without giving reason and without any detrimental effect to medical or dental treatment and care.

Signed.....Date.....
Chief Investigator

Signed.....Date.....
Child's signature (if child wishes to sign)

Signed..... Date.....

Name.....Relationship to the child.....

APPENDIX 11.

Identification code.....

Version 5.0. 21/12/05

1. How important do you think it is to look after **your** mouth and teeth?

Please indicate with an x where you feel is most appropriate on the line.

NOT AT ALL IMPORTANT

VERY IMPORTANT

The following questions are placed so we can put all the data into certain categories for data analysis. This project's data will be compared to national data gained in the Child Dental Health Survey which has the same categories. If you do not wish to answer the questions please move to question 6.

2. Could you tell us about the current job of the child's father or male head of the household or the last job he did if he is currently not doing any paid work? If he is no longer living in the house with the child please go to question 4.

Occupation of father/male guardian.....

3. What age did/will the father or male guardian finish full time education?

4. Could you tell us about the current job of the child's mother or female guardian or the last job she did if she is currently not doing any paid work? If she is no longer living in the house with the child please go to question 6.

Occupation of mother/female guardian.....

5. What age did the mother or female guardian finish full time education?

Identification code.....

Version 5.0 21/12/05

13. If so who examined your child's teeth?
Please tick appropriate answer

Local dentist
hospital dentist
community dentist.

<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>

14. Is your child's own dentist still willing to see your child despite the past medical treatment?

yes	<input type="checkbox"/>	no	<input type="checkbox"/>
don't know			<input type="checkbox"/>
not applicable			<input type="checkbox"/>

15. Did you have any information on how to look after your child's mouth and teeth during cancer treatment?

yes	<input type="checkbox"/>	no	<input type="checkbox"/>
don't know			<input type="checkbox"/>

16. Have any possible effects of the medical treatment on your child's mouth and teeth been discussed with you?

yes	<input type="checkbox"/>	no	<input type="checkbox"/>
don't know			<input type="checkbox"/>

17. Did your child have to go into hospital and stay for treatment because of a sore mouth during his/her chemotherapy?

yes	<input type="checkbox"/>	no	<input type="checkbox"/>
-----	--------------------------	----	--------------------------

18. Did your child have any problems with his/her mouth or teeth during chemotherapy?

yes	<input type="checkbox"/>	no	<input type="checkbox"/>
-----	--------------------------	----	--------------------------

If no please move to question 20.

19. If so what kind of problems occurred?
Please tick any appropriate answers

sore mouth
decayed teeth
mouth infection

<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>
<input type="checkbox"/>

other (please specify).....

Identification code.....

Version 5.0 21/12/05

20. Has your child had any dental treatment carried out since chemotherapy finished? yes no
If no please move to question 23.

21. If so what kind of treatment was this? teeth filled
Please tick any appropriate answers teeth taken out under local anaesthetic
 teeth taken out under general anaesthetic
 Painting/sealing of teeth
 Cleaning of teeth
 orthodontic treatment (braces)
 other (please specify).....

22. If so who provided the treatment for your child? local dentist
Please tick appropriate answer hospital dentist
 community dentist.

23. Do you think your child has adequate dental care? yes no
 don't know

24. Is there anything you would like to say about the dental treatment of your child?
Please write any comments below.

Thank you for your time.

APPENDIX 12

[Not available in this web version]

APPENDIX 13
[Not available in this web version]

APPENDIX 14
[Not available in this web version]

APPENDIX 15
[Not available in this web version]

APPENDIX 16

CHI SQUARE TEST RESULTS

1. The relationship between the presence of opacities and the level of fluoride in the water supply.

	Fluoride(F)	No Fluoride	Row Total
Actual Opacities	3	11	14
No opacities	6	35	41
Col.Total	9	46	55

	Fluoride(F)	No Fluoride	Chi square probability	
Expected Opacities	2.29	11.71	0.553	(N/S)
No opacities	6.71	34.29		

2. The relationship between the type of opaque defect and the level of fluoride in the water supply.

	Fluoride(F)	No Fluoride	Row Total
Actual Demarcated opacities	8	4	12
Diffuse opacities	33	9	42
Col.Total	41	13	54

	Fluoride(F)	No Fluoride	Chi square probability	
Expected Demarcated opacities	9.11	2.89	0.395	N/S)
Diffuse opacities	31.89	10.11		

3. The relationship between the age at which chemotherapy was received and the presence of microdont teeth.

	microdontia	no microdontia	Row total
Actual Chemotherapy age<3.5years	9	70	79
Chemotherapy age>3.5years	0	41	41
Col.Total	9	111	120

	microdontia	no microdontia	Chi square probability	
Expected Chemotherapy age<3.5years	6.13	72.87	0.025	Significant
Chemotherapy age>3.5years	2.87	34.13		

4. The relationship between the use of high dose chemotherapy and stem cell rescue as a treatment and microdont teeth.

	microdontia	no microdontia	Row total
Actual HDCSCR	3	11	14
No HDCSCR	6	35	41
Col.Total	9	46	55

	microdontia	no microdontia	Chi square probability	
Expected HDCSCR	2.29	11.71	0.553	(N/S)
No HDCSCR	6.71	34.29		