# Inequality in survival of people with head and neck cancer

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**BSc (Hons)**

**Submitted in fulfilment of the requirements for the Degree of Doctor of Philosophy**


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**July 2021**

# Abstract


### Background

Socioeconomic inequalities in the relationship between lower socioeconomic status and circumstances with poorer survival of people with head and neck cancer have previously been described. However, the extent and nature of socioeconomic inequality in survival of people with head and neck cancer is poorly understood and explanations for these inequalities are yet to be thoroughly investigated. In particular, the underlying determinants of inequality in survival of people with head and neck cancer is yet to be explored by comparing factors that might be more modifiable with factors that might be more difficult to modify or control. In addition, no study exists from the United Kingdom (UK) that has explored socioeconomic inequality in survival of people with head and neck cancer using individual measurements of socioeconomic status, such as household income or education level, and few studies have investigated the long-term impact of inequality on survival of people with head and neck cancer beyond five-years. Finally, no studies have examined inequality in survival of people with head and neck cancer by utilising metrics of inequality. Further investigations into socioeconomic inequality in survival of people with head and neck cancer need to be conducted to describe and compare inequality with the aim to explain the underlying drivers of inequality in survival for people with head and neck cancer in the short-term, middle-term, and long-term follow-up.

### Aim

This thesis has the potential to shine a light on the issue of socioeconomic inequality in survival of people with head and neck cancer. This thesis aims to inform the patients, public, clinicians, and policy makers who are involved with head and neck cancer services on the magnitude of socioeconomic inequality in survival of people with head and neck cancer, and what factors can explain these inequalities. A series of epidemiological studies of existing UK cohort studies will be conducted to explore this topic from different angles with the aim to inform policy and practice to further the development and delivery of head and neck cancer services.

The overall aim of this thesis is to: describe the trends in socioeconomic determinants and inequalities in survival from head and neck cancer over calendar time and follow-up time; to understand socioeconomic inequality in survival of people with head and neck cancer; and to explain the underlying determinants and explanations of socioeconomic inequality in survival of people with head and neck cancer. In addition, multiple measurements of

survival will be utilised and compared, including overall survival, disease-specific survival, and net survival estimates, as well as measurements of inequality including the slope index of inequality and the relative index of inequality. Finally, both area-based measurements and individual measurements of socioeconomic status will be utilised and compared for their association with inequality in survival of people with head and neck cancer.

**Methods**

Four studies were conducted with the aim to explore the magnitude, extent, and underlying determinants of survival and inequality in survival of people with head and neck cancer in the UK.

Chapter 2 provides an overview analysis of socioeconomic determinants in survival by utilising data from the Scottish Cancer Registry of people diagnosed with head and neck cancer between 1986 to 2015. Due to the limitations around the availability of data in cancer registries, the explanations for socioeconomic inequality were not explored in this chapter and therefore, this chapter was an epidemiological analysis of the trends and magnitude of socioeconomic inequalities in survival over time.

Chapter 3 analyses the determinants of survival from head and neck cancer by utilising the Scottish Audit of Head and Neck Cancer (SAHNC), a population-based clinical cohort study of people with head and neck cancer who were diagnosed between 1999 and 2001. Multiple patient, tumour, and treatment factors were examined for their predictive ability with survival, including area-based socioeconomic deprivation. Several methods of measuring survival were compared and contrasted in this chapter, including overall survival, disease-specific survival, and net survival estimates after one year, five years, and 12 years of a diagnosis of head and neck cancer.

Chapter 4 also uses the SAHNC cohort and built upon Chapter 3 by exploring the drivers and explanations for the socioeconomic inequality observed after one year, five years, and 12 years of a diagnosis of head and neck cancer. The patient, tumour, and treatment factors were individually examined for their relationship with socioeconomic factors with the aim of determining the underlying causes of socioeconomic inequality in survival of people with head and neck cancer. This chapter also explored these inequalities via different survival metrics – overall survival, disease-specific survival, and net survival estimates.

Chapter 5 investigated the relationship of individual socioeconomic factors and explanations for these relationships using a cohort of people with head and neck cancer that were diagnosed between 2011 and 2014 in a population-based clinical cohort study in

England; Head and Neck 5000 (HN5000). This part of the thesis aimed to undertake an in-depth exploration into the nature and extent of the socioeconomic inequality in survival of people with head and neck cancer by considering both area-based and individual dimensions of socioeconomic circumstances. Multiple demographic, health, behavioural, tumour, and treatment factors were considered to help understand the relationship between socioeconomic factors and head and neck cancer survival. This analysis built upon the previous chapters with multiple individual socioeconomic measurements and several additional potential explanatory factors collected as part of a more recent cohort study of people with head and neck cancer, including human papillomavirus (HPV) status.

**Results**

As a whole, this thesis demonstrated strong and consistent socioeconomic inequalities in survival of people with head and neck cancer. These inequalities in survival of people with head and neck cancer appeared to become worse over calendar time and also across follow-up period after one year, five years, and ten years of a diagnosis of head and neck cancer (Chapter 2 – Scottish Cancer Registry). Chapter 3 found that socioeconomic status was not an independent predictor of survival in a cohort of people with head and neck cancer who were diagnosed in Scotland between the years of 1999 and 2001 (SAHNC), while Chapter 4 investigated the underlying factors that may explain the original inequality that was observed in overall survival, disease-specific survival, and net survival estimates (also the SAHNC). Chapter 4 highlighted that in models that were adjusted by various patient, tumour, and treatment factors, none of the factors could individually explain the socioeconomic inequality in survival alone, suggesting that socioeconomic inequality in survival of people with head and neck cancer is complex, with multiple factors having a combined effect, including background mortality in the long-term follow-up (via net survival estimates). The studies that were carried out in Chapter 2 to Chapter 4 only utilised area-based socioeconomic measurements – mainly Carstairs Deprivation Index.

Chapter 5 added to this picture by exploring inequality by using both an area-based (Index of Multiple Deprivation (IMD) Category) and individual measurements of socioeconomic status including highest education level attained, number of years spent in education, annual household income, proportion of income from benefits, and financial concerns of living with or after cancer. Only data from England in the HN5000 cohort could be included in this analysis since it was not possible to pool and standardise the varying measurements of IMD (including Scottish IMD and Welsh IMD) across these countries of the UK. This study determined that inequalities were present for all of the measurements of socioeconomic status, however inequality in highest education level, number of years spent in education, and financial concerns of living with or after cancer were explained (fully attenuated) by other factors such as age and smoking status. Inequality across both

annual household income and the proportion of income from benefits partly attenuated following the adjustment of all of the potential explanatory factors, however, even after full adjustment, the relationship with survival of these factors of socioeconomic status could not be fully explained by any of the potential patient, tumour, or treatment factors that were included in this study.

The secondary aim of Chapter 3 was to compare methods of measuring survival via the use of overall survival, disease-specific survival, and net survival estimates. The substantial differences between these survival metrics demonstrated the overestimation of deaths that are specific to head and neck cancer when using overall survival, and the underestimation of disease-specific mortality from using death certificates when people have died only from head and neck cancer. These results suggest that people are dying of other causes that are related to their head and neck cancer but are not as a direct result of their cancer, which ultimately increases with time following diagnosis. Therefore, the use of net survival provides a good compromise to traditional methods to estimate the true burden of head and neck cancer in long-term follow-up studies. As a result, throughout Chapter 2 to Chapter 4, net survival estimates have been provided alongside overall survival and disease-specific survival results to compare and contrast the outcomes of people with head and neck cancer. However, in Chapter 5, it was not possible to utilise net survival estimations since lifetables for this time point had not yet been generated at the time of this analysis.

**Discussion and Conclusions**

The thesis studied socioeconomic inequality in survival of people with head and neck cancer in the UK using data from three sources – the Scottish Cancer Registry, the SAHNC cohort study of people with head and neck cancer in Scotland, and the HN5000 cohort study of people with head and neck cancer in England. As a whole, this thesis reported that inequality in survival of people with head and neck cancer is a persistent problem – a problem which seems to be getting worse. Moreover, the main premise of this thesis was to further the understanding of explanatory factors of socioeconomic inequality in survival of people with head and neck cancer. Although socioeconomic inequality in survival utilising an area-based measurement of socioeconomic status was explained by various underlying factors, inequality by annual household income and the proportion of income from benefits only attenuated following the adjustment of all potential explanatory factors for patients in England. Even after full adjustment, inequality in survival by annual household income and the proportion of income from benefits could not be explained by any of the potential underlying factors that were included in this study. Therefore, further investigations considering individual measurements of patients' income following a diagnosis of cancer should be conducted.

In addition, a number of recommendations related to policy, practice, and further research were drawn. This thesis has provided a comprehensive examination of socioeconomic inequalities in survival of people with head and neck cancer – a relatively underexplored field. The research involved in-depth analyses of multiple datasets and from a number of perspectives. It has shown that inequalites in survival are substantial and are a growing problem, and has endeavored to explore the explanatory factors. This work provides a platfrom through which policy and practice development, along with evaluation and research, can be based to reduce inequalties in survival and improve the outcome for people who are diagnosed with head and neck cancer.

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# Acknowledgements

I would like to start by expressing my sincere gratitude to my supervisors, Professor David Conway, and Doctor Alex McMahon for their continued support throughout the duration of my PhD studies, both professionally and personally. I am incredibly grateful that you have always supported me through my PhD, which has included some of the most difficult periods of my life. You have both always been able to encourage and motivate me to "keep on going" over the last seven years. You have never doubted my ability to complete this PhD and have always provided me with the confidence and drive that I could and *would* finish my thesis!

Thank you to the staff at the Community Oral Health Department at the University of Glasgow, where my PhD was based, and for always making me feel welcome whenever I visited. A special thank you to Pauline Daniel, for always holding our hands as PhD students, from our first day right up to when we finish.

Thank you to the Scottish Audit of Head and Neck Cancer team – Kenneth Mackenzie, Shirley-Anne Savage, and especially Catriona Douglas, who showed me immense encouragement throughout the duration of my PhD. Thank you also to the Head and Neck 5000 team at the University of Bristol – to Professor Andy Ness and Doctor Sam Leary for guiding me through my first career in research, to Katrina Hurley and Stu Toms for always being available to answer my (not-so) "quick questions", and to Doctor Miranda Pring who not only contributed my research on the Head and Neck 5000 study, but who also provided me with substantial advice on the pathology and coding for the anatomical groupings of head and neck cancer for the Scottish Cancer Registry study. Finally, thank you to the rest of the team – Professor Steven Thomas, Dr Andrea Waylen, Christine Wood, Chris Lippiatt, Shirley Jenkins, and Sofia Leadbetter.

Thank you to my colleagues and friends at the Universities of Bristol and Cardiff, where I have worked alongside some of my PhD, particularly Philip Pallmann, for all of the support you have provided me, especially in recent months. A special thank you to Sam Clarkstone – you have supported me more than you could ever know over the last year. Thank you for becoming my best friend, always being there for me, and for having faith that we would survive the "events of 2020" unscathed! Thank you also to Nicholas Russel at Cardiff University for all of the support you provided me to construct a template for my thesis, and to Michel Grzebyk for the support provided to program net survival using the *stns* command.

Outside of academia, and on a more personal level, thank you to Julie Summers, Alison Shaw, Katie Evans, and Chris Rudge – you all know why! Thank you to my high-school

friend Ollie, for always encouraging me to better myself, and for always being my personal “grammar guru”! Thank you to Mair and Surindar for hosting me so frequently in your home during my visits to Glasgow for my PhD. A very special thank you to my Aunty Bev and Uncle Scottie for supporting me in all areas of my life, but especially in my education, from tutoring me in my Year Six SATS right up to reading my thesis twenty years on! Thank you, Aunty Bev, for taking the time out of your extremely (!) busy schedule to proofread my entire thesis! You are my hero! But let’s not mention that too much just in case you start getting requests from other PhD students…

Thank you to my Dad and Sue, for always encouraging me to finish my PhD, and for being so proud of me and my achievements. Thank you to both of you for always showing an interest in my work, and for reading all of my publications. Thank you, Dad, for all of the support you have given me through my life, for being the first person to teach me mathematics which led me into this career path, and for always being ready with a cup of tea (or a glass of wine) whenever I have needed it.

My dear husband, Thom – I haven’t enough words to express how grateful I am for everything that you do for me. Thank you for all of your love, understanding, and patience throughout the last seven years. Thank you for always believing in me, for always supporting my decisions, and for always being there for me. You truly are my star.

My final acknowledgement goes to my Mum, who passed away in the third year of my PhD. Thank you for always believing in me and for always having encouraged, supported, and done your utmost to ensure I had the best education you could offer me. This thesis is dedicated to you.

# Author's Declaration

Parts of the research work included in this thesis have been published or submitted with co-authors.

Publications

The following studies were designed, performed, analysed, and written primarily by Kate Ingarfield. Alex D. McMahon supervised the analyses for these papers. Alex D. McMahon and David I. Conway supervised and provided feedback on the written content of the papers. Shirley-Anne Savage provided the linkage for the mortality data for the SAHNC cohort. Catriona M. Douglas and Kenneth MacKenzie provided supervision and advice towards the paper from a medical perspective.

**Chapter 3:** Ingarfield, K., McMahon, A.D., Douglas, C.M., Savage, S.A., Conway, D.I. and MacKenzie, K. (2019) 'Determinants of long-term survival in a population-based cohort study of patients with head and neck cancer from Scotland', *Head Neck,* 41(6), 1908-1917.

**Chapter 4:** Ingarfield, K., McMahon, A.D., Douglas, C.M., Savage, S.A., MacKenzie, K. and Conway D.I. (2018) 'Inequality in the survival of patients with head and neck cancer in Scotland', *Front Oncol, 8*, 673.

The following study was designed, performed, analysed, and written primarily by Kate Ingarifeld. Alex D. McMahon supervised the analysis for this paper. Alex D. McMahon and David I. Conway supervised and provided feedback on the written content of the papers. Andrea Waylen, Steve J. Thomas, Miranda Pring, Katrina Hurley and Stu Toms are the Head and Neck 5000 executive team, and provided feedback on the written content of the paper. Andy Ness is the Director of the Head and Neck 5000 study, and provided advice, supervision and feedback on the wrriten content of the paper. Michael Pawlita and Tim Waterboer provided the HPV serology for the cohort.

**Chapter 5:** Ingarfield, K., McMahon, A.D., Hurley, K., Toms, S., Pring, M., Thomas, S.J., Waylen, A., Pawlita, M., Waterboer, T., Ness, A.R. and Conway, D.I. (2021) 'Inequality in surival of people with head and neck cancer: Head and Neck 5000 cohort study', *Head Neck.*

The following study was designed and performed by Kate Ingarfield in conjuction with Catriona M. Douglas. Alex D. McMahon supervised the analysis. Kate Ingarfield performed the analysis, and wrote the methods and results section of the paper. Catriona M. Douglas wrote the introduction and discussion to the paper. Shirley-Anne Savage provided the linkage to mortality data. Alex D. McMahon, David I. Conway, and Kenneth MacKenzie provided feedback on the written content of the paper.

**Other:** Douglas, C.M., Ingarfield, K., McMahon, A.D., Savage, S.A., Conway, D.I., MacKenzie, K. (2018) 'Presenting symptoms and long-term survival in head and neck cancer', *Clin Otolaryngol,* 43(3), 795-804.

I declare that the thesis is my own composition and has not been submitted in part or whole for any other degree.

Kate Ingarfield
July 2021

# List of abbreviations

| | |
|---|---|
| ACM | All-cause mortality |
| ASR | Age-Standardised Incidence Rate |
| CHI | Community Health Index |
| CI | Confidence Interval |
| CRUK | Cancer Research United Kingdom |
| DEPCAT | DEPrivation CATegory |
| DSM | Disease-specific mortality |
| DKFZ | German Cancer Research Center |
| eDRIS | electronic Data Research and Innovation Service |
| EMBASE | Excerpta Medica database |
| HN5000 | Head and Neck 5000 |
| HNC | Head and Neck Cancer |
| HPV | Human Papillomavirus |
| HR | Hazard Ratio |
| IARC | International Agency for Research on Cancer |
| ICD | International Classification of Diseases |
| IMD | Index of Multiple Deprivation |
| INHANCE | International Head and Neck Cancer Epidemiology |
| ISD | Information Services Division |
| LSHTM | London School of Hygiene and Tropical Medicine |
| NCI | National Cancer Institute |
| NHIRD | National Health Insurance Research Database |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| NRS | National Records of Scotland |
| NSS | National Services Scotland |
| PBPP | Public Benefit and Privacy Panel |
| RII | Relative Index of Inequality |
| SAHNC | Scottish Audit of Head and Neck Cancer |
| SCC | Squamous Cell Carcinoma |
| SEER | Surveillance, Epidemiology, and End Results |
| SES | SocioEconomic Status |
| SIMD | Scottish Index of Multiple Deprivation |
| SII | Slope Index of Inequality |
| TNM | Tumour, Node and Metastases |
| UICC | International Union Against Cancer |
| UK | United Kingdom |
| UKIACR | United Kingdom and Ireland Association of Cancer Registries |
| USA | United States of America |
| WHO | World Health Organization |

# 1 Introduction

## 1.1 Thesis structure

This thesis investigates the association of socioeconomic factors with the survival of people with head and neck cancer. The primary aim of this thesis is to explore the extent and magnitude of socioeconomic inequality in survival of people with head and neck cancer. The secondary aim is to thoroughly examine the drivers and underlying causes of this inequality in the short-term, medium-term, and long-term following a diagnosis of head and neck cancer. Potential explanatory factors for these socioeconomic inequalities are explored including multiple participant, demographic, health, behavioural, tumour and treatment factors. In addition, a thorough methodological assessment of measurements of survival is undertaken to determine the impact of socioeconomic determinants using each method of survival analysis. This includes comparing and contrasting results of overall survival, disease-specific survival, and net survival estimates throughout the thesis.

Chapter 1 provides the background to this thesis. This includes an overview of the burden of head and neck cancer across the world and a brief review of the risk factors of head and neck cancer. In addition, current global survival trends and rates along with the determinants and predictors of survival following a diagnosis of head and neck cancer are reviewed. An in-depth literature review focuses on the existing research that investigates socioeconomic determinants and socioeconomic inequalities in the survival of people with head and neck cancer. This review provides the context, background, and rationale for the studies that were performed as part of the thesis.

The next four chapters include the results and analyses of three cohorts which investigate socioeconomic determinants and socioeconomic inequality and explore explanations for these inequalities in the survival of people with head and neck cancer.

Chapter 2 provides an overview analysis of socioeconomic determinants in survival by utilising data from the Scottish Cancer Registry of people diagnosed with head and neck cancer between 1986 to 2015. The primary aim of this chapter is to describe the historical trends over time of the socioeconomic inequality in survival of people with head and neck cancer in Scotland. In addition to comparing trends over calendar time, the differences in inequality over the follow-up time in one-year, five-year, and 10-year survival will also be compared. These trends are examined for the whole cohort, for males and females, and for people with the three main subsites of head and neck cancer (oral cavity, oropharynx, and larynx). Due to the limitations around the availability of data in cancer registries, the explanations for socioeconomic inequality will not be explored in this chapter and

therefore, this chapter will be an epidemiological overview of inequality in survival over time.

Chapter 3 analyses the determinants of survival from head and neck cancer by utilising the Scottish Audit of Head and Neck Cancer (SAHNC), a population-based clinical cohort study of patients who were diagnosed between 1999 and 2001. Multiple patient, tumour, and treatment factors are examined for their predictive ability with survival, including area-based socioeconomic deprivation. Several methods of measuring survival are compared and contrasted in this chapter, including overall survival, disease-specific survival and net survival estimates after one year, five years, and 12 years of a diagnosis of head and neck cancer.

Chapter 4 also uses the SAHNC cohort and builds upon Chapter 3 by exploring the drivers and explanations for the socioeconomic inequality observed after one year, five years and 12 years of a diagnosis of head and neck cancer. The patient, tumour, and treatment factors will be individually examined for their relationship with socioeconomic status with the aim of determining the underlying causes of socioeconomic inequality in survival of people with head and neck cancer in overall survival, disease-specific survival, and net survival estimates.

Chapter 5 investigates the relationship of individual socioeconomic factors and explanations for these relationships using a cohort of people with head and neck cancer who were diagnosed in England between 2011 and 2014 in a population-based clinical cohort study; Head and Neck 5000 (HN5000). This part of the thesis aims to undertake an in-depth exploration into the nature and extent of the socioeconomic inequality in survival of people with head and neck cancer by considering both area-based and individual dimensions of socioeconomic circumstances. Multiple demographic, health, behavioural, tumour, and treatment factors will be considered to help understand the relationship between socioeconomic factors and head and neck cancer survival. This analysis builds upon the previous chapter with multiple individual socioeconomic measurements and several additional potential explanatory factors collected as part of a more recent cohort study of people with head and neck cancer, including human papillomavirus (HPV) status.

Chapter 6 discusses the findings of this thesis collectively by comparing the results of the four studies which have investigated different aspects of socioeconomic inequality in the survival of those with head and neck cancer. This chapter also explores the potential explanations for these socioeconomic inequalities in relation to the literature and discusses the overall strengths and limitations of the research. Finally, this chapter makes recommendations for further research, policy and practice in relation reducing socioeconomic inequalities in survival of people with head and neck cancer.

## 1.2 Methods used in this thesis

### 1.2.1 Methods of measuring survival

Survival analysis investigates the time it takes for an "event" to occur. In cancer research this event can be, for example, the time to death, the time to progression of cancer, or the time to relapse of cancer. In addition, the event must be a binary variable (for example, alive versus dead, progressed versus not progressed, or relapsed versus not relapsed) and the first occurrence of the event (should this event not be death) is the only endpoint that can be considered. Survival analysis requires a "*clear and well defined case definition*" (dos Santos Silva, 1999) such as a group of people with a specific type of cancer who are from one region. Survival analysis also requires a "*clear and well defined starting point*" (dos Santos Silva, 1999) such as the date of diagnosis of a person's cancer or the date of their initial treatment. Survival analysis computes the length of time between the starting point and the endpoint of interest in a study, known as the "survival time", which is dependent upon the length of time each person in a study was followed-up.

#### 1.2.1.1 Kaplan-Meier method

Kaplan-Meier survival analysis is one method that can be used to analyse survival which generates a Kaplan-Meier survival curve (Altman, 1992). The Kaplan-Meier (or product-limit method) is a mathematical technique that allows the amount of follow-up time to be included into the survival time. This curve graphically demonstrates the probability of survival of a group of people against follow-up time (measured in in days, months, or years). The initial starting point is the date of entry of each person into a study, and therefore can be different for multiple participants. As a result, Kaplan-Meier survival analysis is a powerful method of measuring survival since the initial starting date of the analysis does not need to be the same for everyone included in the study. Over time, as people start to leave the study due to the event of interest, the Kaplan-Meier curve decreases which is represented by a step-down function. Survival probabilities are produced in survival tables which are obtained from the Kaplan-Meier function. From these tables, survival rates such as one-year, five-year, or 10-year survival can be extracted.

**Censored observations**

Censored observations occur due to early termination of follow-up or when the endpoint of interest is not known for an individual included in a study. This may occur due to loss-to-follow up, such as the participant moving address, or it may occur due to the endpoint not

meeting the relevant criteria of the event of interest. All participants who have not experienced the event of interest and are alive at the endpoint of a study are censored at this point in time.

#### 1.2.1.2 Overall and disease-specific survival

In this thesis, two measurements of survival have been estimated from Kaplan-Meier survival analysis including overall survival and disease-specific survival. Overall survival considers the risk of death by all causes. However, disease-specific survival only considers deaths that are specifically caused by the disease of interest but does not include deaths that may have been related to or occurred as a secondary effect to the disease of interest. These events that are not of interest are censored (National Cancer Institute, 2021).

#### 1.2.1.3 Net survival

Net survival is defined as the excess mortality between the observed mortality of a group of people under study and the expected mortality of a disease-free group in the population with the same demographic characteristics as the study group (Pohar Perme *et al.*, 2012). Net survival estimation is useful when cause of death information is unknown and provides a more accurate representation of the mortality from a disease of interest by disentangling other causes of death, particularly in studies which have long-term follow-up where competing causes of death are common.

### 1.2.2 Measurements of socioeconomic status

Health inequalities can cover a range of equality domains (for example, age, sex, race, or ethnicity) (Equality Act, 2010). However, for the purposes of this thesis it will focus on socioeconomic inequalities. Socioeconomic measures that are used in the thesis include area-based measurements and individual measurements.

#### 1.2.2.1 Area-based measurements of socioeconomic status

Throughout this thesis, area-based measurements of socioeconomic status have been obtained from several measurements: Carstairs and Morris Index (Carstairs and Morris, 1989; Carstairs and Morris, 1990), Scottish Index of Multiple Deprivation (SIMD) (Public Health Scotland, 2020b), and English IMD (English Indices of Deprivation, 2020).

### Carstairs and Morris Index

The Carstairs and Morris Index was developed in 1989 and ranks the geographical areas of Scotland from a person's home postcode (Carstairs and Morris, 1989; Carstairs and Morris, 1990). The Index has been produced using census data from the years 1981, 1991, 2001 and 2011, and groups areas at the postcode sector using four indicators that act as a representation of material disadvantage: (a) low occupational social class, (b) lack of car ownership, (c) overcrowded households, and (d) male unemployment. The Carstairs and Morris Index is categorised into one of five groups using the Census data: for the 1981, 1991, and 2001 categories, group one represents the people from the least deprived areas and group five represents the people from the most deprived areas, whereas for the 2011 categories, group one represents the people from the most deprived areas and group five represents the people from the least deprived areas (the order has been reversed).

### Scottish Index of Multiple Deprivation

The SIMD was developed in 2004 and like the Carstairs and Morris Index, it is measured at the postcode sector, however SIMD uses smaller geographical areas ("data zones") than those used in the Carstairs and Morris Index (Public Health Scotland, 2020b). SIMD has been produced using census data from the years 2004, 2006, 2009, 2012, 2016, and 2020 and is calculated from seven domains of deprivation: (a) income employment, (b) education,
(c) housing, (d) health, (e) crime, and (f) geographical access. SIMD is categorised into one of five groups using the Census data: for the 2004 and 2006 categories, group one represents the people from the least deprived areas and group five represents the people from the most deprived areas, whereas for the 2009, 2012, 2016, and 2020 categories, group one represents the people from the most deprived areas and group five represents the people from the least deprived (the order has been reversed).

### English Index of Multiple Deprivation

The English IMD was developed in the year 2000 and like the SIMD, it is measured at the postcode level (English Indices of Deprivation, 2020). However, the English IMD uses Local Authority Districts in England. The English IMD has been produced using census data from 2000, 2004, 2007, and 2010 and is calculated from seven domains of deprivation: a) Income Deprivation, (b) Employment Deprivation, (c) Health Deprivation and Disability, (d) Education Skills and Training Deprivation, (e) Barriers to Housing and Services, (f) Living Environment Deprivation, and (g) Crime. The English IMD is

categorised into one of five groups – group one represents the people from the most deprived areas and group five represents the people from the least deprived areas.

#### 1.2.2.2 Individual measurements of socioeconomic status

Measurements of socioeconomic status using individual determinants have been thoroughly reviewed (Galobardes *et al.*, 2006a; Galobardes *et al.*, 2006b) and have also applied to cancer research in the International Agency for Research on Cancer (IARC) publication on Social Inequalities in Cancer (International Agency for Research on Cancer, 2019). Individual measurements of socioeconomic status that have been used throughout this thesis (namely in Chapter 5) include: (a) highest education level attained, (b) number of years spent in full-time education, (c) total annual household income, (d) proportion of income from benefits, and (e) financial concerns of living with or after cancer. Measurements for education level represent early-life socioeconomic status and are a strong predictor of employment, and thus income, in future years, while annual household income is a direct measure of socioeconomic status by measuring a person's access to material resources and services (Conway *et al.*, 2019).

## 1.3 Head and neck cancer

### 1.3.1 Definition

Approximately 90% of cancers of the head and neck are squamous cell carcinoma (SCC) which arise from the epithelium lining of the oral cavity, pharynx, and larynx (Sanderson and Ironside, 2002). There are many types of head and neck cancers which are discretely categorised using the International Classification of Diseases (ICD-10) from the World Health Organisation (WHO) (World Health Organization, 2016). These include the: (a) lip, (b) oral cavity, (c) pharynx (including the nasopharynx, oropharynx, and hypopharynx), (d) larynx, (e) nasal cavity, (f) middle ear, (g) accessory sinuses, (h) bones of the skull and face, (i) mandible, and (j) other ill-defined sites of the head, face, and neck. A comprehensive list of each subsite along with the detailed information of the location in the head and neck of that subsite (including the individual ICD-10 code) is outlined in Appendix 1.2.

Due to the complexity of head and neck cancer, and the varying symptoms, treatment regimens, and prognoses of each anatomical subsite of the head and neck, there is debate around the inclusion criteria of the major subsites in the overarching definition of "head and neck cancer". As a result, the subsites that are included under the definition of

"head and neck cancer" often vary across different studies. A comprehensive review carried out by Kaste *et al.* (2013) outlined several definitions of head and neck cancer from the National Cancer Institute (NCI), IARC, and Cancer Research United Kingdom (CRUK), as outlined in Table 1.1. The most important difference between these definitions is the inclusion of the oesophagus, parathyroid, or thyroid cancers under the definition set out by CRUK. Several articles include these subsites as a form of head and neck cancer, however for the purpose of this research, it is important to note that these have been excluded from all of the analyses performed in this thesis.

**Table 1.1 – Inclusion criteria of head and neck cancer from three major definitions**

| ICD group | NCI | IARC | CRUK |
|---|---|---|---|
| External lip | ✓ | | |
| Oral cavity | ✓ | | |
| Lip and oral cavity combined | | ✓ | |
| Mouth and oropharynx combined | | | ✓ |
| Tongue | | | ✓ |
| Oropharynx | ✓ | ✓ | |
| Tonsil | | | ✓ |
| Throat | | | ✓ |
| Nasopharynx | ✓ | ✓ | ✓ |
| Hypopharynx | ✓ | ✓ | |
| Larynx | ✓ | ✓ | ✓ |
| Paranasal sinuses and nasal cavity | ✓ | | ✓ |
| Salivary glands | ✓ | ✓ | ✓ |
| Eye and orbit | | | ✓ |
| Oesophagus | | | ✓ |
| Parathyroid | | | |
| Thyroid | | | |

*Abbreviations: NCI – National Cancer Institute, IARC – International Agency for Research on Cancer, CRUK – Cancer Research UK*

In addition, the complex nature of head and neck cancer leads to uncertainty around the inclusion and exclusion criteria of the individual subsites that are to be categorised as part of the major subsites of the head and neck, particularly the oral cavity and oropharynx (Conway *et al.*, 2018). A lack of clarity exists around the boundaries of the anatomical subsites of the head and neck that belong to the oropharynx or oral cavity. This often results in variations of the inclusion criteria between studies that investigate cancers of the oral cavity or oropharynx. Due to variations in how head and neck cancer is defined across the different studies used in this thesis, the anatomical subsites (with the corresponding ICD codes) will be specified in the methods section of each chapter.

### 1.3.2 Risk factors of head and neck cancer

This section focuses on the major risk factors of head and neck cancer by summarising the findings from several publications, particularly studies from the International Head and Neck Cancer Epidemiology (INHANCE) consortium (Conway *et al.*, 2009). The INHANCE consortium aims to improve the understanding of the underlying causes of head and neck cancer via the collaboration of several research groups. The investigators have combined their data from 35 case-control studies to produce a pooled analysis comprising of 25,500

patients and 37,100 controls, and their results have been summarised by Winn *et al.* (2015).

#### 1.3.2.1 Smoking and alcohol consumption

Tobacco smoking and alcohol consumption have been well recognised as the leading causes of primary tumours of the head and neck for many years (Macfarlane *et al.*, 1995; Talamini *et al.*, 1998; Bosetti *et al.*, 2002). Tobacco use and alcohol consumption are associated (Duffy *et al.*, 2007), and a person's intake may be influenced by sociodemographic factors such as cohabitation status, education level and gender (Allison, 2001).

The results of a pooled analysis of 15 case-control studies from the INHANCE consortium reported that cigarette smoking, and excessive alcohol drinking are independent risk factors of head and neck cancer (Hashibe *et al.*, 2007). The article reported that those who never drank alcohol were at a more than two-fold increased risk of developing head and neck cancer if they smoked cigarettes, which became higher based on the frequency, duration, and number of pack-years of cigarette smoking. In addition, the risk of developing cancer of the larynx was substantially stronger than the risk of developing cancer of the oral cavity or pharynx for those who smoked tobacco products. For individuals who never smoked, those who consumed at least three alcoholic beverages a day had a more than two-fold risk of head and neck cancer than those who had never drank alcohol. In a later study performed by Hashibe and colleagues, it was found that approximately 72% of head and neck cancers are attributable to tobacco use, alcohol consumption and a combination of the two behaviours (Hashibe *et al.*, 2009). In addition, the joint effects of smoking and alcohol accounted for 64% of oral cavity cases, 72% of pharyngeal cases, and 89% of laryngeal cases (Hashibe *et al.*, 2009).

In a further study conducted from the INHANCE consortium, smoking and alcohol cessation was investigated (Marron *et al.*, 2010). The study found that quitting tobacco smoking could lead to a reduction in the risk of head and neck cancer by 30% after as little as one to four years, or by 70% after more than 20 years. However, the results were not as clear cut for alcohol cessation, which led to a 40% reduced risk of head and neck cancer after more than 20 years of quitting. Tobacco, betel-leaf, or areca nut chewing are also strongly associated with the risk of developing head and neck cancer among Asian populations, which could be responsible for up to half or oral cancer cases in India (Travasso, 2013).

#### 1.3.2.2 Socioeconomic factors

Low socioeconomic position is an additional and independent risk factor of head and neck cancer, and socioeconomic inequalities in the incidence of head and neck cancer have been observed both between and within developed and developing countries (Conway *et al.*, 2008; Conway *et al.*, 2015). Conway *et al.* (2008) conducted a systematic review and meta-analysis of 41 studies to investigate the relationship between socioeconomic inequality and the risk of oral cancer. Conway and authors concluded that low socioeconomic status was associated with an increased risk of developing oral cancer which was also apparent when adjusting for the major potential confounding factors (such as smoking and alcohol consumption).

A further study undertaken by Conway *et al.* (2015) explored the association between education and income with head and neck cancer risk. Conway and authors used data from the INHANCE consortium of head and neck cancer which included 31 studies. The results from this study demonstrated that lower levels of educational attainment and lower income levels were both associated with a more than two-fold increased risk of head and neck cancer, which remained following adjustment for smoking, alcohol, and dietary risk factors.

#### 1.3.2.3 HPV status

In recent years, HPV has been associated with an increase in the incidence of head and neck cancer. There has been a substantial rise in the incidence of HPV-associated cancers of the oropharynx, with approximately 70% of oropharyngeal cancers being related to HPV positivity (Saraiya *et al.*, 2015). D'Souza *et al.* (2007) conducted one of the first case-control studies that examined the role of HPV infection and the risk of oropharyngeal cancer – in 100 people with oropharyngeal cancer and 200 controls without cancer they discovered that people with HPV type 16 (HPV-16) were substantially more at risk of oropharyngeal cancer.

#### 1.3.2.4 Diet and nutrition

Several studies have noted an association between diet and risk of head and neck cancer. Chuang *et al.* (2012) reported that higher intake of fruit and vegetables were associated with a lower risk of head and neck cancer, while a higher intake of red meats were associated with an increased risk of head and neck cancer. Further studies have suggested a reduction in the risk of head and neck cancer in people who have high intake of vitamin C or vitamin E from food (Edefonti *et al.*, 2015a; Edefonti *et al.*, 2015b), but no

strong associations were observed between vitamin or mineral supplements and the risk of head and neck cancer (Li *et al.*, 2012).

#### 1.3.2.5 Body mass index

Gaudet *et al.* (2010) investigated the association of body mass index (BMI) with the risk of head and neck cancer using 17 studies from the INHANCE consortium. The authors reported that people with a lean body mass (BMI < 18.5kg/$m^2$) were associated with a higher risk of head and neck cancer, while those with higher body mass were associated with a reduced risk of head and neck cancer. This trend was notable prior to and after adjusting for additional head and neck cancer risks, including smoking and alcohol consumption.

### 1.3.3 Incidence and trends of head and neck cancer

In 2020, there were more than 930,000 new cases of head and neck cancer diagnosed across the world (Table 1.2); collectively ranking it as the sixth most common type of cancer (Ferlay *et al.*, 2020). The most prevalent group of head and cancers include the lip and oral cavity, followed by the larynx, which accounted for more than 40% (n = 377,713) and 20% (n = 184,615) of all head and neck cancers combined across the globe in 2020, respectively (Ferlay *et al.*, 2020). Head and neck cancer is more common in men than it is in women, with an approximate ratio of 3:1 of men to women, making head and neck cancer the fourth most common cancer in men and the twelfth most common cancer in women in the United Kingdom (UK) in 2020 (Ferlay *et al.*, 2020).

The incidence of head and neck cancer varies across the globe. In a comprehensive study by Miranda-Filho and Bray (2020), the global patterns and trends in cancers of the lip, tongue and mouth were explored across five continents; Africa, the Americas, Asia, Europe, and Oceania between the years of 1998 and 2012. The authors reported that these cancers had the highest rates in several countries in South and Central Asia, and Oceania. Incidence rates were highest in Papua New Guinea (27.5 per 100,000 persons-year), Pakistan (16.3 per 100,000 persons-year), Latvia (14.6 per 100,000 persons-year), India (13.9 per 100,000 persons-year), and Bangladesh (12.4 per 100,000 persons-year). Although smoking and alcohol consumption are well recognised risk factors for cancers of the lip and oral cavity, the authors report that the high prevalence of betel quid chewing in many of these countries is likely to have a strong association with the high incidence of head and neck cancer. In addition, the incidence of these cancers was consistently higher among males than females, with rates ranging from 0.5 to 21.2 per 100,000 persons-year in males, and 0.5 to 12.0 per 100,000 persons-year in females.

In an earlier study carried out by Shield *et al.* (2017), the incidence of cancers of the lip, oral cavity, and pharynx were examined by country, sex, and age for the year of 2012. A total of 529,500 people were diagnosed with cancer of the lip, oral cavity, or pharynx during this year, and the authors predicted that this figure is expected to increase by 62% to 856,000 cases by 2035. Several studies have noted an increase in the incidence of head and neck cancer since the 1980s (Chaturvedi *et al.*, 2013), particularly for cancers of the oropharynx which has notably risen in economically developed countries such as northern European countries including the UK, Denmark, Estonia, Finland, Latvia, Norway and Sweden (Simard *et al.*, 2014).

In the UK, there were nearly 14,000 new cases of head and neck cancer in 2020 (Table 1.2), with cancers of the lip and oral cavity accounting for more than 45% of all head and neck cancers in the UK (Ferlay *et al.*, 2020). Louie *et al.* (2015) investigated the trends in the incidence of head and neck cancer in England between the years of 1995 and 2011 and provided future projections up to 2025. The authors determined that the age standardised incidence rates (ASR) of head and neck cancer increased from 14.1 per 100,000 population to 20.1 per 100,000 from 1995 to 2011, respectively, for males and from 5.9 per 100,000 population to 8.7 per 100,000 population from 1995 to 2011 for females, respectively.

**Table 1.2 – Number of cases of head and neck cancer in the globe and the UK**

| Subsite of the head and neck (ICD code) | Global | | | UK | | |
|---|---|---|---|---|---|---|
| | Total | Males | Females | Total | Males | Females |
| Lip and oral cavity (C00-C06) | 377,713 | 264,211 | 113,502 | 6,317 | 3,931 | 2,386 |
| Larynx (C32) | 184,615 | 160,265 | 24,350 | 2,618 | 2,115 | 503 |
| Nasopharynx (C11) | 133,354 | 96,371 | 36,983 | 276 | 184 | 92 |
| Oropharynx (C09-C10) | 98,412 | 79,045 | 19,367 | 2,810 | 2,110 | 700 |
| Hypopharynx (C12-C13) | 84,254 | 70,254 | 14,000 | 798 | 585 | 213 |
| Salivary glands (C07-C08) | 53,583 | 29,694 | 23,889 | 980 | 515 | 465 |
| *Total* | *931,931* | *699,840* | *232,091* | *13,799* | *9,440* | *4,359* |

*Numbers based on the Global Cancer Observatory (GLOBOCAN) 2020 "Cancer Today" report (Ferlay et al., 2020).*

Over the last two decades, there has been an increase in the association in the rising incidence of head and neck cancer with HPV (Junor *et al.*, 2010; Chaturvedi *et al.*, 2013; Purkayastha *et al.*, 2016). This trend is particularly common for people with cancer of the oropharynx, for whom around one to two thirds of tumours may be HPV-driven (Kreimer *et al.*, 2005). This trend has notably risen in economically developed countries such as northern European countries including the UK, Denmark, Estonia, Finland, Latvia, Norway and Sweden (Simard *et al.*, 2014). People with HPV-positive tumours have a considerably better prognosis than people with HPV-negative tumours, even following adjustment for other baseline covariates (Ragin and Taioli, 2007; Wang *et al.*, 2015).

### 1.3.4 Staging of head and neck cancer

Cancer staging is useful to help clinicians determine the size and extent of a tumour, and whether it has spread to other parts of the body. This allows doctors to plan appropriate treatment regimens and predict prognosis. Cancer stage is determined at the point of diagnosis via x-rays, scans, or biopsies.

The most commonly used system for staging tumours is the Classification of Malignant Tumours Tumour, Node and Metastases (TNM) system (Sobin *et al.*, 2009; National Cancer Institute, 2015) which was developed by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC). The latest version of the TNM classification of malignant tumours is the Eighth Edition (Brierley *et al.*, 2017). However, the analyses throughout this thesis were performed prior to the release of Eighth Edition, and were therefore performed using the Seventh Edition (Sobin *et al.*, 2009). The major change between the Seventh and Eighth editions is the new system for HPV-positive oropharynx cancer which is now considered unsuitable to stage in the same manner as HPV-negative oropharynx cancer (since these people have substantially worse survival) (Lydiatt *et al.*, 2018). This section provides information on the staging system using the Classification of Malignant Tumours, Seventh Edition.

Primary tumour (T) determines the size of the tumour and is given a value of either “X” or between 0 and 4 based on:

- TX indicates that a tumour cannot be measured.
- T0 indicates that there is no tumour, but abnormal pre-cancerous cells may be present.
- T1 indicates a small tumour that has not spread.
- T2, T3 or T4 indicate the size and extent of the tumour, with the higher value representing a larger tumour or further spread into nearby muscle, bone, or skin.

Regional lymph nodes (N) determines whether the primary cancer has spread into lymph nodes, and is given a value of either “X” or between 0 and 3 based on:

- NX indicates that the lymph nodes cannot be measured.
- N0 indicates that the tumour has not spread into the lymph nodes.
- N1, N2 or N3 indicate the amount and location of the spread of the tumour into the lymph nodes, with the higher value representing more lymph node involvement.

Distant metastases (M) determines whether the tumour cells have spread to other parts of the body, and is given a value of either “X”, 0 or 1 based on:

- MX indicates that distant metastases cannot be measured.
- M0 indicates that the cancer has not spread to other locations in the body.
- M1 indicates that the cancer has spread to other locations in the body.

The above information is then combined using an algorithm to determine an overall "number staging system" of between I and IV. Head and neck cancer is staged according to the individual anatomical location of the primary tumour. Each anatomical site of the head and neck is staged individually under specific groupings that are outlined by the Classification of Malignant Tumours, Seventh Edition, including the relevant ICD-10 codes, as outlined in the following sections.

#### 1.3.4.1 Lip and oral cavity (C00, C02-C06)

Table 1.3 and Table 1.4 indicate a summary of the Tumour and Node classifications, and the final grouped staging classification used in the analyses throughout this thesis for people with cancers of the lip and oral cavity.

**Table 1.3 – Summary staging system for the lip and oral cavity**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Less than or equal to 2cm |
| T2 | Greater than 2cm but less than or equal to 4cm |
| T3 | Greater than 4cm |
| T4a | Lip: Tumour invades cortical bone, inferior alveolar nerve, floor of mouth and skin<br>Oral cavity: Tumour invades cortical bone, deep/extrinsic muscle of tongue, maxillary sinus, or skin of face |
| T4b | Tumour invades masticator space, pterygoid plates, skull base or internal carotid artery |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.4 – Final group staging system for the lip and oral cavity**

| Stage | T stage | N stage | M stage |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage I | T1 | N0 | M0 |
| Stage II | T2 | N0 | M0 |
| Stage III | T3 | N0 | M0 |
| | T1, T2, T3 | N1 | M0 |
| Stage IVa | T1, T2, T3 | N2 | M0 |
| | T4a | N0, N1, N2 | M0 |
| Stage IVb | Any T | N3 | M0 |
| | T4b | Any N | M0 |
| Stage IVc | Any T | Any N | M1 |

#### 1.3.4.2 Oropharynx and hypopharynx (C01, C05.1, C05.2, C09, C10.0, C10.2, C10.3, C12-13)

Table 1.5 to Table 1.7 indicate a summary of the Tumour and Node classifications, and the final grouped staging classification used in the analyses throughout this thesis for people with cancers oropharynx or hypopharynx.

**Table 1.5 – Summary staging system for the oropharynx**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Less than or equal to 2cm |
| T2 | Greater than 2cm but less than or equal to 4cm |
| T3 | Greater than 4cm |
| T4a | Tumour invades the larynx, deep/extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible. |
| T4b | Tumour invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base and carotid artery |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.6 – Summary staging system for the hypopharynx**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Less than or equal to 2cm and limited to one subsite |
| T2 | Greater than 2cm but less than or equal to 4cm and limited to one subsite |
| T3 | Greater than 4cm, or with hemilarynx fixation or extension to oesophagus |
| T4a | Tumour invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue |
| T4b | Tumour invades prevertebral fascia, carotid artery, or mediastinal structures |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.7 – Final group staging system for the oropharynx and hypopharynx**

| Stage | T stage | N stage | M stage |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage I | T1 | N0 | M0 |
| Stage II | T2 | N0 | M0 |
| Stage III | T3 | N0 | M0 |
| | T1, T2, T3 | N1 | M0 |
| Stage IVa | T1, T2, T3 | N2 | M0 |
| | T4a | N0, N1, N2 | M0 |
| Stage IVb | T4b | Any N | M0 |
| | Any T | N3 | M0 |
| Stage IVc | Any T | Any N | M1 |

### 1.3.4.3 Nasopharynx (C11)

Table 1.8 and Table 1.9 indicate a summary of the Tumour and Node classifications, and the final grouped staging classification used in the analyses throughout this thesis for people with cancer of the nasopharynx.

**Table 1.8 – Summary staging system for the nasopharynx**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Tumour only present in the nasopharynx or invades the oropharynx or nasal cavity |
| T2 | Tumour with parapharyngeal extension |
| T3 | Tumour invades bony structures of skull base or paranasal sinuses |
| T4a | Tumour invades intracranial, cranial nerves, hypopharynx, orbit, infratemporal fossa, or masticator space |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Metastases in unilateral cervical, unilateral, or bilateral retropharyngeal lymph nodes, above supraclavicular fossa and is less than or equal to 6cm |
| N2 | Metastases in bilateral cervical above supraclavicular fossa and is less than or equal to 6cm |
| N3a | Metastases in lymph node greater than 6cm |
| N3b | Metastases in the supraclavicular fossa of any size |

**Table 1.9 – Final group staging system for the nasopharynx**

| Stage | T stage | N stage | M stage |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage I | T1 | N0 | M0 |
| Stage II | T1 | N1 | M0 |
| | T2 | N0, N1 | M0 |
| Stage III | T1, T2 | N2 | M0 |
| | T3 | N0, N1, N2 | M0 |
| Stage IVa | T4 | N0, N1, N2 | M0 |
| Stage IVb | Any T | N3 | M0 |
| Stage IVc | Any T | Any N | M1 |

#### 1.3.4.4 Larynx (C32.0, C32.1, C32.2, C10.1)

Table 1.10 to Table 1.13 indicate a summary of the Tumour and Node classifications, and the final grouped staging classification used in the analyses throughout this thesis for people with cancer of the larynx.

**Table 1.10 – Summary staging system for the larynx – supraglottis**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Tumour in one subsite and larynx has normal mobility |
| T2 | Tumour invades mucosa of more than one adjacent subsite of the supraglottis or glottis, or adjacent region outside the supraglottis, and larynx does not have fixation |
| T3 | Larynx has cord fixation or invades the postcricoid area, pre-epiglottic tissues, paraglottic space or thyroid cartilage erosion |
| T4a | Tumour invades through the thyroid cartilage, trachea, soft tissues of the neck, deep/extrinsic muscle of the tongue, strap muscles or thyroid |
| T4b | Tumour invades the prevertebral space, mediastinal structure, or carotid artery. |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.11 – Summary staging system for the larynx – glottis**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1a | Tumour is limited to one vocal cord with normal mobility |
| T2b | Tumour is limited to both vocal cords with normal mobility |
| T2 | Tumour invades supraglottic, subglottis and larynx has impaired mobility |
| T3 | Larynx has cord fixation, or invades the paraglottic space or thyroid cartilage erosion |
| T4a | Tumour invades through the thyroid cartilage, trachea, soft tissues of the neck, deep/extrinsic muscle of the tongue, strap muscles or thyroid |
| T4b | Tumour invades the prevertebral space, mediastinal structure, or carotid artery. |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.12 – Summary staging system for the larynx – subglottis**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Tumour is limited to the subglottis |
| T2 | Tumour extends to vocal cord(s) with normal or impaired mobility |
| T3 | Larynx has cord fixation |
| T4a | Tumour invades through the thyroid cartilage, trachea, soft tissues of the neck, deep/extrinsic muscle of the tongue, strap muscles or thyroid |
| T4b | Tumour invades the prevertebral space, mediastinal structure, or carotid artery. |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.13 – Final group staging system for the larynx**

| Stage | T stage | N stage | M stage |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage I | T1 | N0 | M0 |
| Stage II | T2 | N0 | M0 |
| Stage III | T1, T2 | N1 | M0 |
| | T3 | N0, N1 | M0 |
| Stage IVa | T1, T2, T3 | N2 | M0 |
| | T4a | N0, N1, N2 | M0 |
| Stage IVb | T4b | Any N | M0 |
| | Any T | N3 | M0 |
| Stage IVc | Any T | Any N | M1 |

### 1.3.4.5 Nasal cavity and paranasal sinuses (C30.0, 31.0, 1)

Table 1.14 to Table 1.16 indicate a summary of the Tumour and Node classifications, and the final grouped staging classification used in the analyses throughout this thesis for people with cancers of the nasal cavity or paranasal sinuses.

**Table 1.14 – Summary staging system for the nasal cavity and ethmoid sinus**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Tumour exists in one subsite |
| T2 | Tumour exists in two subsites or invades adjacent nasoethmoidal site |
| T3 | Tumour invades medial wall/floor of orbit, maxillary sinus, palate or cribiform plate |
| T4a | Tumour invades anterior orbit, skin of nose/cheek, anterior cranial fossa (minimal), pterygoid plates or sphenoid/frontal sinuses |
| T4b | Tumour invades orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx or clivus |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.15 – Summary staging system for the maxillary sinus**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Tumour invades mucosa |
| T2 | Tumour causes bone erosion/destruction to the hard palate or middle nasal meatus |
| T3 | Tumour invades posterior bony wall maxillary sinus, subcutaneous tissues, floor/medial wall of orbit, pterygoid fossa, or ethmoid sinus |
| T4a | Tumour invades anterior orbit, skin of nose/cheek, anterior cranial fossa, pterygoid plates, or sphenoid/frontal sinuses |
| T4b | Tumour invades orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx or clivus |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.16 – Final group staging system for the nasal cavity and paranasal sinuses**

| Stage | T stage | N stage | M stage |
|---|---|---|---|
| Stage 0 | Tis | N0 | M0 |
| Stage I | T1 | N0 | M0 |
| Stage II | T2 | N0 | M0 |
| Stage III | T3 | N0 | M0 |
| | T1, T2, T3 | N1 | M0 |
| Stage IVa | T1, T2, T3 | N2 | M0 |
| | T4a | N0, N1, N2 | M0 |
| Stage IVb | T4b | Any N | M0 |
| | Any T | N3 | M0 |
| Stage IVc | Any T | Any N | M1 |

### 1.3.4.6 Major salivary glands (C07, C08)

Table 1.17 and Table 1.18 indicate a summary of the Tumour and Node classifications, and the final grouped staging classification used in the analyses throughout this thesis for people with cancers major salivary glands.

**Table 1.17 – Summary staging system for major salivary glands**

| Stage | Definition |
|---|---|
| **T stage** | |
| TX | Primary tumour cannot be assessed |
| T0 | No evidence of primary tumour |
| Tis | Carcinoma *in situ* |
| T1 | Less than or equal to 2cm, without extraparenchymal extension |
| T2 | Greater than 2cm but less than or equal to 4cm, without extraparenchymal extension |
| T3 | Greater than 4cm, without extraparenchymal extension |
| T4a | Tumour invades skin, mandible, ear canal or facial nerve |
| T4b | Tumour invades skull, pterygoid plates, or carotid artery |
| **N stage** | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Single ipsilateral metastases less than or equal to 3cm |
| N2a | Single ipsilateral metastases greater than 3cm but less than 6cm |
| N2b | Multiple ipsilateral metastases less than or equal to 6cm |
| N2c | Bilateral and contralateral metastases less than or equal to 6cm |
| N3 | Metastases in lymph node greater than 6cm |

**Table 1.18 – Final group staging system for the major salivary glands**

| Stage | T stage | N stage | M stage |
|---|---|---|---|
| Stage I | T1 | N0 | M0 |
| Stage II | T2 | N0 | M0 |
| Stage III | T3 | N0 | M0 |
| | T1, T2, T3 | N1 | M0 |
| Stage IVa | T4a | N0, N1 | M0 |
| | T1, T2, T3, T4a | N2 | M0 |
| Stage IVb | T4b | Any N | M0 |
| | Any T | N3 | M0 |
| Stage IVc | Any T | Any N | M1 |

### 1.3.5 Treatment for head and neck cancer

The primary goal of the treatment for head and neck cancer is to remove the tumour, however due to the location of these tumours and the origin of the complex anatomical sites, another main goal is to consider the patient's quality of life post-treatment by preserving the function of the organs, tissues, and nerves that are involved (Rogers *et al.*, 2016b). The leading treatment for head and neck cancer is surgery, radiotherapy, chemotherapy, targeted therapy, or a combination of two or more of these treatment modalities (Macmillan Cancer Support, 2019).

Multidisciplinary teams of several specialised clinicians in the field of head and neck cancer decide the treatment paths of each individual patient based on a number of factors including the stage of the tumour, the anatomical site of the tumour, the patient's age, their health status at diagnosis, and the future impact of any long-term side effects from the treatment on the patient. Several factors need to be taken into consideration following a person's treatment of head and neck cancer, namely dental status (whether the person can continue to chew and swallow food), disfigurement, the impact on existing comorbidities, or the impact on the carer or family (Rogers *et al.*, 2016b).

### 1.3.6 Determinants of head and neck cancer survival

Globally, more than 467,000 deaths were attributable to head and neck cancer in 2020 (Ferlay *et al.*, 2020) and there were more than 4,000 deaths from head and neck cancer in the UK in 2016 (Cancer Research UK, 2017). Due to the complex nature of head and neck cancers, survival from the disease is complex and difficult to report. Survival significantly varies by the anatomical subsite of the head and neck cancer and the stage of the tumour at diagnosis, both of which impact on treatment decisions. This section explores the existing literature outlining most of the determinants and prognostic factors of the survival of people with head and neck cancer. Following this section, a comprehensive literature review explores previous studies that investigate socioeconomic inequality in survival of people with head and neck cancer across the globe.

#### 1.3.6.1 Age

Age is a strong predictor of survival for people with head and neck cancer. Jones *et al.* (1998) conducted a study of 2,647 people with SCC of the oral cavity, oropharynx, larynx, and hypopharynx to investigate the effects of age on survival. The participants were followed-up for a median of 40.3 years and actuarial survival was computed to examine the findings. The study concluded that there was little difference in survival for those who

were between the years of 40 and 70, but survival substantially decreased in those who were over the age of 70. In addition, the authors reported that the older patients presented with worse disease at the primary site and were less likely to receive radical treatment. A further article assessed the impact of age on survival of 1,160 people with SCC of the oral cavity, oropharynx, and larynx. These patients were diagnosed in Washington University Medical Center between the years of 1980 and 1991 and had a minimum of five-year follow-up. The study showed that people who were younger than 40 years of age had substantially better survival than older patients even after adjusting by race, smoking, comorbidity, tumour site, tumour stage, and histologic variation.

#### 1.3.6.2 Sex

Many groups of cancers exhibit a survival advantage towards females over males. However, there is conflicting evidence on whether the same disparities exist between males and females with head and neck cancer. Several studies have found differences in the survival between males and females, with survival favouring women (Franco *et al.*, 1993; Goldberg *et al.*, 1994; McLean *et al.*, 2006). Goldberg *et al.* (1994) examined people diagnosed on the United States (US) Surveillance, Epidemiology and End Results (SEER) Program of people with cancer of the oral cavity and pharynx who were diagnosed between the years of 1973 and 1987. The SEER database collects data on the incidence, prevalence, and survival of people who have been diagnosed with cancer and aims to reduce the burden of cancer in the United States of America (USA). Goldberg and authors found a difference in mortality rates between men and women with cancer of the oral cavity and pharynx, which favoured females. However, the results of other articles conflict with these findings and suggest no difference in survival between males and females (Kokoska *et al.*, 1995; Garavello *et al.*, 2008; Roberts *et al.*, 2010). Roberts *et al.* (2010) conducted a matched-pair analysis of 286 males and 286 females with SCC of the oral cavity, oropharynx, larynx, and hypopharynx at the University of Texas M.D. Anderson Cancer Center. The patients were diagnosed between the years of 1995 and 2008, and the aim of the study was to investigate whether females had better survival outcomes than males. Males and females were matched based on age (±10 years), race/ethnicity, smoking status, tumour site, tumour stage, and treatment, and recurrence-free survival, disease-specific survival, and overall survival estimates were compared between the two groups. From this small study, there was no evidence of recurrence or poorer survival in men compared with women diagnosed with head and neck cancer.

#### 1.3.6.3 Tobacco smoking behaviour

Many studies have investigated the influence of smoking history on the survival of people with head and neck cancer, with survival favouring those with no history of tobacco use (Browman *et al.*, 2002; Duffy *et al.*, 2009; Sharp *et al.*, 2014; Abrahão *et al.*, 2018; Beynon *et al.*, 2018). Browman *et al.* (2002) explored two-year overall survival of people head and neck cancer who were undergoing radiotherapy in Canada and the USA. In a multivariate analysis that included smoking status at baseline, T stage, N stage, and the number of years smoked (measured in pack-years), the number of years smoked had the strongest association with survival. Browman reported that those who had quit smoking less than 12 weeks before their diagnosis were 40% less at risk of dying than those who continued to smoke, and those who had quit smoking more than one year before diagnosis were 70% less at risk of dying than those who continued to smoke. Sharp *et al.* (2014), examined the relationship between smoking status and survival in 5,652 patients who were registered with the National Cancer Registry in Ireland. Those with a history of smoking, and who remained current smokers at the time of their diagnosis, had substantially reduced five-year disease-specific survival and were 36% more at risk of a cancer-specific death than those who had never smoked.

More recently, Beynon *et al.* (2018) investigated outcomes from the HN5000 cohort study of 1,393 people with cancer of the oral cavity, oropharynx, and larynx who were diagnosed in the UK between the years of 2011 and 2014. Beynon and authors found that even after adjusting for several confounding factors including tumour stage, BMI, comorbidity, treatment, HPV status, education, annual household income, IMD, marital status, ethnicity, and alcohol consumption, poor survival remained associated with tobacco smoking at diagnosis. Abrahão *et al.* (2018) conducted an analysis using data from the Alcohol-Related Cancers and Genetic Susceptibility in Europe (ARCAGE) case-control study. A total of 1,210 people were included in the study, of whom 91% were ever smokers, and a strong association between smoking and survival was observed, measured as overall smoking history, duration, and intensity.

Following a cancer diagnosis, continued smoking while undergoing treatment increases toxicity, decreases treatment efficacy, and may lower survival outcomes (Kashigar *et al.*, 2013). Smoking while undergoing treatment for head and neck cancer can also lead to secondary primary tumours, co-morbidities, and a diminished quality of life (Gritz *et al.*, 2005). Of the patients who are current smokers at their time of diagnosis, only half decide to refrain from smoking during their treatment period (Duffy *et al.*, 2008), and those who are living with their partner and those with higher education levels are less likely to continue smoking following a cancer diagnosis, suggesting that family and social support are important factors associated with quitting smoking and continued abstinence (Allison,

2001). Due to the serious and potentially fatal interactions that smoking has with various treatment modalities for cancer, Gritz *et al.* (2005) has recommended that smoking history, current smoking status, and on-going smoking behaviours are recorded as routine data collection in all oncological trials.

#### 1.3.6.4 Alcohol consumption

Several papers have reported poorer survival for people with head and neck cancer with a history of excessive alcohol consumption (Fountzilas *et al.*, 1992; Deleyiannis *et al.*, 1996; Fortin *et al.*, 2009; Mayne *et al.*, 2009; Lopez *et al.*, 2011), while other papers have reported an association prior to adjustment for other factors, but not following adjustment (Duffy *et al.*, 2009; Beynon *et al.*, 2018).

Deleyiannis *et al.* (1996) carried out a study involving 649 people with head and neck cancer to determine the features of alcohol (such as recency of alcohol use, alcohol-related health problems, alcohol dependency, and weekly and lifetime alcohol consumption) that were associated with five-year survival. Those of higher alcoholic severity, as defined by the Michigan Alcoholism Screening Test (MAST), had an increased risk of dying not only from head and neck cancer, but also cardiovascular disease, pulmonary disease, and alcohol-related diseases. Those who abstained from drinking alcohol after their diagnosis, including those with a history of alcohol-related health problems, had better survival than those who did not abstain from drinking.

Mayne *et al.* (2009) investigated the impact of pre-diagnosis and post-diagnosis use of alcohol and tobacco smoking on survival of 264 people with early-stage cancers of the oral cavity, pharynx, and larynx. Mayne *et al.* (2009) reported that a history of alcohol consumption was associated with poorer survival, with those who drank more than 35 drinks per week having nearly five-times excess risk of death compared to those who did not drink. However, this excess risk was only observed for beer or liquor drinkers, but not for wine drinkers. In addition, continuous drinking following a diagnosis of head and neck cancer led to twice as much risk of dying compared to those who did not drink following their diagnosis.

However, several papers conflict with the message that alcohol consumption affects survival of people with head and neck cancer. Beynon *et al.* (2018) investigated the association of a history of smoking and alcohol consumption with survival of 4,276 people diagnosed with cancer of the oral cavity, larynx, and oropharynx. Beynon *et al.* (2018) did not report an association with drinking behaviours and risk of mortality. Additionally, Duffy *et al.* (2009) also could not confirm an association with alcohol consumption and poor

survival for 504 people with head and neck cancer following adjustment for additional factors.

#### 1.3.6.5 HPV status

The recent rise in the incidence of head and neck cancers that are associated with HPV (mainly for those with tumours of the oropharynx) has led to a surge of research in the field, and the positive impact of HPV-positive tumours on the survival of people with head and neck cancer has been discovered. A meta-analysis of 5,681 people with SCC of the head and neck from 34 studies was carried out by Dayyani *et al.* (2010) to assess the impact of HPV on overall survival. The study confirmed that there was improved survival for individuals with HPV infection, particularly for those with HPV-16 positivity. A systematic review conducted by Wang *et al.* (2015) investigated the evidence of the positive effect of HPV positivity on the prognosis of people with cancer of the oropharynx. A total of 56 eligible studies were eligible which included 1,367 people treated with primary surgery and 4,747 people treated with radiation therapy. The study confirmed the findings of the earlier meta-analysis that HPV-16 positivity led to a substantially improved survival for individuals with cancer of the oropharynx.

A further study by D'Souza *et al.* (2016) explored the effect of HPV on the survival of people with head and neck cancer, and the authors performed stratified analyses by geographic region and anatomical site of the head and neck. Patients were recruited to one of three studies: the Brazilian Head and Neck Genome Project (GENCAPO) in São Paulo, Southern Brazil; the Caroline Head and Neck Cancer Study (CHANCE) in North Carolina, USA; and the ARCAGE study in Europe. A total of 1,362 people who were diagnosed with cancer of the oropharynx, hypopharynx, larynx, or oral cavity between the years of 2002 and 2011 were included in the study. The authors reported that there was a significantly lower risk of death among the people who had HPV-related tumours of the oropharynx compared to those without HPV-related tumours, which was observable across all three continents. However, this difference was not as evident for people with tumours that were outside of the oropharynx.

More recent studies have explored the interaction of HPV and smoking with head and neck cancer. Anantharaman *et al.* (2016) investigated this using data from the ARCAGE study, and the head and neck cancer case-control study nested within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. A total of 1,904 head and neck cancer cases and 3,024 controls were included in the study, and the authors reported that smoking increases the risk of cancer of the oropharynx whether or not the person has HPV-16. In addition, earlier studies have also suggested that smoking

consumption, alcohol consumption, and HPV status are three independent risk factors of head and neck cancer incidence and survival (Gillison *et al.*, 2008; Smith *et al.*, 2012).

#### 1.3.6.6 Comorbidity

Several studies have reported that comorbid conditions have a substantially negative effect on the survival outcomes of people with head and neck cancer (Reid *et al.*, 2001; Allareddy and Konety, 2006; Datema *et al.*, 2010; Eytan *et al.*, 2019b; Eytan *et al.*, 2019a). Eytan *et al.* (2019b) examined the effect of comorbidities on overall survival of people with HPV-related and HPV-unrelated head and neck cancer in the USA. A total of 10,524 people were included in the study, including 2,499 people with HPV-related tumours and 8,025 people with HPV-unrelated tumours who were diagnosed between the years of 2004 and 2011 on the SEER database. The authors determined that those with pneumonia, anaemia, dysphagia, malnutrition, weight loss, hypertension, cerebrovascular disease, or dementia that was present at the time of their diagnosis had an increased risk of death in those with both HPV-related and HPV-unrelated head and neck cancer. In addition, individuals with HPV-unrelated head and neck cancer had an increased risk of death if they had paralysis, rheumatologic disease, hip fracture, anxiety, angina, or myocardial infarction at the time of their diagnosis. However, this was not observed in those with HPV-related head and neck cancer, and dental disease was associated with an increased risk of death for people with HPV-related head and neck cancer, but not HPV-unrelated cancer. A further paper by Eytan *et al.* (2019a) explored the prevalence of comorbidities in older survivors of head and neck cancer using the same cohort of people as the previous study. Eytan *et al.* (2019a) reported that hypertension, chronic obstructive pulmonary disease, diabetes, and hyperlipidaemia were *"highly prevalent"* at the time of diagnosis, while other comorbidities that are related to treatment therapies such as pneumonia, anaemia, dysphagia, weight loss, and malnutrition, were less prevalent at diagnosis but rose substantially in the first one to five years after diagnosis.

Allareddy and Konety (2006) investigated the effects of comorbidity on 24,803 people who were hospitalised for head and neck cancer in the USA from the Nationwide Inpatient Sample of the Healthcare Cost and Utilisation Project between the years of 2000 and 2003. Comorbidity was recorded on various conditions that the inpatient had, and univariate and multivariate logistic regression models were produced to investigate mortality. Individuals who had congestive heart failure, neurologic disorders or coagulopathy were at a substantially increased risk of mortality in a multivariate model. Datema *et al.* (2010) investigated the impact of comorbidity on survival of 1,662 people with SCC of the head and neck at the Leiden University Medical Centre between 1981 and 1998. Comorbidity was measured using the Adult Comorbidity Evaluation (ACE-27) to

assess the impact on short-term mortality. Datema and authors reported that poorer survival was particularly observed in people with cardiovascular comorbidity, respiratory comorbidity, gastrointestinal comorbidity, and diabetes.

#### 1.3.6.7 Anatomical site

Survival from head and neck cancer depends on the anatomical site of the primary tumour within the head and neck. Five-year net survival is highest for people with cancer of the oropharynx at 65.6% (95% CI 64.2% to 67.0%) and lowest for those with cancer of the hypopharynx at 27.8% (95% CI 25.7% to 30.1%) (Cancer Research UK, 2017). Individuals with cancer of the oral cavity had five-year net survival estimates of 56.1% (95% CI 54.7% to 57.4%), while men with cancer of the larynx had five-year net survival estimates of 65.4% (95% CI 64.0% to 66.8%) (Cancer Research UK, 2017).

A study involving people diagnosed with head and neck cancer on the SEER database were included in a site-specific study to investigate survival outcomes (Carvalho *et al.*, 2005). A total of 96,232 cases diagnosed between the years of 1973 and 1999 were identified and included in the analysis. Carvalho and authors determined a substantial difference in survival between those with cancer of the lip and those with cancer of the oral cavity, oropharynx, hypopharynx, and “other mouth and pharynx”, who had approximately a three-fold increased risk of mortality than those with cancer of the lip in a multivariate model (oral cavity HR = 2.83, 95% CI = 2.67 to 3.00; oropharynx HR = 2.84, 95% CI = 2.66 to 3.03; hypopharynx HR = 3.62, 95% CI = 3.38 to 3.88; other mouth and pharynx HR = 3.08, 95% CI 2.66 to 3.56). Additionally, those with cancer of the larynx, nasopharynx, and salivary gland were approximately two times more at risk of mortality than those with cancer of the lip (larynx HR = 1.70, 95% CI = 1.59 to 1.80; nasopharynx HR = 1.97, 95% CI = 1.81 to 2.14; salivary gland HR = 1.97, 95% CI = 1.83 to 2.12).

#### 1.3.6.8 Tumour stage

Tumour staging is important to determine the extent and spread of disease by considering the size of the tumour (T), the nodal involvement (N) and whether any distant metastases (M) have emerged from the primary site. As a result, tumour stage is highly associated with survival – a person with a tumour of higher stage is likely to have substantially poorer survival. Rudolph *et al.* (2011) carried out a systematic review and meta-analysis to assess the effects of tumour stage on survival of people with cancer of the larynx. The authors reviewed 29 articles and reported that five-year survival by tumour stage varied between 0% and 100% depending on the T- and N-category of the tumour, with an overall five-year relative survival rate of 64.2% (95% CI 63.7% to 64.7%) for all stages combined.

## 1.4 Literature review: Socioeconomic determinants and inequalities in survival of people with head and neck cancer

In the 1997 landmark IARC publication *Social Inequalities in Cancer*, Auvinen (1997) assessed the socioeconomic factors that are associated with cancer survival and identified gaps in the understanding the determinants of survival from cancer. Auvinen concluded that there was an "*urgent need*" to understand the drivers of socioeconomic inequality in cancer survival, and more than twenty years later, the evidence-base is not much further forward. In 2019 IARC produced an updated publication: *Reducing Social Inequalities in Cancer: Evidence and Priorities for Research* (International Agency for Research on Cancer, 2019), in which Dr Christopher P. Wild, director of IARC, wrote that "*cancer is undoubtedly a disease of inequalities*" and that "*tackling these inequalities is a matter of social justice and human rights*".

Explanations for socioeconomic inequalities in survival of people with cancer are complex and are rarely described for cancers of the head and neck. Auvinen (1997) reviewed articles with the aim of explaining the possible explanations for the differences in all-cancer patient survival by socioeconomic status. Although Auvinen reported that cancer stage at diagnosis is particularly important, in many of the studies included in the review, socioeconomic inequalities in survival of people with cancer by social class remained following the adjustment for stage. Woods *et al.* (2006) carried out a comprehensive review to determine the origins of socioeconomic inequalities in all-cancer survival and concluded that stage at diagnosis, access to health services, and comorbidity may explain some of the association.

This section of the thesis reviews the current evidence of socioeconomic inequality in survival of people with head and neck cancer and provides the basis and rationale for this research.

### 1.4.1 Literature search strategy

Searches in several databases were conducted between October 2014 and March 2020 to identify studies that investigated the effects of socioeconomic status on survival outcomes of people with head and neck cancer. The databases searched included Medline 1950-; Embase 1980-; and Pubmed. The following search was conducted:

> (survival or survivor or mortality or outcome* or prognosis or death).m_titl. and (socio* or economic or social or inequalit* or income or financ* or education* or

depriv* or poverty).m_titl. and (cancer or tumour or tumor or malignan* or carcinoma or neoplasm* or (squamous cell)) adj3 ((head and neck) or (head or neck) or oral or mouth or laryn* or pharyn* or oropharyn* or hypopharyn* or nasopharyn* or sinus* or tonsil* or jaw or tongue or lip* or cheek* or gum* or palat* or gingiva or maxilla or (parotid gland*) or oesophag* or esophag* or UATD or (upper aerodigestive tract) or (upper aero-digestive tract)).tw.

This returned 240 articles which were screened for suitability for this literature review. A final 40 papers were selected for inclusion for a full review as outlined in the following section. This review is also summarised briefly in Appendix 1.3.

### 1.4.2 Inclusion criteria for the literature review

This literature review focusses on articles with the following criteria:

1. Studies that involved any form of head and neck cancer.
2. Studies that involved all types of cancers providing a subgroup of people with head and neck cancer was included and sub-categorised throughout the analysis.
3. Studies that measured any type of socioeconomic status including area-based or individual measurements.
4. Studies that assessed survival or prognosis.
5. Studies written in English.

### 1.4.3 Exclusion criteria for the literature review

The articles that were excluded from this literature review satisfied any of the following criteria:

1. Studies that investigated people with cancer of the thyroid.
2. Studies that investigated skin cancer of the face or neck.
3. Studies that focussed only on mortality rates rather than survival.
4. Studies that only reported inequalities in racial disparities, marital status, or religious status.

### 1.4.4 Effect of socioeconomic status on survival of people with head and neck cancer in the United Kingdom

#### 1.4.4.1 Overview of studies in the United Kingdom

A total of 11 articles were found which investigated socioeconomic determinants and inequalities in survival of people with head and neck cancer in the UK. Five of these studies were produced by a group of researchers from the London School of Hygiene and Tropical Medicine (LSHTM) (Coleman *et al.*, 2001; Coleman *et al.*, 2004; Shack *et al.*, 2007; Rachet *et al.*, 2008; Ellis *et al.*, 2012). All of the papers that were produced by the LSHTM involved cancer registry data from across the UK – four included people from England and Wales (Coleman *et al.*, 2001; Coleman *et al.*, 2004; Rachet *et al.*, 2008; Ellis *et al.*, 2012), and one included individuals from Scotland (Shack *et al.*, 2007). Two of the studies in England and Wales investigated individuals with all types of cancer (Coleman *et al.*, 2001; Coleman *et al.*, 2004), but included a sub-cohort of people with cancer of the larynx, while the other studies examined only those with cancer of the larynx (Shack *et al.*, 2007; Rachet *et al.*, 2008; Ellis *et al.*, 2012). Of the six UK-based studies that were produced outside of the LSHTM, four articles included data from cancer registry sources (Edwards and Jones, 1999; Paterson *et al.*, 2002; Warnakulasuriya *et al.*, 2007; Anandan *et al.*, 2008), one included data from hospital records (Rylands *et al.*, 2016), and the final study analysed data from a cohort study (Robertson *et al.*, 2010). Four of the papers focused on people who were diagnosed with any type of head and neck cancer (Edwards and Jones, 1999; Paterson *et al.*, 2002) or cancer of the oral cavity (Warnakulasuriya *et al.*, 2007; Rylands *et al.*, 2016) in England, while two studies focused on individuals with any type of head and neck cancer (Robertson *et al.*, 2010) or cancer of the nasopharynx (Anandan *et al.*, 2008) in Scotland. All of the UK-based studies used area-based measurements of socioeconomic status and none of the studies used individual-level measurements. All of the articles produced by the LSHTM reported relative survival, as did two other studies outside of the LSHTM (Paterson *et al.*, 2002; Anandan *et al.*, 2008). Four papers reported overall or disease-specific measurements of survival analysis (Edwards and Jones, 1999; Warnakulasuriya *et al.*, 2007; Robertson *et al.*, 2010; Rylands *et al.*, 2016). All of the studies provided up to five-years of follow-up and only one study provided follow-up beyond five-years (Rachet *et al.*, 2008).

#### 1.4.4.2 Studies from the United Kingdom

The earliest article, written by **Edwards and Jones (1999)**, investigated one-, two-, and five-year crude and cause-specific survival of people with head and neck cancer. Data were utilised from the Thames, West Midlands, West of Scotland, and Yorkshire cancer

registries of 25,903 individuals who were diagnosed with head and neck cancer between the years of 1984 and 1993. Edwards and Jones linked the data to Carstairs 1991 Categories and grouped people by quintile 1 (most deprived), quintiles 2 and 3, and quintiles 4 and 5 (least deprived). Edwards and Jones discovered that those who were living in less deprived areas had substantially better crude and cause-specific survival than the people who were living in more deprived areas. In addition, the authors produced a multivariate analysis which adjusted by subsite, extent of the spread of the disease and age which suggested that deprivation had an independent effect on both crude and cause-specific survival following the adjustment by these variables. Although this study investigated some of the potential explanatory factors of socioeconomic inequality, many determinants were not included due to the limitations of cancer registry data, such as smoking and alcohol behaviours. Moreover, this study noted that there were high proportions of missing data for the people who were living in the most deprived areas in this study, which could have led to biased results.

Two of the largest UK-based national studies of population-based cancer survival were produced by the Cancer and Public Health Unit at the LSHTM. These articles investigated the trends of socioeconomic inequalities in cancer survival in England and Wales (Coleman *et al.*, 2001; Coleman *et al.*, 2004). The studies included all diagnoses of cancer from the regional cancer registries. However, the authors also included a stratified analysis for each cancer subsite which included individuals with cancer of the larynx. The first paper written by **Coleman *et al.* (2001)** included nearly three million people who were diagnosed with one of 39 solid tumours or eight types of leukaemia and lymphoma in England and Wales between the years of 1971 and 1990. The participants were followed up for five years to produce one-year and five-year relative survival estimations. The study utilised Carstairs 1991 Categories and variance-weighted least squares regression to produce a “deprivation gap” in the fitted rates between the least deprived and most deprived groups. A total of 8,671 people with cancer of the larynx were included in this analysis and there was a gap of 9.3% in the relative survival estimates of those who resided in the least deprived and most deprived areas, in favour of those from the least deprived regions. However, the study had several limitations, particularly around the origin of the data from national databases of cancers which do not include information on the stage of the tumour or any behavioural information of the participants that are included. As a result, the determinants of socioeconomic inequality in survival of people with cancer was not investigated as part of this study.

A robust study undertaken by **Paterson *et al.* (2002)** included 20,131 people with head and neck cancer from four regional cancer registries in England and Wales between the years of 1981 and 1994. This study examined the effect of deprivation on one-year and

five-year relative survival using Carstairs 1991 Categories from several perspectives including age group, sex, and calendar year. Firstly, the authors reported that survival of the individuals who lived in the most deprived areas was substantially worse than those who lived in the least deprived areas. Secondly, they found that the socioeconomic inequality in survival was not apparent for those who were below the age of 39, while differences were more pronounced in those above the age of 39. Thirdly, Paterson and colleagues investigated the association of deprivation with survival by grouping the data into the years of 1981 to 1985, 1986 to 1990, and 1991 to 1994 and found that the effect of deprivation on relative survival was stronger in the period of 1981 to 1985 and 1991 to 1994, with survival favouring those who lived in the least deprived areas. Lastly, the authors discovered that there was no difference in survival between the deprivation groups for those who survived beyond 18 months. This thorough analysis provided a snapshot of inequality for those who were diagnosed with head and neck cancer between the years of 1981 and 1994. However, there were several limitations due to the use of cancer registry data which does not contain information on the stage of the person's tumour or data on smoking or alcohol consumption. Therefore, the underlying causes of socioeconomic inequality could not be explored as part of this analysis.

A second comprehensive study carried out by **Coleman *et al.* (2004)** was similar to the group's earlier paper (Coleman *et al.*, 2001) and analysed cancer registry data on 2.2 million people. These individuals had been diagnosed with one of the 20 most common cancers in England and Wales between the years of 1986 and 1999. The authors linked Carstairs 1995 Categories to those who were diagnosed between the years of 1986 and 1995 and 2000 English and Welsh IMD scores to those who were diagnosed between the years of 1996 and 1999. Similar to the earlier study, relative survival up to five-years and a "deprivation gap" were presented for each of the cancer sites which included 5,666 individuals with cancer of the larynx. However, unlike the previous article, comparisons of the difference in the deprivation gap every five years were also provided. Coleman and colleagues discovered that the deprivation gap in relative survival for males with cancer of the larynx was increasing and in the period of 1996 to 1999 reached 17%, which was in favour of those from the least deprived areas, and this was the highest out of all 20 cancers presented. The authors concluded that for many cancers, survival improved for those who were from the least deprived areas and as a result, led to a widening in the deprivation gap in the late 1990s in favour of those from the least deprived areas. The aim of this paper was to examine trends in survival over time and therefore, the underlying causes of socioeconomic inequality were not explored. Similar to the other papers that have been reviewed in this section, the limitations around the use of cancer registry data also apply to this study.

A further study conducted by **Shack *et al.* (2007)** investigated the socioeconomic inequality in survival of people with cancer in Scotland. This study investigated a cohort of 357,658 adults with any primary cancer registered on the Scottish Cancer Registry between the years of 1986 and 2000 and followed-up to 2005. The people who were diagnosed with cancer between the years of 1986 and 1995 were linked to Carstairs 1995 Categories, while those who were diagnosed with cancer between the years of 1996 and 2000 were linked to 2004 SIMD scores. Like the group's previous studies, five-year relative survival was computed and the "deprivation gap" was presented for all of the data which included a sub-cohort of 1,128 men with laryngeal cancer. This study demonstrated that the deprivation gap in five-year relative survival was at nearly 11% for men with cancer of the larynx in favour of those from the least deprived areas of Scotland and, in addition, was becoming approximately 3% wider every five years. However, the authors could not explain the reasoning behind the widening socioeconomic inequality for men with cancer of the larynx due to the limitations around cancer registry data which does not hold data such as stage, or health and behavioural information.

**Warnakulasuriya *et al.* (2007)** examined the trends in crude survival for 12,791 people with cancer of the oral cavity and pharynx. Data were extracted from the Thames Cancer Registry between the years of 1995 and 2002, and the results between those who were less than 45 and those who were aged 45 and over were compared. As part of this analysis, the authors also investigated the association of stage, treatment, cancer network of residence, and socioeconomic status with survival. A total of 483 individuals who were younger than 45 years of age and 4,836 people who were older than 45 years were included in the analysis to explore the effect of socioeconomic status on relative survival, which was measured using IMD scores. Univariate unadjusted Cox proportional hazards models for all-cause mortality demonstrated a clear difference in survival for both the younger and older groups of people, with survival favouring those from less deprived regions. The authors reported that socioeconomic inequality attenuated following adjustment for disease stage and treatment modality, particularly for those who were younger than 45 years of age. However, this analysis was restricted to those who lived in South-East England, so is not necessarily generalisable to the rest of the UK. In addition, since this study investigated data from the Thames Cancer Registry, there were limitations in the availability of additional potential explanatory factors for socioeconomic inequality such as health and behavioural factors.

A fourth small report produced by the LSHTM investigated survival of men with cancer of the larynx who were diagnosed between the years of 1986 and 1999 in England and Wales **(Rachet *et al.*, 2008)**. This study used the same data sources and methods that were used in the groups' earlier papers (Coleman *et al.*, 2001; Coleman *et al.*, 2004).

Rachet and colleagues took a deeper look at the 17% deprivation gap of males from the earlier article (Coleman *et al.*, 2004) and reported that this gap had increased by 3.7% every five years, and that survival was consistently in favour of those from the least deprived areas. In addition, this paper investigated 10-year relative survival and discovered that the gap in 10-year relative survival for men diagnosed in the early 1990s was also wide at 11%, in favour of the people from the least deprived regions. The authors outlined that due to the widening socioeconomic inequality observed in this study, the gap between the most and least deprived males could continue to grow up to 20% or more in recent years. However, like the earlier papers, the underlying causes of socioeconomic inequality were not explored.

A small study carried out by **Anandan *et al.* (2008)** included 556 people with cancer of the nasopharynx whose data were extracted from the Scottish Cancer Registry between the years of 1975 and 2001. The study investigated the effects of Carstairs 1991 Categories on one-year, three-year, and five-year relative survival, and overall survival. A difference between those from the least deprived and most deprived areas was discovered, with survival in favour of the people who resided in the areas that were least deprived. However, since this study was restricted to those with nasopharynx cancer, the sample size was small and therefore may not be generalisable to the whole population of people with head and neck cancer. In addition, due to the limitations of cancer registry data the explanations for socioeconomic inequality were not investigated.

In a population-wide cohort study in Scotland including 1,909 people from the SAHNC who were diagnosed with head and neck cancer between the years of 1999 and 2001, **Robertson *et al.* (2010)** aimed to explain the effects of socioeconomic status on five-year overall survival and disease-specific survival. In this study, socioeconomic status was measured using 2001 Deprivation Category (DEPCAT) scores which were categorised into three groups – affluent, intermediate, and deprived. The authors reported that the people who were in the deprived group experienced a 33% (HR = 1.33, 95% CI = 1.06 to 1.68) increased risk of all-cause mortality compared to those in the affluent group. However, in a multivariate Cox proportional hazards model, socioeconomic status was no longer an independent predictor of all-cause mortality or disease-specific mortality following the adjustment for other baseline covariates including WHO Performance Status, tumour stage, age at diagnosis, anatomical site of the tumour, smoking status, and alcohol consumption. This was the only UK-based study to investigate the underlying causes of socioeconomic inequality in survival of people with head and neck cancer. However, Robertson reports the limitations around the use of an area-based measurement of socioeconomic status and that the participants of the study may have under-reported their levels of smoking and alcohol consumption.

**Ellis *et al.* (2012)** undertook a fifth and more thorough study with the LSHTM involving men and women who had been diagnosed with laryngeal cancer. This more recent analysis reported socioeconomic inequalities in survival of 24,234 men and 5,186 women who were diagnosed with cancer of the larynx and recorded on the national cancer registries of England and Wales between the years of 1991 and 2006. The English and Welsh IMD scores were used and both one-year and five-year relative survival was reported along with the "deprivation gap" that was described earlier (Coleman *et al.*, 2001; Coleman *et al.*, 2004; Rachet *et al.*, 2008). Ellis and colleagues reported that there was no difference in relative survival between the least deprived and most deprived groups of females with laryngeal cancer after one year and five years. However, the difference was much clearer for males, with a deprivation gap of 7% and 13% between the least deprived and most deprived males after one year and five years, respectively, in favour of the least deprived group. In addition, the authors outlined that there were differing results depending on the subsite of the laryngeal tumour, which included glottal and supraglottic tumours. These findings suggested that females with tumours of the glottis had a deprivation gap in favour of the least deprived group, while females with supraglottic tumours had a deprivation gap in favour of the most deprived group. However, similar to the group's earlier studies, there were limitations around the use of data from cancer registry sources which did not allow further investigations into the explanations for socioeconomic inequality to be explored.

**Rylands *et al.* (2016)** reported findings from a cohort of 523 people recorded with an SCC of the oral cavity in the University Hospital Aintree database between 2008 and 2012. The data were linked to 2010 IMD scores which grouped people into national quartiles, and two-year and five-year overall survival estimates were reported. Interestingly, the authors reported that there was not an obvious gradient in survival across the IMD quartiles, however there was a difference between binary groups of the most deprived compared to those from the least deprived group, in favour of the least deprived group, although this was minimal. This was a small study of people diagnosed at a single centre in the North of England and so these results are likely to be unreliable. In addition, the authors only investigated overall survival estimates and cause of death was not considered in a cause-specific or relative survival setting.

### 1.4.5 Effect of socioeconomic status on survival of people with head and neck cancer in Europe

#### 1.4.5.1 Overview of studies in Europe

Only five studies from Europe met the eligibility criteria for this literature review. Two of these articles included people from Turin, Italy (Rosso *et al.*, 1996; Boffetta *et al.*, 1997), one included people from The Netherlands (de Graeff *et al.*, 2001), and the final two studies included individuals from Denmark (Andersen *et al.*, 2008; Dalton *et al.*, 2019). Four of these papers investigated survival of either all types of head and neck cancer or cancer of the mouth, pharynx, and larynx (Rosso *et al.*, 1996; de Graeff *et al.*, 2001; Andersen *et al.*, 2008; Dalton *et al.*, 2019), while the fifth study included people with cancer of the larynx (Boffetta *et al.*, 1997). All five of the studies involved cancer registry data and contrastingly to the studies from the UK, all of the European studies used individual measures of socioeconomic status, and none of them used area-based measurements. Two articles investigated outcomes using overall survival (Boffetta *et al.*, 1997; de Graeff *et al.*, 2001), two studies utilised relative survival (Andersen *et al.*, 2008; Dalton *et al.*, 2019), and the fifth paper used case fatality ratios (Rosso *et al.*, 1996). Only one of the studies investigated the underlying causes of socioeconomic inequality in survival by education level (Boffetta *et al.*, 1997).

#### 1.4.5.2 Studies in Europe

The earliest European article was undertaken by **Rosso *et al.* (1996)** and examined social differences in cancer survival in Turin, Italy. This study used the Piedmont Cancer Registry which was linked to census data to provide measurements of socioeconomic status. The authors examined level of education status and estimated the case fatality ratios for all-cause mortality. People with cancer who were diagnosed between the years of 1985 and 1987 and followed-up to 1993 were included. A total of 11,653 people with cancer were eligible for the study, including 294 people with cancer of the mouth and pharynx and 274 individuals with cancer of the larynx. Case fatality ratios were displayed following adjustment for age, area of birth, sex, and housing tenure (owners or renters). No trend by education was apparent for individuals with cancer of the mouth and pharynx, and only a weak trend for those with cancer of the larynx was observed in favour of those with higher levels of education. However, the sample size for this study was small and only included data from one city in Italy and therefore, these results need to be interpreted with caution.

A second small cohort study of 355 people with cancer of the larynx from Turin, Italy was undertaken by **Boffetta *et al.* (1997)**. Individuals were recruited between the years of 1979 and 1982 and followed-up until 1994. The authors presented overall and relative survival with the aim of determining the prognostic factors of survival by exploring age, sex, tumour site, stage, smoking alcohol, nutrient intake, and two measurements for socioeconomic status including education level and occupation. Although statistically insignificant, the authors reported that there was an association between education level and survival following adjustment for tumour site, stage, and tobacco smoking, in favour of those with higher levels of education. However, the same limitations as those for the earlier European study also apply to this study since the sample size was small and the inclusion criteria was restricted to people in one city in Italy.

A small cohort study by **de Graeff *et al.* (2001)** in the 1990s was conducted to evaluate the effects of sociodemographic factors on the survival of people with head and neck cancer. The study was carried out on 208 people in The Netherlands who were diagnosed with SCC of the oral cavity, oropharynx, hypopharynx, and larynx and recruited between the years of 1994 and 1996. The people were followed up either until progression of their cancer or death from their cancer. However, the length of follow-up was not defined. Although the study was primarily focussed on the association between quality of life and survival, de Graeff produced one univariate analysis which included family income and occupational level. This analysis reported no association between income and occupation and survival. However, there were several limitations to this study including the small sample size of people from a small area in The Netherlands and the number of events (including progression and deaths) were low.

As part of a thorough analysis to examine the effects of socioeconomic inequality in incidence and survival of 3.22 million people registered with cancer on the Central Population Register in Denmark, **Andersen *et al.* (2008)** examined a sub-cohort of 3,058 individuals with cancers of the mouth, pharynx, and larynx. People over the age of 30 in Denmark were diagnosed between the years of 1994 and 2003 for the occurrence of cancer and were followed-up until 2006. This was defined in a separate paper (Dalton *et al.*, 2008) and was justified since people who were younger than 30 may still be in education and thus, have not yet established their socioeconomic position. Anderson and colleagues' article assessed 3,058 people with cancers of the mouth or pharynx and 1,799 people with cancer of the larynx. Socioeconomic status was measured using a variety of indicators including level of education, disposable income, affiliation to work market, social class, housing tenure, size of dwelling, and district type. For people with cancer of the mouth and pharynx, better survival was observed for both males and females if they had higher education, higher income, were homeowners, lived in dwellings of larger square

meter, or had better affiliation to the labour market. However, more disposable income was not associated with better survival outcomes for females. For males with cancer of the larynx, better survival was observed for those who were of higher education levels, higher levels of income, homeowners, had larger dwelling sizes, or who were of the creative core or creative professional social class. For females with cancer of the larynx, better survival was reported for those who had more income, were employed, homeowners, or lived in a larger dwelling. Interestingly, females with cancer of the larynx who had basic or high school levels of education had better survival after one-year than those with higher levels of education, however by five-years, this had reversed and the females who had obtained higher education levels had better survival. The population-wide data from Denmark with multiple individual-level socioeconomic measures are strengths of this study. However, as per several other articles included in this literature review, the explanations of socioeconomic determinants and socioeconomic inequalities observed could not be assessed due to limitations of available data from a cancer registry.

**Dalton *et al.* (2019)** explored the trends in socioeconomic inequality in cancer survival from 1987 to 2013. A total of 142,430 people with a diagnosis of cancer from Denmark were included in the study, which included a sub-cohort of 3,928 people with cancer of the head and neck. One-year and five-year relative survival was reported, and socioeconomic position was assessed by utilising the individuals' disposable income in the year prior to their diagnosis. The authors reported that although relative survival improved over the period from 1987 to 2013, this improvement was more prominent in those who had higher income levels, particularly for those with cancer of the head and neck. Inequality in survival of people with head and cancer had increased over time. This was the only study discovered that investigated inequality utilising an individual measurement for levels of income.

### 1.4.6 Effect of socioeconomic status on survival of people with head and neck cancer in the Americas

#### 1.4.6.1 Overview of studies in the Americas

A total of 19 articles were found involving people with head and neck cancer in the Americas. This included 11 studies in the USA six studies in Canada and two studies in South America. Of the 11 papers from the USA, seven studies included people from across the entire USA (Konski *et al.*, 2003; Chen and Halpern, 2007; Megwalu, 2017; Shin *et al.*, 2017; Xu *et al.*, 2017; Gaubatz *et al.*, 2019; Stubbs *et al.*, 2020), two papers included individuals from Florida (Molina *et al.*, 2008; Guo *et al.*, 2015), one study included individuals from California (Chu *et al.*, 2011a), and one study included people

from Texas (Reitzel *et al.*, 2012). Four articles utilised data from the National Cancer Database (Chen and Halpern, 2007; Shin *et al.*, 2017; Gaubatz *et al.*, 2019; Stubbs *et al.*, 2020), two studies utilised data from the SEER programme (Megwalu, 2017; Xu *et al.*, 2017), three involved extracts from local cancer registries (Molina *et al.*, 2008; Chu *et al.*, 2011a; Guo *et al.*, 2015), one involved data from a single-site cancer centre (Reitzel *et al.*, 2012), and the final paper used data which was collected as part of a randomised controlled trial (Konski *et al.*, 2003). Of these articles, seven of them included all types of head and neck cancers (Konski *et al.*, 2003; Molina *et al.*, 2008; Chu *et al.*, 2011a; Reitzel *et al.*, 2012; Guo *et al.*, 2015; Xu *et al.*, 2017; Gaubatz *et al.*, 2019), one included people with cancer of the pharynx (Shin *et al.*, 2017), one included individuals with cancer of the oropharynx (Megwalu, 2017), and one included people with cancer of the larynx (Chen and Halpern, 2007). All of the studies reported overall survival or disease-specific survival. All of the papers used neighbourhood-level measurements of socioeconomic status.

Of the six Canadian articles found, three studies included people in Ontario who were identified from the Ontario Cancer Registry (Mackillop *et al.*, 1997; Groome *et al.*, 2006; Booth *et al.*, 2010), one study included people in Toronto diagnosed at the Toronto Princess Margaret Cancer Centre (Chu *et al.*, 2016), one paper involved people from all of Canada diagnosed on the Canadian Cancer Registry (McDonald *et al.*, 2014), and the final paper included people in British Columbia diagnosed on the British Columbia Cancer Registry (Auluck *et al.*, 2016). Three of the articles included individuals with any type of head and neck cancer (Mackillop *et al.*, 1997; McDonald *et al.*, 2014; Chu *et al.*, 2016), two included people with laryngeal cancer (Groome *et al.*, 2006; Booth *et al.*, 2010), and the final study included people with cancer of the oral cavity or oropharynx (Auluck *et al.*, 2016). All of the studies presented either overall survival or disease-specific survival, and only three articles presented results beyond five-years of follow-up (Mackillop *et al.*, 1997; Groome *et al.*, 2006; Chu *et al.*, 2016). Four of the Canadian articles utilised a measurement of income to describe socioeconomic status (Mackillop *et al.*, 1997; Groome *et al.*, 2006; Booth *et al.*, 2010; McDonald *et al.*, 2014), while the other two studies used measurements of neighbourhood deprivation (Auluck *et al.*, 2016; Chu *et al.*, 2016).

One South American study included people in Brazil with all types of head and neck cancer diagnosed from eight different hospitals (Lopez *et al.*, 2011), while the second study included people from Argentina, Brazil, Columbia, and Uruguay. Both studies investigated all-cause mortality with at least three years of follow-up and education level was used as the measurement of socioeconomic status in both studies.

#### 1.4.6.2 Studies in the USA

**Konski *et al.* (2003)** investigated the effects of education on overall survival of 1,073 people who had been recruited to a randomised controlled trial between the years of 1991 and 1997. The trial aimed to evaluate radiotherapy fractionation schedules in participants with advanced stage SCC of the head and neck. In this article, the authors performed a nested cohort study from the trial data and analysed five-year overall survival from the time of randomisation. The paper evaluated the results of those who had attended college or technical school against those who had not attended school up to those who had graduated from high school or a general education diploma. There was a difference in overall survival up to five-years after randomisation – in a multivariate analysis adjusting for stage, site, and race, the people who attended college or technical school still had a substantially improved survival. However, this was a small study which only included people who had been included in a randomised controlled trial to investigate radiotherapy treatment, and therefore is not necessarily generalisable to the entire population of people with head and neck cancer.

A large population-based study of people whose data had been collected by the National Cancer Database between the years of 1995 and 1998 was conducted by **Chen and Halpern (2007)**. The study explored the predictive factors of survival for individuals who had been diagnosed with advanced SCC of the larynx between the years of 1995 and 1998. A total of 7,019 people were included in the study and the authors utilised area-level characteristics as a measurement of socioeconomic status, including the percentage of high school graduates and median household income. The authors investigated Cox proportional hazards ratios for five-year all-cause mortality. This study did not confirm a difference for individuals who resided in areas with overall lower education or income levels following the adjustment for treatment, sex, race, hospital type, or insurance status. However, only those with advanced SCC of the larynx were included, and therefore these results are not necessarily applicable to the entire population of people with head and neck cancer.

**Molina *et al.* (2008)** investigated the association of community poverty level with the survival of 20,915 people diagnosed with head and neck cancer in Florida between the years of 1998 and 2002. The authors investigated five-year overall survival using a variety of demographic, social, and clinical information, and recorded socioeconomic status using community poverty levels. This study reported that people from lower socioeconomic communities presented at a younger age, with tumours of higher stage, and with significantly lower median survival times compared to those who were from less deprived areas. The authors also discovered that area-based socioeconomic status was an independent predictor of survival in a stepwise multivariate Cox regression analysis which

included participant demographics (age, gender, race, ethnicity, tobacco use, and alcohol consumption), comorbidities, clinical characteristics (tumour grade, stage, and location of treatment), and treatment modality. This was one of the few studies from around the world that investigated the underlying causes of socioeconomic inequality in survival of people with head and neck cancer, however it only utilised an area-based measure and did not examine trends by the individual subsites of the head and neck.

A large cohort study undertaken by **Chu *et al.* (2011b)** investigated the influence of socioeconomic status on the cancer-specific survival of Asians and Pacific Islanders. The study included a total of 53,544 people with head and neck cancer who were identified on the Californian Cancer Registry between the years of 1988 and 2007. Chu and colleagues utilised neighbourhood-level socioeconomic status in quintiles using education, income, occupation, and cost of living. The authors presented median survival of the cohort over the study period and produced multivariate Cox regression models for all-cause and disease-specific mortality. For all of the people included in the analysis, those who were of lower socioeconomic status were more at risk of cancer-specific deaths, and those with cancer of the oropharynx had the greatest difference in survival between the lowest and highest socioeconomic groups. This association continued to be significant after the adjustment for additional baseline covariates including stage, age, and year of diagnosis. For Asian and Pacific Islanders, the same differences were observed for males, however the number of female Asian and Pacific Islanders was too low to determine whether there was an association with socioeconomic status and cancer-specific survival. Due to the limitations of cancer registry data, further possible determinants of socioeconomic inequality in survival could not be investigated. Additionally, individual-level measurements of socioeconomic status were not available for this study.

A smaller study conducted by **Reitzel *et al.* (2012)** investigated the effects of neighbourhood deprivation on the overall survival, disease-specific survival, and disease-free survival results of a cohort of 1,151 people with head and neck cancer. The individuals were treated at the University of Texas MD Anderson Cancer Centre between the years of 1996 and 2009. The participants were linked to neighbourhood deprivation which considered education, employment status, and poverty. This study did not demonstrate an influence of neighbourhood deprivation on people with head and neck cancer, however when the results were stratified by the site of the head and neck, those with cancer of the oropharynx had differing results. For those with oropharyngeal cancer, a high level of neighbourhood deprivation was associated with poor overall survival even following the adjustment of additional covariates such as age, sex, stage, smoking status, and annual household income. This suggested that those with cancer of the oropharynx were at an increased risk of worse outcomes if they resided in areas of low education

level, low-income level, high levels of unemployment, single-parent households, and no vehicle availability.

**Guo *et al.* (2015)** investigated the effects of neighbourhood-level poverty on overall survival and disease-specific survival of 25,157 people who were diagnosed with head and neck cancer. The data for the participants included in the study were extracted from the Florida Cancer Data System between the years of 1996 and 2010. Following adjustment for demographic and clinical information, socioeconomic inequality remained between those who resided in the poorer areas of Florida, who had a substantially higher risk of all-cause and disease-specific mortality. The authors also investigated the effect of individual smoking on socioeconomic inequality in survival and concluded that smoking accounted for a large part of the inequality observed. However, several potential explanatory factors for socioeconomic inequality were not available including alcohol consumption and comorbid conditions.

**Megwalu (2017)** analysed data on 18,791 people with cancer of the oropharynx who were recorded on the SEER database between the years of 2004 and 2012. Megwalu conducted a thorough investigation of the effects of several neighbourhood-level socioeconomic factors on five-year overall survival and disease-specific survival, which included high school completion rate, bachelor's degree completion rate, family poverty rate, median household income, unemployment rate, white collar occupation rate, and socioeconomic index (which were all categorised as "high" and "low"). The study reported that worse five-year overall survival and disease-specific survival was observed for people who were residing in areas with lower rates of high school completion, low bachelor's degree completion rates, higher percentage of families living below the poverty line, high unemployment rates, low percentage of individuals working in white-collar professions, and low socioeconomic indices. In addition, Megwalu performed multivariate analyses which confirmed that this observation remained for people from low socioeconomic neighbourhoods following the adjustment for age, sex, race, marital status, year of diagnosis, cancer site, stage, and treatment.

A study undertaken by **Xu *et al.* (2017)** also utilised the SEER database by extracting 37,995 people with non-metastatic head and neck cancer diagnosed between the years of 2007 and 2012. The authors presented five-year overall survival and disease-specific survival and investigated the effects of neighbourhood-level median household income, education level, unemployment rate, and residence status on survival. The median follow-up time was 24 months. This study outlined that only those who resided in areas of lower median income had a lower overall survival and disease-specific survival in multivariate analyses following the adjustment for age, sex, race, marital status, insurance status, cancer subsite, stage, and treatment. However, this study did not include information on

behavioural data such as smoking and alcohol consumption and therefore, these could not be assessed for their association with socioeconomic inequality in survival.

**Shin *et al.* (2017)** investigated the impact of socioeconomic status on the survival of people with head and neck cancer. Individuals were identified from the National Cancer Database if they were diagnosed between the years of 2004 and 2013. Five-year overall survival was evaluated with a median follow-up time of approximately 25 months. A total of 35,559 people with SCC of the pharynx were included, and socioeconomic status was determined using neighbourhood-level median household income and the proportion of participants who had attained a high school diploma. Shin and authors demonstrated a trend in survival across the median household income groups, suggesting that those who resided in areas of lower median household income had a substantially lower overall survival than those who live in areas of higher median household incomes. The same trend was also clear for those who resided in areas with a lower proportion high school diploma attainment. However, following the adjustment for insurance status, race, comorbidity, cancer site, and stage, the socioeconomic inequality no longer remained for either median household income or the proportion of people who attained a high school diploma.

A study involving data from the National Cancer Database was undertaken by **Gaubatz *et al.* (2019)** to investigate the impact of neighbourhood-level income on the mortality of people with head and neck cancer in the USA. Data were utilised from the National Cancer Database on all people who had a diagnosis of head and neck cancer between the years of 2004 and 2014. The study consisted of 260,035 people and investigated the effects of neighbourhood-level median household income on 90-day all-cause mortality. The authors reported that the participants who resided in areas with lower median household income had poorer 90-day survival following adjustment for comorbidity, stage, tumour site, HPV status, facility type, waiting times for treatment, and treatment type. However, the follow-up period of this study was short and therefore conclusions around the socioeconomic inequality in long-term survival cannot be drawn from this article.

#### 1.4.6.3 Studies from Canada

An early study involving people recorded on the Ontario Cancer Registry conducted by **Mackillop *et al.* (1997)** investigated the effects of income on the survival of people with one of eight different types of cancers, including nearly 16,000 people with head and neck cancer. The study included individuals who were diagnosed with cancer between the years of 1982 and 1991, and overall survival was reported for a period of seven years after diagnosis. Mackillop and colleagues linked information from the 1986 Canadian census to provide median household income as a measurement for socioeconomic status.

The study highlighted strong associations between income and overall survival for people with head and neck cancer, favouring those with higher levels of income. In addition, those who earned lower income also experienced higher rates of death from their head and neck cancer. Finally, the authors reported that the association between income and cancer survival was stronger for those with head and neck cancer than it was for any other cancer. However, these analyses were not adjusted for any confounding factors and therefore explanatory factors for socioeconomic inequality in survival were not investigated.

A later study by **Groome *et al.* (2006)** investigated the effects of income on survival of people with cancer of the larynx. The study included 661 people with cancer of the glottis and 495 people with cancer of the supraglottis. Individuals were diagnosed on the Ontario Cancer Registry between the years of 1982 and 1995 and were followed-up for an average of 62 months. The authors reported cause-specific survival and discovered that those with cancer of the glottis who resided in areas of lower income had substantially worse survival than those who were from areas of higher income. However, this difference was not apparent for those with cancer of the supraglottic. This was a small study with limitations around access to information such as smoking and alcohol consumption due to the use of data from a national cancer registry. Therefore, the explanations for socioeconomic inequality in survival of people with cancer of the larynx could not be explored.

A more recent study undertaken by **Booth *et al.* (2010)** investigated the impact of socioeconomic status on survival of people who were diagnosed with cancer on the Ontario Cancer Registry and at Regional Cancer Centres between the years of 2003 and 2007, including a sub-cohort of 854 individuals with laryngeal cancer. The study investigated the effect of median household income on five-year overall survival and three-year disease-specific survival. The authors recorded a small difference across the median income groups for overall survival and disease-specific survival for those who were recorded in the Ontario Cancer Registry. Results did not demonstrate substantial differences in overall survival and disease-specific survival across the median household income groups. However, there were several limitations to this study including the use of cancer registry data which does not include information on behavioural data. In addition, the sample size of people with cancer of the larynx included in this analysis was small and therefore these results may not be reliable.

**McDonald *et al.* (2014)** examined the relationship between average household income and survival of 30,228 people with cancer of the head and neck. Individuals were identified from the Canadian Cancer Registry between the years of 1992 and 2005 and were followed up to 2007 to provide two-year survival. McDonald and colleagues reported

that lower income was strongly associated with worse survival outcomes for those with head and neck cancer. In addition, time trends were also examined and the gap in survival increased over time for individuals with oropharyngeal cancer, but this trend was not observed for those with cancer of the oral cavity. However, the study did not contain additional information such as tumour stage or behavioural information, and therefore could not investigate explanatory factors of the observed socioeconomic inequality.

**Auluck *et al.* (2016)** investigated the effects of neighbourhood deprivation on survival of people with SCC of the oral cavity and oropharynx. The participants were identified on the British Columbia Cancer Registry between the years of 1981 and 2009 and provided five-year cancer-specific survival rates. The study included 2,059 people with cancer of the oropharynx and 4,319 people with cancer of the oral cavity. Auluck and colleagues reported significantly better disease-specific survival for men with cancer of the oropharynx who resided in affluent areas, however there was no difference for men with cancer of the oral cavity. Interestingly, women with cancer of the oropharynx and oral cavity did not exhibit the same difference as men with cancer of the oropharynx. The authors also presented trends in the deprivation gap and reported that there was an increase in the deprivation gap for men between 1981-1995 and 1996-2009. However, the reverse was observed for women. Finally, this study also investigated whether socioeconomic status was an independent predictor of survival and discovered that the association of socioeconomic status on survival remained following the adjustment for age, sex, stage, and time period.

**Chu *et al.* (2016)** explored the prognostic importance of neighbourhood-level socioeconomic status on overall survival of 2,124 people with newly diagnosed head and neck cancer. The participants were diagnosed at the Toronto's Princess Margaret Cancer Centre between the years of 2003 and 2010 and were followed-up for up to 8 years. Chu and colleagues reported that although low socioeconomic status was associated with poorer survival in a univariate model, it was no longer associated with poorer survival following the adjustment for other variables including age, gender, stage, comorbidity, smoking status, alcohol use, and HPV type 16 status. The authors outlined that those of lower socioeconomic status had comorbidities, tumours of higher stage, were smokers and alcohol users, and were often associated with HPV type 16 negative tumours.

#### 1.4.6.4 Studies form South America

A small cohort study of people in Brazil was carried out by **Lopez *et al.* (2011)** which included 445 individuals with cancers of the oral cavity, oropharynx, larynx, and hypopharynx. Individuals were diagnosed between the years of 1998 and 2002 and followed up until 2005. Socioeconomic status was defined using the number of years the

participants had spent in education and a multivariate Cox proportional hazards regression model for disease-specific mortality was generated. The model was adjusted by age and sex, and the authors concluded that there were differing results for each subsite of the head and neck. For people with cancer of the oral cavity, oropharynx, and hypopharynx the risk of death from head and neck cancer increased as the number of years the participant spent in education increased. However, the results were contrasting for those with cancer of the larynx since these people had a lower risk of disease-specific mortality as the number of years in education increased. However, the hazard ratios were all non-significant and the sample sizes for each subgroup of the head and neck were very small, so these findings are unlikely to be reliable.

**Abrahão *et al.* (2020)** investigated the predictors of survival in a cohort of 1,463 people diagnosed with SCC of the head and neck from Argentina, Brazil, Columbia, and Uruguay between the years of 2011 and 2017. Participants for the study were collected from the InterCHANGE study, a multicentre case-control study to investigate the risk factors and outcomes of people with SCC of the head and neck. Patients were followed up to 2018 and the authors reported three-year overall survival and included the education level of the patients as an explanatory factor. In a univariate Cox proportional hazards model, those who were “illiterate” were 44% more at risk of all-cause mortality compared to those with “superior” education levels (HR = 1.44, 95% CI = 0.63 to 3.32). However, in a multivariate model including age, sex, rate, cancer stage, smoking history, alcohol consumption, and anatomical site, education level was no longer a predictor of survival.

### 1.4.7 Effect of socioeconomic status on survival of people with head and neck cancer in other parts of the world

#### 1.4.7.1 Overview of studies from other parts of the world

A total of six articles were found involving people with head and neck cancer in other parts of the world. This included five studies in Taiwan (Wong *et al.*, 2006; Lee *et al.*, 2012; Chang *et al.*, 2013; Chien *et al.*, 2018; Lai *et al.*, 2018) and one study in Australia (Yu *et al.*, 2008). Of the studies carried out in Taiwan, three of them utilised data from the National Health Insurance Research Database (NHIRD) (Lee *et al.*, 2012; Chang *et al.*, 2013; Lai *et al.*, 2018), one used Taiwan Cancer Registry data (Chien *et al.*, 2018), and the final study used hospital-based records (Wong *et al.*, 2006). Two papers included all types of head and neck cancers (Chien *et al.*, 2018; Lai *et al.*, 2018), two studies included people with oral cavity cancer (Wong *et al.*, 2006; Lee *et al.*, 2012), and the final study included individuals with cancer of the nasopharynx (Chang *et al.*, 2013). Two articles examined overall survival (Wong *et al.*, 2006; Lai *et al.*, 2018), two studies investigated

cumulative survival (Lee *et al.*, 2012; Chang *et al.*, 2013), and one paper reported net survival estimates (Chien *et al.*, 2018). Two-year follow-up was assessed in one of the studies (Lee *et al.*, 2012), five-year follow-up was included in three of the studies (Wong *et al.*, 2006; Chang *et al.*, 2013; Chien *et al.*, 2018), and one paper included up to 12.5 years of follow-up (Lai *et al.*, 2018). Two studies investigated income as a measurement of socioeconomic status (Chien *et al.*, 2018; Lai *et al.*, 2018), one article assessed neighbourhood-level socioeconomic status (Chang *et al.*, 2013), one study included both a neighbourhood-level of socioeconomic status and occupation (Lee *et al.*, 2012), and the final study investigated both occupation and education as measurements for socioeconomic status (Wong *et al.*, 2006). The Australian article used data from the New South Wales Central Cancer Registry and included people with cancer of the oral cavity, pharynx, and larynx. Additionally, the authors reported five-year relative survival proportions and defined socioeconomic status using an area-based measurement (Yu *et al.*, 2008).

#### 1.4.7.2 Studies in Taiwan

The earliest article in Taiwan written by **Wong *et al.* (2006)** investigated the impact of education on five-year survival of people with cancer of the oral cavity. This was a hospital-based study including 1,010 people treated at the Taichung Veterans General Hospital from 1995 to 2002 and followed-up to 2004. Interestingly, there was no observed difference in survival between those who had varying levels of education. However, this study was small and more than 78% of the cohort were junior high school graduates or below which suggests bias in the proportion of people who were selected across the education groups.

A later study carried out by **Lee *et al.* (2012)** investigated the effects of individual and neighbourhood socioeconomic status on survival. This study used data from Taiwan's NHIRD of people who were diagnosed between the years of 2005 and 2008 and included a total of 3,607 individuals with cancer of the oral cavity. The authors reported two-year cumulative survival and compared results by occupation and neighbourhood household income from the 2001 Taiwan Census. The authors recorded differences between the socioeconomically advantaged and disadvantaged groups, with survival favouring the advantaged groups. In addition, people of lower socioeconomic position remained at a higher risk of all-cause mortality following adjustment for age, gender, comorbidity, urbanisation, area of residence, treatment modality, hospital characteristics, and year of diagnosis. This was one of the few studies that explored the explanations for socioeconomic inequality in survival. However, the database did not include information on tumour stage or behavioural data such as smoking and alcohol consumption and

therefore, these risk-factors could not be explored for their association with socioeconomic inequality in survival.

A further study was conducted by **Chang *et al.* (2013)** which investigated both individual and neighbourhood-level measurements of socioeconomic status and their effect with five-year cumulative survival. This study included 4,691 people who were diagnosed with nasopharyngeal cancer between the years of 2002 and 2006 on Taiwan's NHIRD. The four-factor Hollingshead scale (Hollingshead AdB, 1975) was used which uses enrolee category as a proxy for individual-level socioeconomic status. From this, the participants of the study were grouped according to their occupational status. In addition, the authors also used neighbourhood household income averages from Taiwan's 2001 Census as an area-based measurement for socioeconomic status. The authors reported that socioeconomic status remained a significant predictor of survival when adjusting by factors including age, gender, comorbidity, urbanisation, area of residence, treatment, and hospital characteristics. In addition, the authors suggested that those with worse socioeconomic status were treated in hospitals with lower healthcare resources, such as lower number of physicians per patient. However, similar to the previous study, the same limitations apply including the lack of staging and behavioural data to investigate their association with survival.

**Chien *et al.* (2018)** investigated the impact of household income on five-year net survival which included data from the Taiwan NHIRD. A total of 5,307 people with cancer of the larynx and 65,624 people with cancer of oral cavity, oropharynx, and larynx diagnosed between the years of 1992 and 2011 were included in the study. The authors investigated five-year net survival proportions and reported that socioeconomic inequality existed for people with cancer of the larynx, oral cavity, and oropharynx. However, the underlying causes of socioeconomic inequalities were not explored in this study due to the limitations of these data around the collection of information such as stage and behavioural factors.

A large population-based registry study conducted by **Lai *et al.* (2018)** explored the outcomes of 40,985 people with head and neck cancer. The individuals were recorded on the Taiwan NHIRD between the years of 2000 and 2013 and had only been treated with radiotherapy. The authors used income as a measurement of socioeconomic status and reported overall survival with an endpoint of December 2013. The authors reported that low income or living in residential areas of lower socioeconomic status had a detrimental effect on survival, regardless of the location in Taiwan that the person had lived. However, the underlying causes of socioeconomic inequality were not investigated as part of this study due to the limitations around data availability on cancer registry studies.

#### 1.4.7.3 Studies in Australia

**Yu *et al.* (2008)** investigated the impact of socioeconomic status on cancer survival for people diagnosed in Australia. People diagnosed on the New South Wales Central Cancer Registry between 1992 and 2000 were included in the study, along with a sub cohort of 6,331 people with head and neck cancer. The authors confirmed socioeconomic inequality in five-year relative survival for both men and women from an area-based measurement of socioeconomic status, in favour of those who lived in the least deprived regions. However, investigations into the potential determinants of socioeconomic inequality were not carried out as part of this study.

### 1.4.8 Summary and gaps in the literature

Collectively, the international and UK literature demonstrates consistent and clear findings of socioeconomic inequalities in the relationship between lower socioeconomic status and circumstances with poorer survival of people with head and neck cancer. Given the heterogeneity of the studies, their findings could not be formally pooled or combined to estimate the extent of socioeconomic inequalities, nor how it varied by global region, over time, or even by head and neck cancer subsite. It was not also possible to be assertive on or weigh the effects of differing possible explanatory factors. However, in the small number of studies which had modelled explanatory factors, the effect of socioeconomic status was fully explained or attenuated, with limited evidence available on an independent socioeconomic status effect on survival of people with head and neck cancer following consideration for potential underlying factors.

Few studies investigated the underlying causes of inequality in survival of people with head and neck cancers. Of the studies that did investigate the explanatory factors of socioeconomic inequality, few included all of the potential confounders, and only two studies included tumour HPV status as a factor of interest. Additionally, few of the studies included in the literature review investigated the long-term impact of inequality on survival of people with head and neck cancer beyond five-years. Further investigations into the underlying causes of socioeconomic inequality need to be conducted with the aim to explain inequality in survival observed for people with head and neck cancer in the short-term, middle-term, and long-term follow-up.

In addition, of the studies that explored the underlying factors of inequality, there were no groupings of the factors that may explain socioeconomic inequalities in head and neck cancer survival. These have not been viewed through patient, tumour, or treatment factor groupings, and in particular, assessing the underlying determinants have not been grouped as per factors that might be more modifiable (for example, through behaviours

such as smoking and alcohol) compared with factors that might be more difficult to modify or control (for example, tumour site, stage, and treatment regimens).

None of the studies included in this literature review from the UK explored socioeconomic inequality in survival of people with head and neck cancer using individual measurements of socioeconomic status such as household income or education level. Outside of the UK, all of the studies in Europe and only eight studies outside of Europe investigated socioeconomic inequality using either education level, household income, or type of occupation. This limitation to the UK-based literature provides a gap in the evidence of socioeconomic inequality in survival of people with head and neck cancer. No study formally analysed the extent of absolute and relative inequalities in survival using recommended metrics including relative index of inequality (RII) and slope index of inequality (SII) as per IARC 2019 suggestions. Moreover, the trends in survival inequality over calendar time had also not been reported in the literature.

Despite the burden of both incidence and mortality of head and neck cancers being greatest in lower income countries, particularly in South East Asia (Ferlay *et al.*, 2020), there is a lack of research on head and neck cancer survival or outcomes from this part of the world. This itself is an inequality, since inequalities between countries exist and are well recognised (International Agency for Research on Cancer, 2019), however, this is beyond the scope of this thesis.

## 1.5 Aims and objectives of this thesis

This thesis aims to inform patients, clinicians, policy makers, and the public in the UK that are involved with head and neck cancer on the magnitude of socioeconomic inequality observed in survival of people with head and neck cancer and what factors might explain these inequalities. This thesis has the potential to shine a light on the issue of socioeconomic inequality in survival of people with head and neck cancer. A series of epidemiological studies of multiple existing UK cohort studies will explore this topic from different angles. The findings could inform policy and practice in the further development and delivery of head and neck cancer services.

The extent and nature of socioeconomic inequality in survival of people with head and neck cancer across the UK (and Scotland) is poorly understood and explanations for this inequality are yet to be thoroughly investigated by exploring potential underlying patient, tumour, and treatment explanatory factors. The overall aims of this thesis are to:

1. Describe trends in socioeconomic determinants and socioeconomic inequalities in head and neck cancer survival over calendar time and follow-up time.

2. Understand socioeconomic inequality in survival of people with head and neck cancer.
3. Explain the underlying determinants and explanations of socioeconomic inequality in survival of people with head and neck cancer.

The individual aims and objectives of each chapter follow.

### 1.5.1 Chapter 2 aims and objectives

The aim of Chapter 2 is to describe the trends over time and follow-up time of the inequality in survival of people with head and neck cancer in Scotland by utilising the Scottish Cancer Registry. The objectives of this chapter are to:

1. Determine the trends in inequality over calendar time from 1986 to 2015.
2. Compare the patterns in inequality over follow-up time in one-year, five-year, and 10-year survival.
3. Examine these trends and patterns for all of the patients (and by sex), and across the three main subsites of head and neck cancer (oral cavity, oropharynx, and larynx).

### 1.5.2 Chapter 3 aims and objectives

The primary aim of Chapter 3 is to determine the factors that are independently associated with survival at three time points – one year, five years, and 12 years after a diagnosis of head and neck cancer by utilising the SAHNC cohort study of people with head and neck cancer who were diagnosed in Scotland between the years of 1999 and 2001 (Scottish Audit of Head and Neck Cancers Steering Group, 2004). The secondary aim of this chapter is to compare several methods of measuring survival via the use of overall survival, disease-specific survival, and net survival estimates to provide an in-depth and comprehensive picture of the factors that are associated with survival of people with head and neck cancer in Scotland. The objectives of this chapter are to:

1. Explore the patient, tumour and treatment factors that are associated with one-year, five-year, and 12-year overall survival and disease-specific survival.
2. Compare the outcomes of three different survival metrics: overall survival, disease-specific survival, and net survival estimates.

### 1.5.3 Chapter 4 aims and objectives

Following on from the research of Chapter 3, and also using the SAHNC cohort, the aims of Chapter 4 are to explore the drivers of inequality in survival of people with head and neck cancer using an area-based measurement of socioeconomic status (Scottish Audit of Head and Neck Cancers Steering Group, 2004). This chapter explores socioeconomic inequality in Scotland one year, five years, and 12 years after a diagnosis of head and neck cancer. The objectives of this chapter are to:

1. Explore the underlying patient, tumour and treatment factors that are associated with socioeconomic inequality in survival of people with head and neck cancer.
2. Examine the differences in socioeconomic inequality in survival of people with head and neck cancer via overall survival, disease-specific survival, and net survival estimates.

### 1.5.4 Chapter 5 aims and objectives

The aim of Chapter 5 is to explore the underlying determinants of both area-based and individual measurements of socioeconomic status of people diagnosed with head and neck cancer by utilising the HN5000 cohort study (Ness *et al.*, 2014; Ness *et al.*, 2015). The objectives of this chapter are to:

1. Explore the underlying demographic, health, behavioural, tumour, and treatment factors that are associated with socioeconomic inequality in survival of people with head and neck cancer.
2. Compare socioeconomic inequality in both area-based and induvial measurements of socioeconomic status.

### 1.5.5 Chapter 6 aims and objectives

Chapter 6 begins with a summary of the collective thesis findings from the four studies that were conducted throughout this thesis in relation to the prior knowledge and gaps that were identified in the literature review. This chapter goes on to discuss the thesis strengths and limitations, and finally makes recommendations for policy, practice, and further research on socioeconomic inequalities in head and neck cancer outcomes and survival. Finally, the thesis will end with a conclusion section.

# 2 Trends over time in inequality in survival of people with head and neck cancer in Scotland: population-based cancer registry study

## 2.1 Introduction

This chapter investigates the trends over time in inequality in survival of people with head and neck cancer in Scotland. This study utilises data from the Scottish Cancer Registry of all of the head and neck cancer registrations between the years of 1986 and 2015.

Cancer registration is the collection, maintenance, and management of data on new diagnoses of cancer that occur in a population (International Agency for Research on Cancer, 1991). The Scottish Cancer Registry is a member of the United Kingdom and Ireland Association of Cancer Registries (UKIACR), and has been collecting information on cancer incidence, mortality, and survival since 1958. The Scottish Cancer Registry database follows the international standards for cancer registration in order to maintain its' quality and completeness of data (International Agency for Research on Cancer, 1991). The aim of the database is to improve cancer services by monitoring incidence, evaluating outcomes, and investigating the effectiveness of cancer prevention and screening programmes. The Scottish Cancer Registry is collected by the Information Service Division (ISD) of the NHS Scotland (now Public Health Scotland), with the aim to "*collect, validate, analyse and store accurate, timely and comprehensive data on cancer*" (ISD Scotland, 2010b). The database holds information such as personal and demographic data, and details on the tumour diagnosis, including the anatomical site of the tumour and its' histology. In addition, the Scottish Cancer Registry holds geographical data including Carstairs and Morris Indices, SIMD, and data on the Scottish Cancer Network in which a person's malignancy was diagnosed and treated. The database provides the opportunity to investigate the trends in socioeconomic inequality in survival of people with head and neck cancer, and to examine long-term survival after one year, five years, and 10 years of a diagnosis of head and neck cancer in Scotland.

### 2.1.1 Aims and objectives

The aim of Chapter 2 is to describe the trends over time and follow-up time of the inequality in survival of people with head and neck cancer in Scotland by utilising the Scottish Cancer Registry. The objectives of this chapter are to:

1. Determine the trends in inequality over calendar time from 1986 to 2015.
2. Compare the patterns in inequality over follow-up time in one-year, five-year, and 10-year survival.
3. Examine these trends and patterns for all of the patients (and by sex), and across the three main subsites of head and neck cancer (oral cavity, oropharynx, and larynx).

## 2.2 Methods

### 2.2.1 Data extraction

Data were requested and extracted from the Scottish Cancer Registry on all of the registrations who had had at least one head and neck malignancy diagnosed between 1st January 1986 and 31st December 2015.

#### 2.2.1.1 Measurement of Socioeconomic Status

Socioeconomic status was obtained from the area-based Carstairs and Morris 1991 Indices (Carstairs and Morris, 1989; McLoone, 2000). The index ranks the geographical areas of Scotland (from the person's home postcode) into one of five groups using 1991 Census data – group one represents the people who resided in the least deprived areas of Scotland and group five represents the people who resided in the most deprived areas of Scotland. The index categorises groups areas at the postcode level based on:
(a) low social class, (b) lack of car ownership, (c) overcrowding, and (d) male unemployment.

To standardise the results over time and compare trends over time, the Carstairs and Morris 1991 index was used in the primary analysis linked across all years of data from the cancer registry (as opposed to using the index with the most recent census data updates for different time periods and decades).

However, two sensitivity analyses were conducted to compare various measurements of socioeconomic status. The first sensitivity analysis utilised the nearest Carstairs and

Morris Index that coincided with the date of the registrant's diagnosis of head and neck cancer. Carstairs and Morris 1991 Categories were used for the people who were diagnosed between 1986 and 1995, Carstairs and Morris 2001 Categories (McLoone, 2004) were used for the people who were diagnosed between 1996 and 2005, and Carstairs and Morris 2011 Categories (Brown *et al.*, 2014) were used for the people who were diagnosed between 2006 and 2015. The second sensitivity analysis utilised the earliest defined SIMD category from 2004 census data (Public Health Scotland, 2020b). Due to the recency of SIMD in comparison to Carstairs and Morris 1991 Index, this sensitivity analysis only included individuals who were diagnosed from 2001 onwards (as it was not possible to link SIMD with more historic data). The SIMD 2004 is calculated using data from multiple sources in seven domains of deprivation: (a) income employment, (b) education, (c) housing, (d) health, (e) crime, and (f) geographical access (Scottish Executive, 2004). Like the Carstairs and Morris Index, SIMD is measured at the postcode level, however SIMD 2004 uses smaller geographical areas ("data zones") than those used in the Carstairs and Morris Indices.

#### 2.2.1.2 Baseline characteristics

**Demographic data**

Data on sex and the age at which a person was diagnosed with cancer, along with information on their primary tumour (see section 2.2.5) that was recorded on the Scottish Cancer Registry were included.

**Tumour information**

Information was recorded on the anatomical site of the tumour which was determined using ICD-10 codes (World Health Organization, 2016). Data were requested on all of the registrations that had diagnoses of cancer(s) of the (a) lip (C00), (b) oral cavity (C02-C04, C05.0, C06), (c) oropharynx (C01, C05.1, C05. 2, C09, C10), (d) hypopharynx (C12, C13), (e) larynx (C32, C10.1), (f) major salivary glands (C07, C08), and (g) other sites of the head and neck (C14.0, C30.1, C41.1, C69.5). The pathology of the tumour was also recorded in the Scottish Cancer Registry, and for the purposes of this analysis was grouped as: (a) SCC, and (b) non-SCC.

**Treatment information**

The treatment modality that the people received for their cancer was only recorded on the Scottish Cancer Registry for those who were diagnosed from 1996 onwards. This was grouped as: (a) surgery only, (b) radiotherapy only, (c) surgery and radiotherapy,

(d) chemoradiotherapy only, (e) surgery and chemoradiotherapy, (f) chemotherapy with or without surgery, and (g) no treatment.

### 2.2.2 Data verification

The computer system that stores the Scottish Cancer Registry performs over 500 validity and feasibility checks to validate each record (ISD Scotland, 2010a). In addition, the quality of the data is verified by using "*routine indicators, computer validation and ad hoc studies of data accuracy and case ascertainment*" (ISD Scotland, 2010a). A study carried out by Brewster *et al.* (2002) generated a random sample of 3,500 registrations diagnosed between April and September 1997. Brewster confirmed that the quality of these data was high, with medical records available for 90.7% of registrations.

### 2.2.3 Data linkage

Scottish Cancer Registry data were linked to mortality records from the National Records of Scotland (NRS) which included death certification up to 31st December 2017. The records were linked using an established probability matching technique that was based on the Howard Newcombe principle (Newcombe *et al.*, 1959). This method matches records to the mortality data using a unique Community Health Index (CHI) number that is assigned to every person who is registered with the NHS in Scotland.

### 2.2.4 Information governance approvals

The information governance and data linkage approvals for this study were obtained from the NHS Privacy Advisory Committee (now known as the Public Benefits and Privacy Panel (PBPP)) (Appendix 2.1). Amendments to the data linkage were requested in 2017, and this request was subsequently approved (Appendix 2.2).

### 2.2.5 Eligible cases

Scottish Cancer Registry data were provided on all of the individuals with at least one head and neck cancer, along with any other malignancy within or outside of the head and neck. All of the data provided contained people with diagnoses between 1st January 1986 and 31st December 2015. Due to this, the following algorithm was developed and performed in order to identify a single record containing a person's primary tumour:

1. If a person had records containing a non-malignant tumour or duplicate skin cancer records, the records were removed.

2. If a person had duplicate records with the same ICD code and the same date of incidence, the duplicate records were removed, and a single entry was kept.
3. If a person had both a head and neck tumour and a non-head and neck tumour diagnosed on the same date, the record containing the non-head and neck tumour was removed.
4. If a person had multiple head and neck tumours diagnosed on the same date, the record containing the main subsite of the head and neck was kept (i.e., oral cavity over larynx, larynx over oropharynx, oropharynx over hypopharynx etc.).
5. Following the above, the primary tumour of a person was identified from the earliest diagnosed tumour, and all of the future entries were removed.

Following the removal of non-primary tumours, registrations were subsequently deleted if:

1. Their primary tumour was found to not be a head and neck malignancy.
2. They were younger than 18 years of age.
3. They were missing Carstairs 1991 Category.

### 2.2.6 Statistical analyses

Frequency tables for each of the demographic data, tumour, and treatment information and socioeconomic status were produced along with the proportion of deaths that had occurred by 31st December 2017 for the whole cohort. In addition, frequency tables that displayed the cross-tabulation of socioeconomic status with the demographic data, and tumour, and treatment information were generated for the whole cohort and the proportions across each of the groups were compared using the Pearson's chi-square test.

One-year, five-year, and 10-year net survival with 95% CIs were calculated using the Pohar-Perme method (Pohar Perme *et al.*, 2012; Pohar Perme *et al.*, 2016) by using lifetables that were standardised by calendar year, age, sex, and Carstairs 1991 Category. These lifetables were provided by the Cancer Survival Group at the LSHTM (Cancer Survival Group, 2019), and covered the period of 1991 to 2010. Therefore, the lifetables were extended back to 1986 using the data from 1991, and up to 2015 using the data from 2010. All of the net survival results were computed using the *stns* command in Stata, Version 16 (StataCorp., 2019). All of the survival estimates were generated for the whole cohort, for males and females, and for the three main anatomical sites of the head and neck (oral cavity, oropharynx, and larynx) separately.

Overall survival and disease-specific survival were calculated using the Kaplan-Meier method with 95% confidence intervals (CIs). Disease-specific survival estimates were

generated by specifying the event indicator as those who had “died from head and neck cancer” which was extracted from the primary cause of death information on the person’s death certificate. Cause of death information for disease-specific survival was extracted from the data recorded on the person’s death certificate which was obtained from their NRS mortality data linkage. One-year, five-year, and 10-year overall survival and disease-specific survival estimates were investigated for their relationship with inequality over time for all of the time periods. These results were produced in SAS Software, version 9.4.

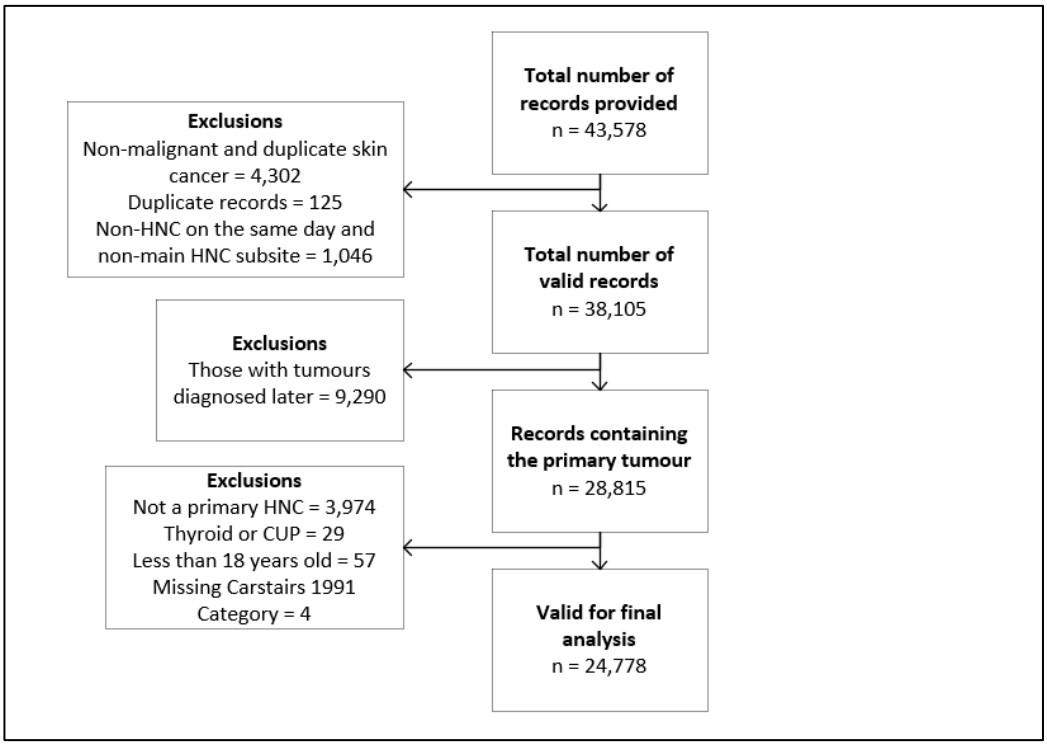
The SII and RII were calculated with 95% CIs for each of the survival estimates and Cox proportional hazards models. The SII is based on the linear regression of the mid-point of survival or mortality for each Carstairs 1991 Category (Regidor, 2004), while the RII can be estimated by dividing the SII by the population rate (Pamuk, 1985). These results were produced using SAS Software, version 9.4.

## 2.3 Results

### 2.3.1 Eligible cases

A total of 43,579 registrations were included in the original database provided by the electronic Data Research and Innovation Service (eDRIS) at ISD, Scotland for diagnoses between the 1st January 1986 and 31st December 2015 (Figure 2.1). Following the defined algorithm in Section 2.2.5, 4,302 (9.4%) of the records were removed due to having tumours that were not malignant or duplicate skin cancer records. A total of 125 (0.3%) of the records were duplicate records and were removed, and 1,046 (0.9%) of the records were removed since these people had tumours both inside and outside of the head and neck, or multiple tumours within the head and neck diagnosed on the same day – the record containing the main site of the head and neck cancer was kept. A total of 9,290 (24.2%) records were removed since these records were for people who had a tumour that was diagnosed at an earlier date. From the remaining registrations, those who did not have a head and neck cancer as their primary tumour (n = 3,974/8.6%) were removed. Records for people who had cancer of the thyroid or cancer of unknown primary (n = 29/0.1%) were removed. Those who were younger than 18 years old (n = 57/0.1%), and people who were missing a Carstairs 1991 Category (n = 4) were also removed. The final database had a total of 24,778 individuals recorded with a primary head and neck cancer during the study period on the Scottish Cancer Registry. These results were compared with other publications of incident head and neck cancers and were found to be similar (Shack *et al.*, 2007; Purkayastha *et al.*, 2016).

**Figure 2.1 – Flow chart of eligible cases included in the Scottish Cancer Registry study**




## 2.3.2 Baseline characteristics

### 2.3.2.1 Whole cohort

The numbers and proportions of the baseline characteristics are displayed in Table 2.1 on Page 63 for all of the people included in this study, along with the proportion of deaths that had occurred by 31st December 2017. The median age of the whole cohort was 63 years with an interquartile range of 55 to 72 years. There was a ratio of 2.4:1 of males to females, and people were more likely to have either a tumour of the oral cavity (n = 8,189; 33.0%) or a tumour of the larynx (n = 7,706; 31.1%). A total of 21,403 (86.4%) individuals had tumours that were SCC. For those who had their treatment recorded from 1996, surgery only (n = 4,384; 26.5%) was the most common treatment modality used, while 1,828 (11.1%) people received no treatment for their cancer. Over time, there was a rise in the number of individuals who had a primary diagnosis of head and neck cancer, which increased from 3,257 (13.1%) in 1986-1990 to 4,865 (19.6%) in 2011-2015. The highest proportion of the cohort were diagnosed in the West of Scotland Cancer Network (n = 12,850; 51.9%). There was a trend in the proportion of people across the Carstairs 1991 Categories with 3,623 (14.6%) individuals from the least deprived areas, and 6,594 (26.6%) individuals from the most deprived areas.

#### 2.3.2.2 Comparison between males and females

The numbers and proportions of the baseline characteristics for males and females are displayed in Appendix 2.3 and Appendix 2.4, respectively, along with the proportion of deaths for males and females that had occurred by 31st December 2017. The median age of the male population was 63 years (IQR = 55 to 71), while females were slightly older with a median age of 66 years (IQR = 56 to 75). Males were more likely to have tumours of the larynx (n = 6,133/35.0%), while females were more likely to have tumours of the oral cavity (n = 3,027/41.6%). A total of 15,448 (88.2%) males had tumours that were SCC, while females had a slightly lower proportion of SCC tumours (n = 5,955/81.9%). Of the people who had their treatment recorded from 1996, males were less likely than females to have been treated by surgery only (males = 2,823/24.1%, and females = 1,561/32.3%). From 1986, there was a rise in the number of both males and females who had a primary head and neck cancer from 2,280 (13.0%) in 1986-1990 to 3,445 (19.0%) in 2011-2015 for males, and from 977 (13.2%) in 1886-1990 to 1,420 (19.5%) in 2011-2015 for females. The highest proportion of both males and females were from the West of Scotland Cancer Network (males = 9,095/51.9%, females = 3,755/51.7%). There was a trend in the proportion of males across the Carstairs 1991 Categories with 2,506 (14.3%) males from the least deprived region, and 4,770 (27.2%) males from the most deprived region. There was also a trend in the proportions of females across the Carstairs 1991 Categories, however compared to males, there was a slightly lower proportion of females in the most deprived region (n = 1,824/25.1%).

#### 2.3.2.3 Comparison between those with cancer of the oral cavity, oropharynx, and larynx

The numbers and proportions of the baseline characteristics for people with cancer of the oral cavity, oropharynx, and larynx are displayed in Appendix 2.5 to Appendix 2.7, respectively, along with the proportion of deaths that had occurred by 31st December 2017. The median age of those with cancer of the oral cavity, oropharynx, and larynx was 63 years (IQR = 55 to 72), 59 years (IQR = 52 to 67), and 65 years (IQR = 57 to 72), respectively. People with cancer of the larynx were substantially more likely to be male with a ratio of 3.9:1 of males to females, which was much higher compared with people who were diagnosed with cancers of the oral cavity or oropharynx at 1.7:1 and 2.6:1 of males to females, respectively. Of those who had their treatment recorded from 1996 onwards, people with cancer of the oral cavity were more likely to have been treated with surgery only (n = 2,327/41.1%), while people with cancer of the larynx were more likely to have been treated with radiotherapy only (n = 1,914/40.0%). Those who had cancer of the oropharynx were more likely to have been treated with chemoradiotherapy (n =

694/26.1%). Over time, there was a rise in the number of individuals who had a head and neck cancer, which for those with oral cavity and larynx cancer was from 954 (11.6%) and 1,131 (14.7%) in 1986-1990, to 1,682 (20.5%) and 1,215 (15.8%) in 2011-2015, respectively. The most prominent difference over time was for individuals with cancer of the oropharynx which increased from 272 (8.0%) in 1896-1990 to 1,015 (30.0%) in 2011-2015. People with cancer of the larynx were slightly more likely to have resided in the West of Scotland (n = 4,2274/54.9%) compared to people with cancer of the oral cavity (n = 4,208/51.4%), and oropharynx (n = 1,686/49.9%). People with cancer of the oral cavity or oropharynx had similar trends across the Carstairs 1991 Categories which increased from 1,278 (15.6%) and 511 (15.1%) in the least deprived category to 2,102 (25.7%) and 873 (25.8%) in the most deprived category, respectively. The most prominent difference across the Carstairs 1991 Categories was for individuals with cancer of the larynx which increased from 938 (12.2%) individuals residing in the least deprived category to 2,311 (30.0%) individuals residing the most deprived category.

### 2.3.3 Death rates by December 2017

#### 2.3.3.1 Whole cohort

A total of 18,322 (73.9%) deaths had occurred by 31st December 2017 when the Scottish Cancer Registry was linked to the mortality data from the NRS (Table 2.1, Page 63). People were more likely to die if they were older, had tumours of the hypopharynx, or were treated with chemotherapy with or without surgery. They were also more likely to die if they resided in the West of Scotland Cancer Network or were from the most deprived regions (79.4% versus 66.5%). There was a slightly higher proportion of deaths of males (n = 13,040; 74.5%) than females (n = 5,282; 72.5%), and a slightly higher proportion of death for those with cancer of SCC (n = 16,043; 75.0%) compared to those with non-SCC tumours (n = 2,279; 67.5%).

#### 2.3.3.2 Comparison between males and females

For males and females, a total of 13,040 (74.5%) and 5,282 (72.7%) deaths, respectively, had occurred by 31st December 2017 when the Scottish Cancer Registry was linked to the mortality data from the NRS (Appendix 2.3 and Appendix 2.4). Males had a higher proportion of deaths compared to females if they were younger, had tumours of the salivary gland, or tumours that were non-SCC. There were no differences between the proportion of deaths for males and females by age, year of diagnosis, Scottish Cancer Network, or Carstairs 1991 Category.

#### 2.3.3.3 Comparison between those with cancer of the oral cavity, oropharynx, and larynx

For people who were diagnosed with tumours of the oral cavity, oropharynx, and larynx a total of 6,028 (73.6%), 2,204 (65.2%), and 5,854 (76.0%) deaths had occurred by 31st December 2017 when the Scottish Cancer Registry was linked to the mortality data from the NRS (Appendix 2.5 to Appendix 2.7). Females with tumours of the larynx had a higher proportion of deaths at 77.7% (n = 1,222) compared with females who had tumours of the oral cavity at 72.0% (n = 2,179). In addition, the proportion of deaths for those residing in the least deprived Carstairs 1991 Category was higher for people with cancer of the larynx at 79.5% (n = 1,838) compared to those with cancer of the oral cavity at 65.7% (n = 840), respectively. Individuals who had cancer of the oropharynx consistently had a lower proportion of deaths compared to people with cancer of the oral cavity or larynx.

**Table 2.1 – Baseline characteristics and proportion of deaths for the whole cohort**

| Variable | Frequency (Column %) | Died by 30th September 2017 (Row %) |
|---|---|---|
| **Total** | 24,778 (100.0%) | 18,322 (73.9%) |
| **Age at incidence** | | |
| Less than 45 | 1,382 (5.6%) | 541 (39.1%) |
| 45 to 54 | 4,238 (17.1%) | 2,553 (60.2%) |
| 55 to 64 | 7,601 (30.7%) | 5,418 (71.3%) |
| 65 to 74 | 6,988 (28.2%) | 5,663 (81.0%) |
| 75 and over | 4,569 (18.4%) | 4,147 (90.8%) |
| **Sex** | | |
| Male | 17,508 (70.7%) | 13,040 (74.5%) |
| Female | 7,270 (29.3%) | 5,282 (72.7%) |
| **ICD group** | | |
| Oral cavity | 8,189 (33.0%) | 6,028 (73.6%) |
| Larynx | 7,706 (31.1%) | 5,854 (76.0%) |
| Oropharynx | 3,379 (13.6%) | 2,204 (65.2%) |
| Hypopharynx | 1,586 (6.4%) | 1,447 (91.2%) |
| Lip | 1,379 (5.6%) | 948 (68.7%) |
| Salivary gland | 1,175 (4.7%) | 720 (61.3%) |
| Other | 1,364 (5.5%) | 1,121 (82.2%) |
| **Pathology** | | |
| SCC | 21,403 (86.4%) | 16,043 (75.0%) |
| Non-SCC | 3,375 (13.6%) | 2,279 (67.5%) |
| **Treatment** | | |
| Surgery only | 4,384 (17.7%) | 2,278 (52.0%) |
| Radiotherapy only | 3,096 (12.5%) | 2,161 (69.8%) |
| Surgery and radiotherapy | 2,762 (11.1%) | 1,917 (69.4%) |
| Chemoradiotherapy | 2,412 (9.7%) | 1,430 (59.3%) |
| Surgery and chemoradiotherapy | 1,502 (6.1%) | 832 (55.4%) |
| Chemotherapy +/- surgery | 552 (2.2%) | 439 (79.5%) |
| No treatment | 1,828 (7.4%) | 1,727 (94.5%) |
| Unknown | 8,242 (33.3%) | 7,538 (91.5%) |
| **Year group** | | |
| 1986-1990 | 3,257 (13.1%) | 3,033 (93.1%) |
| 1991-1995 | 3,760 (15.2%) | 3,446 (91.6%) |
| 1996-2000 | 4,151 (16.8%) | 3,551 (85.5%) |
| 2001-2005 | 4,226 (17.1%) | 3,212 (76.0%) |
| 2006-2010 | 4,519 (18.2%) | 2,875 (63.6%) |
| 2011-2015 | 4,865 (19.6%) | 2,205 (45.3%) |
| **Network of residence** | | |
| West of Scotland (WoSCAN) | 12,850 (51.9%) | 9,834 (76.5%) |
| East of Scotland (SCAN) | 6,154 (24.8%) | 4,362 (70.9%) |
| North of Scotland (NOSCAN) | 5,774 (23.3%) | 4,126 (71.5%) |
| **Carstairs 1991 Category** | | |
| 1 – Least deprived | 3,623 (14.6%) | 2,408 (66.5%) |
| 2 | 4,487 (18.1%) | 3,180 (70.9%) |
| 3 | 4,818 (19.4%) | 3,550 (73.7%) |
| 4 | 5,256 (21.2%) | 3,950 (75.2%) |
| 5 – Most deprived | 6,594 (26.6%) | 5,234 (79.4%) |

### 2.3.4 Cross-tabulations of Carstairs 1991 Category by each baseline characteristic

#### 2.3.4.1 Whole cohort

The cross-tabulations of each IMD Category with the baseline characteristics are displayed in Table 2.2. Compared to people who resided in the least deprived areas, those who resided in the most deprived regions were more likely to be younger, be males, and have cancer of the larynx that was SCC. From 1996 onwards, those who were in the most deprived category were also more likely to be treated with chemoradiotherapy or receive no treatment at all. Those who resided in the most deprived regions were also more likely to reside in the West of Scotland.

#### 2.3.4.2 Comparison between males and females

The cross-tabulations of each IMD Category with the baseline characteristics are displayed in Appendix 2.8 and Appendix 2.9. The trends by the Carstairs 1991 Categories for both males and females coincided with the trends observed for the whole cohort. Males and females who resided in the most deprived areas were more likely to be between the ages of 45 and 64 and have cancer of the larynx that was SCC. From 1996 onwards, both males and females who were in the most deprived categories were less likely to be treated with surgery only and were more likely to receive no treatment.

#### 2.3.4.3 Comparison between those with cancer of the oral cavity, oropharynx, and larynx

The cross-tabulations of each IMD Category with the baseline characteristics are displayed in Appendix 2.10 and Appendix 2.12. People who resided in the most deprived regions were more likely to be between the ages of 45 and 54 if they had cancer of the oral cavity, between the ages of 45 and 64 if they had cancer of the oropharynx and be younger than 64 years of age if they had cancer of the larynx. The people who lived in the most deprived region and who had cancer of the oral cavity were more likely to be male, while those with cancer of the larynx were more likely to be female.

**Table 2.2 – Cross-tabulation of Carstairs 1991 Category with baseline characteristics for the whole cohort**

| | Carstairs 1991 Category (row %) | | | | | |
|---|---|---|---|---|---|---|
| **Variable** | **1 – Least deprived** | **2** | **3** | **4** | **5 – Most deprived** | **Chi-sq. p-value** |
| **Age at incidence** | | | | | | <0.001 |
| Less than 45 | 232 (6.4%) | 258 (5.7%) | 265 (5.5%) | 285 (5.4%) | 342 (5.2%) | |
| 45 to 54 | 565 (15.6%) | 705 (15.7%) | 793 (16.5%) | 896 (17.0%) | 1,279 (19.4%) | |
| 55 to 64 | 977 (27.0%) | 1,318 (29.4%) | 1,480 (30.7%) | 1,693 (32.2%) | 2,133 (32.3%) | |
| 65 to 74 | 1,021 (28.2%) | 1,278 (28.5%) | 1,335 (27.7%) | 1,496 (28.5%) | 1,858 (28.2%) | |
| 75 and over | 828 (22.9%) | 928 (20.7%) | 945 (19.6%) | 886 (16.9%) | 982 (14.9%) | |
| **Sex** | | | | | | 0.002 |
| Male | 2,506 (69.2%) | 3,109 (69.3%) | 3,403 (70.6%) | 3,720 (70.8%) | 4,770 (72.3%) | |
| Female | 1,117 (30.8%) | 1,378 (30.7%) | 1,415 (29.4%) | 1,536 (29.2%) | 1,824 (27.7%) | |
| **ICD group** | | | | | | <0.001 |
| Oral cavity | 1,278 (35.3%) | 1,520 (33.9%) | 1,575 (32.7%) | 1,714 (32.6%) | 2,102 (31.9%) | |
| Larynx | 938 (25.9%) | 1,245 (27.7%) | 1,513 (31.4%) | 1,699 (32.3%) | 2,311 (35.0%) | |
| Oropharynx | 511 (14.1%) | 647 (14.4%) | 645 (13.4%) | 703 (13.4%) | 873 (13.2%) | |
| Hypopharynx | 200 (5.5%) | 274 (6.1%) | 274 (5.7%) | 379 (7.2%) | 459 (7.0%) | |
| Lip | 258 (7.1%) | 324 (7.2%) | 323 (6.7%) | 262 (5.0%) | 212 (3.2%) | |
| Salivary gland | 264 (7.3%) | 246 (5.5%) | 241 (5.0%) | 209 (4.0%) | 215 (3.3%) | |
| Other | 174 (4.8%) | 231 (5.1%) | 247 (5.1%) | 290 (5.5%) | 422 (6.4%) | |
| **Pathology** | | | | | | <0.001 |
| SCC | 2,987 (82.4%) | 3,826 (85.3%) | 4,135 (85.8%) | 4,619 (87.9%) | 5,836 (88.5%) | |
| Non-SCC | 636 (17.6%) | 661 (14.7%) | 683 (14.2%) | 637 (12.1%) | 758 (11.5%) | |
| **Treatment** | | | | | | <0.001 |
| Surgery only | 732 (20.2%) | 873 (19.5%) | 906 (18.8%) | 914 (17.4%) | 959 (14.5%) | |
| Radiotherapy only | 467 (12.9%) | 512 (11.4%) | 605 (12.6%) | 672 (12.8%) | 840 (12.7%) | |
| Surgery and radiotherapy | 441 (12.2%) | 567 (12.6%) | 554 (11.5%) | 537 (10.2%) | 663 (10.1%) | |
| Chemoradiotherapy | 295 (8.1%) | 433 (9.7%) | 455 (9.4%) | 552 (10.5%) | 677 (10.3%) | |
| Surgery and chemoradiotherapy | 262 (7.2%) | 310 (6.9%) | 290 (6.0%) | 305 (5.8%) | 335 (5.1%) | |
| Chemotherapy +/- surgery | 66 (1.8%) | 78 (1.7%) | 119 (2.5%) | 114 (2.2%) | 175 (2.7%) | |
| No treatment | 233 (6.4%) | 288 (6.4%) | 349 (7.2%) | 380 (7.2%) | 578 (8.8%) | |
| Unknown | 1,127 (31.1%) | 1,426 (31.8%) | 1,540 (32.0%) | 1,782 (33.9%) | 2,367 (35.9%) | |
| **Network** | | | | | | <0.001 |
| West of Scotland (WoSCAN) | 1,222 (33.7%) | 1,394 (31.1%) | 1,930 (40.1%) | 2,737 (52.1%) | 5,567 (84.4%) | |
| East of Scotland (SCAN) | 1,008 (27.8%) | 1,489 (33.2%) | 1,531 (31.8%) | 1,686 (32.1%) | 440 (6.7%) | |
| North of Scotland (NOSCAN) | 1,393 (38.4%) | 1,604 (35.7%) | 1,357 (28.2%) | 833 (15.8%) | 587 (8.9%) | |

### 2.3.5 Follow-up time

The median follow-up time for each of the whole cohort, males and females, and those with cancers of the oral cavity, oropharynx, and larynx are outlined below.

**Whole cohort:** The median follow-up time was 8.4 years (IQR = 4.8 to 14.3 years) and 2.0 years (IQR = 0.7 to 6.1 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

**Males:** The median follow-up time was 8.3 years (IQR = 4.7 to 14.1 years) and 2.0 years (IQR = 0.7 to 6.0 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

**Females:** The median follow-up time was 8.6 years (IQR = 5.0 to 14.8 years) and 1.9 years (IQR = 0.6 to 6.4 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

**Oral cavity:** The median follow-up time was 8.1 years (IQR = 4.6 to 13.3 years) and 1.8 years (IQR = 0.6 to 5.4 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

**Larynx:** The median follow-up time was 9.4 years (IQR = 5.3 to 15.3 years) and 3.1 years (IQR = 1.0 to 8.0 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

**Oropharynx:** The median follow-up time was 6.6 years (IQR = 4.0 to 10.8 years) and 1.5 years (IQR = 0.6 to 4.6 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

### 2.3.6 Survival results

Net survival after one year, five years, and 10 years for each demographic are displayed in Table 2.3. Net survival after one year, five years, and 10 years was 77.8% (95% CI 77.2% to 78.3%), 54.4% (95% CI 53.7% to 55.2%), and 43.9% (95% CI 42.8% to 45.0%), respectively. Similar trends and differences were observed for overall survival (Appendix 2.13) and disease-specific survival (Appendix 2.14); however, the overall survival results were lower, with one-year, five-year, and 10-year overall survival at 75.1% (95% CI 74.6% to 75.7%), 47.0% (95% CI 46.4% to 47.6%), and 32.1% (95% CI 31.4% to 32.7%), respectively, while the disease-specific results were higher with one-year, five-year, and 10-year disease-specific survival at 80.2% (95% CI 79.7% to 80.7%), 61.8% (95% CI 61.1% to 62.4%), and 56.0% (55.3% to 56.7%), respectively.

Net survival was the same between males and females, which after 10 years was 43.5% (95% CI 42.2% to 44.8%) and 44.7% (95% CI 42.6% to 46.7%), respectively. People with cancer of the lip had the highest net survival, which after 10 years was 82.6% (95 CI 74.1% to 91.1%), while people with cancer of the hypopharynx had the lowest net survival, which after 10 years was 15.0% (95% CI 12.7% to 17.3%). Those who were treated with surgery only had the highest net survival, which after 10 years was 67.9% (95% CI 64.0% to 71.8%), while those who received chemotherapy with or without surgery had the lowest net survival, which after 10 years was 24.8% (95% CI 20.4% to 29.1%). The individuals who resided within the West of Scotland Cancer Network had the lowest net survival at all three time points, which after 10 years was 40.3% (95% CI 38.8% to 41.8%). Over time, one-year net survival did not improve from the period of 1986-1990 at 78.5% (95% CI 77.0% to 80.0%) to 2011-2015 at 78.8% (95% CI 77.6% to 80.0%). There was a slight improvement in five-year net survival which increased from 53.5% (95% CI 51.3% to 55.7%) in 1986-1990 to 57.6% (95% CI 55.8% to 59.4%) in 2011-2015. However, there was also no improvement in 10-year net survival from the period of 1986-1991 at 43.5% (95% CI 40.7% to 46.2%) to 2006-2010 at 44.6% (95% CI 42.1% to 47.1%).

There was a trend in net survival across the Carstairs 1991 Categories at all three time points. After 10 years, the people who were from the most deprived regions had a much lower net survival compared to the people who were from the least deprived areas at 36.9% (95% CI 35.1% to 38.8%) and 48.8% (95% CI 45.9% to 51.7%), respectively.

**Table 2.3 – Net survival by each baseline characteristic**

| Variable | One-year net survival (95% CI) | Five-year net survival (95% CI) | 10-year net survival (95% CI) |
|---|---|---|---|
| **Total** | 77.8 (77.2, 78.3) | 54.4 (53.7, 55.2) | 43.9 (42.8, 45.0) |
| **Age at incidence** | | | |
| Less than 45 | 89.8 (88.2, 91.4) | 73.8 (71.4, 76.2) | 67.6 (64.9, 70.3) |
| 45 to 54 | 84.6 (83.5, 85.7) | 61.8 (60.3, 63.4) | 51.9 (50.2, 53.7) |
| 55 to 64 | 81.0 (80.1, 81.9) | 55.5 (54.3, 56.8) | 43.5 (42.1, 45.0) |
| 65 to 74 | 75.7 (74.6, 76.8) | 51.4 (49.9, 52.8) | 39.2 (37.4, 41.0) |
| 75 and over | 65.3 (63.7, 66.9) | 44.3 (42.0, 46.6) | 36.6 (32.3, 40.9) |
| **Sex** | | | |
| Male | 78.4 (77.7, 79.0) | 53.9 (53.0, 54.8) | 43.5 (42.2, 44.8) |
| Female | 76.3 (75.2, 77.3) | 55.6 (54.2, 57.0) | 44.7 (42.6, 46.7) |
| **ICD group** | | | |
| Oral cavity | 75.7 (74.7, 76.7) | 51.5 (50.2, 52.8) | 41.0 (39.2, 42.9) |
| Larynx | 84.0 (83.1, 84.9) | 61.5 (60.1, 62.8) | 48.1 (46.2, 50.0) |
| Oropharynx | 75.6 (74.1, 77.1) | 52.0 (50.1, 53.9) | 40.6 (38.2, 43.0) |
| Hypopharynx | 55.1 (52.5, 57.6) | 22.2 (19.9, 24.5) | 15.0 (12.7, 17.3) |
| Lip | 97.9 (96.4, 99.3) | 89.6 (85.8, 93.4) | 82.6 (74.1, 91.1) |
| Salivary gland | 84.8 (82.5, 87.1) | 62.8 (59.3, 66.2) | 58.3 (53.5, 63.1) |
| Other | 59.8 (57.1, 62.5) | 31.9 (29.1, 34.6) | 23.6 (20.6, 26.5) |
| **Treatment** | | | |
| Surgery only | 91.5 (90.6, 92.5) | 77.1 (75.3, 79.0) | 67.9 (64.0, 71.8) |
| Radiotherapy only | 81.6 (80.2, 83.1) | 57.5 (55.3, 59.7) | 44.2 (41.0, 47.3) |
| Surgery and radiotherapy | 86.9 (85.5, 88.2) | 57.6 (55.4, 59.8) | 43.4 (40.6, 46.1) |
| Chemoradiotherapy | 82.9 (81.3, 84.4) | 53.3 (51.0, 55.6) | 39.8 (36.9, 42.8) |
| Surgery and chemoradiotherapy | 88.3 (86.6, 90.0) | 57.5 (54.8, 60.3) | 46.6 (43.2, 50.0) |
| Chemotherapy +/- surgery | 57.8 (53.6, 62.0) | 33.2 (28.9, 37.4) | 24.8 (20.4, 29.1) |
| No treatment | 18.6 (16.7, 20.4) | 9.8 (8.2, 11.4) | 7.6 (5.8, 9.4) |
| Unknown | 76.6 (75.6, 77.6) | 50.9 (49.6, 52.3) | 40.8 (39.1, 42.5) |
| **Network of residence** | | | |
| West of Scotland (WoSCAN) | 76.0 (75.2, 76.8) | 51.8 (50.7, 52.8) | 40.3 (38.8, 41.8) |
| East of Scotland (SCAN) | 80.2 (79.1, 81.3) | 58.7 (57.2, 60.3) | 49.1 (46.7, 51.5) |
| North of Scotland (NOSCAN) | 79.0 (77.9, 80.2) | 55.7 (54.1, 57.2) | 46.2 (44.0, 48.4) |
| **Year group** | | | |
| 1986-1990 | 78.5 (77.0, 80.0) | 53.5 (51.3, 55.7) | 43.5 (40.7, 46.2) |
| 1991-1995 | 75.6 (74.2, 77.1) | 49.6 (47.6, 51.6) | 39.8 (37.2, 42.3) |
| 1996-2000 | 77.2 (75.8, 78.5) | 54.4 (52.5, 56.2) | 43.0 (40.3, 45.6) |
| 2001-2005 | 78.2 (76.9, 79.5) | 54.4 (52.6, 56.2) | 44.8 (42.7, 46.9) |
| 2006-2010 | 77.9 (76.7, 79.2) | 55.9 (54.2, 57.6) | 44.6 (42.1, 47.1) |
| 2011-2015 | 78.8 (77.6, 80.0) | 57.6 (55.8, 59.4) | N/A |
| **Carstairs Category** | | | |
| 1 – Least deprived | 81.0 (79.7, 82.4) | 60.2 (58.2, 62.2) | 48.8 (45.9, 51.7) |
| 2 | 79.6 (78.3, 80.8) | 57.0 (55.2, 58.8) | 48.1 (45.2, 51.0) |
| 3 | 80.1 (78.9, 81.3) | 55.9 (54.1, 57.6) | 44.5 (41.8, 47.2) |
| 4 | 76.5 (75.3, 77.7) | 54.3 (52.7, 55.9) | 44.9 (42.7, 47.1) |
| 5 – Most deprived | 74.0 (72.9, 75.1) | 48.5 (47.0, 50.0) | 36.9 (35.1, 38.8) |
| *SII (95% CI)* | 9.1 (3.7, 14.6) | 13.7 (7.1, 20.2) | 14.7 (3.8, 25.6) |
| *RII (95% CI)* | 0.12 (0.05, 0.19) | 0.25 (0.13, 0.37) | 0.34 (0.09, 0.58) |

### 2.3.7 Trends over time in survival by Carstairs 1991 Category

#### 2.3.7.1 Whole cohort

The trends over time in net survival by Carstairs 1991 Category for the whole cohort are displayed in Table 2.4. There was inequality in net survival for all of the people who were diagnosed with head and neck cancer between the years of 1986-1990 and 2011-2015 after one year, five years, and 10 years. However, the inequality was stronger in more recent years, which was particularly noticeable after five years of follow-up. After five years, the people who were diagnosed in 1986-1990 and who were in the least deprived and most deprived groups had net survival estimates of 54.0% (95% CI 48.3% to 59.6%) and 49.2% (95% CI 45.2% to 53.3%), respectively. However, as the people in group three had the highest net survival estimate of 55.8% (95% CI 50.8% to 60.8%), the SII and RII did not display inequality at 6.6 (95% CI -6.0 to 19.3) and 0.12 (95% CI -0.11 to 0.36), respectively. However, inequality in five-year survival was much clearer for those who were diagnosed between the years of 2011-2015, and net survival for those who were in the least deprived and most deprived groups were 66.9% (95% CI 62.6% to 71.2%) and 51.8% (95% CI 48.1% to 55.5%), respectively, with an SII and RII of 19.2 (95% CI 16.1 to 22.3) and 0.32 (95% CI 0.27 to 0.37), respectively.

By 10 years of follow-up, for the people who were in the least deprived and most deprived groups and who were diagnosed in 1986-1990, net survival estimates were 47.5% (95% CI 40.4% to 54.7%) and 39.0% (95% CI 34.2% to 43.9%), respectively, with an SII and RII of 8.4 (95% CI -4.2 to 20.9) and 0.19 (95% CI -0.10 to 0.48), respectively. These results were stronger than the SII and RII results after one year and five years of follow-up. Results for those who were diagnosed in 2011-2015 were similar but the inequality was substantially worse by five years than it was after one year of follow-up. After one year, the individuals in the least deprived and most deprived groups had net survival estimates of 82.8% (95% CI 80.0% to 85.6%) and 73.5% (95% CI 70.9% to 76.2%), respectively, with an SII and RII of 7.1 (95% CI 2.5 to 11.7) and 0.09 (95% CI 0.03 to 0.15), respectively. However, after five years for follow-up, the people who were diagnosed between the years of 2011-2015 and who were in the least deprived and most deprived groups had net survival estimates of 66.9% (95% CI 62.6% to 71.2%) and 51.8% (95% CI 48.1% to 55.5%), respectively, with an SII and RII of 19.2 (95% CI 16.1 to 22.3) and 0.32 (95% CI 0.27 to 0.37), respectively. The same trends were also observed for the results from overall survival (Appendix 2.15) and disease-specific survival (Appendix 2.21).

**Table 2.4 – Net survival by Carstairs 1991 Category per year group of diagnosis for the whole cohort**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 81.0 (77.1, 84.9) | 77.2 (73.3, 81.2) | 82.4 (79.1, 85.6) | 82.8 (79.6, 86.0) | 79.3 (76.0, 82.6) | 82.8 (80.0, 85.6) |
| 2 | 79.1 (75.5, 82.8) | 77.9 (74.5, 81.3) | 81.3 (78.2, 84.5) | 77.8 (74.7, 80.8) | 78.4 (75.5, 81.4) | 82.3 (79.7, 84.8) |
| 3 | 81.3 (78.0, 84.8) | 79.5 (76.3, 82.7) | 80.0 (77.1, 83.0) | 80.2 (77.3, 83.2) | 80.2 (77.5, 83.0) | 79.7 (77.0, 82.4) |
| 4 | 75.2 (71.7, 78.6) | 74.8 (71.6, 78.0) | 73.0 (70.8, 77.0) | 78.2 (75.3, 81.0) | 78.6 (75.9, 81.3) | 77.8 (75.0, 80.5) |
| 5 – Most deprived | 77.4 (74.4, 80.3) | 71.6 (68.6, 74.5) | 72.4 (69.6, 75.2) | 74.8 (72.1, 77.6) | 74.8 (72.2, 77.4) | 73.5 (70.9, 76.2) |
| *SII (95% CI)* | *5.3 (-5.8, 16.4)* | *8.8 (-1.8, 19.4)* | *14.4 (5.3, 23.5)* | *7.7 (-1.6, 17.1)* | *5.3 (-3.3, 13.9)* | *7.1 (2.5, 11.7)* |
| *RII (95% CI)* | *0.07 (-0.07, 0.21)* | *0.12 (-0.02, 0.26)* | *0.19 (0.07, 0.30)* | *0.10 (-0.02, 0.22)* | *0.07 (-0.04, 0.18)* | *0.09 (0.03, 0.15)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 54.0 (48.3, 59.6) | 54.7 (49.0, 60.4) | 59.6 (54.8, 64.4) | 62.0 (57.6, 66.5) | 61.0 (56.7, 65.3) | 66.9 (62.6, 71.2) |
| 2 | 54.8 (49.4, 60.1) | 51.0 (46.3, 55.8) | 60.0 (55.5, 64.6) | 54.2 (50.1, 58.2) | 58.1 (54.0, 62.1) | 62.8 (58.8, 66.7) |
| 3 | 55.8 (50.8, 60.8) | 52.1 (47.5, 56.7) | 57.0 (52.8, 61.3) | 56.2 (52.0, 60.4) | 56.8 (53.0, 60.6) | 57.1 (53.0, 61.1) |
| 4 | 55.3 (50.6, 60.1) | 51.4 (47.2, 55.6) | 53.5 (49.5, 57.4) | 54.6 (50.8, 58.4) | 57.3 (53.7, 61.0) | 52.6 (48.5, 56.7) |
| 5 – Most deprived | 49.2 (45.2, 53.3) | 43.2 (39.4, 46.9) | 46.9 (43.4, 50.4) | 49.5 (45.9, 53.0) | 50.2 (46.9, 53.5) | 51.8 (48.1, 55.5) |
| *SII (95% CI)* | *6.6 (-6.0, 19.3)* | *12.7 (-0.8, 26.3)* | *17.5 (8.8, 26.3)* | *11.9 (-0.9, 24.7)* | *11.8 (1.5, 22.1)* | *19.2 (16.1, 22.3)* |
| *RII (95% CI)* | 0.12 (-0.11, 0.36) | 0.26 (-0.02, 0.53) | 0.32 (0.16, 0.48) | 0.22 (-0.02, 0.45) | 0.21 (0.03, 0.39) | 0.32 (0.27, 0.37) |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 47.5 (40.4, 54.7) | 41.2 (32.3, 50.1) | 46.9 (40.9, 53.0) | 51.6 (46.5, 56.7) | 48.2 (41.7, 54.7) | N/A |
| 2 | 43.1 (36.7, 49.4) | 45.3 (39.1, 51.4) | 49.5 (40.5, 58.5) | 47.0 (41.9, 52.1) | 49.1 (43.7, 54.4) | N/A |
| 3 | 45.1 (38.5, 51.7) | 38.7 (33.3, 44.0) | 45.6 (39.5, 51.7) | 48.4 (43.0, 53.8) | 43.6 (36.5, 50.7) | N/A |
| 4 | 45.4 (39.2, 51.6) | 42.7 (37.2, 48.2) | 44.7 (39.6, 49.8) | 44.9 (40.5, 49.3) | 49.4 (44.5, 54.3) | N/A |
| 5 – Most deprived | 39.0 (34.2, 43.9) | 33.7 (29.4, 37.9) | 33.9 (29.7, 38.1) | 37.9 (33.9, 42.0) | 38.9 (34.9, 43.0) | N/A |
| *SII (95% CI)* | *8.4 (-4.2, 20.9)* | *11.1 (-7.9, 30.0)* | *18.2 (0.0, 36.3)* | *15.5 (4.1, 27.0)* | *10.4 (-10.1, 31.0)* | *N/A* |
| *RII (95% CI)* | *0.19 (-0.10, 0.48)* | *0.28 (-0.20, 0.76)* | *0.43 (0.00, 0.84)* | *0.34 (0.09, 0.60)* | *0.23 (-0.22, 0.68)* | *N/A* |

#### 2.3.7.2 Comparison between males and females

The trends over time in net survival by Carstairs 1991 Category for males and females are displayed in Table 2.5 and Table 2.6, respectively. Net survival results for males and females after one year, five years, and 10 years between 1986-1990 to 2011-2015 were comparable to the results for the whole cohort by widening over calendar time and follow-up time. For those who were diagnosed between the years of 1986-1990, inequality in five-year net survival was stronger for males than it was for females, with males exhibiting an SII and RII of 8.4 (95% CI 2.1 to 13.6) and 0.16 (95% CI 0.06 to 0.26), respectively, and females exhibiting an SII and RII of 1.5 (95% CI -27.8 to 30.8) and 0.03 (95% CI -0.50 to 0.56), respectively. This difference in five-year net survival was also apparent for those who were diagnosed between the years of 2011-2015, with males exhibiting an SII and RII of 22.9 (95% CI 10.3 to 35.5) and 0.40 (95% CI 0.18 to 0.62), respectively and females exhibiting an SII and RII of 12.1 (95% CI% 4.1 to 20.1) and 0.21 (95% CI 0.07 to 0.34), respectively. However, this difference in inequality was not as clear by 10-years. The same trends were also observed for the results from overall survival (Appendix 2.16 and Appendix 2.17) and disease-specific survival (Appendix 2.22 and Appendix 2.23).

**Table 2.5 – Net survival by Carstairs 1991 Category per year group of diagnosis for males**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 82.8 (78.2, 87.5) | 77.5 (72.7, 82.3) | 84.7 (81.1, 88.4) | 81.9 (77.9, 85.9) | 82.7 (79.0, 86.4) | 81.6 (78.2, 85.0) |
| 2 | 80.7 (76.4, 85.0) | 80.7 (76.8, 84.7) | 83.2 (79.5, 86.9) | 76.9 (73.3, 80.6) | 79.3 (75.8, 82.9) | 85.2 (82.3, 88.1) |
| 3 | 82.0 (78.0, 86.0) | 82.5 (78.8, 86.1) | 79.9 (76.4, 83.4) | 80.5 (76.9, 84.1) | 81.0 (77.7, 84.2) | 79.7 (76.5, 82.9) |
| 4 | 74.8 (70.6, 78.9) | 75.8 (72.1, 79.6) | 74.7 (71.1, 78.4) | 77.7 (74.3, 81.1) | 79.3 (76.1, 82.5) | 77.4 (74.1, 80.6) |
| 5 – Most deprived | 78.3 (74.9, 81.8) | 72.1 (68.7, 75.5) | 72.6 (69.3, 75.9) | 74.6 (71.3, 77.8) | 74.6 (71.5, 77.7) | 73.9 (70.9, 77.0) |
| *SII (95% CI)* | *6.6 (-7.3, 20.5)* | *10.7 (-5.8, 27.1)* | *16.5 (11.4, 21.6)* | *6.9 (-3.8, 17.7)* | *8.7 (-0.2, 17.6)* | *12.5 (1.1, 23.9)* |
| *RII (95% CI)* | *0.08 (-0.09, 0.26)* | *0.14 (-0.08, 0.35)* | *0.21 (0.15, 0.28)* | *0.09 (-0.05, 0.23)* | *0.11 (0.0, 0.22)* | *0.16 (0.01, 0.30)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 55.5 (48.4, 62.6) | 54.7 (47.8, 61.6) | 59.8 (54.1, 65.5) | 60.9 (55.5, 66.3) | 63.0 (57.9, 68.2) | 67.7 (62.8, 72.7) |
| 2 | 54.4 (47.7, 61.1) | 52.2 (46.5, 58.0) | 60.9 (55.5, 66.3) | 53.0 (48.2, 57.8) | 58.0 (53.1, 62.9) | 63.8 (59.1, 68.4) |
| 3 | 54.5 (48.4, 60.5) | 53.1 (47.6, 58.5) | 56.0 (51.0, 60.9) | 56.7 (51.6, 61.8) | 57.7 (53.2, 62.3) | 57.3 (52.6, 62.0) |
| 4 | 52.7 (47.0, 58.3) | 50.5 (45.6, 55.5) | 50.5 (45.7, 55.2) | 53.3 (48.8, 57.9) | 57.5 (53.2, 61.8) | 50.6 (45.7, 55.5) |
| 5 – Most deprived | 49.0 (44.1, 53.8) | 42.5 (38.2, 46.9) | 47.7 (43.5, 51.8) | 48.1 (43.9, 52.3) | 48.5 (44.7, 52.4) | 50.7 (46.2, 55.2) |
| *SII (95% CI)* | *8.4 (2.1, 13.6)* | *15.0 (2.5, 27.5)* | *17.9 (9.6, 26.2)* | *12.5 (-1.8, 26.8)* | *15.6 (2.1, 29.2)* | *22.9 (10.3, 35.5)* |
| *RII (95% CI)* | *0.16 (0.06, 0.26)* | *0.30 (0.05, 0.56)* | *0.33 (0.18, 0.49)* | *0.23 (-0.03, 0.50)* | *0.28 (0.04, 0.52)* | *0.40 (0.18, 0.62)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 47.9 (38.7, 57.1) | 38.2 (27.9, 48.5) | 47.7 (40.4, 55.0) | 50.8 (44.7, 56.8) | 47.7 (39.3, 56.1) | N/A |
| 2 | 40.8 (33.1, 48.5) | 47.3 (39.5, 55.2) | 50.3 (43.1, 57.6) | 47.4 (41.3, 53.6) | 48.9 (42.4, 55.4) | N/A |
| 3 | 41.7 (33.6, 49.7) | 40.6 (34.1, 47.1) | 43.0 (35.7, 50.4) | 47.6 (41.1, 54.2) | 44.6 (35.2, 54.0) | N/A |
| 4 | 44.5 (37.0, 51.9) | 45.3 (39.1, 51.5) | 43.1 (37.4, 48.8) | 46.4 (41.2, 51.6) | 49.2 (43.6, 54.9) | N/A |
| 5 – Most deprived | 37.8 (31.9, 43.7) | 32.6 (27.7, 37.5) | 34.2 (29.5, 39.0) | 38.3 (33.3, 43.2) | 37.6 (32.9, 42.3) | N/A |
| *SII (95% CI)* | *8.4 (-7.4, 24.2)* | *11.4 (-18.7, 41.4)* | *18.8 (4.3, 33.3)* | *14.2 (2.0, 26.3)* | *12.0 (-9.3, 33.3)* | *N/A* |
| *RII (95% CI)* | *0.20 (-0.18, 0.58)* | *0.28 (-0.46, 1.03)* | *0.44 (0.10, 0.78)* | *0.31 (0.04, 0.58)* | *0.27 (-0.21, 0.74)* | *N/A* |

**Table 2.6 – Net survival by Carstairs 1991 Category per year group of diagnosis for females**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 77.3 (80.2, 84.4) | 76.6 (69.4, 83.8) | 76.4 (69.8, 83.0) | 84.5 (79.2, 89.9) | 71.4 (64.9, 77.9) | 85.5 (80.6, 90.4) |
| 2 | 75.6 (68.9, 82.4) | 71.3 (64.8, 77.8) | 77.2 (71.3, 83.2) | 79.7 (74.2, 85.1) | 76.3 (70.8, 81.8) | 75.7 (70.6, 80.9) |
| 3 | 79.7 (73.5, 86.0) | 71.4 (64.6, 78.2) | 80.3 (74.7, 85.9) | 79.6 (74.4, 84.9) | 78.5 (73.4, 83.6) | 79.6 (74.5, 84.6) |
| 4 | 76.0 (69.8, 82.3) | 72.0 (65.8, 78.3) | 72.2 (66.6, 77.8) | 79.4 (74.2, 84.5) | 76.9 (71.7, 82.1) | 78.7 (73.6, 83.7) |
| 5 – Most deprived | 75.0 (69.3, 80.7) | 69.9 (64.3, 75.6) | 71.9 (66.7, 77.0) | 75.5 (70.4, 80.7) | 75.4 (70.4, 80.4) | 72.5 (67.6, 77.5) |
| *SII (95% CI)* | *2.7 (-7.1, 12.5)* | *5.7 (-3.3, 14.6)* | *8.2 (-6.8, 23.2)* | *8.9 (1.1, 16.7)* | *-2.8 (-16.0, 10.4)* | *11.1 (-7.5, 29.7)* |
| *RII (95% CI)* | *0.03 (-0.09, 0.16)* | *0.08 (-0.05, 0.20)* | *0.11 (-0.09, 0.31)* | *0.11 (0.01, 0.21)* | *-0.04 (-0.21, 0.14)* | *0.14 (-0.10, 0.38)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 50.9 (41.6, 60.3) | 54.7 (45.0, 64.4) | 59.0 (50.3, 67.7) | 64.2 (56.5, 72.0) | 56.1 (48.4, 63.7) | 65.1 (56.7, 73.4) |
| 2 | 55.4 (46.6, 64.1) | 48.3 (40.2, 56.5) | 58.1 (50.0, 66.1) | 56.8 (49.2, 64.3) | 58.0 (50.8, 64.2) | 60.6 (53.2, 68.0) |
| 3 | 58.9 (50.4, 67.5) | 49.6 (41.2, 58.0) | 59.8 (51.6, 68.0) | 55.1 (47.9, 62.3) | 54.5 (47.7, 61.2) | 56.8 (48.9, 64.6) |
| 4 | 61.2 (52.8, 69.7) | 53.4 (45.6, 61.3) | 60.0 (52.7, 67.3) | 57.8 (50.7, 64.8) | 56.8 (50.1, 63.5) | 57.4 (49.8, 65.0) |
| 5 – Most deprived | 49.9 (42.7, 57.2) | 45.0 (37.6, 52.5) | 44.9 (38.7, 51.1) | 53.1 (46.6, 59.7) | 54.8 (48.5, 61.0) | 54.2 (47.5, 61.0) |
| *SII (95% CI)* | *1.5 (-27.8, 30.8)* | *7.5 (-11.3, 26.3)* | *16.7 (-11.6, 45.0)* | *9.8 (-4.9, 24.5)* | *2.1 (-5.5, 9.7)* | *12.1 (4.1, 20.1)* |
| *RII (95% CI)* | *0.03 (-0.50, 0.56)* | *0.15 (-0.23, 0.53)* | *0.30 (-0.21, 0.81)* | *0.17 (-0.09, 0.43)* | *0.04 (-0.10, 0.17)* | *0.21 (0.07, 0.34)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 46.4 (35.6, 57.2) | 48.6 (32.6, 64.5) | 44.7 (34.4, 55.1) | 53.2 (44.0, 62.4) | 49.4 (40.3, 58.5) | N/A |
| 2 | 48.3 (37.5, 59.1) | 40.5 (31.0, 50.0) | 47.7 (26.6, 68.8) | 45.7 (36.9, 54.6) | 49.5 (40.2, 58.8) | N/A |
| 3 | 52.0 (41.6, 62.5) | 32.7 (23.6, 41.8) | 52.2 (41.5, 62.8) | 49.8 (40.3, 59.2) | 41.3 (32.9, 49.8) | N/A |
| 4 | 47.2 (36.5, 57.9) | 36.1 (25.2, 47.0) | 47.9 (37.7, 58.1) | 41.1 (33.1, 49.1) | 49.7 (40.1, 59.3) | N/A |
| 5 – Most deprived | 42.2 (34.0, 50.5) | 36.5 (28.6, 44.8) | 32.9 (24.7, 41.2) | 37.1 (30.0, 44.2) | 42.6 (34.6, 50.6) | N/A |
| *SII (95% CI)* | *6.8 (-11.0, 24.6)* | *11.6 (-12.3, 35.4)* | *16.7 (-18.5, 51.8)* | *18.5 (2.3, 34.7)* | *6.4 (-15.2, 28.1)* | *N/A* |
| *RII (95% CI)* | *0.15 (-0.23, 0.52)* | *0.30 (-0.32, 0.93)* | *0.38 (-0.42, 1.17)* | *0.41 (0.05, 0.78)* | *0.14 (-0.33, 0.61)* | *N/A* |

#### 2.3.7.3 Comparison between those with oral cavity, oropharynx, and cancer of the larynx

The trends over time in net survival by Carstairs 1991 Category for people with cancer of the oral cavity, oropharynx, and larynx are displayed in Table 2.52 to Table 2.54, respectively. Net survival results for those with cancer of the oral cavity, oropharynx, and larynx after one year, five years, and 10 years between 1986-1990 to 2011-2015 were comparable to the results for the whole cohort by widening over calendar time and follow-up time.

For those who were diagnosed between the years of 1986-1990, there was no inequality in net survival after one year or five years for those diagnosed with cancer of the oral cavity, oropharynx, or larynx. However, results for those who were diagnosed between the years of 1986-1990 differed after 10 years of follow-up: for those with cancer of the oral cavity and larynx, there was no inequality present, however for those with cancer of the oropharynx, there was strong inequality with the least deprived and most deprived groups exhibiting 10-year net survival of 31.3% (95% CI 13.2% to 49.4%) and 15.7% (95% CI 5.3% to 26.1%), respectively, and an SII and RII of 22.6 (95% CI 2.0 to 43.3) and 0.88 (95% CI 0.08 to 1.68), respectively. However, for those who were diagnosed between the years of 2011-2015, inequality was present after one year and five years of follow-up. The same trends were also observed for the results from overall survival (Appendix 2.18 to Appendix 2.20) and disease-specific survival (Appendix 2.24 to Appendix 2.26).

**Table 2.7 – Net survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the oral cavity**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 75.0 (66.9, 83.2) | 75.1 (68.2, 81.9) | 76.1 (69.9, 82.4) | 84.9 (79.8, 89.9) | 77.9 (72.5, 83.4) | 83.1 (78.7, 87.5) |
| 2 | 75.3 (68.3, 82.3) | 72.9 (66.8, 78.9) | 79.6 (74.0, 85.2) | 72.4 (66.7, 78.1) | 73.4 (68.1, 78.7) | 83.4 (79.2, 87.6) |
| 3 | 72.3 (65.3, 79.3) | 76.0 (69.8, 82.1) | 76.7 (71.2, 82.1) | 78.1 (72.9, 83.2) | 82.3 (77.9, 86.8) | 77.5 (72.6, 82.3) |
| 4 | 67.2 (60.3, 74.1) | 71.9 (65.8, 77.9) | 70.0 (64.1, 76.0) | 77.2 (72.4, 82.0) | 76.4 (71.7, 81.2) | 78.9 (74.3, 83.5) |
| 5 – Most deprived | 73.3 (67.8, 78.9) | 68.0 (62.5, 73.4) | 71.9 (67.0, 76.7) | 74.1 (69.3, 78.9) | 73.8 (69.3, 78.4) | 72.7 (68.0, 77.4) |
| *SII (95% CI)* | *3.8 (-13.6, 21.2)* | *8.5 (-2.5, 19.4)* | *9.2 (-5.2, 23.6)* | *7.3 (-14.7, 29.3)* | *3.4 (-16.9, 23.8)* | *13.1 (2.5, 23.7)* |
| *RII (95% CI)* | *0.05 (-0.19, 0.29)* | *0.12 (-0.03, 0.27)* | *0.12 (-0.07, 0.32)* | *0.09 (-0.19, 0.38)* | *0.04 (-0.22, 0.31)* | *0.17 (0.03, 0.30)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 39.7 (29.9, 49.5) | 45.7 (36.5, 54.9) | 54.1 (45.9, 62.2) | 63.4 (56.1, 70.6) | 59.7 (52.6, 66.7) | 67.3 (60.4, 74.2) |
| 2 | 43.9 (35.2, 52.6) | 47.3 (39.5, 55.1) | 52.8 (45.1, 60.5) | 48.7 (41.8, 55.7) | 55.6 (49.1, 62.2) | 64.8 (58.3, 71.3) |
| 3 | 47.6 (38.7, 56.4) | 46.6 (38.3, 54.9) | 51.7 (44.6, 58.8) | 55.0 (48.1, 61.9) | 63.4 (57.0, 69.8) | 56.4 (49.3, 63.5) |
| 4 | 49.6 (41.3, 57.9) | 47.7 (40.1, 55.2) | 46.9 (39.5, 54.3) | 48.9 (42.6, 55.2) | 54.2 (47.9, 60.5) | 52.6 (45.5, 59.6) |
| 5 – Most deprived | 43.6 (36.3, 50.8) | 39.2 (32.9, 45.6) | 45.7 (39.7, 51.6) | 45.6 (39.6, 51.5) | 47.5 (42.0, 53.1) | 48.2 (41.5, 54.8) |
| *SII (95% CI)* | *-3.2 (-23.2, 16.7)* | *8.4 (-8.1, 24.9)* | *11.7 (6.3, 17.0)* | *16.6 (-7.4, 40.6)* | *14.6 (-10.4, 39.6)* | *25.4 (17.9, 32.9)* |
| *RII (95% CI)* | *-0.07 (-0.51, 0.37)* | *0.19 (-0.18, 0.55)* | *0.23 (0.13, 0.34)* | *0.32 (-0.14, 0.79)* | *0.26 (-0.19, 0.71)* | *0.44 (0.31, 0.57)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 32.9 (22.0, 43.7) | 36.6 (25.6, 47.6) | 41.0 (31.1, 50.8) | 56.7 (48.1, 64.2) | 41.9 (28.4, 55.3) | N/A |
| 2 | 30.3 (20.8, 39.8) | 39.2 (30.6, 47.7) | 38.4 (28.7, 48.0) | 45.1 (37.2, 53.0) | 46.5 (38.4, 54.7) | N/A |
| 3 | 35.8 (25.5, 46.2) | 30.1 (21.6, 38.6) | 49.1 (39.6, 58.7) | 48.3 (39.5, 57.1) | 44.6 (29.8, 59.5) | N/A |
| 4 | 38.2 (27.6, 48.7) | 36.8 (26.4, 47.3) | 33.1 (25.4, 40.7) | 37.4 (30.5, 44.4) | 50.1 (41.3, 58.9) | N/A |
| 5 – Most deprived | 35.1 (27.1, 43.0) | 32.8 (25.5, 40.0) | 31.6 (23.2, 37.9) | 33.9 (27.4, 40.5) | 44.2 (37.6, 50.8) | N/A |
| *SII (95% CI)* | *-5.2 (-19.1, 8.6)* | *5.3 (-13.0, 23.6)* | *14.4 (-18.4, 47.2)* | *26.1 (7.5, 44.8)* | *-2.7 (-19.4, 14.1)* | *N/A* |
| *RII (95% CI)* | *-0.15 (-0.54, 0.25)* | *0.15 (-0.37, 0.68)* | *0.38 (-0.49, 1.24)* | *0.61 (0.18, 1.04)* | *-0.06 (-0.43, 0.31)* | *N/A* |

**Table 2.8 – Net survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the oropharynx**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 72.2 (56.5, 87.9) | 62.9 (48.1, 77.8) | 87.7 (79.4, 95.9) | 83.0 (74.8, 91.2) | 77.4 (69.6, 85.2) | 83.9 (78.1, 89.8) |
| 2 | 71.5 (58.2, 84.8) | 75.7 (64.6, 86.9) | 71.3 (61.3, 81.4) | 77.4 (69.3, 85.5) | 82.5 (76.1, 88.9) | 83.7 (78.5, 88.8) |
| 3 | 79.4 (67.2, 91.7) | 58.0 (45.3, 70.7) | 78.5 (69.8, 87.2) | 80.7 (73.1, 88.2) | 81.8 (75.4, 88.3) | 78.6, 72.6, 84.6) |
| 4 | 55.9 (43.8, 68.0) | 60.9 (49.2, 72.5) | 71.5 (62.0, 81.0) | 74.2 (65.7, 82.6) | 80.1 (73.9, 86.4) | 79.8 (73.9, 85.7) |
| 5 – Most deprived | 69.1 (58.1, 80.0) | 65.0 (55.3, 74.8) | 67.9 (59.4, 76.3) | 67.4 (59.0, 75.8) | 70.8 (64.1, 77.6) | 74.4 (68.9, 79.9) |
| *SII (95% CI)* | *10.3 (-38.0, 58.7)* | *4.5 (-31.9, 40.9)* | *18.8 (-8.0, 45.7)* | *17.6 (1.7, 33.5)* | *10.3 (-12.0, 32.7)* | *12.2 (3.7, 20.7)* |
| *RII (95% CI)* | *0.15 (0.56, 0.86)* | *0.07 (-0.50, 0.63)* | *0.25 (-0.11, 0.61)* | *0.23 (0.02, 0.44)* | *0.13 (-0.15, 0.42)* | *0.15 (0.05, 0.26)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 35.5 (17.0, 54.0) | 35.1 (20.1, 50.0) | 56.0 (42.8, 69.1) | 57.7 (46.6, 68.9) | 55.0 (45.4, 64.7) | 71.6 (63.4, 79.7) |
| 2 | 42.0 (24.8, 59.3) | 43.0 (29.6, 56.3) | 39.1 (27.2, 51.0) | 52.8 (42.7, 62.8) | 66.4 (58.0, 74.8) | 64.9 (56.9, 73.0) |
| 3 | 34.0 (18.9, 49.1) | 22.8 (11.4, 34.3) | 57.4 (46.2, 68.7) | 50.2 (40.2, 60.3) | 56.5 (47.6, 65.3) | 62.8 (54.9, 70.7) |
| 4 | 34.4 (22.1, 46.7) | 35.0 (22.6, 47.3) | 44.2 (33.1, 55.3) | 57.5 (47.3, 67.6) | 56.6 (48.4, 64.8) | 59.7 (51.1, 68.2) |
| 5 – Most deprived | 34.5 (22.5, 46.4) | 36.6 (25.8, 47.4) | 35.9 (26.9, 45.0) | 47.8 (38.2, 57.4) | 48.5 (40.7, 56.2) | 56.3 (48.8, 63.8) |
| *SII (95% CI)* | *5.5 (-10.6, 21.7)* | *0.1 (-40.5, 40.7)* | *19.6 (-25.4, 64.5)* | *7.5 (-14.1, 29.1)* | *14.0 (-14.2, 42.1)* | *17.5 (10.5, 24.6)* |
| *RII (95% CI)* | *0.15 (-0.30, 0.60)* | *0.00 (-1.17, 1.17)* | *0.43 (-0.56, 1.42)* | *0.14 (-0.26, 0.55)* | *0.25 (-0.25, 0.75)* | *0.28 (0.17, 0.39)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 31.3 (13.2, 49.4) | 31.5 (16.1, 46.9) | 42.4 (27.7, 57.1) | 47.5 (35.8, 59.3) | 53.8 (43.5, 64.2) | N/A |
| 2 | 35.9 (17.5, 54.3) | 27.9 (15.2, 40.6) | 32.2 (19.6, 44.8) | 42.7 (31.6, 53.8) | 57.1 (47.1, 67.1) | N/A |
| 3 | 25.2 (11.0, 39.4) | 12.8 (1.9, 23.8) | 46.2 (33.1, 59.4) | 41.5 (30.0, 53.0) | 48.7 (39.0, 58.4) | N/A |
| 4 | 26.7 (13.4, 40.0) | 31.3 (17.3, 45.4) | 37.4 (25.3, 49.5) | 47.2 (36.2, 58.2) | 49.6 (40.1, 59.1) | N/A |
| 5 – Most deprived | 15.7 (5.3, 26.1) | 14.9 (5.7, 24.1) | 26.1 (17.2, 35.1) | 31.7 (22.0, 41.4) | 33.2 (24.4, 41.9) | N/A |
| *SII (95% CI)* | *22.6 (2.0, 43.3)* | *15.4 (-29.8, 60.6)* | *16.9 (-21.2, 55.0)* | *14.4 (-13.7, 42.4)* | *26.8 (-0.4, 54.0)* | *N/A* |
| *RII (95% CI)* | *0.88 (0.08, 1.68)* | *0.68 (-1.32, 2.69)* | *0.47 (-0.59, 1.53)* | *0.35 (-0.33, 1.02)* | *0.57 (-0.01, 1.14)* | *N/A* |

**Table 2.9 – Net survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the larynx**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 84.5 (77.9, 91.1) | 84.5 (77.9, 91.1) | 86.3 (80.8, 91.8) | 82.1 (75.6, 88.5) | 86.9 (81.3, 92.6) | 84.7 (78.6, 90.9) |
| 2 | 87.7 (82.5, 93.0) | 87.5 (82.5, 92.5) | 87.0 (82.0, 92.0) | 84.3 (79.3, 89.4) | 83.1 (77.6, 88.6) | 83.8 (78.2, 89.4) |
| 3 | 88.5 (83.6, 93.5) | 86.9 (82.3, 92.5) | 87.9 (83.5, 92.3) | 82.9 (77.8, 88.0) | 84.6 (79.9, 89.3) | 86.3 (81.7, 90.9) |
| 4 | 83.8 (78.6, 89.1) | 86.2 (81.8, 90.6) | 81.4 (76.9, 86.0) | 85.1 (80.5, 89.6) | 85.1 (80.7, 89.6) | 79.3 (74.2, 84.5) |
| 5 – Most deprived | 84.6 (80.5, 88.7) | 82.1 (78.0, 86.3) | 81.7 (77.5, 85.9) | 83.9 (79.8, 87.9) | 79.9 (75.5, 84.3) | 78.3 (73.7, 82.8) |
| *SII (95% CI)* | *3.0 (-7.6, 13.7)* | *5.5 (-4.4, 15.3)* | *8.2 (-2.6, 19.1)* | *-1.5 (-7.1, 4.1)* | *6.6 (-3.8, 17.0)* | *9.8 (2.0, 21.6)* |
| *RII (95% CI)* | *0.04 (-0.09, 0.16)* | *0.06 (-0.05, 0.18)* | *0.10 (-0.03, 0.23)* | *-0.02 (-0.08, 0.05)* | *0.08 (-0.05, 0.20)* | *0.12 (-0.02, 0.26)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 58.6 (48.0, 69.2) | 70.0 (58.7, 81.3) | 68.6 (59.7, 77.5) | 62.5 (53.7, 71.4) | 74.1 (65.8, 82.4) | 70.0 (59.7, 80.4) |
| 2 | 65.3 (55.3, 75.3) | 58.5 (50.4, 66.7) | 70.6 (63.0, 78.1) | 59.1 (51.6, 66.7) | 60.5 (51.8, 69.1) | 65.6 (56.5, 74.7) |
| 3 | 61.0 (52.5, 69.5) | 63.0 (55.7, 70.3) | 66.1 (58.6, 73.5) | 63.3 (55.8, 70.8) | 56.9 (49.9, 64.0) | 60.7 (52.5, 69.0) |
| 4 | 64.8 (56.6, 72.9) | 64.0 (57.1, 70.9) | 60.9 (54.4, 67.4) | 64. 3(57.6, 71.1) | 66.3 (59.6, 73.0) | 54.8 (46.5, 63.2) |
| 5 – Most deprived | 57.4 (51.0, 63.8) | 55.9 (49.9, 61.9) | 57.2 (51.0, 63.4) | 56.7 (50.6, 62.8) | 57.3 (51.3, 63.3) | 56.5 (49.4, 63.6) |
| *SII (95% CI)* | *5.3 (-14.1, 24.6)* | *11.0 (-11.2, 33.2)* | *17.3 (9.0, 25.5)* | *6.6 (-7.6, 20.8)* | *10.6 (-22.1, 43.3)* | *16.3 (0.6, 31.9)* |
| *RII (95% CI)* | *0.09 (-0.23, 0.40)* | *0.18 (-0.18, 0.54)* | *0.27 (0.14, 0.40)* | *0.11 (-0.12, 0.35)* | *0.17 (-0.36, 0.70)* | *0.27 (0.01, 0.53)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 45.2 (32.4, 58.0) | 54.1 (33.7, 74.6) | 50.3 (39.0, 61.6) | 43.8 (33.9, 53.7) | 63.2 (51.5, 74.9) | N/A |
| 2 | 47.7 (36.4, 59.0) | 53.7 (42.7, 64.8) | 61.1 (51.1, 71.1) | 46.7 (37.7, 55.8) | 49.2 (38.4, 59.9) | N/A |
| 3 | 43.7 (33.6, 53.8) | 49.9 (41.0, 58.8) | 44.1 (32.2, 56.0) | 52.2 (42.1, 62.3) | 43.1 (32.1, 54.1) | N/A |
| 4 | 50.9 (40.4, 61.4) | 53.9 (45.5, 62.4) | 52.7 (44.4, 61.1) | 54.6 (46.6, 62.6) | 53.2 (43.8, 62.6) | N/A |
| 5 – Most deprived | 43.3 (35.5, 51.1) | 45.8 (38.3, 53.3) | 42.7 (35.2, 50.2) | 40.5 (33.4, 47.6) | 39.9 (32.4, 47.5) | N/A |
| *SII (95% CI)* | *2.7 (-16.0, 21.5)* | *9.7 (-5.2, 24.5)* | *13.3 (-21.1, 47.7)* | *5.9 (-29.2, 40.9)* | *18.6 (-17.9, 54.9)* | *N/A* |
| *RII (95% CI)* | *0.06 (-0.35, 0.47)* | *0.19 (-0.10, 0.48)* | *0.27 (-0.43, 0.97)* | *0.12 (-0.62, 0.87)* | *0.39 (-0.37, 1.15)* | *N/A* |

### 2.3.8 Sensitivity analyses

Two sensitivity analyses were conducted using varying measurements of socioeconomic status. The first sensitivity analysis utilised the nearest Carstairs and Morris index to the date of the registrant's diagnosis of head and neck cancer. Carstairs and Morris 1991 Categories were used for the people who were diagnosed between 1986 and 1995, Carstairs and Morris 2001 Categories (McLoone, 2004) were used for the people who were diagnosed between 1996 and 2005, and Carstairs and Morris 2011 Categories (Brown *et al.*, 2014) were used for the people who were diagnosed between 2006 and 2015. The second sensitivity analysis utilised the earliest defined SIMD categories from 2004 census data. Due to the recency of SIMD in comparison to Carstairs and Morris 1991 Index, this sensitivity analysis only included individuals who were diagnosed in more recent years from 2001 onwards.

#### 2.3.8.1 Trends over time using the nearest Carstairs Category

The trends over time in net survival by the nearest Carstairs Category for the whole cohort are displayed in Appendix 2.27. Since the same Carstairs 1991 Categories were used for those diagnosed between the years of 1986 and 1995, these results were the same as they were in the main analysis. For the remaining time periods, the results were also similar to the main analysis and inequality was present over the entire period. In addition, and in the same fashion as the main analysis, inequality became stronger over calendar time and over the follow-up period in the sensitivity analysis which used the nearest Carstairs Category by the year of the persons diagnosis. These results were also obtained for overall survival and disease-specific survival (Appendix 2.28 and Appendix 2.29).

#### 2.3.8.2 Trends over time using SIMD 2004 Categories

The trends over time in net survival by SIMD 2004 Categories for those who were diagnosed from 2001 onwards are displayed in Appendix 2.30. Inequality remained present for the time periods between 2001 and 2015 when using SIMD 2004 Categories compared to Carstairs 2001 Categories. Inequality was strongest in the most recent time period of 2011-2015 in the same fashion as the trends that were observed in the main analysis. In addition, and similarly to the main analysis, inequality also became clearer over the follow-up period and was worse after five years and 10 years than it was after one year. These results were also obtained for overall survival and disease-specific survival (Appendix 2.31 and Appendix 2.32).

## 2.4 Discussion

The aim of this chapter was to provide an overview of the time-trends in inequality in survival of people with head and neck cancer in Scotland. In addition to comparing trends over calendar time, the differences in inequality over follow-up time in one-year, five-year, and 10-year net survival were compared. These trends were examined for the whole cohort, by males and females, and across the three main subsites of head and neck cancer (oral cavity, oropharynx, and larynx). There are several key findings from this study which are outlined below.

***Survival of the whole cohort***

Net survival estimates after one year, five years, and 10 years were 77.8% (95% CI 77.2% to 78.3%), 54.4% (95% CI 53.7% to 55.2%), and 43.9% (95% CI 42.8% to 45.0%), respectively (Table 2.3). Overall survival after one year, five years, and 10 years was 75.1% (95% CI 74.6% to 75.7%), 47.0% (95% CI 46.4% to 47.6%), and 32.1% (95% CI 31.4% to 32.7%), respectively (Appendix 2.13), while disease-specific survival was higher at 80.2% (95% CI 79.7% to 80.7%), 61.8% (95% CI 61.1% to 62.4%), and 56.0% (95% CI 55.3% to 56.7%), respectively (Appendix 2.14). Over time, one-year net survival did not improve from the period of 1986-1990 at 78.5% (95% CI 77.0% to 80.0%) to 2011-2015 at 78.8% (95% CI 77.6% to 80.0%). There was a slight improvement in five-year net survival which increased from 53.5% (95% CI 51.3% to 55.7%) in 1986-1990 to 57.6% (95% CI 55.8% to 59.4%) in 2011-2015. However, there was also no improvement in 10-year net survival from the period of 1986-1991 at 43.5% (95% CI 40.7% to 46.2%) to 2006-2010 at 44.6% (95% CI 42.1% to 47.1%).

***Trends in inequality in survival over calendar time***

Inequality in net survival estimates was evident for all of the time periods of diagnosis, however inequality observed in the period of 2011-2015 was higher than it was at any other time period before it. For this time period of diagnosis, the least deprived and most deprived groups had five-year net survival estimates of 66.9% (95% CI 62.6% to 71.2%) and 51.8% (95% CI 48.1% to 55.5%), respectively (Table 2.4). Additionally, the SII and RII for these results were 19.2 (95% CI 16.1 to 22.3) and 0.32 (95% CI 0.27 to 0.37), which was the highest of all of the models for net survival for those diagnosed between 2011-2015 compared to those diagnosed during other time periods. The same pattern was observed for overall survival and disease-specific survival and for those with cancer of the oral cavity, oropharynx, and larynx, and for males and females individually (Appendix 2.15 to Appendix 2.20, and Appendix 2.29).

***Trends in inequality in survival over follow-up period***

In addition to inequality becoming worse over calendar time, inequality also became wider in the longer follow-up period since diagnosis. For example, for the people who were diagnosed in the period 2006-2010, the SIIs for net survival increased from 5.3 (95% CI -5.8 to 16.4), to 6.6 (95% CI -6.0 to 19.3) and 8.4 (95% CI -4.2 to 20.9) after one year, five years, and 10 years, respectively (Table 2.23). This observation was apparent for net survival, disease-specific survival, and overall survival estimates for all of the cohort, for males and females individually and for those who had cancer of the oral cavity, oropharynx, and larynx (Appendix 2.15 to Appendix 2.20, and Appendix 2.29).

***Comparisons with previous studies***

Only two previous studies have utilised Scottish Cancer Registry data to investigate the inequality in survival of people with head and neck cancer. A sub cohort of men diagnosed with cancer of the larynx was included in a large study of people diagnosed on the Scottish Cancer Registry between the years of 1986 and 2000 and followed up to 2005 (Shack *et al.*, 2007). Shack et al (2007) utilised 1995 Carstairs Index to investigate five-year relative survival. Similar to the present investigations, the study confirmed a deprivation gap in five-year relative survival for men with cancer of the larynx and in addition, concluded that inequality was widening by approximately 3% every five years. A second study investigated a cohort of registrations on the Scottish Cancer Registry with cancer of the nasopharynx diagnosed between the years of 1975 and 2001 (Anandan *et al.*, 2008). This study also showed inequality in survival, but trends over time were not investigated.

A study involving English and Welsh registry data investigated inequality utilising both Carstairs 1995 Index and the Index of Multiple Deprivation for men with cancer of the larynx diagnosed between 1996 and 1999 (Coleman *et al.*, 2004)**.** Coleman and colleagues investigated inequality in relative survival and confirmed that survival was improving for those who resided in areas of lower levels of deprivation, while those in the most deprived areas did not exhibit an improvement in survival over time. A further report on these data suggested that the gap between the least deprived and most deprived groups of England and wales could grow to up to 20% or more "*in the near future*" (Rachet *et al.*, 2008).

***Limitations and strengths***

There are several limitations to this study. The main limitation is the accessibility of data. Since this study involved cancer registry data, there were no additional data available such as tumour stage or health and behavioural information, and therefore investigations

into the explanations of inequality in survival of people with head and neck cancer could not be explored. Secondly, socioeconomic status was measured using the area based Carstairs 1991 Index (Carstairs and Morris, 1990; McLoone, 2000), which is derived from the 1991 Census based on the proportion of male unemployment, social class, lack of car ownership, and overcrowding in a dwelling. This study involved cancer registry data, and therefore further data on individual measurements of socioeconomic status (including education level and amount of income) were not available. Additionally, Carstairs 1991 Categories may not accurately represent rural and urban populations as it may be essential for people in these areas to own a car. However, as other indices such as education level or income were not available for this analysis, Carstairs 1991 Categories were the best measurement available. In addition, a further limitation of this study is the use of Carstairs 1991 Indices for the entire follow-up period, rather than the use of the Carstairs Categories at the nearest point in time (such as Carstairs 2001 and Carstairs 2011 Indices). Carstairs 1991 Indices were deemed the most appropriate for this study to ensure a consistent and standardised comparison of the impact of socioeconomic status over time, since the more recent Carstairs Indices may re-allocate some areas into different socioeconomic groups. In addition, we performed a sensitivity analysis which utilised Carstairs 2001 and Carstairs 2011 Indices for people who were diagnosed from 1996 onwards, and these results were the same as the results to the main analysis (Appendix 2.27). A second sensitivity analysis utilised data from the 2004 SIMD for people who were diagnosed from 2001 onwards. These results also demonstrated the same trends observed to those of the main analysis (Appendix 2.30).

This study has several strengths. Firstly, the Scottish Cancer Registry is a reliable source of all of the head and neck cancer registrations in Scotland during the study period of 1986 to 2015. Scottish Cancer Registry data is high quality data and well complete (Brewster *et al.*, 1997; Brewster *et al.*, 2002), and mortality (death record) linkage is thought to be highly accurate with detection of approximately 98.3% of the potential linkages (Newcombe *et al.*, 1959; Kendrick and Clarke, 1993). Scottish Cancer Registry data were provided on all of the individuals with at least one head and neck cancer, along with any other malignancy within or outside of the head and neck that the person may also have had. All of the data that were provided included people with diagnoses between 1st January 1986 and 31st December 2015. We cross-checked these data (n = 43,578) with the published Head and Neck Cancer Statistics from ISD Scotland (ISD Scotland, 2018). However, for accurate comparisons of individual cases of people with a primary head and neck cancer, an algorithm was developed and performed in order to identify a single record containing a person's primary tumour (Section 2.2.6). Following the execution of this algorithm, a total of 24,778 individual primary head and neck cancers were identified during the study period. These results were compared with other publications of incident

primary head and neck cancers and were found to be similar (Shack *et al.*, 2007; Purkayastha *et al.*, 2016). A further strength of this study is the large sample size of nearly 25,000 people with a primary head and neck tumour diagnosed in Scotland between the years of 1986 and 2015. Due to the long time period of this analysis, this allowed investigations into long-term survival to be conducted, which is rarely examined for people with head and neck cancer. An additional strength of this analysis is the use of the Scottish Cancer Registry data to provide a comprehensive analysis to investigate inequality in survival of people with head and neck cancer from a wide range of perspectives based on the availability of the data. This included investigations of net survival, overall survival, and disease-specific survival after one year, five years, and 10 years while also comparing survival over both follow-up time and calendar time for the whole cohort, and by sex and cancer subsites.

### 2.4.1 Conclusion

Inequalities in survival of people with head and neck cancer in Scotland are wide and have increased over time. This large population-based cancer registry analysis shows that those living in the most deprived areas have substantially worse survival prospects. This study demonstrates that inequality became worse over time for people with head and neck cancer and was at its widest in those diagnosed in the most recent period (2011-2015). This study also confirms that inequality became worse in the longer follow-up period, particularly five years and 10 years after a diagnosis of head and neck cancer.

These results demonstrate the public health and health service challenge of inequalities in survival of people with head and neck cancer over a period of nearly 30 years, the burden falling amongst those from the most deprived communities, and of a worsening picture of inequalities. This warrants further investigation into understanding the underlying causes of inequality in survival of people with head and neck cancer, with the aim of developing interventions, services, or policies to address this public health problem.

# 3 Determinants of survival in a population-based cohort study of people with head and neck cancer in Scotland (SAHNC)

## 3.1 Introduction

The SAHNC is a prospective clinical cohort study of people with head and neck cancer. The SAHNC cohort study recruited individuals who were diagnosed in Scotland under the National Health Services (NHS) between September 1999 and August 2001.

The SAHNC cohort study was set up by (what was previously known as) the Clinical Resource Audit Group (CRAG) which was part of the Scottish Executive Health Department (SEHD). The aim of the SEHD was to promote clinical effectiveness in Scotland and to facilitate and provide funding for projects such as prospective clinical cohort studies. A multidisciplinary National Steering Committee was convened to supervise the SAHNC cohort study. The group met on six occasions to organise, manage, and oversee the study over the two-year recruitment period. The aims of the study, as outlined in the *Scottish Audit of Head and Neck Cancers: A Prospective Audit* (Scottish Audit of Head and Neck Cancers Steering Group, 2004), were to:

> *"1. Identify referral patterns for people with head and neck cancers from the primary care unit to the treatment units.*
> *2. Identify variations in clinical practice in the investigation and treatment of all types of head and neck cancers in Scotland from presentation to death.*
> *3. Identify good and inappropriate practice based on clinical outcomes and identify possible reasons for these.*
> *4. Identify areas which require further investigation/action.*
> *5. Establish a central core data set which will be the basis of ongoing quality assurance for the management of head and neck tumours. This is an essential feature of clinical governance.*
> *6. Set up recommendations for the development of national treatment protocols and head and neck treatment guidelines."*

### 3.1.1 Aims and objectives

In this thesis, the SAHNC cohort study provides a unique and valuable opportunity to explore the association of various patient, tumour, and treatment factors with survival of

people with head and neck cancer in Scotland. The primary aim of Chapter 3 is to determine the factors that are independently associated with survival at three time points – one year, five years, and 12 years after a diagnosis of head and neck cancer by utilising the SAHNC cohort study of people with head and neck cancer who were diagnosed in Scotland between the years of 1999 and 2001 (Scottish Audit of Head and Neck Cancers Steering Group, 2004). The secondary aim of this chapter is to compare methods of measuring survival via the use of overall, disease-specific, and net survival estimates to provide an in-depth and comprehensive picture of the factors that are associated with survival of people with head and neck cancer in Scotland. The objectives of this chapter are to:

1. Explore the patient, tumour and treatment factors that are associated with one-year, five-year, and 12-year overall survival and disease-specific survival.
2. Compare the outcomes by the different survival metrics: overall survival, disease-specific survival, and net survival estimates.

## 3.2 Methods

### 3.2.1 Data collection

The baseline data collection for the SAHNC cohort study was undertaken between 1st September 1999 and 31st August 2001. A total of 61 hospitals contributed towards the study and were based in the health board areas of Argyll and Clyde, Ayrshire, Forth Valley, Grampian, Greater Glasgow, Highlands and Islands, Lanarkshire, Lothian, and Tayside.

Data collection proformas were produced for the study by the multidisciplinary National Steering Committee with the aim to request information from clinicians and research nurses who were based at each of the contributing hospitals. Each hospital site was provided with the proformas at baseline and was asked to complete and return them to the appointed data manager within that region. The data collection proformas that were collected contained detailed information on various patient, tumour, and treatment factors which are outlined below.

#### 3.2.1.1 Patient factors

The term “patient factors” has been used in this analysis as an overarching title for the factors under investigation which are not directly linked to any of the tumour or treatment factors (defined in detail below). The patient factors relate to all of the personal

information about the people who were recruited to the SAHNC cohort study, as well as socio-demographic information, behavioural history, and health status. The patient factors that were collected and included in this analysis included age at diagnosis, sex, socioeconomic status, smoking status, alcohol consumption, and WHO Performance Status.

Socioeconomic status was obtained by linking the SAHNC data to the area-based Carstairs and Morris 2001 Categories using the patients' home postcodes (Carstairs and Morris, 1989; Carstairs and Morris, 1990; McLoone, 2004). The categories rank the geographical areas of Scotland into one of five groups using 2001 Census data – group one represents the people from the least deprived areas and group five represents the people from the most deprived areas. The Carstairs and Morris 2001 Categories groups areas based on: (a) male unemployment rates, (b) lack of car ownership, (c) overcrowding in private households, and (d) low occupational social class.

Smoking status and alcohol consumption were recorded at baseline and no further information was documented regarding the persons behaviour while they were undergoing their treatment. Smoking status was defined on the questionnaire as: (a) current smoker (up to time of diagnosis), (b) previous smoker, and (c) never smoked. There was no further information collected in addition to this, such as pack-years. Alcohol consumption was defined on the questionnaire as: (a) current (problem) drinker, (b) previous (problem) drinker, and (c) occasional drinker/never drank.

WHO Performance Status was used to record the physical fitness of each patient at the time of their diagnosis and was defined as: (a) normal activity, (b) strenuous activity restricted, (c) up and about for more than 50% of their waking hours, (d) confined to a bed or a chair for more than 50% of their waking hours, and (e) confined to a bed or a chair for 100% of their waking hours (Oken *et al.*, 1982).

#### 3.2.1.2 Tumour factors

The term "tumour factors" has been used in this analysis as an overarching title for the factors under investigation that are directly related to the person's cancer diagnosis. The tumour factors that were collected included information on the specific anatomical site of the head and neck malignancy, the stage of the tumour, and the histological type of the tumour.

The anatomical site of the head and neck tumour was determined using ICD-10 codes (World Health Organization, 2016). This included tumours of the (a) lip (C00); (b) oral cavity (C02-C04, C05.0, C06); (c) oropharynx (C01, C05.1, C05.2, C09, C10); (d)

hypopharynx (C12, C13); (e) larynx (C32, C10.1); (f) nasopharynx, nasal cavity, and sinuses (C11, C30.0, C31); (g) salivary glands (C07, C08); (h) and other ill-defined areas of the head and neck (C14, C30.1, C41, C44, C76, C77).

The stage of each tumour was classified using the TNM Classification of Malignant Tumours from the UICC (Sobin and Wiettekind, 2002). The TNM Classification groups tumours into four categories from stage I to stage IV. Each anatomical site of the head and neck is staged individually according to the Tumour (T), Node (N) and Metastases (M) categorisation that was assigned by the treating clinician at the time of the patient's diagnosis (as outlined in section 1.3.4). The histological type of the tumour was grouped as: (a) SCC and (b) non-SCC.

#### 3.2.1.3 Treatment factors

The term "treatment factors" has been used in this analysis as an overarching title for the factors under investigation that are directly related to the patient's cancer treatment. The treatment factors that were collected included information on the type of treatment modality the people received for their diagnosis of head and neck cancer, and also the geographical location of the treating hospital.

The treatment modality groupings were decided in consultation with head and neck cancer clinicians in multidisciplinary meetings. For the purpose of this study, the treatment combinations were grouped into five categories: (a) surgery only; (b) radiotherapy only; (c) surgery combined with radiotherapy; (d) chemotherapy only, chemotherapy combined with surgery, chemotherapy combined with radiotherapy, and chemotherapy combined with both surgery and radiotherapy; or (e) no treatment.

The geographical location of the treating hospital in which the patients received their care was based on the service that was delivered in the three Scottish Cancer Networks. These were located in one of three geographic regions: (a) West of Scotland Network (WoSCAN) (Ayrshire and Arran, Forth Valley, Greater Glasgow, Clyde, and Lanarkshire), (b) South East Scotland Cancer Network (SCAN) (Borders, Dumfries and Galloway, Fife, and Lothian), or (c) North of Scotland Cancer Network (NOSCAN) (Grampian, Highland, Orkney, Shetland, Tayside, and Western Isles).

### 3.2.2 Data verification

All of the data that were collected as part of the SAHNC cohort study were cross-checked against pathology forms and radiotherapy treatment lists. The data were also cross-checked using SMR data which are routinely collected by hospital medical records

departments and logged with ISD Scotland. A quality assurance appraisal was also carried out on 10% of the data from the West of Scotland, and it was reported that the data were of “high quality”.

### 3.2.3 Data linkage

On 30th September 2013, the SAHNC data were linked to mortality records from the NRS. The records were linked using an established probability matching technique based on the Howard Newcombe principle (Newcombe *et al.*, 1959). This method matches people to NRS mortality data using their unique CHI number registered with NHS, Scotland. Information governance and approval for the mortality linkage were obtained from the NHS Privacy Advisory Committee (now known as the Public Benefits and Privacy Panel) (Appendix 3.1).

### 3.2.4 Cause of death

The causes of death of those who had died in the SAHNC cohort study were extracted from the information recorded on their death certificates that were obtained from the NRS mortality data linkage. Primary and secondary causes of death were recorded using ICD-10 codes and were grouped into three categories: (a) died from head and neck cancer, (b) died from another form of cancer, and (c) died from other non-cancer causes.

### 3.2.5 Eligible cases

Since this was a survival study, those unable to be matched to CHI numbers were excluded to enable successful data linkage of all of the patients included in this analysis to the NRS mortality records. For the successful computation of net survival, those who were unable to be matched to Carstairs 2001 Category due to invalid or missing postcode data were also excluded from the study. Due to the long-term follow-up of this study, people over the age of 85 were excluded since the life-expectancy for an 85 year old male and female in between the years of 2014 and 2016 was only 5.5 years and 6.4 years, respectively (National Records of Scotland, 2017).

### 3.2.6 Statistical analyses

Frequency tables of each of the patient, tumour, and treatment factors were produced along with the proportion of deaths that had occurred by September 2013. The primary and secondary causes of deaths for each of the patients who had died were examined via the use of frequency tables and graphically over time.

One-year, five-year, and 12-year overall survival and disease-specific survival estimates were calculated using the Kaplan-Meier method with 95% confidence intervals. Overall survival was computed using any cause of death as an event. Disease-specific survival was computed using an event for the people who had “died from head and neck cancer” which was recorded on their death certificate as their primary cause of death. In addition, Cox proportional hazards models with 95% confidence intervals that were minimally adjusted by age and sex for all-cause mortality and disease-specific mortality were produced to compare mortality across the groups of people by each patient, tumour, and treatment factor after one year, five years, and 12 years.

Mutually adjusted forward stepwise multivariate Cox proportional hazards models were used to determine which variables had an independent association with all-cause mortality and disease-specific mortality after one year, five years, and 12 years. Age at diagnosis, tumour stage and treatment modality were forced into the mutually adjusted models due to their strong association with survival in the minimally adjusted models. As a precaution, these results were checked using a backwards stepwise routine to reduce dimensionality with the aim to find a core group of variables that explained mortality. In addition, two sensitivity analyses were performed by removing those who did not receive any treatment since these people were likely to have died soon after their diagnosis of head and neck cancer. In addition, a second sensitivity analysis was performed by removing those who had cancer of the oropharynx since we did not have access to HPV information for this study.

Since this was a large study, many of the p-values were very small and therefore, chi-square statistics were added to the analysis tables for overall survival, disease-specific survival, all-cause mortality, and disease-specific mortality as a way of visually ranking the importance of each determinant in the models. All overall survival, disease-specific survival results and Cox proportional hazards models were computed using SAS Software, Version 9.4.

Additionally, net survival with 95% confidence intervals was calculated using the Pohar-Perme method (Pohar Perme *et al.*, 2012; Pohar Perme *et al.*, 2016) by using lifetables that were standardised by calendar year, age, sex, and Carstairs 2001 Category. The lifetables were provided by the Cancer Survival Group at the LSHTM (Cancer Survival Group, 2019). All of the net survival results and the graphs for the estimated net survival function were computed using the *stns* command and the *stns graph* command in Stata, version 14 (Clerc-Urmes *et al.*, 2014; StataCorp., 2017).

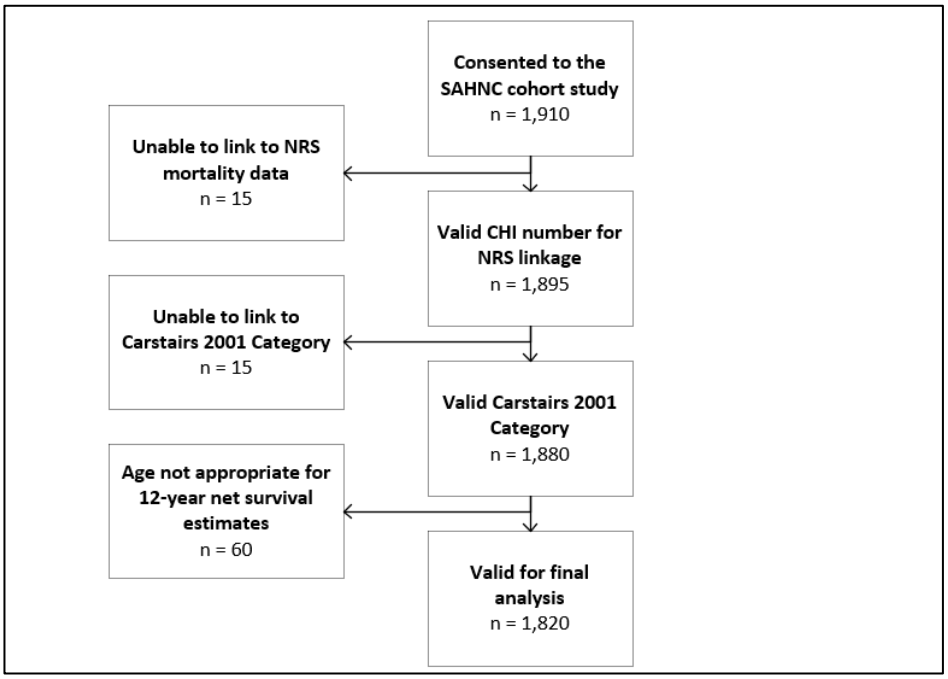
# 3.3 Results

## 3.3.1 Eligible cases

A total of 1,910 people with head and neck cancer who were diagnosed between 1st September 1999 and 31st August 2001 were recruited to the SAHNC cohort study. This accounted for 77% of all of the head and neck cancer cases that were diagnosed and recorded in the Scottish Cancer Registry during the same period (Scottish Audit of Head and Neck Cancers Steering Group, 2004).

Figure 3.1 outlines the number of people that were excluded from the cohort for the purpose of this analysis. Of the 1,910 people who were recruited to the SAHNC cohort study, 1,985 were successfully linked to the NRS mortality data – 15 people were unable to be matched to the mortality data due to having an invalid CHI number. A further 15 people were excluded as they were unable to be matched to the Carstairs 2001 Category due to having an invalid or a missing postcode. In addition, 60 patients over the age of 85 were also excluded due to the low life expectancy of people of this age. The remaining 1,820 patients were eligible to be included in this study.

**Figure 3.1 – Flow chart of eligible cases included in the SAHNC cohort study**




## 3.3.2 Baseline characteristics

The numbers and proportions of the baseline patient, tumour, and treatment factors are displayed in Table 3.1 to Table 3.3, along with the proportions of deaths that had occurred by September 2013 per group within each variable.

### 3.3.2.1 Description of the patient factors

The patients' ages at diagnosis ranged from 13 to 85, with a median age of 63 years. There was a ratio of 2.5:1 of males to females, and a total of 937 (51.5%) individuals were from the two most deprived Carstairs 2001 Category in Scotland. There were 1,539 (84.6%) people recorded as current or previous smokers at the time of their diagnosis, compared with only 221 (12.1%) recorded as never having smoked in their lifetime. A total of 708 (39.0%) patients were recorded as having had a current or previous problem with their levels of alcohol consumption compared with 891 (49.0%) who were recoded as either being an occasional drinker or never having drank alcohol. There were 825 (45.3%) people who had a normal WHO Performance Status at the time of their diagnosis, and none of the patients in the cohort were confined to a bed or a chair for 100% of their waking hours.

**Table 3.1 – Baseline characteristics and total number of deaths per determinant by September 2013 for each patient factor**

| Variable | Frequency N (Column %) | Died by September 2013 N (Row %) |
|---|---|---|
| **Total** | 1,820 (100.0%) | 1,384 (76.0%) |
| **Age at diagnosis** | | |
| Less than 45 | 99 (5.4%) | 38 (38.4%) |
| 45 to 54 | 288 (15.8%) | 183 (63.5%) |
| 55 to 64 | 592 (32.5%) | 426 (72.0%) |
| 65 to 74 | 551 (30.3%) | 470 (85.3%) |
| 75 and over | 290 (15.9%) | 267 (92.1%) |
| **Sex** | | |
| Male | 1,300 (71.4%) | 1,000 (76.9%) |
| Female | 520 (28.6%) | 384 (73.9%) |
| **Carstairs 2001 Category** | | |
| 1 (Least deprived) | 241 (13.2%) | 183 (75.9%) |
| 2 | 317 (17.4%) | 226 (71.3%) |
| 3 | 325 (17.9%) | 248 (76.3%) |
| 4 | 409 (22.5%) | 311 (76.0%) |
| 5 (Most deprived) | 528 (29.0%) | 416 (78.8%) |
| **Smoking behaviour** | | |
| Never smoked | 221 (12.1%) | 133 (60.2%) |
| Previous smoker | 405 (22.3%) | 301 (74.3%) |
| Current smoker | 1,134 (62.3%) | 906 (79.9%) |
| Not recorded | 60 (3.3%) | 44 (73.3%) |
| **Alcohol consumption** | | |
| Never/occasionally drank | 891 (49.0%) | 629 (70.6%) |
| Previous problem drinker | 212 (11.7%) | 180 (84.9%) |
| Current problem drinker | 496 (27.3%) | 410 (82.7%) |
| Not recorded | 221 (12.1%) | 165 (74.7%) |
| **WHO Performance Status** | | |
| Normal activity | 825 (45.3%) | 511 (61.9%) |
| Strenuous activity restricted | 465 (25.6%) | 401 (86.2%) |
| Up and about >50% | 137 (7.5%) | 130 (94.9%) |
| Confined to bed/chair >50% | 97 (5.3%) | 96 (99.0%) |
| Not recorded | 296 (16.3%) | 246 (83.1%) |

### 3.3.2.2 Description of the tumour factors

Those who had cancer of the larynx represented the largest group of patients with head and neck cancer at 32.1% (n = 584). This was followed by 28.8% (n = 506) of people with

cancer of the oral cavity, and the lowest prevalence of head and neck cancer was those with cancer of the nasal cavity (n = 85/4.7%) or lip (n = 85/4.7%). Most of the patients were diagnosed with stage IV tumours which represented 662 (36.4%) cases, and 1,585 (87.0%) had a tumour which was of SCC histology.

**Table 3.2 – Baseline characteristics and total number of deaths per determinant by September 2013 for each tumour factor**

| Variable | Frequency N (Column %) | Died by September 2013 N (Row %) |
|---|---|---|
| **Anatomical site** | | |
| Larynx | 584 (32.1%) | 427 (73.1%) |
| Oral cavity | 506 (28.8%) | 395 (78.1%) |
| Oropharynx | 323 (17.8%) | 261 (80.8%) |
| Hypopharynx | 119 (6.5%) | 112 (94.1%) |
| Nasal cavity | 85 (4.7%) | 64 (75.3%) |
| Lip | 85 (4.7%) | 40 (47.1%) |
| Other/salivary gland | 118 (6.5%) | 85 (72.0%) |
| **Tumour stage** | | |
| I | 383 (21.0%) | 218 (56.9%) |
| II | 369 (20.3%) | 266 (72.1%) |
| III | 273 (15.0%) | 213 (78.0%) |
| IV | 662 (36.4%) | 586 (88.5%) |
| Unknown | 133 (7.3%) | 101 (75.9%) |
| **Histology** | | |
| SCC | 1,585 (87.1%) | 1,209 (76.3%) |
| Non-SCC | 235 (12.9%) | 175 (74.5%) |

### 3.3.2.3 Description of the treatment factors

The most common treatment modality received was “radiotherapy only,” by which a total 507 (27.9%) patients were treated. This was followed by “surgery only,” by which 477 (26.2%) people were treated, and a combination of surgery and radiotherapy, by which 458 (25.2%) individuals were treated. A total of 1,001 (55.0%) people were treated within the West of Scotland (WoSCAN) cancer network, 440 (24.2%) were treated in the East of Scotland (SCAN) cancer network, and 379 (20.8%) were treated in the North of Scotland (NOSCAN) cancer network.

**Table 3.3 – Baseline characteristics and total number of deaths per determinant by September 2013 for each treatment factor**

| Variable | Frequency N (Column %) | Died by September 2013 N (Row %) |
|---|---|---|
| **Treatment modality** | | |
| Surgery only | 477 (26.2%) | 164 (34.4%) |
| Radiotherapy only | 507 (27.9%) | 130 (25.6%) |
| Surgery and radiotherapy | 458 (25.2%) | 98 (21.4%) |
| Surgery, radiotherapy, and chemotherapy | 65 (3.6%) | 20 (4.6%) |
| Radiotherapy and chemotherapy | 143 (7.9%) | 21 (4.8%) |
| Chemotherapy +/- surgery | 41 (2.3%) | 1 (0.2%) |
| No treatment | 129 (7.1%) | 2 (1.6%) |
| **Network/region** | | |
| WoSCAN (West of Scotland) | 1,001 (55.0%) | 787 (78.6%) |
| SCAN (East of Scotland) | 440 (24.2%) | 316 (71.8%) |
| NOSCAN (North of Scotland) | 379 (20.8%) | 281 (74.1%) |

#### 3.3.2.4 Death rates by September 2013

A total of 1,384 (76.0%) deaths had occurred by September 2013 when the SAHNC data was linked to the NRS mortality data (Table 3.1). The patients were more likely to have died if they were older, from more deprived regions, were current or previous smokers, currently or previously drank alcohol to problematic levels, or had worse WHO Performance Status (Table 3.1). They were also more likely to die if they had cancers of the hypopharynx or oropharynx, had tumours of higher stage (Table 3.2), or were either treated with a treatment modality that was combined with chemotherapy or received no treatment at all (Table 3.3). There was a slight difference in the proportions of people who died across the three Scottish Cancer Networks, whereby those from the West of Scotland (WoSCAN) network had a higher rate of death (n = 787/78.6%) compared to those who were treated in the other two Scottish Cancer Networks (SCAN = 316/71.8%, NOSCAN = 281/74.1%). Interestingly, there was no substantial difference in the proportions of deaths between males and females by September 2013 (Table 3.1).

### 3.3.3 Cause of death

Table 3.4 displays a cross-tabulation of the primary and secondary causes of death of the 1,384 (76.0%) patients who had died during the follow-up period to September 2013. A total of 677 (48.9%) primary causes of death were as a result of head and neck cancer. Of the 677 people whose primary cause of death was as a result of head and neck cancer, a total of 658 (97.2%) individuals also had “head and neck cancer” recorded as their secondary cause of death on their death certificates. The primary cause of 308 (22.3%) deaths was as a result of “other types of cancers”; however, 79 (25.6%) of these people had “head and neck cancer” recorded as their secondary cause of death, which suggests that the underlying cause of their death may have been as a result of head and neck cancer. The primary cause of 399 (38.8%) deaths was as a result of “other non-cancer” causes of death, however 83 (20.8%) of these individuals had “head and neck cancer” recorded as their secondary cause of death, which also suggests that the underlying cause of their death may have been as a result of head and neck cancer. Thus, a total of 839 (60.6%) of deaths could have been in some way related to the patients’ head and neck cancer, but it was not recorded as a primary cause of death on their death certificate.

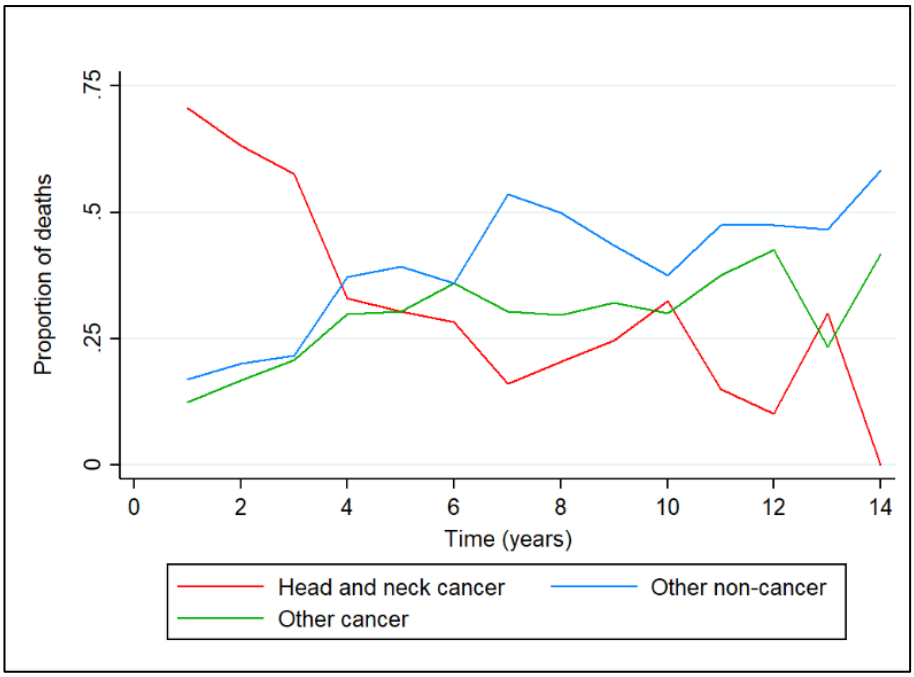
Figure 3.2 displays the proportions of primary causes of death as a result of head and neck cancer, other types of cancer, and other types of deaths per year of follow-up until September 2013. Deaths resulting from head and neck cancer represented the highest proportion of deaths in the first two years after diagnosis. However, after four years, deaths from other causes, represented a higher proportion of deaths than those from

head and neck cancer. By September 2013, the most common cause of death was “death from other non-cancer causes”.

**Table 3.4 – Primary and secondary causes of death by September 2013**

| | **Primary cause of death by September 2013 N (Col. %)** | | | |
|---|---|---|---|---|
| **Secondary cause of death by September 2013** | Head and neck cancer | Other types of cancer | Other non-cancer | **Total** |
| Head and neck cancer | 658 (97.2%) | 79 (25.6%) | 83 (20.8%) | **820 (59.2%)** |
| Other types of cancer | 1 (0.1%) | 224 (72.7%) | 13 (3.3%) | **238 (17.2%)** |
| Other non-cancer | 18 (2.7%) | 5 (1.6%) | 303 (75.9%) | **326 (23.6%)** |
| **Total, N (row %)** | **677 (48.9%)** | **308 (22.3%)** | **399 (28.8%)** | **1,384 (100.0%)** |

**Figure 3.2 – Proportions of deaths per year by head and neck cancer, other cancer, and other types of deaths**



### 3.3.4 Overall survival, disease-specific survival, and net survival results

Overall survival, disease-specific survival, and net survival estimates after one year, five years, and 12 years of diagnosis are displayed in Table 3.5 to Table 3.7 on Page 116 to Page 118. The Kaplan-Meier plots for the results of overall survival and disease-specific survival, and the graph for the estimated net survival function for the whole cohort are displayed in Figure 3.3 to Figure 3.5. Overall survival after one year, five years, and 12 years was 76.0% (95% CI 74.0% to 77.9%), 46.1% (95% CI 43.8% to 48.4%), and 26.3% (95% CI 24.3% to 28.3%), respectively, while disease-specific survival was 82.3% (95% CI 80.4% to 84.0%), 64.1% (95% CI 61.7% to 66.4%), and 56.9% (95% CI 54.3% to 59.4%), respectively. One-year, five-year, and 12-year net survival estimates were 78.3% (95% CI 76.2% to 80.3%), 53.8% (95% CI 51.1% to 56.5%), and 41.4% (95% CI 37.6% to 45.1%), respectively. Results for disease-specific survival were higher than the overall survival results at all three time points. This observation would be expected since disease-specific survival eliminates other causes of death that are not related to head and neck cancer. Over time, overall survival and disease-specific survival became further apart, which demonstrates the high proportion of deaths that were caused by disease-specific factors in the short-term follow-up, and the increase in other causes of death as the follow-up period continued. The net survival results were also higher than those for overall survival after five years and 12 years but were lower than the results for disease-specific survival, suggesting that disease-specific survival does not fully capture all disease-related deaths, particularly in the long-term.

**Figure 3.3 – Kaplan-Meier plot for overall survival for the whole cohort**

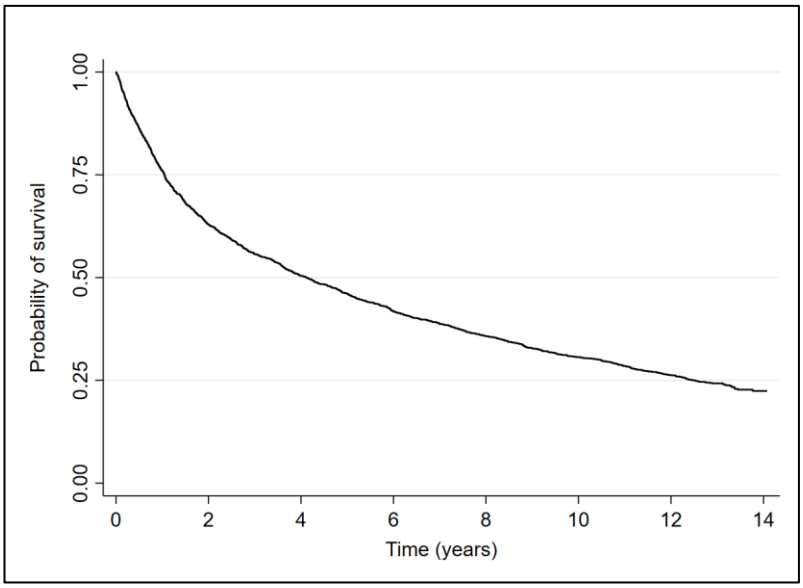



**Figure 3.4 – Kaplan-Meier plot for disease-specific survival for the whole cohort**

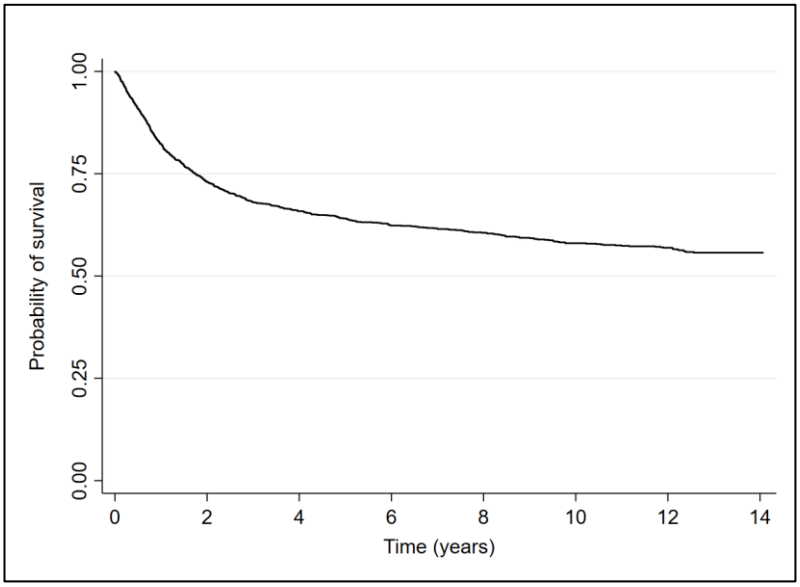
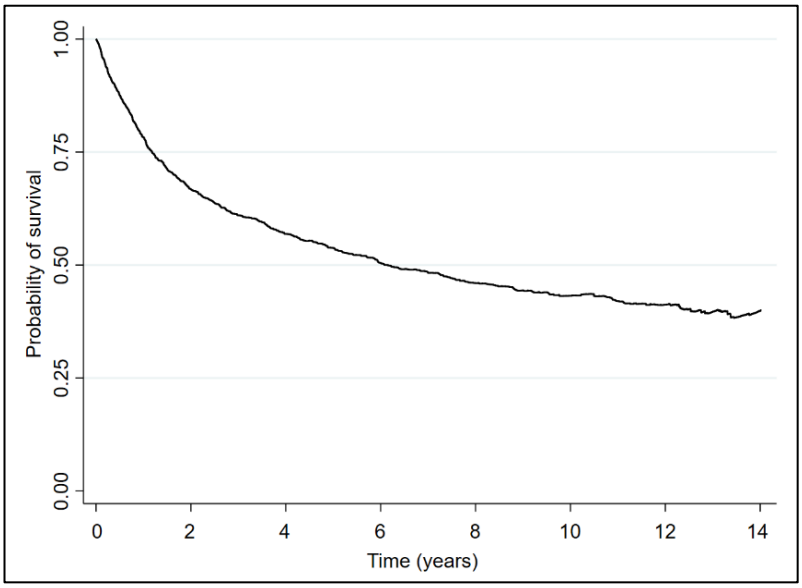



**Figure 3.5 – Graph of the estimated net survival function for the whole cohort**



#### 3.3.4.1 Overall survival, disease-specific survival, and net survival by patient factors

***Age at diagnosis***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the age at diagnosis of the patients that were recruited to the SAHNC cohort are displayed in Figure 3.6 to Figure 3.8. As the age of the patients at diagnosis increased, the overall survival, disease-specific survival, and net survival results decreased. After 12 years, the survival between those who were less than 45 years old and those who were aged 75 and over reduced from 62.6% (95% CI 52.3% to 71.3%) to 10.3% (95% CI 7.2% to 14.2%) for overall survival, from 72.1% (95% CI 61.7% to 80.1%) to 45.3% (95% CI 37.9% to 52.4%) for disease-specific survival, and from 64.9% (95% CI 55.0% to 74.7%) to 43.2 (95% CI 28.0% to 58.4%) for net survival. The overall survival, disease-specific survival, and net survival results were similar for those who were less than 45 years old, suggesting that these people were more likely to have died as a result of their head and neck cancer. However, as the patients age increased, the differences between overall survival, disease-specific survival and net survival became clearer, suggesting that those who were older were more likely to die of other causes that were not related to their head and neck cancer. This was particularly noticeable between the survival results for people who were aged 75 and over, with 12-year overall survival, disease-specific survival, and net survival results of 10.3% (95% CI 14.9% to 21.3%), 54.2% (95% CI 49.1% to 59.1%), and 35.8% (95% CI 29.5% to 58.4%), respectively.

**Figure 3.6 – Kaplan-Meier plot for overall survival by age group**

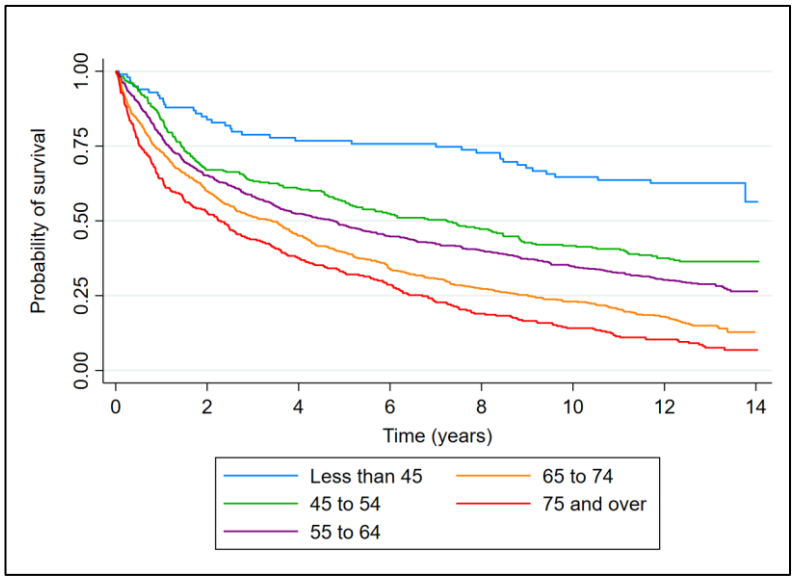



**Figure 3.7 – Kaplan-Meier plot for disease-specific survival by age group**

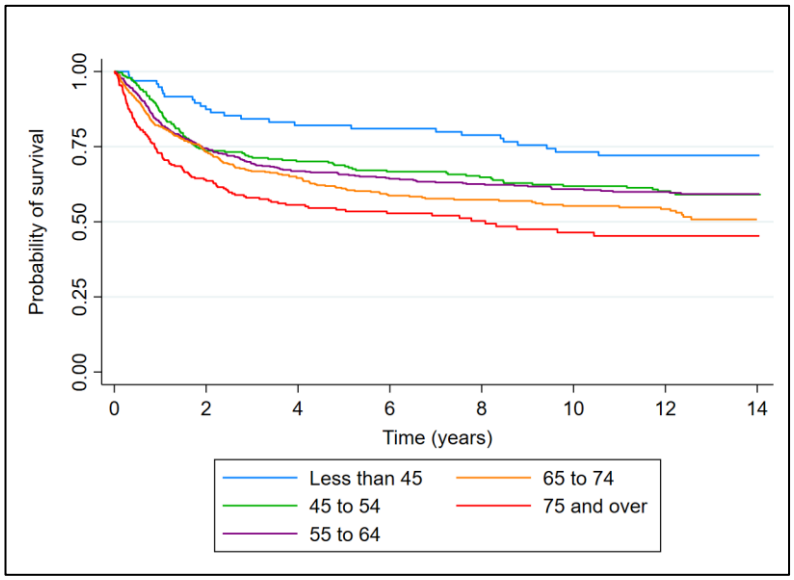
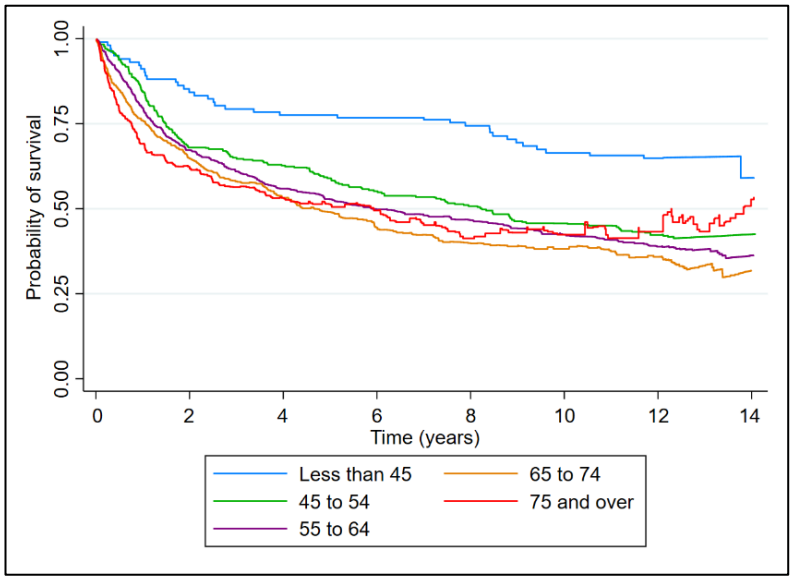



**Figure 3.8 – Graph of the estimated net survival function by age group**



***Sex***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the sex of the patients in the SAHNC cohort are displayed in Figure 3.9 to Figure 3.11. After one year, males and females had similar survival estimates at 76.2% (95% CI 73.7% to 78.4%) and 75.8% (95% CI 71.9% to 79.2%) for overall survival, 82.0% (95% CI 79.8% to 84.1%) and 82.8% (95% CI 79.2% to 85.9%) for disease-specific survival, and 78.5% (95% CI 76.1% to 80.9%) and 77.6% (95% CI 73.8% to 81.4%) for net survival, respectively. By five and 12 years, there were small differences between overall survival and disease-specific survival for males and females whereby after 12 years, males had a slightly lower overall survival of 24.9% (95% CI 22.6% to 27.3%) compared to females who had an overall survival of 29.6% (95% CI 25.8% to 33.6%). Likewise, after 12 years the males also had a lower disease-specific survival of 55.3% (95% CI 52.2% to 58.3%) compared to the females who had a disease-specific survival of 60.9% (95% CI 56.0% to 65.5%). However, 12-year net survival results for males and females were similar at 40.5% (95% CI 36.2% to 44.8%) and 43.0% (95% CI 36.1% to 49.8%), respectively.

**Figure 3.9 – Kaplan-Meier plot for overall survival by sex**

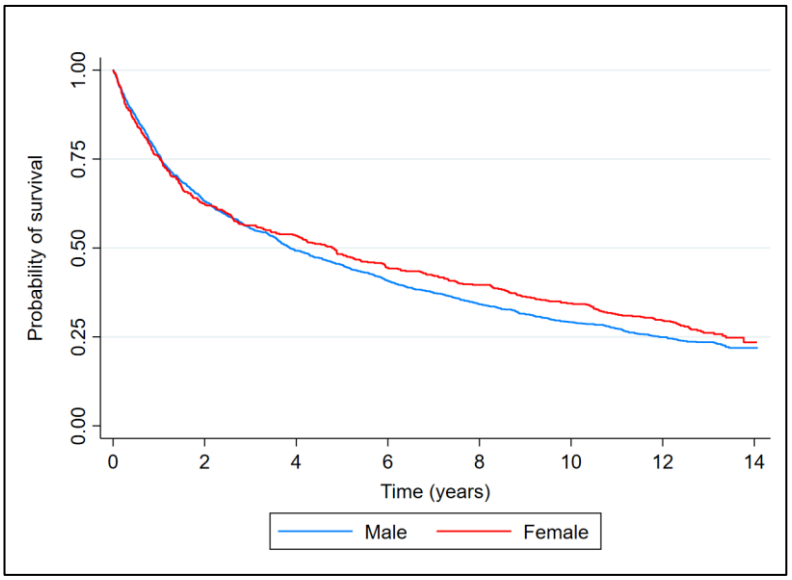



**Figure 3.10 – Kaplan-Meier plot for disease-specific survival by sex**

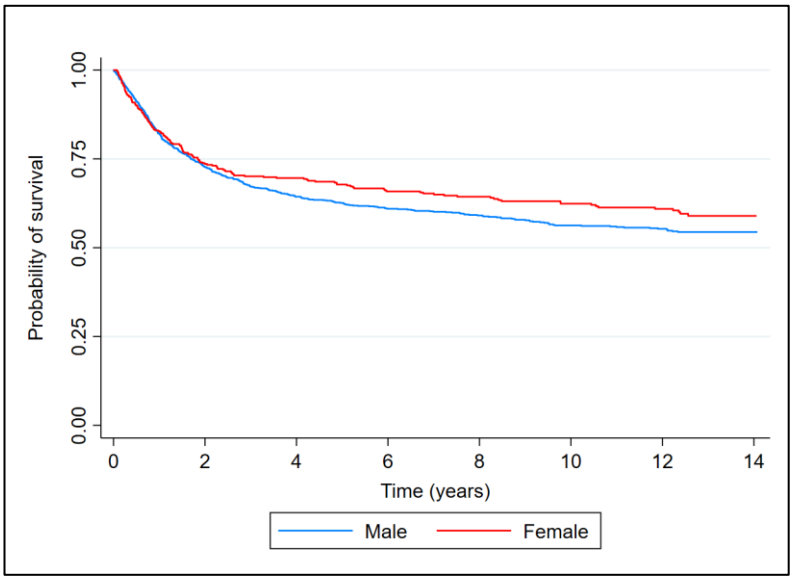
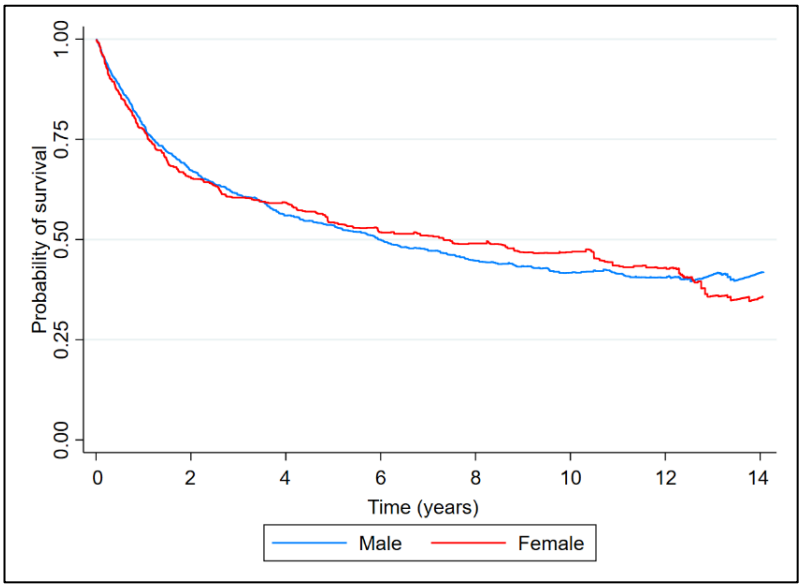



**Figure 3.11 – Graph of the estimated net survival function by sex**



***Carstairs 2001 Category***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for Carstairs 2001 Category are displayed in Figure 3.12 to Figure 3.14. Compared to the individuals who were from the least deprived Carstairs 2001 Category, after one year, those from the most deprived group had a substantially lower overall survival, disease-specific survival, and net survival of 71.8% (95% CI 67.7%, to 75.4%), 79.1% (95% CI 75.2%, to 82.4%), and 73.7% (95% CI 69.7% to 77.6%), respectively. In contrast, the people who were in the least deprived group had overall survival, disease-specific survival, and net survival results of 83.4% (95% CI 78.1% to 87.5%), 88.8% (95% CI 83.9% to 92.2%), and 86.1% (95% CI 81.3% to 91.0%), respectively. By five years and 12 years, the people from the most deprived area continued to have the lowest overall survival, disease-specific survival, and net survival, which after 12 years was 22.9% (95% CI 19.4% to 26.5%), 51.1% (95% CI 46.0% to 55.9%), and 35.7% (95% CI 29.6% to 58.5%), respectively. The people in the second least deprived group had the highest overall survival and disease-specific survival results which after 12 years were 30.6% (95% CI 25.6% to 35.7%) and 65.6% (95% CI 59.6% to 70.9%), respectively. However, the inequality by net survival after 12 years was not as well defined since those in the second most deprived group had the highest net survival result of 46.6% (95% CI 38.4% to 41.8%).

**Figure 3.12 – Kaplan-Meier plot for overall survival by Carstairs 2001 Category**

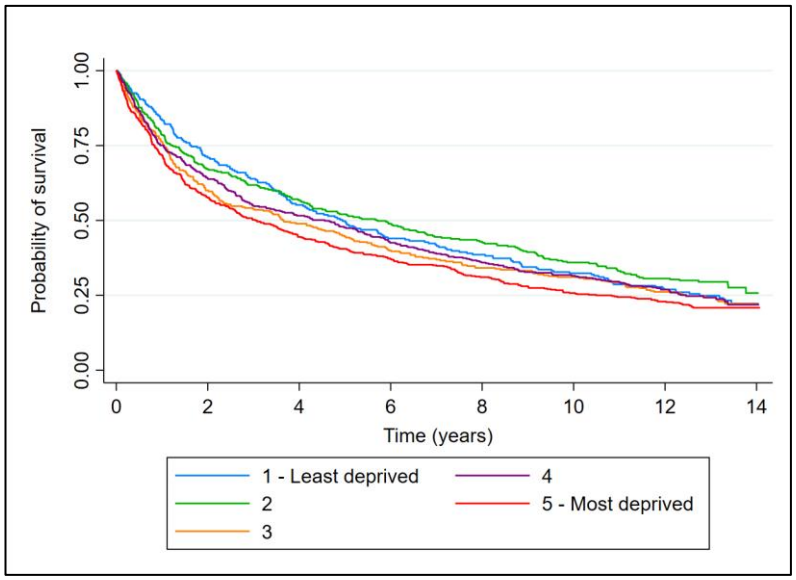



**Figure 3.13 – Kaplan-Meier plot for disease-specific survival by Carstairs 2001 Category**

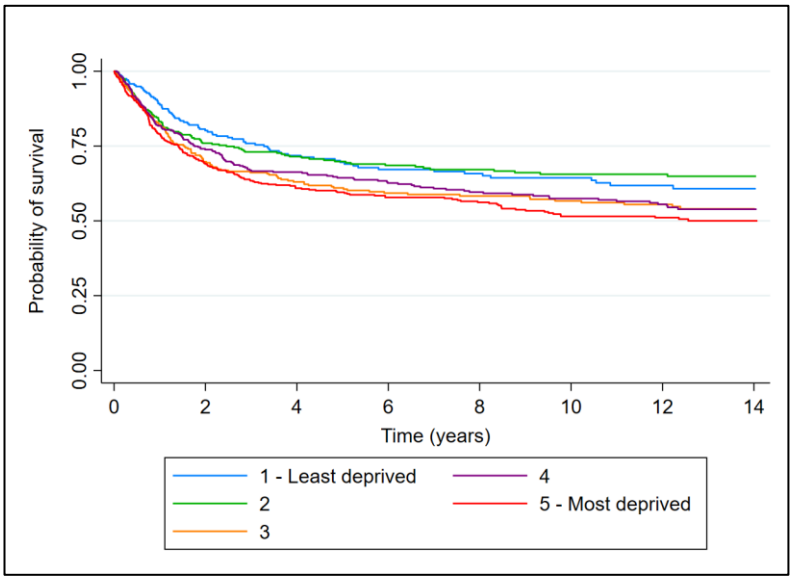
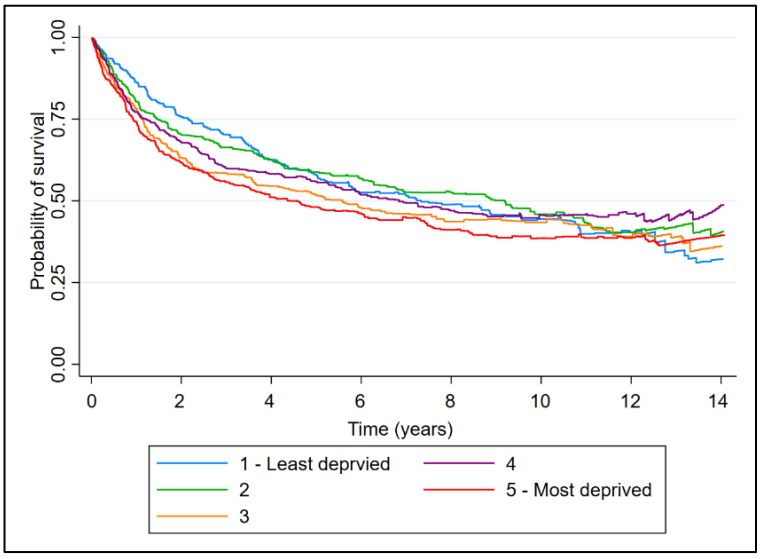



**Figure 3.14 – Graph of the estimated net survival function by Carstairs 2001 Category**



***Smoking behaviour***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the smoking behaviour that the patients had at the time of their diagnosis are displayed in Figure 3.15 to Figure 3.17. Those who had never smoked had 12-year overall survival, disease-specific survival, and net survival results of 43.9% (95% CI 37.3% to 50.3%), 66.9% (95% CI 59.8% to 73.0%), and 70.6% (95% CI 57.1% to 84.1%), respectively. The difference between these results suggests that the people who had never smoked were more likely to die of other causes that were not related to their head and neck cancer. In contrast, the individuals who were current smokers had a substantially lower overall survival, disease-specific survival, and net survival result at all three time points, which after 12 years was 22.3% (95% CI 19.9% to 24.8%), 53.2% (95% CI 49.9% to 56.5%), and 32.4% (95% CI 28.6% to 36.2%), respectively. The substantial difference in overall survival and disease-specific survival, suggests that those who were current smokers may be dying as an indirect result of their head and neck cancer which is not being captured by the disease-specific results. Interestingly, the patients who were previous smokers had similar disease-specific survival and net survival results to those who were never smokers after one year and five years. After 12 years, the results for disease-specific survival remained similar to those after five years. However, the net survival results for those who had never smoked were substantially higher than that of the previous smokers at 70.6% (95% CI 57.1% to 84.1%) and 49.9% (95% CI 40.5% to 59.2%), respectively. This substantial difference suggests that in the long-term the patients who previously smoked are dying as an indirect result of their head and neck cancer, which is not being reflected on their cause of death certificates.

**Figure 3.15 – Kaplan-Meier plot for overall survival by smoking behaviour**

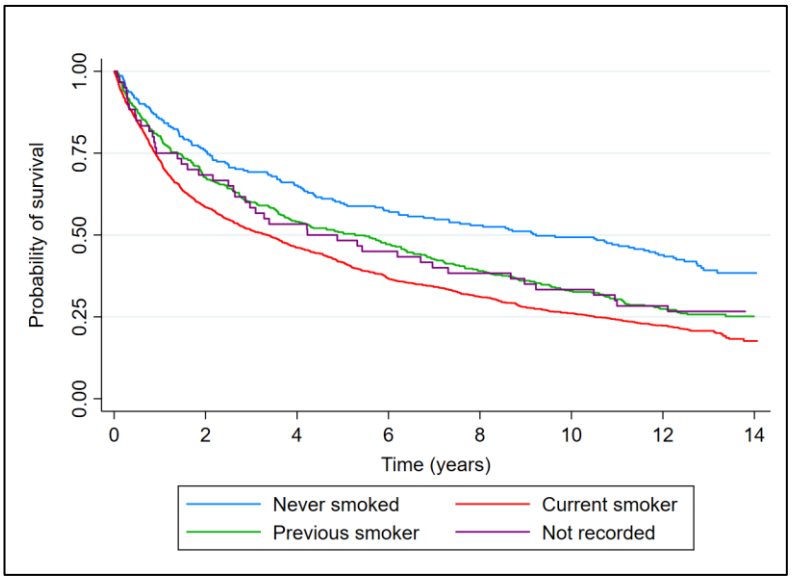



**Figure 3.16 – Kaplan-Meier plot for disease-specific survival by smoking behaviour**

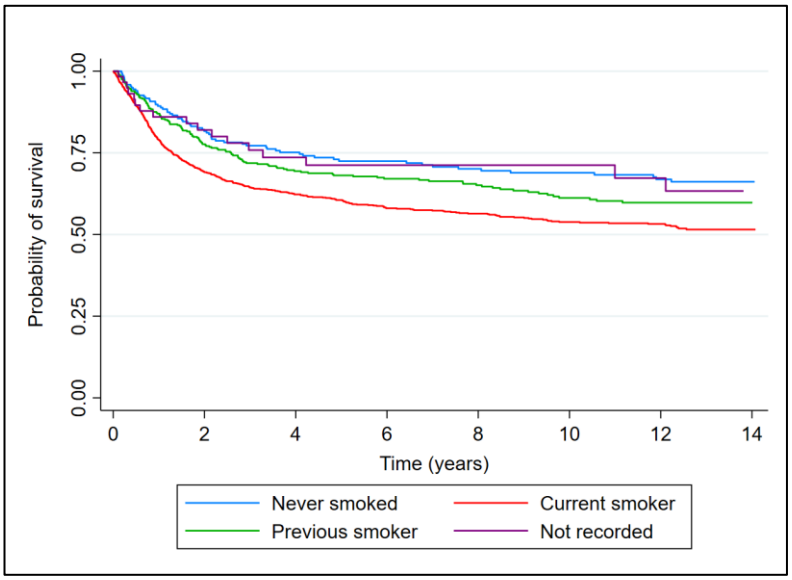
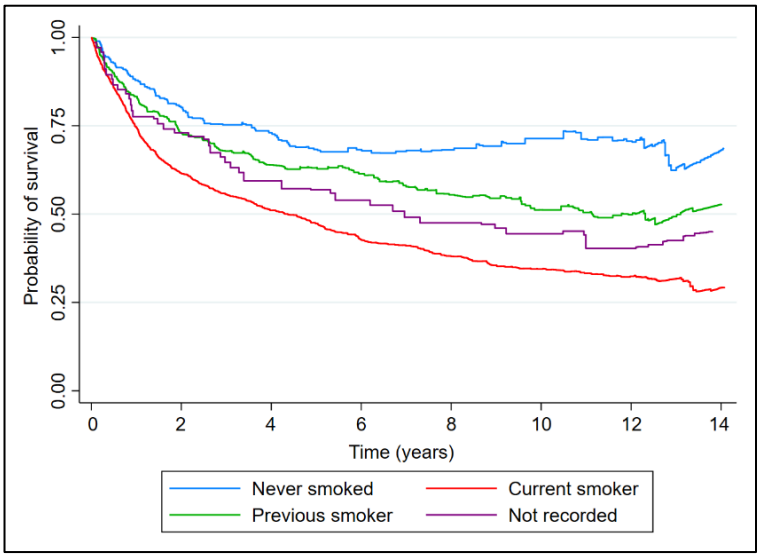



**Figure 3.17 – Graph of the estimated net survival function by smoking behaviour**



### *Alcohol consumption*

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the level of alcohol that the patients had consumed before their diagnosis are displayed in Figure 3.18 to Figure 3.20. The people who had a current problem with their levels of alcohol consumption obtained similar overall survival, disease-specific survival, and net survival results as those who were reported having had a previous problem with their alcohol consumption at all three time points. At 12 years, for those who had a current problem with their alcohol consumption and for those who had a previous problem with their alcohol consumption, their results were 18.2% (95% CI 14.9% to 21.7%) and 17.0% (95% CI 12.3% to 22.3%) for overall survival, respectively, 45.9% (95% CI 40.5% to 51.1%) and 49.7% (95% CI 42.1% to 56.9%) for disease-specific survival, respectively, and 23.5% (95% CI 18.6% to 28.4%) and 23.4% (95% CI 15.9% to 30.9%) for net survival, respectively. The individuals who reported as never having drunk alcohol or who occasionally drank alcohol consistently had a substantially higher overall survival, disease-specific survival, and net survival results than those who drank to problematic levels at all three time points. These results were 32.3% (95% CI 29.3% to 35.4%), 62.1% (95% CI 58.5% to 65.5%), and 70.6% (95% CI 57.1% to 84.1%) for overall survival, disease-specific survival, and net survival results after 12 years, respectively. The substantial difference between overall survival and disease-specific survival suggests that the patients who never or occasionally drank were likely to have died from other causes that were not related to their head and neck cancer. In addition, the results from the Kaplan-Meier plots indicate that those who did not report their levels of alcohol consumption could also have been never or occasional drinkers.

**Figure 3.18 – Kaplan-Meier plot for overall survival by alcohol consumption**

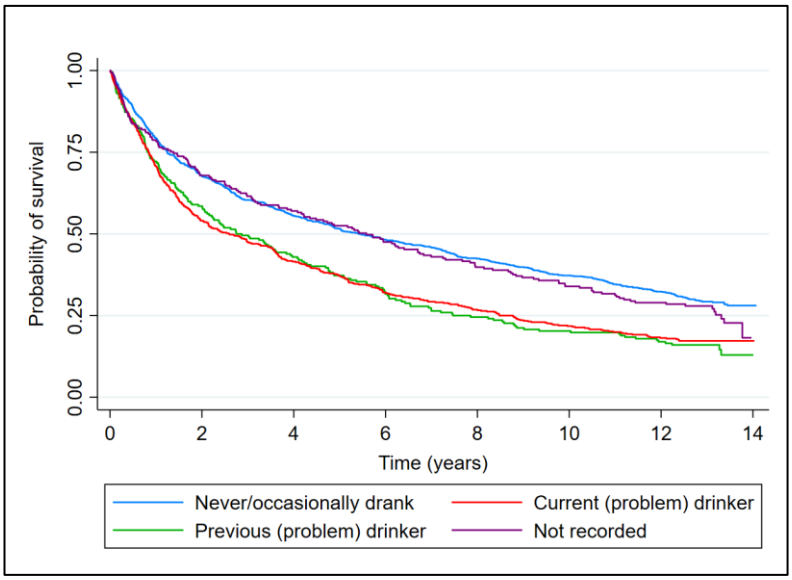



**Figure 3.19 – Kaplan-Meier plot for disease-specific survival by alcohol consumption**

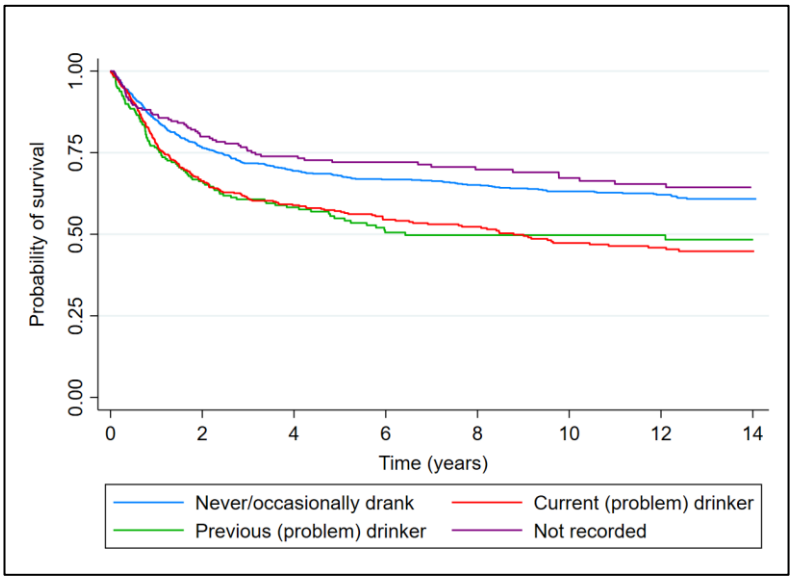
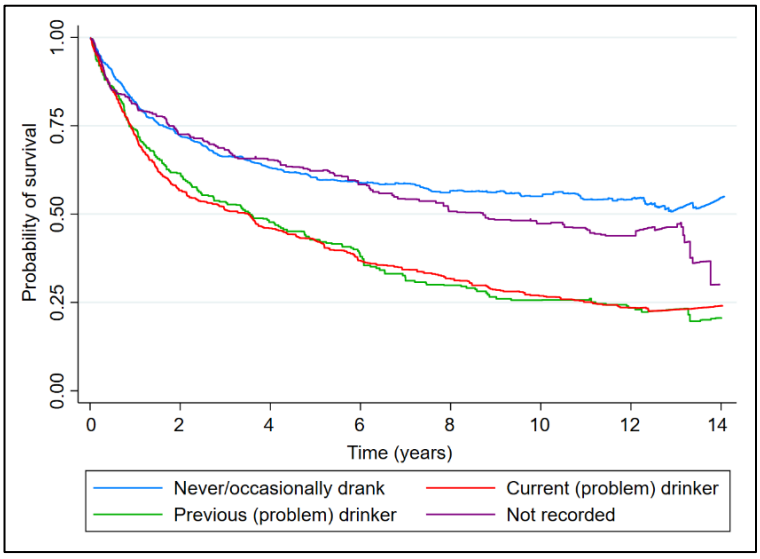



**Figure 3.20 – Graph of the estimated net survival function by alcohol consumption**



***WHO Performance Status***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the WHO Performance Status that the patients experienced at the time of their diagnosis are displayed in Figure 3.21 to Figure 3.23. There was a clear and prominent gradient observed by WHO Performance Status – as the patient's WHO Performance Statuses decreased, the overall survival, disease-specific survival, and net survival also decreased at all three time points. This was particularly noticeable after 12 years by which time the people who had normal activity levels at diagnosis compared to those who had restricted strenuous activity levels at diagnosis had an overall survival estimate of 40.6% (95% CI 37.2% to 43.9%) and 16.1% (95% CI 13.0% to 19.6%), respectively. The results for the patients with normal activity levels at diagnosis compared to those who had restricted strenuous activity levels at diagnosis had disease-specific survival and net survival results of 70.4% (95% CI 66.8% to 73.7%) and 49.7% (95% CI 44.1% to 55.0%), and 59.0% (95% CI 53.5% to 64.9%) and 33.1% (95% CI 26.7% to 41.1%), respectively. These results suggest that a small amount of restriction to a person's activity levels had a substantial negative effect on their outcome following a diagnosis of head and neck cancer.

**Figure 3.21 – Kaplan-Meier plot for overall survival by WHO Performance Status**

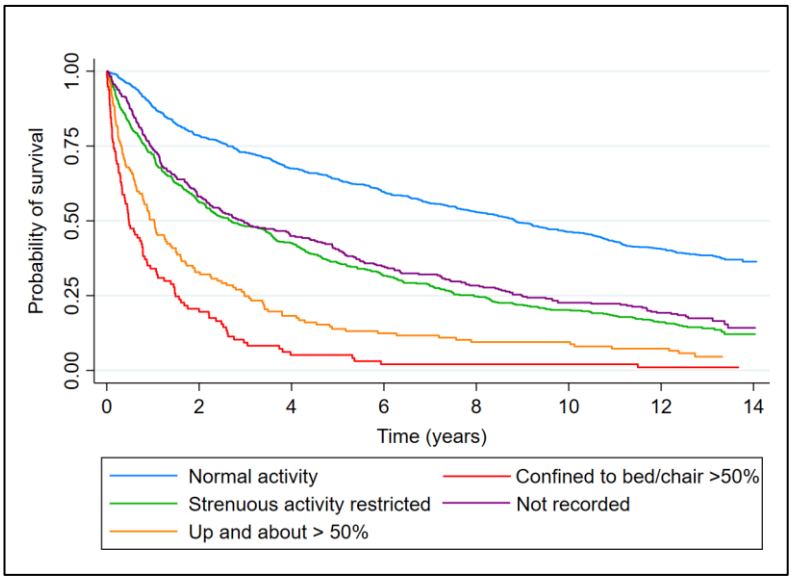



**Figure 3.22 – Kaplan-Meier plot for disease-specific survival by WHO Performance Status**

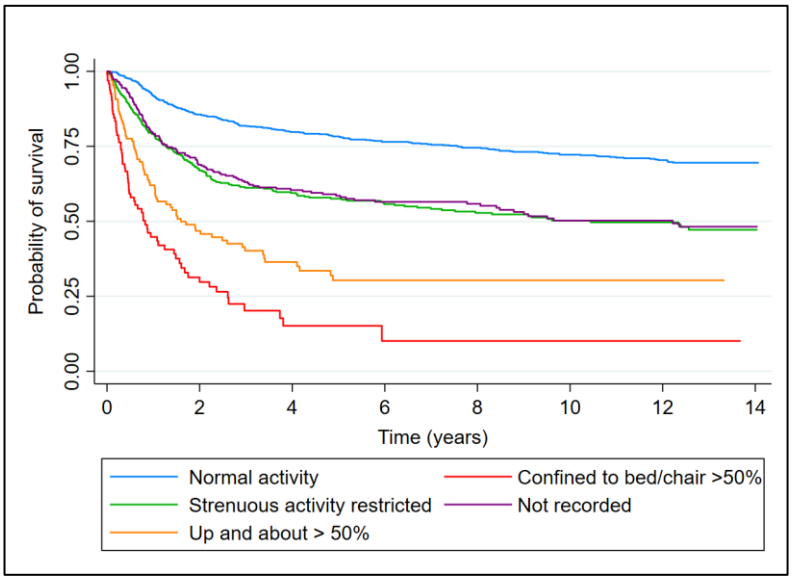
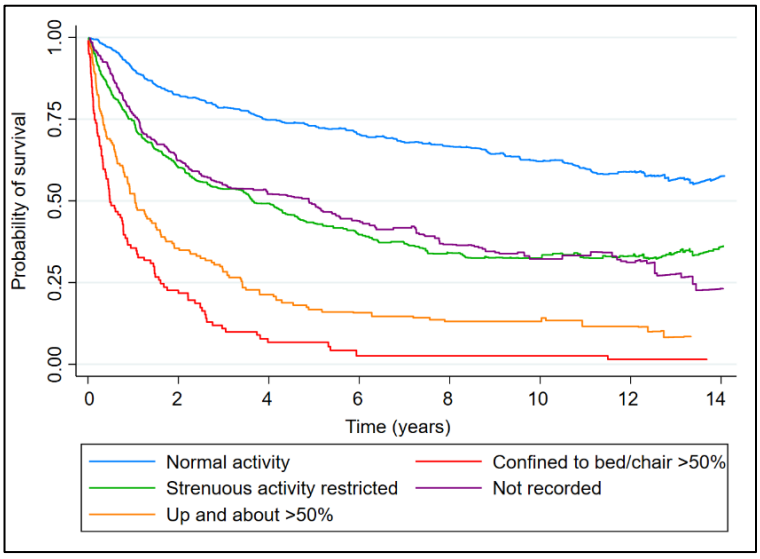



**Figure 3.23 – Graph of the estimated net survival function by WHO Performance Status**



#### 3.3.4.2 Overall survival, disease-specific survival, and net survival by tumour factors

***Anatomical site***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the anatomical site of the patients' tumour are displayed in Figure 3.24 to Figure 3.26. Clear variations in overall survival, disease-specific survival, and net survival results were seen across the anatomical sites after one year, five years, and 12 years. The highest overall survival, disease-specific survival, and net survival was from people with cancers of the lip at 56.5% (95% CI 45.3% to 66.2%), 91.3% (95% CI 81.5% to 96.0%), and 98.3% (95% CI 76.3% to 120.2%) after 12 years, respectively. The results for disease-specific and net survival for individuals with cancer of the lip were substantially higher than the results for overall survival, which suggests that very few deaths of those with cancer of the lip occur as a result of their disease. The lowest overall survival, disease-specific survival, and net survival was among people with cancers of the hypopharynx at 9.2% (95% CI 4.9% to 15.3%), 23.6% (95% CI 14.5% to 33.9%), and 15.8% (95% CI 7.0% to 24.7%) at 12 years, respectively. The results for overall and net survival were similar, suggesting that these people are more likely to die as a result of their head and neck cancer. However, the disease-specific survival results were slightly higher, which suggests that disease-specific survival does not fully capture the deaths as a result of hypopharyngeal cancer. Individuals with cancer of the oropharynx did not demonstrate the obvious survival advantage that is usually seen in this cancer subgroup from HPV positivity and had a 12-year overall survival of 21.4% (95% CI 17.1% to 26.0%), which was lower than the other two major head and neck groups of the oral cavity and larynx.

**Figure 3.24 – Kaplan-Meier plot for overall survival by anatomical site**

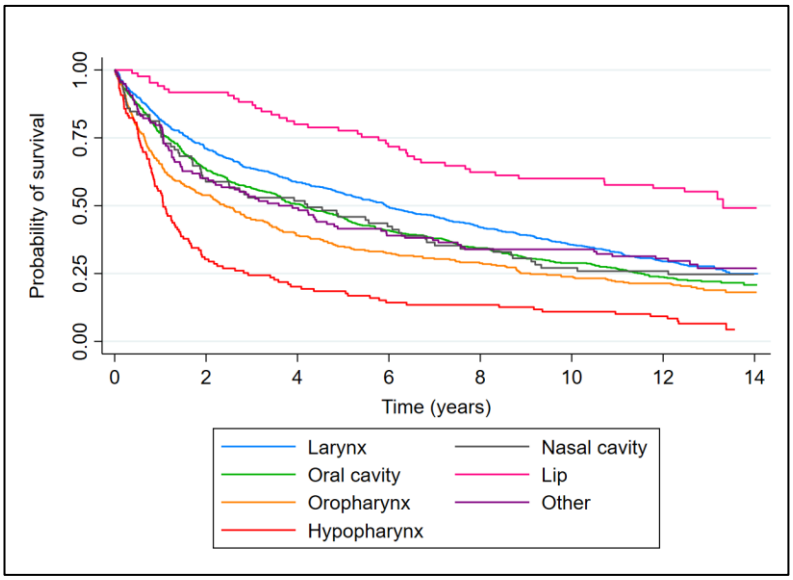



**Figure 3.25 – Kaplan-Meier plot for disease-specific survival by anatomical site**

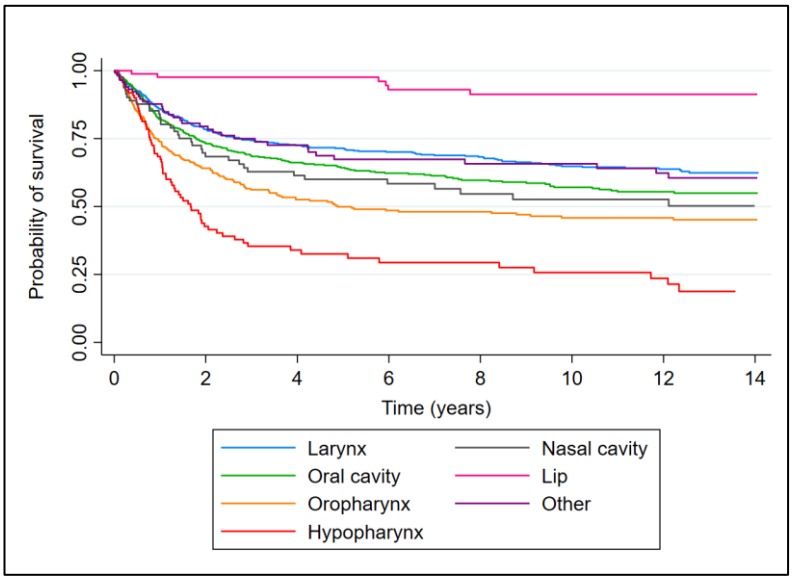
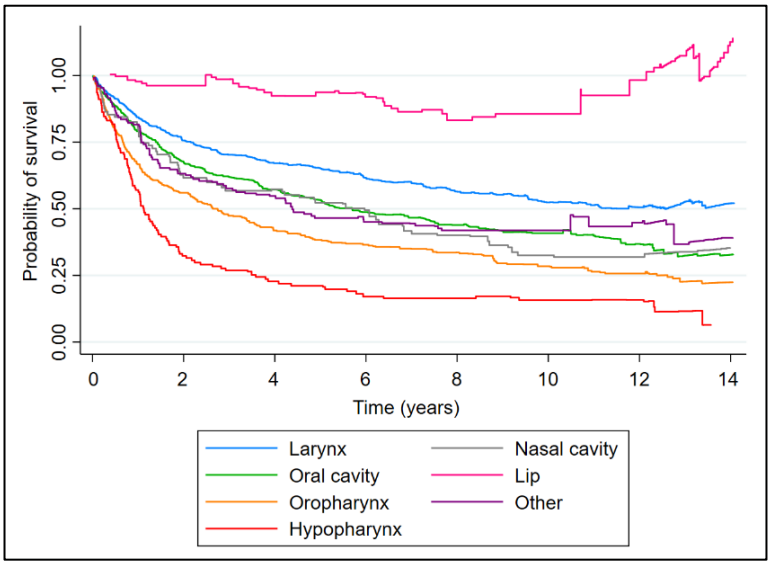



**Figure 3.26 – Graph of the estimated net survival function by anatomical site**



***Tumour stage***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the stage of the patient's tumour are displayed in Figure 3.27 to Figure 3.29. As the tumour stage of the person's cancer increased, the one-year, five-year, and 12-year overall survival, disease-specific survival, and net survival results also decreased at all three time points. Individuals who had stage I cancer had 12-year overall survival, disease-specific survival, and net survival of 46.0% (95% CI 40.9% to 50.9%), 84.0% (95% CI 79.4% to 87.8%), and 72.2% (95% CI 62.7% to 81.6%), respectively. However, those who had stage IV cancer had 12-year overall survival, disease-specific survival, and net survival results of 13.9% (95% CI 11.4% to 16.7%), 35.3% (95% CI 31.0% to 39.6%), and 21.6% (95% CI 17.1% to 26.0%), respectively. The disease-specific and net survival results after five years were substantially higher than the results for overall survival for those with stage I or stage II tumours. This suggests that the people who were diagnosed with early staged tumours were more likely to have died from other causes that were not related to their head and neck cancer.

**Figure 3.27 – Kaplan-Meier plot for overall survival by tumour stage**

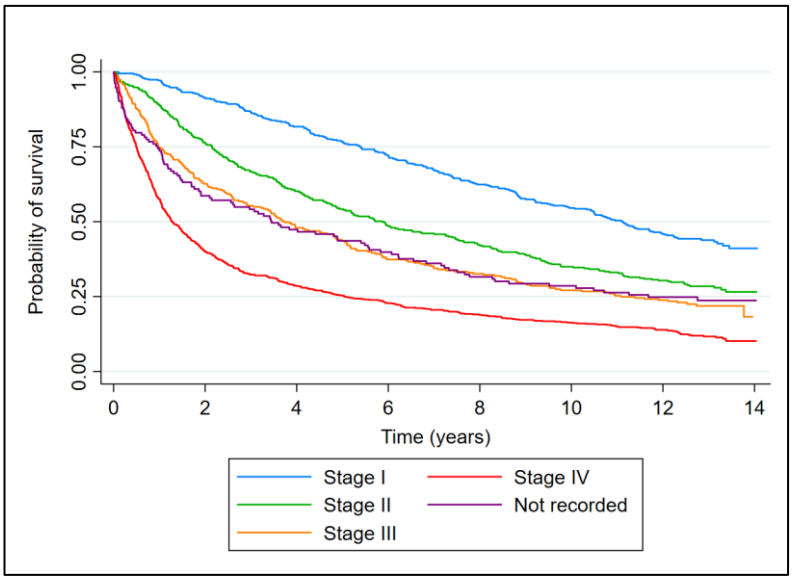



**Figure 3.28 – Kaplan-Meier plot for disease-specific survival by tumour stage**

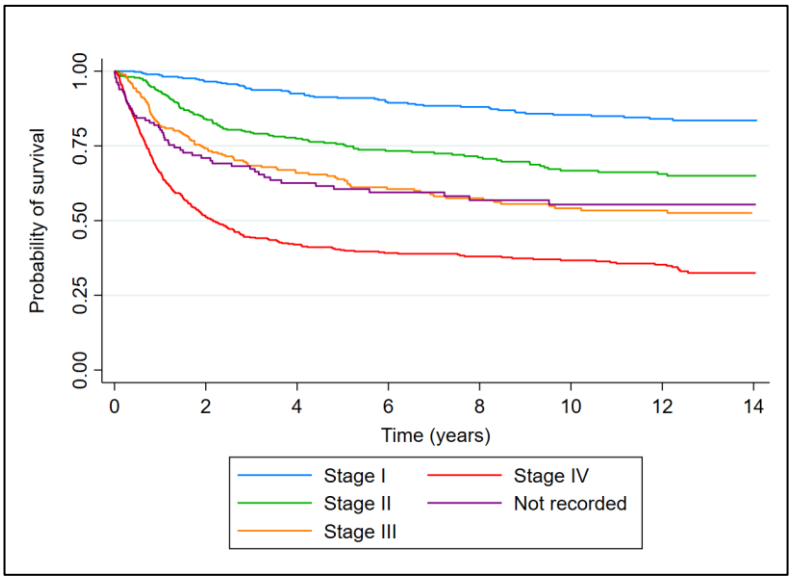
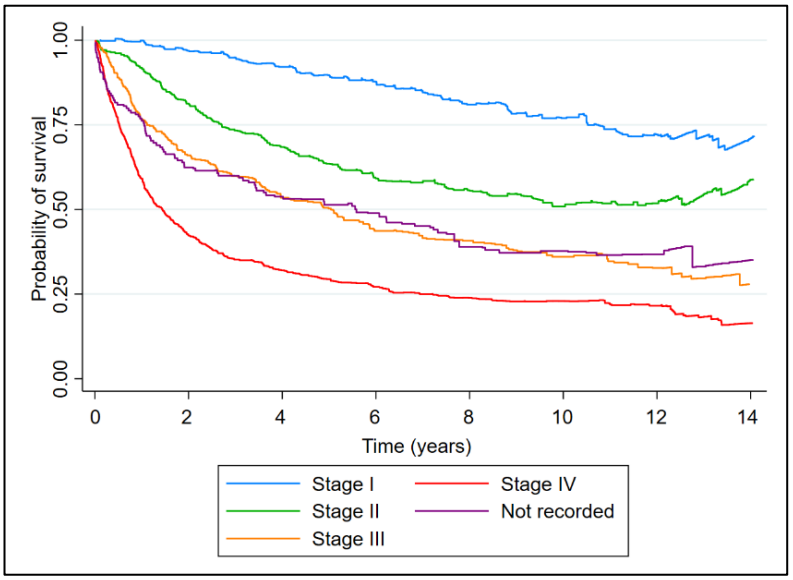



**Figure 3.29 – Graph of the estimated net survival function by tumour stage**



#### 3.3.4.3 Overall survival, disease-specific survival, and net survival by treatment factors

***Treatment modality***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the treatment modality that the patients received are displayed in Figure 3.30 to Figure 3.32. Those who were treated with chemotherapy with or without surgery, or who received no treatment had the worst overall survival, disease-specific survival, and net survival results at all three time points, which after just one year was 9.8% (95% CI 3.1% to 21.0%) and 10.9% (95% CI 6.2% to 16.9%); 17.2% (95% CI 5.6% to 34.0%) and 18.1% (95% CI 10.7% to 26.9%); and 10.0% (95% CI 1.3% to 18.7%) and 11.2% (95% CI 6.8% to 16.7%), respectively. Those who were treated with surgery only had the highest overall survival, disease-specific survival, and net survival results, which after one year was 88.9% (95% CI 85.7% to 91.4%), 93.5% (95% CI 90.8% to 95.4%) and 91.7% (95% CI 88.8% to 94.6%), respectively. The substantial difference between overall survival, and disease-specific survival and net survival results suggest that in the long-term, those who were treated with surgery only were more likely to die as a result of other causes of death that are not related to their head and neck cancer. The overall survival, disease-specific survival, and net survival results for the individuals who were treated with surgery only were followed by those who were treated with either radiotherapy only or surgery and radiotherapy, the results of which were similar at 82.1% (95% CI 78.4% to 85.1%) and 83.0% (95% CI 79.2% to 86.1%); 87.0% (95% CI 83.7% to 89.7%) and 86.5% (95% CI 82.9% to 89.3%); and 84.8% (95% CI 81.3% to 88.2%) and 84.9% (95% CI 81.4% to 88.5%), respectively, after one year.

**Figure 3.30 – Kaplan-Meier plot for overall survival by treatment modality**

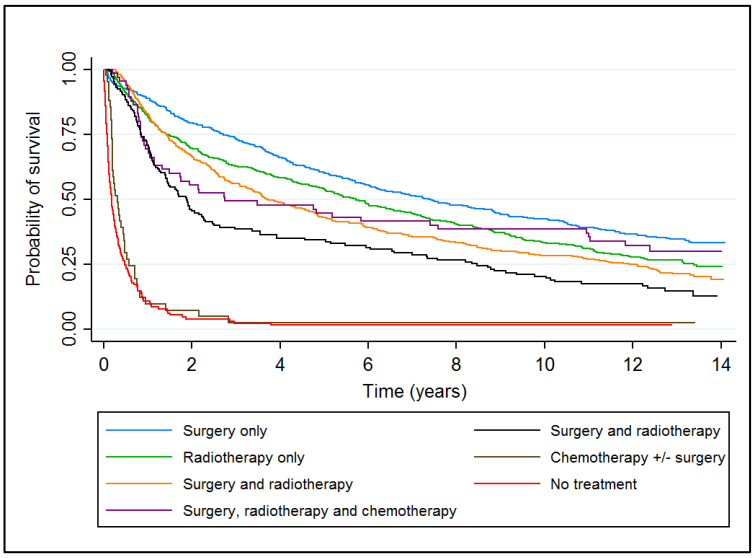



**Figure 3.31 – Kaplan-Meier plot for disease-specific survival by treatment modality**

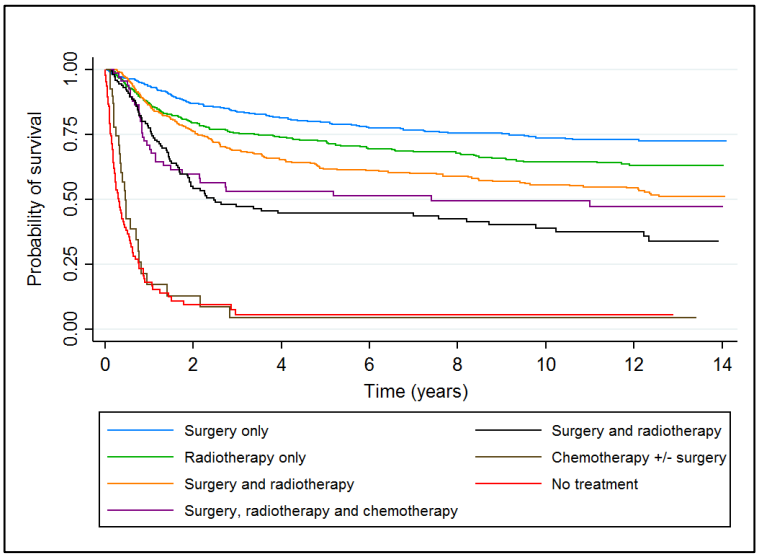
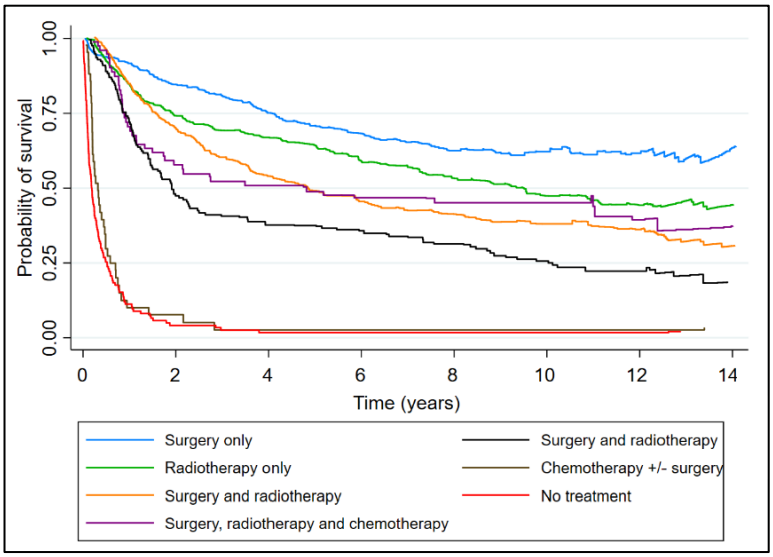



**Figure 3.32 – Graph of the estimated net survival function by treatment modality**



***Scottish Cancer Network***

The Kaplan-Meier plots for overall survival and disease-specific survival, and the graph for the estimated net survival function for the Scottish Cancer Network that the people were treated in are displayed in Figure 3.33 to Figure 3.35. One-year overall survival was similar across the three Scottish Cancer Networks at 77.6% (95% CI 73.0% to 81.5%) for NOSCAN, 76.4% (95% CI 72.1% to 80.1%) for SCAN and 75.3% (95% CI 72.5% to 77.9%) for WoSCAN. However, the results varied slightly at 12 years, by which time WoSCAN had the lowest overall survival of 24.0% (95% CI 21.4% to 26.7%) compared to SCAN at 30.0% (95% CI 25.8% to 34.3%). Like the results for overall survival, one-year disease-specific survival was similar across the three Scottish Cancer Networks at 82.5% (95% CI 79.9% to 84.8%) for WoSCAN, 82.0% (95% CI 78.0% to 85.4%) for the SCAN and 81.9% (95% CI 77.6% to 85.5%) for NOSCAN. However, the results varied slightly at 12 years by which time WoSCAN had the lowest disease-specific survival at 54.8% (95% CI 51.1% to 58.3%) compared to the SCAN at 60.0% (95% CI 54.8% to 64.8%). One-year and five-year net survival results were similar across the three Scottish Cancer Networks, however the results varied slightly at 12 years when WoSCAN obtained lower net survival of 36.9% (95% CI 32.0% to 41.7%), and SCAN obtained 12-year net survival of 50.0% (95% CI 42.0% to 58.1%).

**Figure 3.33 – Kaplan-Meier plot for overall survival by Scottish Cancer Network**

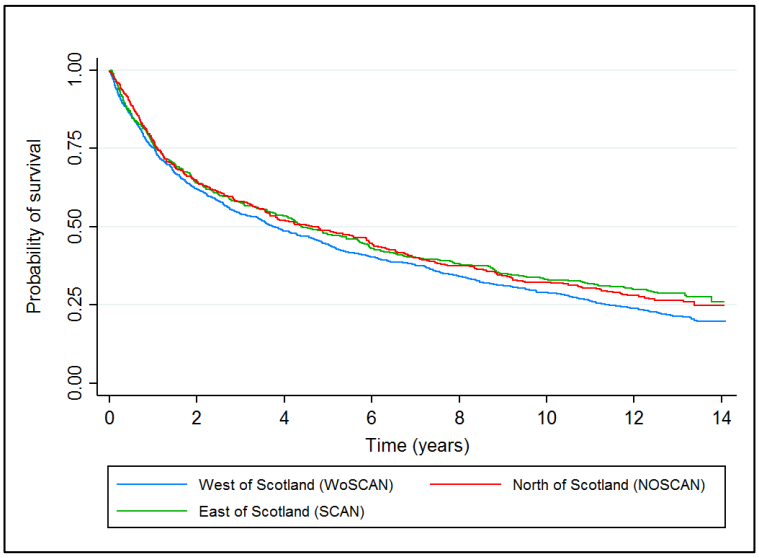



**Figure 3.34 – Kaplan-Meier plot for disease-specific survival by Scottish Cancer Network**

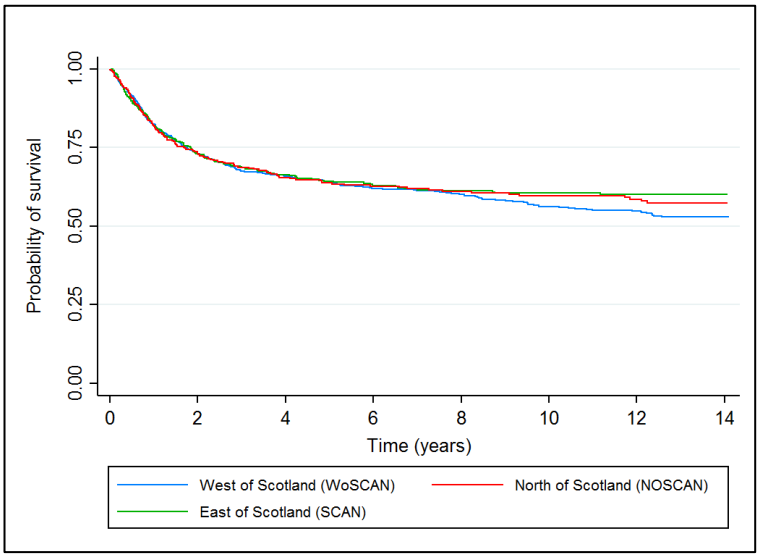



**Figure 3.35 – Graph of the estimated net survival function by Scottish Cancer Network**

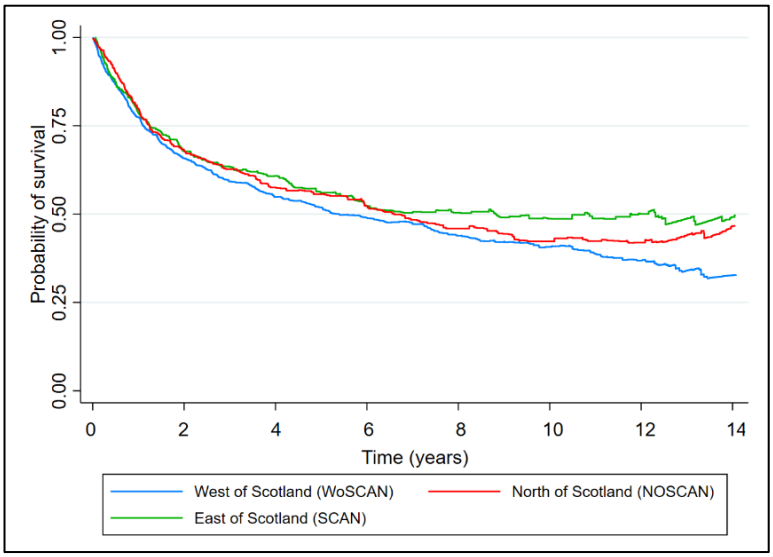


**Table 3.5 – One-year overall survival, disease-specific survival, and net survival results for each patient, tumour, and treatment factor**

| Variable | One-year overall survival %, (95% CI) | One-year disease-specific survival %, (95% CI) | One-year net survival %, (95% CI) |
|---|---|---|---|
| **Whole cohort** | 76.0 (74.0, 77.9) | 82.3 (80.4, 84.0) | 78.3 (76.2, 80.3) |
| **Age at diagnosis** | | | |
| Less than 45 | 90.9 (83.3, 95.2) | 94.8 (88.0, 97.8) | 91.1 (85.5, 96.8) |
| 45 to 54 | 83.7 (78.9, 87.5) | 86.5 (81.9, 90.0) | 84.2 (80.0, 88.6) |
| 55 to 64 | 78.4 (74.8, 81.5) | 83.1 (79.7, 85.9) | 79.6 (76.2, 83.0) |
| 65 to 74 | 73.1 (69.2, 76.6) | 81.7 (78.1, 84.8) | 75.9 (72.1, 79.8) |
| 75 and over | 64.1 (58.3, 69.4) | 72.9 (67.2, 77.8) | 69.1 (63.2, 75.0) |
| **Sex** | | | |
| Male | 76.2 (73.7, 78.4) | 82.0 (79.8, 84.1) | 78.5 (76.1, 80.9) |
| Female | 75.8 (71.9, 79.2) | 82.8 (79.2, 85.9) | 77.6 (73.8, 81.4) |
| **Carstairs 2001 Category** | | | |
| 1 (Least deprived) | 83.4 (78.1, 87.5) | 88.8 (83.9, 92.2) | 86.1 (81.3, 91.0) |
| 2 | 78.6 (73.6, 82.7) | 83.2 (78.5, 86.9) | 80.9 (76.2, 85.5) |
| 3 | 76.3 (71.3, 80.6) | 82.2 (77.5, 86.1) | 78.6 (73.8, 83.3) |
| 4 | 75.1 (70.6, 79.0) | 81.8 (77.5, 85.3) | 77.2 (72.8, 81.5) |
| 5 (Most deprived) | 71.8 (67.7, 75.4) | 79.1 (75.2, 82.4) | 73.7 (69.7, 77.6) |
| **Smoking behaviour** | | | |
| Never smoked | 85.5 (80.2, 89.5) | 89.3 (84.4, 92.8) | 87.9 (83.1, 92.7) |
| Previous smoker | 80.3 (76.0, 83.8) | 87.0 (83.2, 90.0) | 83.3 (79.2, 87.3) |
| Current smoker | 72.8 (70.1, 75.2) | 79.0 (76.4, 81.3) | 74.6 (71.9, 77.2) |
| Not recorded | 75.0 (62.0, 84.1) | 86.0 (73.9, 92.7) | 77.6 (66.2, 88.9) |
| **Alcohol consumption** | | | |
| Never/occasionally drank | 79.2 (76.4, 81.8) | 85.0 (82.4, 87.2) | 81.7 (78.9, 84.4) |
| Previous problem drinker | 72.2 (65.6, 77.7) | 76.6 (70.2, 81.8) | 74.0 (67.9, 80.2) |
| Current problem drinker | 70.8 (66.6, 74.6) | 77.8 (73.7, 81.3) | 72.4 (68.3, 76.5) |
| Not recorded | 78.7 (72.7, 83.6) | 86.7 (81.2, 90.6) | 81.3 (75.7, 86.9) |
| **WHO Performance Status** | | | |
| Normal activity | 88.1 (85.7, 90.2) | 91.9 (89.8, 92.6) | 90.2 (88.0, 92.5) |
| Strenuous activity restricted | 72.3 (68.0, 76.1) | 79.1 (74.9, 82.6) | 74.6 (70.5, 78.9) |
| Up and about >50% | 50.4 (41.7, 58.4) | 62.0 (52.7, 70.0) | 52.2 (44.2, 61.6) |
| Confined to bed/chair >50% | 34.0 (24.8, 43.4) | 44.8 (33.7, 55.2) | 35.6 (27.0, 46.8) |
| Not recorded | 74.0 (68.6, 78.6) | 79.2 (74.0, 83.5) | 76.5 (71.5, 81.8) |
| **Anatomical site** | | | |
| Larynx | 81.9 (78.5, 84.8) | 85.9 (82.8, 88.5) | 84.4 (81.1, 87.6) |
| Oral cavity | 76.9 (67.2, 85.1) | 82.1 (78.4, 85.3) | 79.1 (75.3, 82.9) |
| Oropharynx | 65.3 (59.9, 70.2) | 73.8 (68.5, 78.4) | 66.7 (61.4, 72.0) |
| Hypopharynx | 55.5 (46.1, 63.9) | 68.4 (58.5, 76.4) | 57.0 (47.9, 66.2) |
| Nasal cavity | 77.7 (67.2, 85.1) | 82.8 (72.6, 89.4) | 79.5 (70.4, 88.5) |
| Lip | 94.1 (86.4, 97.5) | 97.6 (90.8, 99.4) | 97.7 (92.4, 100.3) |
| Other/salivary gland | 79.7 (71.2, 85.9) | 87.7 (80.2, 92.6) | 81.6 (74.1, 89.0) |
| **Tumour stage** | | | |
| I | 97.1 (94.9, 98.4) | 98.7 (96.9, 99.5) | 99.9 (98.2, 101.7) |
| II | 89.2 (85.5, 91.9) | 93.3 (90.2, 95.5) | 91.9 (88.6, 95.2) |
| III | 74.7 (69.1, 79.5) | 81.7 (76.4, 85.9) | 76.6 (71.3, 81.9) |
| IV | 57.6 (53.7, 61.2) | 66.2 (62.4, 69.8) | 59.1 (55.2, 63.0) |
| Unknown | 73.7 (65.3, 80.3) | 80.3 (72.2, 86.2) | 76.2 (68.5, 83.9) |
| **Treatment modality** | | | |
| Surgery only | 88.9 (85.7, 91.4) | 93.5 (90.8, 95.4) | 91.7 (88.8, 94.6) |
| Radiotherapy only | 82.1 (78.4, 85.1) | 87.0 (83.7, 89.7) | 84.8 (81.3, 88.2) |
| Surgery and radiotherapy | 83.0 (79.2, 86.1) | 86.4 (82.9, 89.3) | 84.9 (81.4, 88.5) |
| Surgery, radiotherapy and chemotherapy | 69.2 (56.5, 78.9) | 70.7 (58.0, 80.2) | 70.5 (59.2, 81.9) |
| Radiotherapy and chemotherapy | 70.6 (62.4, 77.4) | 77.5 (69.6, 83.6) | 72.0 (64.4, 79.6) |
| Chemotherapy +/- surgery | 9.8 (3.1, 21.0) | 17.2 (5.6, 34.0) | 10.0 (1.3, 18.7) |
| No treatment | 10.9 (6.2, 16.9) | 18.1 (10.7, 26.9) | 11.2 (6.8, 16.7) |
| **Network/region** | | | |
| WoSCAN (West Scotland) | 75.3 (72.5, 77.9) | 82.5 (79.9, 84.8) | 77.4 (74.7, 80.2) |
| SCAN (East Scotland) | 76.4 (72.1, 80.1) | 82.0 (78.0, 85.4) | 78.7 (74.6, 82.8) |
| NOSCAN (North Scotland) | 77.6 (73.0, 81.5) | 81.9 (77.6, 85.5) | 79.7 (75.4, 84.0) |

**Table 3.6 – Five-year overall survival, disease-specific survival, and net survival results for each patient, tumour, and treatment factor**

| Variable | Five-year overall survival %, (95% CI) | Five-year disease-specific survival %, (95% CI) | Five-year net survival %, (95% CI) |
|---|---|---|---|
| **Whole cohort** | 46.1 (43.8, 48.4) | 64.1 (61.7, 66.4) | 53.8 (51.1, 56.5) |
| **Age at diagnosis** | | | |
| Less than 45 | 76.8 (67.1, 83.9) | 82.1 (72.8, 88.5) | 77.5 (69.2, 85.9) |
| 45 to 54 | 56.6 (50.7, 62.1) | 68.8 (62.9, 74.0) | 58.9 (53.0, 64.9) |
| 55 to 64 | 48.5 (44.4, 52.4) | 65.7 (61.5, 69.6) | 52.8 (48.4, 57.2) |
| 65 to 74 | 39.6 (35.5, 43.6) | 61.1 (56.4, 65.4) | 49.1 (44.0, 54.1) |
| 75 and over | 32.8 (27.4, 38.2) | 54.0 (47.6, 60.0) | 51.3 (42.8, 59.9) |
| **Sex** | | | |
| Male | 45.2 (42.5, 47.9) | 62.6 (59.7, 65.3) | 53.5 (50.3, 56.8) |
| Female | 48.3 (43.9, 52.5) | 67.8 (63.3, 71.9) | 54.3 (49.3, 59.3) |
| **Carstairs 2001 Category** | | | |
| 1 (Least deprived) | 49.8 (43.3, 55.9) | 69.6 (62.9, 75.3) | 58.1 (50.4, 65.8) |
| 2 | 50.1 (46.4, 57.4) | 69.8 (64.2, 74.8) | 58.8 (52.5, 65.2) |
| 3 | 44.6 (39.2, 49.9) | 61.0 (55.1, 66.4) | 51.8 (45.5, 58.1) |
| 4 | 47.7 (42.8, 52.4) | 64.4 (59.2, 69.1) | 55.9 (50.1, 61.6) |
| 5 (Most deprived) | 40.5 (36.3, 44.7) | 59.6 (54.9, 63.9) | 48.1 (43.0, 53.2) |
| **Smoking behaviour** | | | |
| Never smoked | 59.7 (52.9, 65.9) | 72.5 (65.8, 78.0) | 68.3 (60.4, 76.2) |
| Previous smoker | 50.9 (45.9, 55.6) | 68.1 (63.0, 72.7) | 63.1 (57.0, 69.2) |
| Current smoker | 41.6 (38.7, 44.5) | 60.6 (57.4, 63.5) | 47.4 (44.0, 50.7) |
| Not recorded | 48.3 (35.3, 60.2) | 71.2 (56.6, 81.7) | 56.9 (41.5, 72.4) |
| **Alcohol consumption** | | | |
| Never/occasionally drank | 51.6 (48.3, 54.9) | 68.0 (64.6, 71.1) | 60.4 (56.4, 64.4) |
| Previous problem drinker | 37.3 (30.8, 43.7) | 54.9 (47.4, 61.7) | 42.8 (35.3, 50.3) |
| Current problem drinker | 37.1 (32.9, 41.3) | 57.1 (52.2, 61.7) | 42.5 (37.6, 47.4) |
| Not recorded | 52.5 (45.7, 58.8) | 72.1 (65.2, 77.9) | 62.2 (54.2, 70.3) |
| **WHO Performance Status** | | | |
| Normal activity | 64.0 (60.6, 67.2) | 78.3 (75.2, 81.1) | 73.0 (69.3, 76.9) |
| Strenuous activity restricted | 35.9 (31.6, 40.3) | 57.5 (52.5, 62.2) | 43.2 (38.1, 48.9) |
| Up and about >50% | 13.9 (8.7, 20.2) | 30.3 (21.2, 40.0) | 16.7 (10.9, 25.6) |
| Confined to bed/chair >50% | 5.2 (1.9, 10.8) | 15.1 (7.1, 26.0) | 6.8 (3.1, 15.0) |
| Not recorded | 40.5 (34.9, 46.1) | 58.5 (52.2, 64.3) | 49.0 (42.6, 56.4) |
| **Anatomical site** | | | |
| Larynx | 54.6 (50.5, 58.6) | 71.4 (67.4, 75.1) | 65.2 (60.3, 70.1) |
| Oral cavity | 45.7 (41.3, 49.9) | 64.3 (59.6, 68.5) | 53.2 (48.0, 58.4) |
| Oropharynx | 35.0 (29.8, 40.2) | 49.9 (43.8, 55.7) | 38.3 (32.5, 44.1) |
| Hypopharynx | 18.5 (12.1, 25.9) | 32.6 (23.0, 42.4) | 21.2 (13.1, 29.2) |
| Nasal cavity | 45.9 (35.1, 56.0) | 60.0 (48.2, 70.0) | 52.3 (40.3, 64.3) |
| Lip | 77.6 (67.2, 85.1) | 97.6 (90.8, 99.4) | 93.7 (81.6, 105.7) |
| Other/salivary gland | 41.5 (32.6, 50.2) | 67.4 (56.8, 75.9) | 46.5 (36.1, 56.9) |
| **Tumour stage** | | | |
| I | 76.8 (72.2, 80.7) | 91.0 (87.5, 93.6) | 89.7 (84.5, 94.9) |
| II | 54.2 (49.0, 59.1) | 75.6 (70.6, 79.9) | 63.5 (57.3, 69.7) |
| III | 43.6 (37.6, 49.4) | 63.9 (57.3, 69.7) | 50.3 (43.5, 57.2) |
| IV | 25.4 (22.1, 28.7) | 40.2 (36.0, 44.3) | 29.4 (25.5, 33.3) |
| Unknown | 43.6 (35.1, 51.8) | 60.5 (51.0, 68.8) | 51.4 (41.2, 61.6) |
| **Treatment modality** | | | |
| Surgery only | 60.2 (55.6, 64.4) | 79.6 (75.5, 83.1) | 70.9 (65.5, 76.3) |
| Radiotherapy only | 54.0 (49.6, 58.3) | 72.3 (68.0, 76.2) | 64.4 (59.1, 69.7) |
| Surgery and radiotherapy | 43.0 (38.4, 47.5) | 61.7 (56.7, 66.3) | 49.1 (43.9, 54.3) |
| Surgery, radiotherapy and chemotherapy | 44.6 (32.3, 56.2) | 53.1 (40.1, 64.4) | 48.9 (35.3, 62.4) |
| Radiotherapy and chemotherapy | 34.3 (26.6, 42.0) | 44.6 (35.7, 53.0) | 37.5 (29.0, 46.1) |
| Chemotherapy +/- surgery | 2.4 (0.2, 11.0) | 4.3 (0.3, 17.9) | 2.6 (1.5, 6.8) |
| No treatment | 1.6 (0.3, 5.0) | 5.6 (1.7, 13.1) | 1.7 (0.4, 3.9) |
| **Network/region** | | | |
| WoSCAN (West Scotland) | 44.5 (41.4, 47.5) | 64.1 (60.8, 67.2) | 51.9 (48.3, 55.6) |
| SCAN (East Scotland) | 47.5 (42.8, 52.1) | 64.2 (59.3, 68.7) | 56.0 (50.4, 61.7) |
| NOSCAN (North Scotland) | 48.8 (43.7, 53.7) | 63.7 (58.4, 68.6) | 55.6 (49.8, 61.5) |

**Table 3.7 – 12-year overall survival, disease-specific survival, and net survival results for each patient, tumour, and treatment factor**

| Variable | 12-year overall survival %, (95% CI) | 12-year disease-specific survival %, (95% CI) | 12-year net survival %, (95% CI) |
|---|---|---|---|
| **Whole cohort** | 26.3 (24.3, 28.3) | 56.9 (54.3, 59.4) | 41.4 (37.6, 45.1) |
| **Age at diagnosis** | | | |
| Less than 45 | 62.6 (52.3, 71.3) | 72.1 (61.7, 80.1) | 64.9 (55.0, 74.7) |
| 45 to 54 | 37.5 (31.9, 43.0) | 60.2 (53.8, 66.0) | 42.2 (35.9, 48.5) |
| 55 to 64 | 30.2 (26.6, 34.0) | 60.0 (55.5, 64.2) | 38.8 (34.0, 43.7) |
| 65 to 74 | 18.0 (14.9, 21.3) | 54.2 (49.1, 59.1) | 35.8 (29.5, 42.2) |
| 75 and over | 10.3 (7.2, 14.2) | 45.3 (37.9, 52.4) | 43.2 (28.0, 58.4) |
| **Sex** | | | |
| Male | 24.9 (22.6, 27.3) | 55.3 (52.2, 58.3) | 40.5 (36.2, 44.8) |
| Female | 29.6 (25.8, 33.6) | 60.9 (56.0, 65.5) | 43.0 (36.1, 49.8) |
| **Carstairs 2001 Category** | | | |
| 1 (Least deprived) | 27.0 (21.5, 32.7) | 61.8 (54.4, 68.4) | 40.4 (30.7, 50.0) |
| 2 | 30.6 (25.6, 35.7) | 65.6 (59.6, 70.9) | 43.8 (35.0, 52.6) |
| 3 | 26.2 (21.5, 31.0) | 55.5 (49.2, 61.3) | 40.7 (31.5, 49.9) |
| 4 | 26.9 (22.7, 31.3) | 55.5 (49.9, 60.8) | 46.6 (38.4, 54.7) |
| 5 (Most deprived) | 22.9 (19.4, 26.5) | 51.1 (46.0, 55.9) | 35.7 (29.6, 41.8) |
| **Smoking behaviour** | | | |
| Never smoked | 43.9 (37.3, 50.3) | 66.9 (59.8, 73.0) | 70.6 (57.1, 84.1) |
| Previous smoker | 27.4 (23.2, 31.8) | 59.8 (54.1, 65.0) | 49.9 (40.5, 59.2) |
| Current smoker | 22.3 (19.9, 24.8) | 53.2 (49.9, 56.5) | 32.4 (28.6, 36.2) |
| Not recorded | 28.3 (17.6, 40.0) | 67.3 (51.2, 79.1) | 40.3 (22.2, 58.5) |
| **Alcohol consumption** | | | |
| Never/occasionally drank | 32.3 (29.3, 35.4) | 62.1 (58.5, 65.5) | 54.1 (48.0, 60.1) |
| Previous problem drinker | 17.0 (12.3, 22.3) | 49.7 (42.1, 56.9) | 23.4 (15.9, 30.9) |
| Current problem drinker | 18.2 (14.9, 21.7) | 45.9 (40.5, 51.1) | 23.5 (18.6, 28.4) |
| Not recorded | 29.0 (23.1, 35.0) | 65.4 (57.6, 72.1) | 43.9 (33.8, 54.0) |
| **WHO Performance Status** | | | |
| Normal activity | 40.6 (37.2, 43.9) | 70.4 (66.8, 73.7) | 59.0 (53.5, 64.9) |
| Strenuous activity restricted | 16.1 (13.0, 19.6) | 49.7 (44.1, 55.0) | 33.1 (26.7, 41.1) |
| Up and about >50% | 7.3 (3.7, 12.5) | 30.3 (21.2, 40.0) | 11.6 (5.9, 22.9) |
| Confined to bed/chair >50% | 1.0 (0.1, 5.0) | 10.1 (2.8, 23.1) | 1.5 (0.3, 9.0) |
| Not recorded | 19.3 (15.0, 23.9) | 50.2 (43.4, 56.7) | 31.2 (23.7, 41.1) |
| **Anatomical site** | | | |
| Larynx | 29.5 (25.8, 33.2) | 63.8 (59.2, 67.9) | 50.5 (43.4, 57.7) |
| Oral cavity | 23.7 (20.1, 27.5) | 55.4 (50.3, 60.3) | 36.8 (30.1, 43.6) |
| Oropharynx | 21.4 (17.1, 26.0) | 45.8 (39.6, 51.8) | 25.7 (19.7, 31.8) |
| Hypopharynx | 9.2 (4.9, 15.3) | 23.6 (14.5, 33.9) | 15.8 (7.0, 24.7) |
| Nasal cavity | 25.9 (17.1, 35.5) | 52.6 (40.2, 63.6) | 31.9 (19.5, 44.4) |
| Lip | 56.5 (45.3, 66.2) | 91.3 (81.5, 96.0) | 98.3 (76.3, 120.2) |
| Other/salivary gland | 30.5 (22.5, 38.9) | 62.3 (51.0, 71.7) | 44.8 (29.9, 59.7) |
| **Tumour stage** | | | |
| I | 46.0 (40.9, 50.9) | 84.0 (79.4, 87.8) | 72.2 (62.7, 81.6) |
| II | 30.4 (25.7, 35.1) | 65.6 (59.6, 70.9) | 51.8 (42.8, 60.9) |
| III | 23.8 (18.9, 29.0) | 53.4 (46.2, 60.0) | 32.7 (24.4, 41.0) |
| IV | 13.9 (11.4, 16.7) | 35.3 (31.0, 39.6) | 21.6 (17.1, 26.0) |
| Unknown | 24.8 (17.9, 32.4) | 55.4 (45.4, 64.3) | 36.8 (24.5, 49.1) |
| **Treatment modality** | | | |
| Surgery only | 36.7 (32.4, 41.0) | 72.8 (68.1, 77.0) | 61.7 (53.1, 70.2) |
| Radiotherapy only | 27.6 (23.8, 31.6) | 63.1 (58.1, 67.7) | 44.3 (37.0, 51.5) |
| Surgery and radiotherapy | 24.9 (21.0, 28.9) | 54.2 (48.8, 59.3) | 36.2 (29.7, 42.6) |
| Surgery, radiotherapy and chemotherapy | 32.3 (21.4, 43.7) | 47.3 (34.3, 59.2) | 39.4 (23.4, 55.5) |
| Radiotherapy and chemotherapy | 17.5 (11.8, 23.1) | 37.3 (28.3, 46.3) | 22.3 (13.8, 30.8) |
| Chemotherapy +/- surgery | 2.4 (0.2, 11.0) | 4.3 (0.3, 17.9) | 2.6 (1.5, 6.8) |
| No treatment | 1.6 (0.3, 5.0) | 5.6 (1.7, 13.1) | 1.7 (0.4, 3.9) |
| **Network/region** | | | |
| WoSCAN (West Scotland) | 24.0 (21.4, 26.7) | 54.8 (51.1, 58.3) | 36.9 (32.0, 41.7) |
| SCAN (East Scotland) | 30.0 (25.8, 34.3) | 60.0 (54.8, 64.8) | 50.0 (42.0, 58.1) |
| NOSCAN (North Scotland) | 28.0 (23.5, 32.6) | 58.6 (52.9, 63.8) | 41.9 (34.7, 49.2) |

### 3.3.5 Minimally adjusted Cox proportional hazards models for all-cause mortality and disease-specific mortality

The Cox proportional hazards models that were minimally adjusted for age and sex for one-year, five-year, and 12-year all-cause mortality and disease-specific mortality are displayed in Table 3.8 to Table 3.13 on Page 124 to Page 129.

#### 3.3.5.1 Minimally adjusted Cox proportional hazards models for all-cause mortality and disease-specific mortality for the patient factors

***Carstairs 2001 Category***

Following adjustment for age and sex, the patients in the most deprived group were 96% (HR = 1.96, 95% CI 1.38 to 2.77) and 43% (HR = 1.43, 95% CI 1.15 to 1.76) more at risk of all-cause mortality after one year and five years, respectively, compared to those who were from the least deprived group. However, by 12 years, the people in the most deprived category only had a 27% (HR = 1.27, 95% CI 1.06 to 1.52) higher risk of all-cause mortality compared to those who were from the least deprived group. Following adjustment for age and sex, the individuals in the most deprived group were two-fold (HR = 2.09, 95% CI 1.36 to 3.22), 55% (HR = 1.55, 95% CI 1.17 to 2.06), and 51% (HR = 1.51, 95% CI 1.16 to 1.96) more at risk of disease-specific mortality compared to those from the least deprived groups after one year, five years, and 12 years, respectively. The results for disease-specific mortality following age and sex adjustment were substantially higher than the results from the models for all-cause mortality after 12-years, suggesting that the patients from the most deprived regions were more at risk of disease-specific mortality than they were of all-cause mortality.

***Smoking behaviour***

The patients who were reported as current smokers at the time of their diagnosis were at a substantially higher risk of all-cause mortality than those who were reported as never having smoked in their lifetime at all three time points following adjustment for age and sex. The individuals who were reported as current smokers were 88% (HR = 1.88, 95% CI 1.56 to 2.27) more at risk of all-cause mortality at 12 years compared to those who were reported as never having smoked in their lifetime. Interestingly, the people who were reported as being previous smokers at the time of their diagnosis had a smaller excess risk of all-cause mortality compared to those who were reported as never having smoked in their lifetime (one-year HR = 1.21, 95% CI 0.87 to 1.67; five-year HR = 1.13, 95% CI 0.88 to 1.45, 12-year HR = 1.20, 95% CI 0.98 to 1.48) following adjustment for age and sex. Like the results for all-cause mortality, the patients who were reported as current

smokers at the time of their diagnosis had a substantially higher risk of disease-specific mortality than those who were reported as never having smoked in their lifetime at all three time points following adjustment for age and sex. The individuals who were reported as current smokers were 70% (HR = 1.70, 95% CI 1.30 to 2.22) more at risk of disease-specific mortality at 12 years compared to those who were reported as never having smoked. Similar to the results for all-cause mortality, the people who were reported as being previous smokers at the time of their diagnosis had no excess risk of disease-specific mortality compared to those who were reported as never having smoked in their lifetime (one-year HR = 0.99, 95% CI 0.68 to 1.44; five-year HR = 1.04, 95% CI 0.75 to 1.44; 12-year HR = 1.07, 95% CI 0.79 to 1.45) following adjustment for age and sex.

***Alcohol consumption***

Patients who were reported as having a current problem with their levels of alcohol consumption at the time of their diagnosis were at a substantially higher risk of all-cause mortality than those who were reported as never having drank or who occasionally drank at diagnosis at all three time points following adjustment for age and sex. Those who were reported as having a current problem with alcohol consumption were 77% (HR = 1.77, 95% CI 1.55 to 2.02) more at risk of all-cause mortality after 12 years compared to the individuals who were reported as never having drank or who occasionally drank before their diagnosis. The people who were reported as having a previous problem with their alcohol consumption were at a lower risk of all-cause mortality than those who were reported as having a current problem with their alcohol consumption after one year, five years, and 12 years following adjustment for age and sex. After 12 years, those who were reported as having a previous problem with their alcohol consumption were 63% (HR = 1.63, 95% CI 1.38 to 1.93) more at risk of all-cause mortality than the people who were reported as never having drank or who occasionally drank following adjustment for age and sex, which was noticeably lower than those who were reported as having a current problem with their levels of alcohol consumption.

Following adjustment for age and sex, the individuals who were reported as having a current problem with their consumption of alcohol were at a higher risk of disease-specific mortality than those who were reported as never having drank or who occasionally drank. The patients who were reported as having a current problem with alcohol were 73% (HR = 1.73, 95% CI 1.43 to 2.08) more at risk of disease-specific mortality after 12 years compared to those who were reported as never having drank or who occasionally drank before their diagnosis. Like the results for all-cause mortality, those who were reported as having a previous problem with their alcohol consumption were at a lower risk of disease-specific mortality than those who were reported as having a current problem with their alcohol consumption after one year, five years, and 12 years following adjustment for age

and sex. After 12 years, the people who were reported as having a previous problem with their alcohol consumption were 63% (HR = 1.63, 95% CI 1.29 to 2.08) more at risk of disease-specific mortality than the people who were reported as never having drank or who occasionally drank following adjustment for age and sex, which was noticeably lower than those who were reported as having a previous problem with their alcohol consumption.

***WHO Performance Status***

The patients who had a worse WHO Performance Status were at a considerably higher risk of all-cause mortality following adjustment for age and sex at all three time points. The individuals who were reported as being confined to a bed or a chair for more than 50% of their waking hours were at a more than seven-fold (HR = 7.08, 95% CI 5.34 to 9.40) higher risk of all-cause mortality after one year. By 12 years, this risk had reduced, but those who were reported as being confined to a bed or a chair for more than 50% of their waking hours remained at a near six-fold (HR = 5.74, 95% CI 4.56 to 7.22) increased risk of all-cause mortality compared to the people who were of a normal WHO Performance Status following adjustment for age and sex. Like the results for all-cause mortality, the people who had worse WHO Performance Status continued to be at a substantially higher risk of disease-specific mortality following adjustment for age and sex at all three time points. Those who were reported as being confined to a bed or a chair for more than 50% of their waking hours had a more than seven-fold increased risk of disease-specific mortality after one year, five years, and 12 years (one-year HR = 7.86, 95% CI 5.61 to 11.03; five-year HR = 7.64, 95% CI 5.66 to 10.31; 12-year HR = 7.25, 95% CI 5.40 to 9.71). However, unlike the results for all-cause mortality, the results for disease-specific mortality by WHO Performance Status did not attenuate over time.

#### 3.3.5.2 Minimally adjusted Cox proportional hazards models for all-cause mortality and disease-specific mortality for the tumour factors

***Anatomical site***

Following adjustment for age and sex, the patients with cancer of the lip had a 77% (HR = 0.23, 95% CI 0.17 to 0.33) lower risk of all-cause mortality after 12 years compared to those with cancer of the oropharynx. However, the individuals with cancer of the hypopharynx had a 42% (HR = 1.42, 95% CI 1.14 to 1.78) higher risk of all-cause mortality after 12 years compared to those with cancer of the oropharynx following adjustment for age and sex. The same differences were observed following adjustment for age and sex whereby people with cancer of the lip had a 92% (HR = 0.08, 95% CI 0.03 to 0.17) lower risk of disease-specific mortality after 12 years compared to those with cancer

of the oropharynx. However, people with cancer of the hypopharynx had a 50% (HR = 1.50, 95% CI 1.13 to 1.99) higher risk of disease-specific mortality after 12 years compared to those with cancer of the oropharynx.

***Tumour stage***

The patients who were diagnosed with cancers that were stage IV were substantially more at risk of all-cause mortality than those who were diagnosed with cancers that were stage I. This was particularly apparent after one year, by which time the individuals who had stage IV tumours were 10 times (HR = 10.24, 95% CI 7.17 to 14.63) more at risk of all-cause mortality than those who were diagnosed with stage I tumours. By 12 years, the people who had stage IV tumours remained at an increased risk of all-cause mortality compared to those who had stage I tumours, however this risk had reduced to 3.5-fold (HR = 3.51, 95% CI 3.00 to 4.11). The increase in the risk of individuals with stage IV tumours was stronger for disease-specific mortality, and those who were diagnosed with stage IV tumours were more than 20 times (HR = 20.52, 95% CI 11.51 to 36.59) more at risk of disease-specific survival after one year compared to those who were diagnosed with stage I tumours following adjustment for age and sex. A similar pattern to the results for all-cause mortality was observed over time for disease-specific mortality, whereby those who were diagnosed with stage IV tumours had a reduction in the excess risk of disease-specific mortality after 12 years, but remained nearly 8 times (HR = 7.80, 95% CI 5.83 to 10.45) more at risk.

#### 3.3.5.3 Minimally adjusted Cox proportional hazards models for all-cause mortality and disease-specific mortality for the treatment factors

***Treatment modality***

Following adjustment for age and sex, the patients who were treated with radiotherapy only were 24% (HR = 1.24, 95% CI 1.06 to 1.44) more at risk of all-cause mortality than those who were treated with surgery only after 12 years. Despite having similar survival results to those who were treated with radiotherapy, the people who were treated with a combination of surgery and radiotherapy were 57% (HR = 1.57, 95% CI 1.35 to 1.83) more at risk of all-cause mortality compared to those who were treated with surgery only after 12 years following adjustment for age and sex. The individuals who received chemotherapy with or without surgery, or who received no treatment were substantially more at risk of all-cause mortality than those who were treated with surgery only after 12 years following age and sex adjustment (chemotherapy group HR = 10.48, 95% CI 7.47 to 14.71; no treatment HR = 12.17, 95% CI 9.77 to 15.16). Like the results for all-cause mortality, the people who were treated with radiotherapy only were at a 45% (HR = 1.45,

95% CI 1.14 to 1.86) higher risk of disease-specific mortality compared to those who were treated with surgery only following adjustment for age and sex. Also like the results for all-cause mortality, even though the survival results for those who were treated with radiotherapy only or with surgery and radiotherapy were similar, the people who were treated with surgery and radiotherapy had a higher risk of disease-specific mortality of two-fold (HR = 2.08, 95% CI 1.64 to 2.64) after 12 years following adjustment for age and sex. The patients who were treated with chemotherapy with or without surgery, or who received no treatment were considerably more at risk of disease-specific survival than those who were treated with surgery only (chemotherapy group HR = 15.26, 95% CI 9.90 to 23.53; no treatment HR = 18.98, 95% CI 14.13 to 25.50)

***Scottish Cancer Network***

Following adjustment for age and sex, there was no excess risk in all-cause or disease-specific mortality for any of the three Scottish Cancer Networks at one year or five years. However, by 12 years, the patients who were treated in the West of Scotland were 22% (HR = 1.22, 95% CI 1.07 to 1.39) more at risk than those who were treated in the East of Scotland. This difference was not reflected in the results for disease-specific mortality, since the people who were treated in the West of Scotland had no increased risk of disease-specific mortality than those who were treated in the East of Scotland (HR = 1.15, 95% CI 0.95 to 1.39).

**Table 3.8 – Minimally adjusted* hazard ratios for all-cause mortality after one year for each patient, tumour, and treatment factor**

| Variable | One-year all-cause mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Carstairs 2001 Category** | | | <0.001 | 19.61 |
| 1 (Least deprived) | 1.00 (Ref.) | - | | |
| 2 | 1.35 (0.92, 2.00) | 0.402 | | |
| 3 | 1.53 (1.05, 2.25) | 0.009 | | |
| 4 | 1.62 (1.12, 2.33) | 0.096 | | |
| 5 (Most deprived) | 1.96 (1.38, 2.77) | <0.001 | | |
| **Smoking behaviour** | | | <0.001 | 43.51 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.21 (0.87, 1.67) | 0.253 | | |
| Current smoker | 2.02 (1.51, 2.71) | <0.001 | | |
| Not recorded | 1.08 (0.62, 1.86) | 0.787 | | |
| **Alcohol consumption** | | | <0.001 | 46.79 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.51 (1.19, 1.93) | <0.001 | | |
| Current problem drinker | 1.81 (1.50, 2.18) | <0.001 | | |
| Not recorded | 0.89 (0.68, 1.17) | 0.416 | | |
| **WHO Performance Status** | | | <0.001 | 243.60 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 2.37 (1.93, 2.91) | <0.001 | | |
| Up and about >50% | 4.81 (3.72, 6.22) | <0.001 | | |
| Confined to bed/chair >50% | 7.08 (5.34, 9.40) | <0.001 | | |
| Not recorded | 2.17 (1.71, 2.74) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 115.13 |
| Larynx | 0.44 (0.35, 0.55) | <0.001 | | |
| Oral cavity | 0.61 (0.49, 0.75) | <0.001 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.36 (1.03, 1.79) | 0.031 | | |
| Nasal cavity | 0.69 (0.47, 1.01) | 0.056 | | |
| Lip | 0.12 (0.06, 0.24) | <0.001 | | |
| Other/salivary gland | 0.74 (0.54, 1.03) | 0.073 | | |
| **Tumour stage** | | | <0.001 | 244.59 |
| I | 1.00 (Ref.) | - | | |
| II | 3.16 (2.13, 4.71) | <0.001 | | |
| III | 5.39 (3.64, 7.99) | <0.001 | | |
| IV | 10.24 (7.17, 14.63) | <0.001 | | |
| Unknown | 5.69 (3.68, 8.82) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 670.50 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.58 (1.22, 2.04) | <0.001 | | |
| Surgery and radiotherapy | 1.81 (1.40, 2.34) | <0.001 | | |
| Surgery, radiotherapy and chemotherapy | 2.94 (1.92, 4.50) | <0.001 | | |
| Radiotherapy and chemotherapy | 3.46 (2.54, 4.71) | <0.001 | | |
| Chemotherapy +/- surgery | 16.78 (11.40, 24.70) | <0.001 | | |
| No treatment | 19.58 (14.83, 25.85) | <0.001 | | |
| **Network/region** | | | 0.360 | 2.04 |
| WoSCAN (West Scotland) | 1.14 (0.94, 1.37) | 0.181 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.04 (0.83, 1.32) | 0.711 | | |

*Adjusted by age and tumour sex

**Table 3.9 – Minimally adjusted* hazard ratios for all-cause mortality after five years for each patient, tumour, and treatment factor**

| Variable | Five-year all-cause mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Carstairs 2001 Category** | | | <0.001 | 20.58 |
| 1 (Least deprived) | 1.00 (Ref.) | - | | |
| 2 | 0.99 (0.78, 1.26) | 0.776 | | |
| 3 | 1.22 (0.97, 1.54) | 0.110 | | |
| 4 | 1.14 (0.91, 1.43) | 0.266 | | |
| 5 (Most deprived) | 1.43 (1.15, 1.76) | 0.001 | | |
| **Smoking behaviour** | | | <0.001 | 59.68 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.13 (0.88, 1.45) | 0.341 | | |
| Current smoker | 1.86 (1.49, 2.32) | <0.001 | | |
| Not recorded | 1.20 (0.80, 1.80) | 0.368 | | |
| **Alcohol consumption** | | | <0.001 | 74.87 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.58 (1.30, 1.91) | <0.001 | | |
| Current problem drinker | 1.83 (1.58, 2.13) | <0.001 | | |
| Not recorded | 0.96 (0.79, 1.18) | 0.728 | | |
| **WHO Performance Status** | | | <0.001 | 319.64 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 2.12 (1.81, 2.48) | <0.001 | | |
| Up and about >50% | 4.07 (3.28, 5.04) | <0.001 | | |
| Confined to bed/chair >50% | 6.60 (5.19, 8.38) | <0.001 | | |
| Not recorded | 1.96 (1.63, 2.34) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 158.98 |
| Larynx | 0.47 (0.40, 0.57) | <0.001 | | |
| Oral cavity | 0.66 (0.55, 0.78) | <0.001 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.43 (1.13, 1.82) | 0.003 | | |
| Nasal cavity | 0.75 (0.55, 1.01) | 0.062 | | |
| Lip | 0.18 (0.11, 0.28) | <0.001 | | |
| Other/salivary gland | 0.75 (0.58, 0.99) | 0.040 | | |
| **Tumour stage** | | | <0.001 | 299.14 |
| I | 1.00 (Ref.) | - | | |
| II | 2.14 (1.69, 2.72) | <0.001 | | |
| III | 3.22 (2.53, 4.11) | <0.001 | | |
| IV | 5.36 (4.34, 6.61) | <0.001 | | |
| Unknown | 3.04 (2.27, 4.07) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 684.14 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.24 (1.04, 1.50) | 0.020 | | |
| Surgery and radiotherapy | 1.69 (1.41, 2.03) | <0.001 | | |
| Surgery, radiotherapy and chemotherapy | 2.02 (1.42, 2.87) | <0.001 | | |
| Radiotherapy and chemotherapy | 2.60 (2.04, 3.31) | <0.001 | | |
| Chemotherapy +/- surgery | 12.63 (8.90, 17.90) | <0.001 | | |
| No treatment | 14.39 (11.39, 18.18) | <0.001 | | |
| **Network/region** | | | 0.161 | 3.65 |
| WoSCAN (West Scotland) | 1.13 (0.97, 1.31) | 0.106 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.01 (0.84, 1.21) | 0.931 | | |

*Adjusted by age and tumour sex

**Table 3.10 – Minimally adjusted* hazard ratios for all-cause mortality after 12 years for each patient, tumour, and treatment factor**

| Variable | 12-year all-cause mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Carstairs 2001 Category** | | | 0.005 | 15.10 |
| 1 (Least deprived) | 1.00 (Ref.) | - | | |
| 2 | 0.94 (0.77, 1.15) | 0.441 | | |
| 3 | 1.09 (0.89, 1.32) | 0.479 | | |
| 4 | 1.08 (0.89, 1.30) | 0.406 | | |
| 5 (Most deprived) | 1.27 (1.06, 1.52) | 0.012 | | |
| **Smoking behaviour** | | | <0.001 | 72.33 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.20 (0.98, 1.48) | 0.081 | | |
| Current smoker | 1.88 (1.56, 2.27) | <0.001 | | |
| Not recorded | 1.27 (0.90, 1.79) | 0.170 | | |
| **Alcohol consumption** | | | <0.001 | 86.53 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.63 (1.38, 1.93) | <0.001 | | |
| Current problem drinker | 1.77 (1.55, 2.02) | <0.001 | | |
| Not recorded | 1.02 (0.86, 1.22) | 0.796 | | |
| **WHO Performance Status** | | | <0.001 | 320.45 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.94 (1.70, 2.22) | <0.001 | | |
| Up and about >50% | 3.49 (2.86, 4.25) | <0.001 | | |
| Confined to bed/chair >50% | 5.74 (4.56, 7.22) | <0.001 | | |
| Not recorded | 1.81 (1.55, 2.11) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 156.92 |
| Larynx | 0.54 (0.46, 0.64) | <0.001 | | |
| Oral cavity | 0.71 (0.60, 0.83) | <0.001 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.42 (1.14, 1.78) | 0.002 | | |
| Nasal cavity | 0.77 (0.59, 1.02) | 0.066 | | |
| Lip | 0.23 (0.17, 0.33) | <0.001 | | |
| Other/salivary gland | 0.72 (0.56, 0.92) | 0.009 | | |
| **Tumour stage** | | | <0.001 | 282.10 |
| I | 1.00 (Ref.) | - | | |
| II | 1.60 (1.33, 1.91) | <0.001 | | |
| III | 2.22 (1.84, 2.69) | <0.001 | | |
| IV | 3.51 (3.00, 4.11) | <0.001 | | |
| Unknown | 2.10 (1.65, 2.66) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 650.19 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.24 (1.06, 1.44) | 0.006 | | |
| Surgery and radiotherapy | 1.57 (1.35, 1.83) | <0.001 | | |
| Surgery, radiotherapy and chemotherapy | 1.68 (1.23, 2.31) | 0.001 | | |
| Radiotherapy and chemotherapy | 2.38 (1.92, 2.94) | <0.001 | | |
| Chemotherapy +/- surgery | 10.48 (7.47, 14.71) | <0.001 | | |
| No treatment | 12.17 (9.77, 15.16) | <0.001 | | |
| **Network/region** | | | 0.007 | 10.02 |
| WoSCAN (West Scotland) | 1.22 (1.07, 1.39) | 0.003 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.08 (0.92, 1.26) | 0.377 | | |

*Adjusted by age and tumour sex

**Table 3.11 – Minimally adjusted* hazard ratios for disease-specific mortality after one year for each patient, tumour, and treatment factor**

| Variable | One-year disease-specific mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Carstairs 2001 Category** | | | 0.028 | 10.87 |
| 1 (Least deprived) | 1.00 (Ref.) | - | | |
| 2 | 1.59 (0.99, 2.54) | 0.284 | | |
| 3 | 1.69 (1.06, 2.69) | 0.017 | | |
| 4 | 1.72 (1.10, 2.69) | 0.004 | | |
| 5 (Most deprived) | 2.09 (1.36, 3.22) | <0.001 | | |
| **Smoking behaviour** | | | <0.001 | 27.25 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 0.99 (0.68, 1.44) | 0.950 | | |
| Current smoker | 1.69 (1.21, 2.35) | 0.001 | | |
| Not recorded | 0.72 (0.35, 1.48) | 0.375 | | |
| **Alcohol consumption** | | | <0.001 | 32.15 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.60 (1.21, 2.13) | 0.001 | | |
| Current problem drinker | 1.70 (1.35, 2.13) | <0.001 | | |
| Not recorded | 0.77 (0.55, 1.09) | 0.137 | | |
| **WHO Performance Status** | | | <0.001 | 180.91 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 2.48 (1.93, 3.18) | <0.001 | | |
| Up and about >50% | 4.97 (3.63, 6.81) | <0.001 | | |
| Confined to bed/chair >50% | 7.86 (5.61, 11.03) | <0.001 | | |
| Not recorded | 2.17 (1.63, 2.88) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 74.84 |
| Larynx | 0.44 (0.34, 0.58) | <0.001 | | |
| Oral cavity | 0.60 (0.46, 0.77) | <0.001 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.27 (0.90, 1.78) | 0.174 | | |
| Nasal cavity | 0.72 (0.46, 1.13) | 0.149 | | |
| Lip | 0.04 (0.01, 0.17) | <0.001 | | |
| Other/salivary gland | 0.53 (0.34, 0.83) | 0.005 | | |
| **Tumour stage** | | | <0.001 | 183.62 |
| I | 1.00 (Ref.) | - | | |
| II | 5.68 (3.06, 10.55) | <0.001 | | |
| III | 9.57 (5.17, 17.72) | <0.001 | | |
| IV | 20.52 (11.51, 36.59) | <0.001 | | |
| Unknown | 10.66 (5.53, 20.55) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 495.41 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.72 (1.24, 2.39) | 0.001 | | |
| Surgery and radiotherapy | 2.12 (1.53, 2.94) | <0.001 | | |
| Surgery, radiotherapy and chemotherapy | 4.45 (2.78, 7.12) | <0.001 | | |
| Radiotherapy and chemotherapy | 4.33 (2.98, 6.31) | <0.001 | | |
| Chemotherapy +/- surgery | 18.33 (11.32, 29.70) | <0.001 | | |
| No treatment | 24.15 (17.07, 34.19) | <0.001 | | |
| **Network/region** | | | 0.905 | 0.20 |
| WoSCAN (West Scotland) | 1.03 (0.82, 1.29) | 0.804 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.06 (0.81, 1.40) | 0.656 | | |

*Adjusted by age and tumour sex

**Table 3.12 – Minimally adjusted* hazard ratios for disease-specific mortality after five years for each patient, tumour, and treatment factor**

| Variable | Five-year disease-specific mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Carstairs 2001 Category** | | | 0.005 | 15.00 |
| 1 (Least deprived) | 1.00 (Ref.) | - | | |
| 2 | 1.06 (0.77, 1.46) | 0.693 | | |
| 3 | 1.41 (1.04, 1.92) | 0.029 | | |
| 4 | 1.28 (0.95, 1.72) | 0.107 | | |
| 5 (Most deprived) | 1.55 (1.17, 2.06) | 0.002 | | |
| **Smoking behaviour** | | | <0.001 | 32.40 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.04 (0.75, 1.44) | 0.801 | | |
| Current smoker | 1.72 (1.29, 2.29) | <0.001 | | |
| Not recorded | 0.93 (0.53, 1.65) | 0.804 | | |
| **Alcohol consumption** | | | <0.001 | 40.96 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.64 (1.29, 2.09) | <0.001 | | |
| Current problem drinker | 1.65 (1.36, 2.01) | <0.001 | | |
| Not recorded | 0.79 (0.59, 1.06) | 0.116 | | |
| **WHO Performance Status** | | | <0.001 | 224.53 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 2.20 (1.78, 2.72) | <0.001 | | |
| Up and about >50% | 4.56 (3.46, 6.00) | <0.001 | | |
| Confined to bed/chair >50% | 7.64 (5.66, 10.31) | <0.001 | | |
| Not recorded | 2.11 (1.66, 2.68) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 116.65 |
| Larynx | 0.42 (0.33, 0.53) | <0.001 | | |
| Oral cavity | 0.58 (0.46, 0.72) | <0.001 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.36 (1.01, 1.83) | 0.041 | | |
| Nasal cavity | 0.73 (0.50, 1.07) | 0.106 | | |
| Lip | 0.04 (0.01, 0.13) | <0.001 | | |
| Other/salivary gland | 0.52 (0.36, 0.77) | 0.001 | | |
| **Tumour stage** | | | <0.001 | 248.49 |
| I | 1.00 (Ref.) | - | | |
| II | 2.93 (1.98, 4.34) | <0.001 | | |
| III | 5.11 (3.46, 7.54) | <0.001 | | |
| IV | 10.12 (7.14, 14.35) | <0.001 | | |
| Unknown | 5.33 (3.44, 8.27) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 525.25 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.47 (1.13, 1.91) | 0.005 | | |
| Surgery and radiotherapy | 2.07 (1.60, 2.68) | <0.001 | | |
| Surgery, radiotherapy and chemotherapy | 3.50 (2.32, 5.28) | <0.001 | | |
| Radiotherapy and chemotherapy | 3.82 (2.80, 5.23) | <0.001 | | |
| Chemotherapy +/- surgery | 16.17 (10.41, 25.13) | <0.001 | | |
| No treatment | 19.93 (14.68, 27.05) | <0.001 | | |
| **Network/region** | | | 0.858 | 0.31 |
| WoSCAN (West Scotland) | 1.06 (0.87, 1.28) | 0.580 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.04 (0.82, 1.32) | 0.748 | | |

*Adjusted by age and tumour sex

**Table 3.13 – Minimally adjusted* hazard ratios for disease-specific mortality after 12 years for each patient, tumour, and treatment factor**

| Variable | 12-year disease-specific mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Carstairs 2001 Category** | | | 0.002 | 17.19 |
| 1 (Least deprived) | 1.00 (Ref.) | - | | |
| 2 | 0.98 (0.73, 1.33) | 0.892 | | |
| 3 | 1.32 (0.99, 1.75) | 0.053 | | |
| 4 | 1.27 (0.97, 1.68) | 0.073 | | |
| 5 (Most deprived) | 1.51 (1.16, 1.96) | 0.002 | | |
| **Smoking behaviour** | | | <0.001 | 32.91 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.07 (0.79, 1.45) | 0.644 | | |
| Current smoker | 1.70 (1.30, 2.22) | <0.001 | | |
| Not recorded | 0.94 (0.55, 1.61) | 0.835 | | |
| **Alcohol consumption** | | | <0.001 | 47.75 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.63 (1.29, 2.06) | <0.001 | | |
| Current problem drinker | 1.73 (1.43, 2.08) | <0.001 | | |
| Not recorded | 0.83 (0.64, 1.09) | 0.184 | | |
| **WHO Performance Status** | | | <0.001 | 222.87 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 2.12 (1.74, 2.59) | <0.001 | | |
| Up and about >50% | 4.13 (3.16, 5.40) | <0.001 | | |
| Confined to bed/chair >50% | 7.25 (5.40, 9.72) | <0.001 | | |
| Not recorded | 2.04 (1.63, 2.54) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 123.79 |
| Larynx | 0.46 (0.37, 0.57) | <0.001 | | |
| Oral cavity | 0.63 (0.50, 0.78) | <0.001 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.50 (1.13, 1.99) | 0.006 | | |
| Nasal cavity | 0.78 (0.54, 1.13) | 0.184 | | |
| Lip | 0.08 (0.03, 0.17) | <0.001 | | |
| Other/salivary gland | 0.56 (0.39, 0.80) | 0.002 | | |
| **Tumour stage** | | | <0.001 | 258.81 |
| I | 1.00 (Ref.) | - | | |
| II | 2.47 (1.77, 3.45) | <0.001 | | |
| III | 4.10 (2.94, 5.71) | <0.001 | | |
| IV | 7.80 (5.83, 10.45) | <0.001 | | |
| Unknown | 4.11 (2.79, 6.05) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 527.92 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.45 (1.14, 1.86) | 0.003 | | |
| Surgery and radiotherapy | 2.08 (1.64, 2.64) | <0.001 | | |
| Surgery, radiotherapy and chemotherapy | 3.14 (2.12, 4.65) | <0.001 | | |
| Radiotherapy and chemotherapy | 3.74 (2.79, 5.02) | <0.001 | | |
| Chemotherapy +/- surgery | 15.26 (9.90, 23.53) | <0.001 | | |
| No treatment | 18.98 (14.13, 25.50) | <0.001 | | |
| **Network/region** | | | 0.326 | 2.24 |
| WoSCAN (West Scotland) | 1.15 (0.95, 1.39) | 0.143 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.07 (0.85, 1.35) | 0.551 | | |

*Adjusted by age and tumour sex

### 3.3.6 Mutually adjusted multivariate Cox proportional hazards model for all-cause mortality

Results for the mutually adjusted Cox proportional hazards model for one-year, five-year, and 12-year all-cause mortality are displayed in Table 3.14 to Table 3.16 on Page 133 to Page 135.

#### 3.3.6.1 Determinants with an independent association with all-cause mortality – summary of findings

In the order that they were entered into the model, the determinants that had an independent association with all-cause mortality following the forced inclusion of age at diagnosis, tumour stage and treatment modality in the forward stepwise mutually adjusted Cox proportional hazards models after one year, five years, and 12 years were WHO Performance Status, alcohol consumption, anatomical site, and smoking behaviour. A description of these effects is outlined below.

#### 3.3.6.2 Patient factors with an independent association with all-cause mortality

***Age at diagnosis***

Following mutual adjustment, the patients who were older continued to have a greater risk of all-cause mortality following mutual adjustment, particularly after 12 years, by which time the people who were 75 years and older had a near 2.5-fold (HR = 2.44, 95% CI 1.97 to 3.01) increase in the risk of all-cause mortality compared to those who were aged between the years of 45 and 54.

***Smoking behaviour***

Following mutual adjustment, the patients who were reported as having been current smokers at the time of their head and neck cancer diagnosis were at a greater risk of all-cause mortality compared to those who were reported as having been previous smokers or who had never smoked at the time of their diagnosis. After one year, five years, and 12 years, the people who were current smokers were 42% (HR = 1.42, 95% CI 1.04 to 1.94), 39% (H = 1.39, 95% CI 1.10 to 1.76), and 45% (HR = 1.45, 95% CI 1.19 to 1.77) more at risk of all-cause mortality than those who had never smoked, respectively. However, after one year, five years, and 12 years, the individuals who were previous smokers were not at an increased risk of all-cause mortality compared to those who never smoked following mutual adjustment (one-year HR = 1.12, 95% CI 0.80 to 1.56; five-year HR = 1.04, 95% CI 0.81 to 1.35; 12-year HR = 1.08, 95% CI 0.87 to 1.34).

***Alcohol consumption***

Following mutual adjustment, the patients who were reported as having a current problem with their consumption of alcohol were 32% (HR = 1.32, 95% CI 1.08 to 1.61) more at risk of one-year all-cause mortality than those who were reported as never having drank or who occasionally drank alcohol. Over time, the risk of all-cause mortality became greater for those who had a current problem with their alcohol consumption at diagnosis, and after 12 years these people were 51% (HR = 1.51, 95% CI 1.31 to 1.73) more at risk of all-cause mortality than those who never drank or who occasionally drank alcohol. A similar pattern was observed for the individuals who were reported as having a previous problem with their alcohol consumption at diagnosis, and after one year these people had no excess risk of all-cause mortality than those who were reported as never having drank or who occasionally drank alcohol (HR = 1.19, 95% CI 0.93 to 1.53). However, by five years this risk had increased to 29% (HR = 1.29, 95% CI 1.06 to 1.57) and after 12 years the risk was higher at 36% (HR = 1.36, 95% CI 1.15 to 1.62) for those who had a previous problem with their alcohol consumption compared to those who never drank or who occasionally drank alcohol following mutual adjustment.

***WHO Performance Status***

The patients who had worse WHO Performance Status at the time of their diagnosis were at a significantly increased risk of all-cause mortality following mutual adjustment at all three time points. Those who were reported as being confined to a bed or a chair for more than 50% of their waking hours were at a more than two-fold increased risk of all-cause mortality after one year, five years, and 12 years (one-year HR = 2.38, 95% CI 1.74 to 3.27; five-year HR = 2.80, 95% CI 2.15 to 3.65; 12-year HR = 2.61, 95% CI 2.03 to 3.36) following mutual adjustment.

#### 3.3.6.3 Tumour factors with an independent association with all-cause mortality

**Anatomical site**

Following mutual adjustment, the patients with cancer of the lip had a 50% (HR = 0.50, 95% CI 0.35 to 0.73) lower risk of all-cause mortality after 12 years compared to those with cancer of the oropharynx. People with cancer of the larynx also had a reduced risk of all-cause mortality by 26% (HR = 0.74, 95% CI 0.63 to 0.88) after 12 years compared to those who were diagnosed with cancer of the oropharynx. However, interestingly there were no differences in overall survival between the patients who had cancers of the oropharynx, hypopharynx, nasal cavity, or other tumours of the head and neck cancer after one year, five years, and 12 years following mutual adjustment.

***Tumour stage***

As the tumour stage of the patients' cancer increased, the one-year, five-year, and 12-year risk of all-cause mortality increased at all three time points following mutual adjustment. Individuals who had stage IV cancer had a near six-fold (HR = 5.89, 95% CI 3.98 to 8.71) increased risk of all-cause mortality compared to those who were diagnosed with stage I cancer after one year. Over time, the difference in risk across the cancer stages attenuated, however after 12 years the people who were diagnosed with stage IV cancer still had a more than two-fold (HR = 2.38, 95% CI 1.97 to 2.88) increased risk of all-cause mortality than those who were diagnosed with a tumour stage I tumour following mutual adjustment.

#### 3.3.6.4 Treatment factors with an independent association with all-cause mortality

***Treatment modality***

Following mutual adjustment, the patients who were treated with a combination of surgery and radiotherapy had no excess risk of all-cause mortality compared to those who were treated with surgery only after one year (HR = 0.97, 95% CI 0.73 to 1.29), five years (HR = 1.01, 95% CI 0.82 to 1.24), and 12 years (HR = 1.02, 95% CI 0.86 to 1.22). After one year, the people who were treated with radiotherapy only were 62% (HR = 1.62, 95% CI 1.22 to 2.16) more at risk of all-cause mortality following mutual adjustment compared to those who received surgery only. However, by five years and 12 years this excess risk had reduced to around 30% for those who received radiotherapy only compared to those who received surgery only following adjustment for age and tumour stage (five-year HR = 1.32, 95% CI 1.07 to 1.63; 12-year HR = 1.31, 95% CI 1.09 to 1.57).

**Table 3.14 – Mutually adjusted hazard ratios for all-cause mortality after one year for each patient, tumour, and treatment factor**

| Variable | One-year all-cause mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 22.23 |
| Less than 45 | 0.71 (0.42, 1.21) | 0.208 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.00 (0.77, 1.29) | 0.991 | | |
| 65 to 74 | 1.37 (1.05, 1.79) | 0.019 | | |
| 75 and over | 1.60 (1.18, 2.18) | 0.002 | | |
| **Smoking behaviour** | | | 0.024 | 9.40 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.12 (0.80, 1.56) | 0.520 | | |
| Current smoker | 1.42 (1.04, 1.94) | 0.026 | | |
| Not recorded | 0.94 (0.51, 1.73) | 0.835 | | |
| **Alcohol consumption** | | | 0.023 | 10.82 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.19 (0.93, 1.53) | 0.169 | | |
| Current problem drinker | 1.32 (1.08, 1.61) | 0.006 | | |
| Not recorded | 0.86 (0.63, 1.16) | 0.323 | | |
| **WHO Performance Status** | | | <0.001 | 41.46 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.52 (1.23, 1.89) | <0.001 | | |
| Up and about >50% | 2.19 (1.66, 2.90) | <0.001 | | |
| Confined to bed/chair >50% | 2.38 (1.74, 3.27) | <0.001 | | |
| Not recorded | 1.45 (1.13, 1.85) | 0.003 | | |
| **Anatomical site** | | | 0.006 | 18.33 |
| Larynx | 0.72 (0.57, 0.91) | 0.007 | | |
| Oral cavity | 1.00 (0.79, 1.27) | 0.991 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 0.99 (0.74, 1.31) | 0.926 | | |
| Nasal cavity | 0.80 (0.54, 1.20) | 0.279 | | |
| Lip | 0.48 (0.23, 1.03) | 0.058 | | |
| Other/salivary gland | 1.25 (0.88, 1.77) | 0.210 | | |
| **Tumour stage** | | | <0.001 | 88.70 |
| I | 1.00 (Ref.) | - | | |
| II | 2.71 (1.81, 4.05) | <0.001 | | |
| III | 4.17 (2.77, 6.27) | <0.001 | | |
| IV | 5.89 (3.98, 8.71) | <0.001 | | |
| Unknown | 4.36 (2.74, 6.95) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 285.18 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.62 (1.22, 2.16) | <0.001 | | |
| Surgery and radiotherapy | 0.97 (0.73, 1.29) | 0.828 | | |
| Surgery, radiotherapy and chemotherapy | 1.39 (0.88, 2.19) | 0.154 | | |
| Radiotherapy and chemotherapy | 1.70 (1.21, 2.40) | 0.002 | | |
| Chemotherapy +/- surgery | 7.25 (4.77, 11.02) | <0.001 | | |
| No treatment | 7.78 (5.68, 10.66) | <0.001 | | |

**Table 3.15 – Mutually adjusted hazard ratios for all-cause mortality after five years for each patient, tumour, and treatment factor**

| Variable | Five-year all-cause mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 69.51 |
| Less than 45 | 0.56 (0.36, 0.87) | 0.010 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.11 (0.91, 1.36) | 0.306 | | |
| 65 to 74 | 1.65 (1.34, 2.03) | <0.001 | | |
| 75 and over | 2.01 (1.58, 2.56) | <0.001 | | |
| **Smoking behaviour** | | | 0.001 | 16.08 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.04 (0.81, 1.35) | 0.745 | | |
| Current smoker | 1.39 (1.10, 1.76) | 0.006 | | |
| Not recorded | 1.14 (0.72, 1.79) | 0.574 | | |
| **Alcohol consumption** | | | <0.001 | 29.35 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.29 (1.06, 1.57) | 0.012 | | |
| Current problem drinker | 1.50 (1.28, 1.75) | <0.001 | | |
| Not recorded | 0.95 (0.76, 1.20) | 0.688 | | |
| **WHO Performance Status** | | | <0.001 | 79.64 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.51 (1.28, 1.77) | <0.001 | | |
| Up and about >50% | 2.27 (1.81, 2.86) | <0.001 | | |
| Confined to bed/chair >50% | 2.80 (2.15, 3.65) | <0.001 | | |
| Not recorded | 1.44 (1.19, 1.73) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 29.90 |
| Larynx | 0.70 (0.57, 0.85) | <0.001 | | |
| Oral cavity | 0.95 (0.78, 1.15) | 0.570 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.05 (0.82, 1.34) | 0.708 | | |
| Nasal cavity | 0.83 (0.60, 1.14) | 0.243 | | |
| Lip | 0.48 (0.30, 0.78) | 0.003 | | |
| Other/salivary gland | 1.12 (0.84, 1.48) | 0.457 | | |
| **Tumour stage** | | | <0.001 | 96.36 |
| I | 1.00 (Ref.) | - | | |
| II | 1.91 (1.50, 2.43) | <0.001 | | |
| III | 2.46 (1.90, 3.18) | <0.001 | | |
| IV | 3.33 (2.61, 4.26) | <0.001 | | |
| Unknown | 2.61 (1.91, 3.58) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 277.35 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.32 (1.07, 1.63) | 0.011 | | |
| Surgery and radiotherapy | 1.01 (0.82, 1.24) | 0.917 | | |
| Surgery, radiotherapy and chemotherapy | 1.08 (0.74, 1.57) | 0.682 | | |
| Radiotherapy and chemotherapy | 1.39 (1.06, 1.83) | 0.017 | | |
| Chemotherapy +/- surgery | 6.24 (4.29, 9.06) | <0.001 | | |
| No treatment | 6.22 (4.77, 8.10) | <0.001 | | |

**Table 3.16 – Mutually adjusted hazard ratios for all-cause mortality after 12 years for each patient, tumour, and treatment factor**

| Variable | 12-year all-cause mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 139.21 |
| Less than 45 | 0.59 (0.42, 0.84) | 0.004 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.17 (0.98, 1.40) | 0.077 | | |
| 65 to 74 | 1.94 (1.62, 2.32) | <0.001 | | |
| 75 and over | 2.44 (1.97, 3.01) | <0.001 | | |
| **Smoking behaviour** | | | <0.001 | 24.62 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.08 (0.87, 1.34) | 0.488 | | |
| Current smoker | 1.45 (1.19, 1.77) | <0.001 | | |
| Not recorded | 1.22 (0.83, 1.80) | 0.304 | | |
| **Alcohol consumption** | | | <0.001 | 38.81 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.36 (1.15, 1.62) | <0.001 | | |
| Current problem drinker | 1.51 (1.31, 1.73) | <0.001 | | |
| Not recorded | 1.01 (0.83, 1.23) | 0.900 | | |
| **WHO Performance Status** | | | <0.001 | 84.55 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.46 (1.27, 1.68) | <0.001 | | |
| Up and about >50% | 2.13 (1.73, 2.63) | <0.001 | | |
| Confined to bed/chair >50% | 2.61 (2.03, 3.36) | <0.001 | | |
| Not recorded | 1.42 (1.21, 1.66) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 32.79 |
| Larynx | 0.74 (0.63, 0.88) | <0.001 | | |
| Oral cavity | 0.98 (0.82, 1.16) | 0.790 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.06 (0.84, 1.33) | 0.624 | | |
| Nasal cavity | 0.78 (0.59, 1.04) | 0.087 | | |
| Lip | 0.50 (0.35, 0.73) | <0.001 | | |
| Other/salivary gland | 1.02 (0.79, 1.33) | 0.881 | | |
| **Tumour stage** | | | <0.001 | 83.57 |
| I | 1.00 (Ref.) | - | | |
| II | 1.44 (1.20, 1.73) | <0.001 | | |
| III | 1.77 (1.45, 2.17) | <0.001 | | |
| IV | 2.38 (1.97, 2.88) | <0.001 | | |
| Unknown | 1.97 (1.52, 2.56) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 283.86 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.31 (1.09, 1.57) | 0.004 | | |
| Surgery and radiotherapy | 1.02 (0.86, 1.22) | 0.810 | | |
| Surgery, radiotherapy and chemotherapy | 1.00 (0.72, 1.39) | 0.984 | | |
| Radiotherapy and chemotherapy | 1.40 (1.10, 1.78) | 0.006 | | |
| Chemotherapy +/- surgery | 6.01 (4.19, 8.62) | <0.001 | | |
| No treatment | 5.99 (4.67, 7.69) | <0.001 | | |

#### 3.3.6.5 Sensitivity analysis 1 – excluding people who received no treatment in the models for all-cause mortality

The results for the forward stepwise models which excluded the people who received no treatment after one year, five years, and 12 years are displayed in Table 3.17 to Table 3.19. Following the exclusion of the people who received no treatment, a total of 1,691 people remained in this sensitivity analysis. When a forward stepwise multivariate Cox proportional hazards model was performed, the determinants with an independent association with all-cause mortality following the forced inclusion of age at diagnosis, tumour stage, and treatment modality after one year, five years, and 12 years were WHO Performance Status, alcohol consumption, anatomical site, and smoking behaviour. This displayed the same results as the main cohort.

#### 3.3.6.6 Sensitivity analysis 2 – excluding people with oropharynx cancer in the models for all-cause mortality

The results for the forward stepwise models which excluded the people who had cancer of the oropharynx after one year, five years, and 12 years are displayed in Table 3.20 to Table 3.22. Following the exclusion of the people who had cancer of the oropharynx, a total of 1,497 people remained in this sensitivity analysis. The determinants with an independent association with all-cause mortality in a mutually adjusted Cox proportional hazards model following the forced inclusion of age at diagnosis, tumour stage, and treatment modality were WHO Performance Status, alcohol consumption, anatomical site, and smoking behaviour after five years and 12 years. These results were the same as the results for the main cohort of people at both five years and 12 years. However, the results differed slightly after one year and the determinants with an independent association with all-cause mortality after one year included age at diagnosis, tumour stage, treatment modality, WHO Performance Status, alcohol consumption, anatomical site, and Scottish Cancer Network.

**Table 3.17 – Mutually adjusted hazard ratios for all-cause mortality after one year for each patient, tumour, and treatment factor following the exclusion of people who received no treatment (n = 1,691)**

| Variable | One-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 19.22 |
| Less than 45 | 0.80 (0.47, 1.39) | 0.434 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.09 (0.83, 1.43) | 0.522 | | |
| 65 to 74 | 1.52 (1.15, 2.01) | 0.003 | | |
| 75 and over | 1.69 (1.21, 2.37) | 0.002 | | |
| **Smoking status** | | | 0.015 | 10.47 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.10 (0.77, 1.57) | 0.588 | | |
| Current smoker | 1.45 (1.05, 2.01) | 0.025 | | |
| Unknown | 0.74 (0.35, 1.59) | 0.442 | | |
| **Alcohol consumption** | | | 0.006 | 12.59 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.14 (0.87, 1.51) | 0.348 | | |
| Current problem drinker | 1.41 (1.14, 1.74) | 0.002 | | |
| Not recorded | 0.83 (0.58, 1.20) | 0.316 | | |
| **WHO Performance Status** | | | <0.001 | 42.81 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.52 (1.22, 1.91) | 0.001 | | |
| Up and about >50% | 2.59 (1.92, 3.48) | <0.001 | | |
| Confined to bed/chair >50% | 1.98 (1.32, 2.97) | 0.001 | | |
| Not recorded | 1.47 (1.14, 1.89) | 0.003 | | |
| **Anatomical site** | | | <0.001 | 31.07 |
| Larynx | 0.67 (0.52, 0.88) | 0.001 | | |
| Oral cavity | 1.18 (0.90, 1.54) | 0.003 | | |
| Oropharynx | 1.00 (Ref.) | | | |
| Hypopharynx | 1.30 (0.95, 1.78) | 0.105 | | |
| Nasal cavity | 0.90 (0.58, 1.41) | 0.657 | | |
| Lip | 0.60 (0.28, 1.30) | 0.195 | | |
| Other/salivary gland | 1.38 (0.95, 2.00) | 0.093 | | |
| **Stage** | | | <0.001 | 102.05 |
| I | 1.00 (Ref.) | - | | |
| II | 2.55 (1.68, 3.86) | <0.001 | | |
| III | 4.09 (2.68, 6.24) | <0.001 | | |
| IV | 6.72 (4.48, 10.08) | <0.001 | | |
| Unknown | 3.76 (2.25, 6.29) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 129.61 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.74 (1.31, 2.32) | 0.001 | | |
| Surgery and radiotherapy | 0.91 (0.68, 1.22) | 0.533 | | |
| Surgery, radiotherapy and chemotherapy | 1.28 (0.81, 2.03) | 0.294 | | |
| Radiotherapy and chemotherapy | 1.58 (1.11, 2.25) | 0.011 | | |
| Chemotherapy +/- surgery | 7.96 (5.17, 12.26) | <0.001 | | |

**Table 3.18 – Mutually adjusted hazard ratios for all-cause mortality after five years for each patient, tumour, and treatment factor study following the exclusion of people who received no treatment (n = 1,691)**

| Variable | Five-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 65.73 |
| Less than 45 | 0.59 (0.38, 0.93) | 0.022 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.18 (0.96, 1.46) | 0.125 | | |
| 65 to 74 | 1.76 (1.42, 2.18) | <0.001 | | |
| 75 and over | 2.09 (1.62, 2.07) | <0.001 | | |
| **Smoking status** | | | <0.001 | 18.30 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.02 (0.78, 1.32) | 0.904 | | |
| Current smoker | 1.42 (1.11, 1.81) | 0.005 | | |
| Unknown | 1.08 (0.65, 1.79) | 0.771 | | |
| **Alcohol consumption** | | | <0.001 | 28.58 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.24 (1.00, 1.53) | 0.050 | | |
| Current problem drinker | 1.53 (1.30, 1.80) | <0.001 | | |
| Not recorded | 0.94 (0.72, 1.21) | 0.622 | | |
| **WHO Performance Status** | | | <0.001 | 80.83 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.49 (1.26, 1.76) | <0.001 | | |
| Up and about >50% | 2.60 (2.04, 3.31) | <0.001 | | |
| Confined to bed/chair >50% | 2.69 (1.96, 3.68) | <0.001 | | |
| Not recorded | 1.47 (1.21, 1.78) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 44.09 |
| Larynx | 0.67 (0.54, 0.82) | <0.001 | | |
| Oral cavity | 1.03 (0.84, 1.27) | 0.764 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.34 (1.03, 1.74) | 0.030 | | |
| Nasal cavity | 0.96 (0.68, 1.35) | 0.799 | | |
| Lip | 0.56 (0.34, 0.91) | 0.020 | | |
| Other/salivary gland | 1.17 (0.87, 1.58) | 0.297 | | |
| **Stage** | | | <0.001 | 106.27 |
| I | 1.00 (Ref.) | - | | |
| II | 1.87 (1.46, 2.40) | <0.001 | | |
| III | 2.44 (1.88, 3.18) | <0.001 | | |
| IV | 3.63 (2.82, 4.66) | <0.001 | | |
| Unknown | 2.33 (1.65, 3.30) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 118.70 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.38 (1.12, 1.71) | 0.003 | | |
| Surgery and radiotherapy | 0.98 (0.79, 1.21) | 0.831 | | |
| Surgery, radiotherapy and chemotherapy | 1.03 (0.71, 1.50) | 0.880 | | |
| Radiotherapy and chemotherapy | 1.31 (1.00, 1.73) | 0.053 | | |
| Chemotherapy +/- surgery | 6.76 (4.62, 9.88) | <0.001 | | |

**Table 3.19 – Mutually adjusted hazard ratios for all-cause mortality after 12 years for each patient, tumour, and treatment factor following the exclusion of people who received no treatment (n = 1,691)**

| Variable | 12-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 133.95 |
| Less than 45 | 0.61 (0.43, 0.88) | 0.008 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.23 (1.03, 1.47) | 0.024 | | |
| 65 to 74 | 2.03 (1.69, 2.44) | <0.001 | | |
| 75 and over | 2.53 (2.03, 3.15) | <0.001 | | |
| **Smoking status** | | | <0.001 | 27.03 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 1.06 (0.85, 1.32) | 0.591 | | |
| Current smoker | 1.47 (1.20, 1.81) | <0.001 | | |
| Unknown | 1.20 (0.79, 1.81) | 0.397 | | |
| **Alcohol consumption** | | | <0.001 | 36.01 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.32 (1.10, 1.58) | 0.003 | | |
| Current problem drinker | 1.52 (1.32, 1.75) | <0.001 | | |
| Not recorded | 1.00 (0.81, 1.23) | 0.972 | | |
| **WHO Performance Status** | | | <0.001 | 83.17 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.43 (1.24, 1.65) | <0.001 | | |
| Up and about >50% | 2.34 (1.87, 2.92) | <0.001 | | |
| Confined to bed/chair >50% | 2.50 (1.85, 3.38) | <0.001 | | |
| Not recorded | 1.46 (1.24, 1.72) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 41.43 |
| Larynx | 0.73 (0.61, 0.87) | <0.001 | | |
| Oral cavity | 1.05 (0.88, 1.26) | 0.586 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.29 (1.01, 1.64) | 0.043 | | |
| Nasal cavity | 0.93 (0.69, 1.26) | 0.645 | | |
| Lip | 0.58 (0.40, 0.84) | 0.004 | | |
| Other/salivary gland | 1.06 (0.81, 1.39) | 0.675 | | |
| **Stage** | | | <0.001 | 91.03 |
| I | 1.00 (Ref.) | - | | |
| II | 1.41 (1.17, 1.70) | <0.001 | | |
| III | 1.75 (1.42, 2.15) | <0.001 | | |
| IV | 2.52 (2.08, 3.06) | <0.001 | | |
| Unknown | 1.75 (1.32, 2.32) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 121.10 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.37 (1.14, 1.64) | <0.001 | | |
| Surgery and radiotherapy | 1.00 (0.84, 1.20) | 0.981 | | |
| Surgery, radiotherapy and chemotherapy | 0.97 (0.69, 1.36) | 0.855 | | |
| Radiotherapy and chemotherapy | 1.35 (1.05, 1.72) | 0.017 | | |
| Chemotherapy +/- surgery | 6.58 (4.57, 9.47) | <0.001 | | |

**Table 3.20 – Mutually adjusted hazard ratios for all-cause mortality after one year for each patient, tumour, and treatment factor following the exclusion of people who had oropharynx cancer (n = 1,497)**

| Variable | One-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.015 | 12.31 |
| Less than 45 | 0.55 (0.29, 1.05) | 0.070 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.82 (0.61, 1.11) | 0.197 | | |
| 65 to 74 | 1.07 (0.80, 1.44) | 0.640 | | |
| 75 and over | 1.23 (0.88, 1.71) | 0.232 | | |
| **Alcohol consumption** | | | 0.006 | 12.34 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.40 (1.05, 1.86) | 0.020 | | |
| Current problem drinker | 1.38 (1.11, 1.72) | 0.004 | | |
| Not recorded | 0.94 (0.70, 1.27) | 0.681 | | |
| **WHO Performance Status** | | | <0.001 | 42.56 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.45 (1.13, 1.85) | 0.003 | | |
| Up and about >50% | 2.67 (1.95, 3.66) | <0.001 | | |
| Confined to bed/chair >50% | 2.30 (1.59, 3.32) | <0.001 | | |
| Not recorded | 1.40 (1.06, 1.85) | 0.018 | | |
| **Anatomical site** | | | 0.007 | 16.14 |
| Larynx | 1.00 (Ref.) | | | |
| Oral cavity | 1.38 (1.09, 1.75) | 0.008 | | |
| Hypopharynx | 1.34 (0.99, 1.79) | 0.055 | | |
| Nasal cavity | 1.03 (0.68, 1.56) | 0.879 | | |
| Lip | 0.68 (0.32, 1.45) | 0.315 | | |
| Other/salivary gland | 1.67 (1.17, 2.36) | 0.004 | | |
| **Stage** | | | <0.001 | 82.36 |
| I | 1.00 (Ref.) | - | | |
| II | 2.99 (1.94, 4.61) | <0.001 | | |
| III | 4.34 (2.77, 6.79) | <0.001 | | |
| IV | 6.57 (4.29, 10.06) | <0.001 | | |
| Unknown | 4.24 (2.56, 7.01) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 200.22 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.63 (1.19, 2.22) | 0.002 | | |
| Surgery and radiotherapy | 1.01 (0.74, 1.38) | 0.966 | | |
| Surgery, radiotherapy and chemotherapy | 1.26 (0.71, 2.25) | 0.423 | | |
| Radiotherapy and chemotherapy | 2.26 (1.53, 3.34) | <0.001 | | |
| Chemotherapy +/- surgery | 5.78 (3.45, 9.68) | <0.001 | | |
| No treatment | 7.77 (5.47, 11.04) | <0.001 | | |
| **Network/region** | | | 0.040 | 6.45 |
| WoSCAN (West Scotland) | 1.15 (0.91, 1.46) | 0.235 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.43 (1.08, 1.89) | 0.012 | | |

**Table 3.21 – Mutually adjusted hazard ratios for all-cause mortality after five years for each patient, tumour, and treatment factor following the exclusion of people who had oropharynx cancer (n = 1,497)**

| Variable | Five-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 49.06 |
| Less than 45 | 0.42 (0.25, 0.73) | 0.002 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.98 (0.78, 1.24) | 0.882 | | |
| 65 to 74 | 1.40 (1.11, 1.77) | 0.004 | | |
| 75 and over | 1.75 (1.35, 2.28) | <0.001 | | |
| **Smoking status** | | | 0.013 | 10.84 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 0.90 (0.68, 1.19) | 0.462 | | |
| Current smoker | 1.21 (0.93, 1.56) | 0.153 | | |
| Unknown | 0.95 (0.59, 1.54) | 0.840 | | |
| **Alcohol consumption** | | | <0.001 | 23.07 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.48 (1.18, 1.85) | <0.001 | | |
| Current problem drinker | 1.46 (1.23, 1.74) | <0.001 | | |
| Not recorded | 1.04 (0.81, 1.34) | 0.766 | | |
| **WHO Performance Status** | | | <0.001 | 75.91 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.41 (1.18, 1.70) | <0.001 | | |
| Up and about >50% | 2.69 (2.08, 3.48) | <0.001 | | |
| Confined to bed/chair >50% | 2.77 (2.05, 3.73) | <0.001 | | |
| Not recorded | 1.42 (1.15, 1.75) | 0.00 | | |
| **Anatomical site** | | | <0.001 | 26.45 |
| Larynx | 1.00 (Ref.) | - | | |
| Oral cavity | 1.37 (1.13, 1.66) | 0.001 | | |
| Hypopharynx | 1.51 (1.18, 1.94) | 0.001 | | |
| Nasal cavity | 1.17 (0.85, 1.62) | 0.335 | | |
| Lip | 0.71 (0.44, 1.14) | 0.156 | | |
| Other/salivary gland | 1.60 (1.20, 2.13) | 0.001 | | |
| **Stage** | | | <0.001 | 86.43 |
| I | 1.00 (Ref.) | - | | |
| II | 2.07 (1.60, 2.69) | <0.001 | | |
| III | 2.54 (1.92, 3.35) | <0.001 | | |
| IV | 3.48 (2.67, 4.54) | <0.001 | | |
| Unknown | 2.71 (1.94, 3.77) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 180.84 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.31 (1.04, 1.65) | 0.023 | | |
| Surgery and radiotherapy | 1.04 (0.83, 1.30) | 0.732 | | |
| Surgery, radiotherapy and chemotherapy | 1.11 (0.70, 1.75) | 0.663 | | |
| Radiotherapy and chemotherapy | 1.67 (1.22, 2.28) | 0.001 | | |
| Chemotherapy +/- surgery | 5.19 (3.26, 8.28) | <0.001 | | |
| No treatment | 5.73 (4.26, 7.70) | <0.001 | | |

**Table 3.22 – Mutually adjusted hazard ratios for all-cause mortality after 12 years for each patient, tumour, and treatment factor following the exclusion of people who had oropharynx cancer (n = 1,497)**

| Variable | 12-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 101.06 |
| Less than 45 | 0.52 (0.34, 0.78) | 0.002 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.03 (0.84, 1.25) | 0.805 | | |
| 65 to 74 | 1.67 (1.37, 2.04) | <0.001 | | |
| 75 and over | 2.13 (1.69, 2.68) | <0.001 | | |
| **Smoking status** | | | <0.001 | 16.89 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 0.95 (0.75, 1.19) | 0.644 | | |
| Current smoker | 1.28 (1.03, 1.59) | 0.026 | | |
| Unknown | 1.04 (0.69, 1.57) | 0.840 | | |
| **Alcohol consumption** | | | <0.001 | 32.23 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.55 (1.28, 1.89) | <0.001 | | |
| Current problem drinker | 1.46 (1.25, 1.70) | <0.001 | | |
| Not recorded | 1.10 (0.89, 1.35) | 0.389 | | |
| **WHO Performance Status** | | | <0.001 | 79.91 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.37 (1.17, 1.60) | <0.001 | | |
| Up and about >50% | 2.54 (2.00, 3.21) | <0.001 | | |
| Confined to bed/chair >50% | 2.56 (1.93, 3.39) | <0.001 | | |
| Not recorded | 1.39 (1.17, 1.66) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 29.88 |
| Larynx | 1.00 (Ref.) | - | | |
| Oral cavity | 1.33 (1.13, 1.57) | <0.001 | | |
| Hypopharynx | 1.44 (1.15, 1.81) | 0.002 | | |
| Nasal cavity | 1.05 (0.78, 1.39) | 0.764 | | |
| Lip | 0.69 (0.48, 0.99) | 0.043 | | |
| Other/salivary gland | 1.35 (1.04, 1.76) | 0.023 | | |
| **Stage** | | | <0.001 | 84.62 |
| I | 1.00 (Ref.) | - | | |
| II | 1.56 (1.28, 1.90) | <0.001 | | |
| III | 1.83 (1.47, 2.28) | <0.001 | | |
| IV | 2.58 (2.10, 3.17) | <0.001 | | |
| Unknown | 2.14 (1.63, 2.80) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 181.88 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.34 (1.09, 1.63) | 0.004 | | |
| Surgery and radiotherapy | 1.02 (0.84, 1.23) | 0.839 | | |
| Surgery, radiotherapy and chemotherapy | 1.12 (0.75, 1.66) | 0.583 | | |
| Radiotherapy and chemotherapy | 1.56 (1.18, 2.07) | 0.002 | | |
| Chemotherapy +/- surgery | 4.72 (3.00, 7.43) | <0.001 | | |
| No treatment | 5.41 (4.09, 7.16) | <0.001 | | |

### 3.3.7 Mutually adjusted multivariate Cox proportional hazards model for disease-specific mortality

Results for the mutually adjusted Cox proportional hazards model for one-year, five-year, and 12-year disease-specific mortality are displayed in Table 3.23 to Table 3.25 on Page 146 to Page 148.

#### 3.3.7.1 Determinants with an independent association with disease-specific mortality – summary of findings

In the order that they entered the model, the determinants that had an independent association with disease-specific mortality following mutual adjustment and after the forced inclusion of age at diagnosis, tumour stage, and treatment modality after one year were WHO Performance Status, alcohol consumption, and network; and at five years and 12 years included WHO Performance Status, alcohol consumption, and anatomical site. These results were similar to the results for all-cause mortality. However, after one year anatomical site was not an independent predictor of disease-specific mortality, but Scottish Cancer Network was an independent predictor of disease-specific mortality. Interestingly, and unlike the results for all-cause mortality, smoking behaviour was also not an independent predictor in any of the models for one-year, five-year or 12-year disease-specific mortality. A description of these effects is outlined below.

#### 3.3.7.2 Patient factors with an independent association with disease-specific mortality

***Age at diagnosis***

Patients who were older continued to have a greater risk of disease-specific mortality following mutual adjustment, particularly after 12 years by which time those who were 75 years and older had a 58% (HR = 1.58, 95% CI 1.18 to 2.11) increased risk of disease-specific mortality compared to those who were aged between the years of 45 and 54.

***Alcohol consumption***

The patients who were reported as having a current problem with their consumption of alcohol were more than 40% more at risk of disease-specific mortality than those who were reported as never having drank or who occasionally drank alcohol following mutual adjustment after one and five years (one-year HR = 1.42, 95% CI 1.13 to 1.78; five-year HR = 1.45, 95% CI 1.19 to 1.76). Similar to the results for all-cause mortality, over time, the risk of disease-specific mortality became greater for those who had a current problem

with their alcohol consumption at diagnosis, and after 12 years these people were 54% (HR = 1.54, 95% CI 1.28 to 1.86) more at risk of disease-specific mortality than those who never drank or who occasionally drank alcohol.

***WHO Performance Status***

Patients who had a worse WHO Performance Status at diagnosis were at a substantially increased risk of disease-specific mortality following mutual adjustment at all three time points. Individuals who were reported as being confined to a bed or a chair for more than 50% of their waking hours were at a more than 2.5-fold increased risk of disease-specific mortality after one year, five years, and 12 years (one-year HR = 2.51, 95% CI 1.72 to 3.66; five-year HR = 2.72, 95% CI 1.95 to 3.80; 12-year HR = 2.66, 95% CI 1.92 to 3.68) following mutual adjustment. These results were comparable to the results for all-cause mortality following mutual adjustment.

#### 3.3.7.3 Tumour factors with an independent association with disease-specific mortality

***Anatomical site***

Anatomical site was an independent predictor of five-year and 12-year disease-specific mortality, but not one-year disease-specific mortality. Following mutual adjustment, the patients with cancer of the lip had a 75% (HR = 0.25, 95% CI 0.11 to 0.58) lower risk of disease-specific mortality after 12 years compared to those with cancer of the oropharynx. People with cancer of the larynx also had a reduced risk of disease-specific mortality by 22% (HR = 0.78, 95% CI 0.61 to 0.99) after 12 years compared to those who were diagnosed with cancer of the oropharynx. However, interestingly there were no differences between the outcomes for individuals with oropharynx, hypopharynx, nasal cavity, and other tumours of the head and neck after one year, five years, and 12 years following mutual adjustment.

***Tumour stage***

As the stage of the patients' tumour increased, the risk of one-year, five-year, and 12-year disease-specific mortality increased at all three time points following mutual adjustment. Individuals who had stage IV cancer had more than a 12-fold (HR = 12.42, 95% CI 6.77 to 22.83) increased risk of disease-specific mortality compared to those who were diagnosed with stage I cancer after one year. This was substantially higher than the results for all-cause mortality, suggesting that people with stage IV cancers are highly likely to have died from their cancer. Over time, the difference in risk across the tumour stages attenuated in the same way that it did for all-cause mortality, however after 12 years the

patients who were diagnosed with stage IV cancer were still nearly five times (HR = 4.86, 95% CI 3.49 to 6.77) more at risk of disease-specific mortality than the people who were diagnosed with a stage I tumour following mutual adjustment.

#### 3.3.7.4 Treatment factors with an independent association with disease-specific mortality

***Treatment modality***

Following mutual adjustment, the patients who were treated with a combination of surgery and radiotherapy had no excess risk of disease-specific mortality compared to those who were treated with surgery only after one year (HR = 1.12, 95% CI 0.79 to 1.59), five years (HR = 1.07, 95% CI 0.81 to 1.43), or 12 years (HR = 1.14, 95% CI 0.88 to 1.49), which was the same as the results for all-cause mortality. After one year, the individuals who were treated with radiotherapy only were 70% (HR = 1.70, 95% CI 1.21 to 1.59) more at risk of disease-specific mortality following mutual adjustment compared to those who received surgery only. However, by five years and 12 years this excess risk had reduced slightly to 54% for those who received radiotherapy only compared to those who received surgery only following adjustment for age and tumour stage (five-year HR = 1.54, 95% CI 1.15 to 2.06; 12-year HR = 1.54, 95% CI 1.17 to 2.03). These results were comparable to the results for all-cause mortality.

***Network***

Scottish Cancer Network was an independent predictor of one-year disease-specific mortality, but not for five-year or 12-year disease-specific mortality. These results were not observed in the mutually adjusted models for all-cause mortality. Patients who were diagnosed in the North of Scotland Cancer Network were 30% (HR = 1.30, 95% CI 0.98 to 1.73) more at risk of disease-specific mortality than those who were in the East of Scotland Cancer Network. Those who were treated in the West of Scotland Cancer Network were not at an increased risk of disease-specific mortality than those who were treated in the East of Scotland Cancer Network (HR = 0.95, 95% CI 0.74 to 1.20).

**Table 3.23 – Mutually adjusted hazard ratios for disease-specific mortality after one year for each patient, tumour, and treatment factor**

| Variable | One-year disease-specific mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.018 | 11.93 |
| Less than 45 | 0.70 (0.38, 1.27) | 0.236 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.89 (0.66, 1.20) | 0.432 | | |
| 65 to 74 | 1.03 (0.76, 1.40) | 0.856 | | |
| 75 and over | 1.41 (1.00, 2.00) | 0.053 | | |
| **Alcohol consumption** | | | <0.001 | 19.33 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.35 (1.01, 1.80) | 0.041 | | |
| Current problem drinker | 1.42 (1.13, 1.78) | 0.002 | | |
| Not recorded | 0.69 (0.48, 0.97) | 0.035 | | |
| **WHO Performance Status** | | | <0.001 | 31.61 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.60 (1.23, 2.09) | <0.001 | | |
| Up and about >50% | 2.25 (1.60, 3.15) | <0.001 | | |
| Confined to bed/chair >50% | 2.51 (1.72, 3.66) | <0.001 | | |
| Not recorded | 1.51 (1.11, 2.04) | 0.008 | | |
| **Tumour stage** | | | <0.001 | 84.00 |
| I | 1.00 (Ref.) | - | | |
| II | 4.89 (2.62, 9.12) | <0.001 | | |
| III | 7.23 (3.85, 13.57) | <0.001 | | |
| IV | 12.42 (6.77, 22.83) | <0.001 | | |
| Unknown | 7.86 (3.99, 15.51) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 233.82 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.70 (1.21, 2.38) | 0.002 | | |
| Surgery and radiotherapy | 1.12 (0.79, 1.59) | 0.532 | | |
| Surgery, radiotherapy and chemotherapy | 2.08 (1.26, 3.42) | 0.004 | | |
| Radiotherapy and chemotherapy | 2.13 (1.42, 3.19) | <0.001 | | |
| Chemotherapy +/- surgery | 7.27 (4.41, 12.00) | <0.001 | | |
| No treatment | 10.15 (6.93, 14.87) | <0.001 | | |
| **Network/region** | | | 0.043 | 6.29 |
| WoSCAN (West Scotland) | 0.95 (0.74, 1.20) | 0.649 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.30 (0.98, 1.73) | 0.071 | | |

**Table 3.24 – Mutually adjusted hazard ratios for disease-specific mortality after five years for each patient, tumour, and treatment factor**

| Variable | Five-year disease-specific mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 19.77 |
| Less than 45 | 0.66 (0.40, 1.11) | 0.118 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.95 (0.74, 1.23) | 0.721 | | |
| 65 to 74 | 1.24 (0.95, 1.62) | 0.112 | | |
| 75 and over | 1.55 (1.14, 2.10) | 0.005 | | |
| **Alcohol consumption** | | | <0.001 | 24.63 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.41 (1.10, 1.81) | 0.006 | | |
| Current problem drinker | 1.45 (1.19, 1.76) | <0.001 | | |
| Not recorded | 0.76 (0.57, 1.03) | 0.073 | | |
| **WHO Performance Status** | | | <0.001 | 43.61 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.43 (1.15, 1.78) | 0.002 | | |
| Up and about >50% | 2.15 (1.60, 2.89) | <0.001 | | |
| Confined to bed/chair >50% | 2.72 (1.95, 3.80) | <0.001 | | |
| Not recorded | 1.45 (1.13, 1.86) | 0.003 | | |
| **Anatomical site** | | | 0.007 | 17.81 |
| Larynx | 0.73 (0.57, 0.93) | 0.011 | | |
| Oral cavity | 0.91 (0.71, 1.17) | 0.465 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 0.98 (0.73, 1.33) | 0.900 | | |
| Nasal cavity | 0.79 (0.53, 1.17) | 0.242 | | |
| Lip | 0.15 (0.05, 0.47) | 0.001 | | |
| Other/salivary gland | 0.76 (0.51, 1.13) | 0.177 | | |
| **Tumour stage** | | | <0.001 | 99.58 |
| I | 1.00 (Ref.) | - | | |
| II | 2.48 (1.67, 3.69) | <0.001 | | |
| III | 3.71 (2.47, 5.56) | <0.001 | | |
| IV | 6.14 (4.17, 9.03) | <0.001 | | |
| Unknown | 4.83 (3.02, 7.74) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 201.83 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.54 (1.15, 2.06) | 0.004 | | |
| Surgery and radiotherapy | 1.07 (0.81, 1.43) | 0.635 | | |
| Surgery, radiotherapy and chemotherapy | 1.51 (0.98, 2.35) | 0.064 | | |
| Radiotherapy and chemotherapy | 1.68 (1.19, 2.38) | 0.003 | | |
| Chemotherapy +/- surgery | 6.31 (3.96, 10.05) | <0.001 | | |
| No treatment | 7.53 (5.36, 10.59) | <0.001 | | |

**Table 3.25 – Mutually adjusted hazard ratios for disease-specific mortality after 12 years for each patient, tumour, and treatment factor**

| Variable | 12-year disease-specific mortality HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 22.85 |
| Less than 45 | 0.78 (0.51, 1.21) | 0.267 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.94 (0.74, 1.19) | 0.607 | | |
| 65 to 74 | 1.28 (0.99, 1.64) | 0.056 | | |
| 75 and over | 1.58 (1.18, 2.11) | 0.002 | | |
| **Alcohol consumption** | | | <0.001 | 30.95 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.42 (1.12, 1.80) | 0.004 | | |
| Current problem drinker | 1.54 (1.28, 1.86) | <0.001 | | |
| Not recorded | 0.81 (1.15, 1.07) | 0.131 | | |
| **WHO Performance Status** | | | <0.001 | 43.93 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.41 (1.15, 1.73) | 0.001 | | |
| Up and about >50% | 2.06 (1.55, 2.74) | <0.001 | | |
| Confined to bed/chair >50% | 2.66 (1.92, 3.68) | <0.001 | | |
| Not recorded | 1.46 (1.16, 1.84) | 0.001 | | |
| **Anatomical site** | | | 0.005 | 18.47 |
| Larynx | 0.78 (0.61, 0.99) | 0.037 | | |
| Oral cavity | 0.98 (0.78, 1.25) | 0.885 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.10 (0.82, 1.47) | 0.531 | | |
| Nasal cavity | 0.82 (0.56, 1.20) | 0.314 | | |
| Lip | 0.25 (0.11, 0.58) | 0.001 | | |
| Other/salivary gland | 0.80 (0.54, 1.18) | 0.259 | | |
| **Tumour stage** | | | <0.001 | 98.22 |
| I | 1.00 (Ref.) | - | | |
| II | 2.13 (1.52, 2.98) | <0.001 | | |
| III | 3.03 (2.14, 4.29) | <0.001 | | |
| IV | 4.86 (3.49, 6.77) | <0.001 | | |
| Unknown | 3.83 (2.52, 5.83) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 205.62 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.54 (1.17, 2.03) | 0.002 | | |
| Surgery and radiotherapy | 1.14 (0.88, 1.49) | 0.325 | | |
| Surgery, radiotherapy and chemotherapy | 1.45 (0.95, 2.21) | 0.084 | | |
| Radiotherapy and chemotherapy | 1.77 (1.28, 2.45) | <0.001 | | |
| Chemotherapy +/- surgery | 6.49 (4.10, 10.26) | <0.001 | | |
| No treatment | 7.71 (5.54, 10.73) | <0.001 | | |

#### 3.3.7.5 Sensitivity analyses 1 – excluding people who received no treatment

The results for the forward stepwise models for disease-specific mortality which excluded the people who received no treatment after one year, five years, and 12 years are displayed in Table 3.26 to Table 3.28. Following the exclusion of the people who received no treatment, a total of 1,691 people remained in the first sensitivity analysis. After one year, when a forward stepwise multivariate Cox proportional hazards model was performed, the determinants with an independent association with disease-specific mortality following the forced inclusion of age at diagnosis, tumour stage, and treatment modality was WHO Performance Status, alcohol consumption, and anatomical site. The determinants after five and 12 years were WHO Performance Status, alcohol consumption, anatomical site, and smoking status. These results were similar to the results for the main cohort of people for disease-specific mortality; however smoking status was also an independent determinant of disease-specific mortality after five and 12 years following the exclusion of the people who received no treatment.

#### 3.3.7.6 Sensitivity analyses 2 – excluding people with oropharynx cancer

The results for the forward stepwise models for disease-specific mortality which excluded the people who had oropharynx cancer after one year, five years, and 12 years are displayed in Table 3.29 to Table 3.31. Following the exclusion of the people who had cancer of the oropharynx, a total of 1,497 patients were remaining in this sensitivity analysis. The determinants with an independent association with one-year disease-specific mortality in a mutually adjusted Cox proportional hazards model following the forced inclusion of age at diagnosis, tumour stage, and treatment modality were WHO Performance Status, alcohol consumption, and Scottish Cancer Network. These results were similar to the results for the main cohort of people after one year. The determinants with an independent association with disease-specific mortality in a mutually adjusted Cox proportional hazards model following the forced inclusion of age at diagnosis, tumour stage, and treatment modality were WHO Performance Status, alcohol consumption, and anatomical site after five and 12 years with the addition of Scottish Cancer Network. These results were similar to the results for the main cohort of people at both five years and 12 years.

**Table 3.26 – Mutually adjusted hazard ratios for disease-specific mortality after one year for each patient, tumour, and treatment factor following the exclusion of people who received no treatment (n = 1,691)**

| Variable | One-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.315 | 4.74 |
| Less than 45 | 0.81 (0.44, 1.48) | 0.488 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.95 (0.70, 1.30) | 0.760 | | |
| 65 to 74 | 1.12 (0.80, 1.55) | 0.513 | | |
| 75 and over | 1.33 (0.90, 1.96) | 0.151 | | |
| **Alcohol consumption** | | | 0.001 | 15.74 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.28 (0.93, 1.76) | 0.135 | | |
| Current problem drinker | 1.40 (1.09, 1.80) | 0.008 | | |
| Not recorded | 0.60 (0.39, 0.94) | 0.024 | | |
| **WHO Performance Status** | | | <0.001 | 28.92 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.52 (1.16, 2.00) | 0.003 | | |
| Up and about >50% | 2.52 (1.76, 3.61) | <0.001 | | |
| Confined to bed/chair >50% | 2.13 (1.32, 3.44) | 0.002 | | |
| Not recorded | 1.48 (1.08, 2.01) | 0.015 | | |
| **Anatomical site** | | | 0.011 | 16.55 |
| Larynx | 0.81 (0.59, 1.12) | 0.202 | | |
| Oral cavity | 1.32 (0.96, 1.81) | 0.091 | | |
| Oropharynx | 1.00 (Ref.) | | | |
| Hypopharynx | 1.31 (0.90, 1.92) | 0.162 | | |
| Nasal cavity | 1.02 (0.61, 1.70) | 0.931 | | |
| Lip | 0.27 (0.07, 1.16) | 0.078 | | |
| Other/salivary gland | 0.91 (0.55, 1.52) | 0.717 | | |
| **Stage** | | | <0.001 | 87.30 |
| I | 1.00 (Ref.) | - | | |
| II | 5.24 (2.67, 10.29) | <0.001 | | |
| III | 8.01 (4.05, 15.86) | <0.001 | | |
| IV | 15.29 (7.86, 29.74) | <0.001 | | |
| Unknown | 8.47 (3.90, 18.42) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 81.23 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.88 (1.31, 2.70) | <0.001 | | |
| Surgery and radiotherapy | 1.00 (0.70, 1.44) | 0.994 | | |
| Surgery, radiotherapy and chemotherapy | 1.73 (1.04, 2.89) | 0.036 | | |
| Radiotherapy and chemotherapy | 1.78 (1.16, 2.72) | 0.008 | | |
| Chemotherapy +/- surgery | 7.58 (4.49, 12.82) | <0.001 | | |

**Table 3.27 – Mutually adjusted hazard ratios for disease-specific mortality after five years for each patient, tumour, and treatment factor following the exclusion of people who received no treatment (n = 1,691)**

| Variable | Five-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.002 | 17.18 |
| Less than 45 | 0.75 (0.44, 1.25) | 0.269 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 1.00 (0.77, 1.31) | 0.977 | | |
| 65 to 74 | 1.35 (1.03, 1.79) | 0.033 | | |
| 75 and over | 1.64 (1.17, 2.29) | 0.004 | | |
| **Smoking status** | | | 0.037 | 8.47 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 0.92 (0.65, 1.30) | 0.618 | | |
| Current smoker | 1.27 (0.92, 1.74) | 0.141 | | |
| Unknown | 0.88 (0.41, 1.89) | 0.741 | | |
| **Alcohol consumption** | | | 0.005 | 12.84 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.29 (0.99, 1.70) | 0.064 | | |
| Current problem drinker | 1.36 (1.09, 1.69) | 0.007 | | |
| Not recorded | 0.74 (0.51, 1.10) | 0.133 | | |
| **WHO Performance Status** | | | <0.001 | 46.40 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.38 (1.10, 1.73) | 0.006 | | |
| Up and about >50% | 2.53 (1.86, 3.45) | <0.001 | | |
| Confined to bed/chair >50% | 2.66 (1.78, 3.98) | <0.001 | | |
| Not recorded | 1.51 (1.17, 1.96) | 0.002 | | |
| **Anatomical site** | | | <0.001 | 29.53 |
| Larynx | 0.70 (0.53, 0.92) | 0.010 | | |
| Oral cavity | 1.08 (0.83, 1.42) | 0.571 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.39 (1.00, 1.91) | 0.048 | | |
| Nasal cavity | 1.01 (0.66, 1.55) | 0.962 | | |
| Lip | 0.18 (0.06, 0.59) | 0.004 | | |
| Other/salivary gland | 0.81 (0.52, 1.25) | 0.334 | | |
| **Stage** | | | <0.001 | 102.84 |
| I | 1.00 (Ref.) | - | | |
| II | 2.55 (1.69, 3.85) | <0.001 | | |
| III | 3.79 (2.49, 5.77) | <0.001 | | |
| IV | 6.77 (4.52, 10.13) | <0.001 | | |
| Unknown | 4.42 (2.63, 7.43) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 80.91 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.62 (1.20, 2.18) | 0.001 | | |
| Surgery and radiotherapy | 1.03 (0.77, 1.38) | 0.829 | | |
| Surgery, radiotherapy and chemotherapy | 1.52 (0.97, 2.37) | 0.068 | | |
| Radiotherapy and chemotherapy | 1.62 (1.13, 2.31) | 0.008 | | |
| Chemotherapy +/- surgery | 7.03 (4.35, 11.36) | <0.001 | | |

**Table 3.28 – Mutually adjusted hazard ratios for disease-specific mortality after 12 years for each patient, tumour, and treatment factor following the exclusion of people who received no treatment (n = 1,691)**

| Variable | 12-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | <0.001 | 20.33 |
| Less than 45 | 0.85 (0.55, 1.33) | 0.480 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.99 (0.77, 1.26) | 0.909 | | |
| 65 to 74 | 1.38 (1.06, 1.78) | 0.016 | | |
| 75 and over | 1.66 (1.22, 2.28) | 0.002 | | |
| **Smoking status** | | | 0.046 | 7.99 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 0.93 (0.67, 1.28) | 0.650 | | |
| Current smoker | 1.24 (0.93, 1.67) | 0.144 | | |
| Unknown | 0.88 (0.44, 1.77) | 0.727 | | |
| **Alcohol consumption** | | | <0.001 | 17.81 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.30 (1.00, 1.69) | 0.047 | | |
| Current problem drinker | 1.45 (1.18, 1.78) | <0.001 | | |
| Not recorded | 0.80 (0.56, 1.13) | 0.197 | | |
| **WHO Performance Status** | | | <0.001 | 45.05 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.36 (1.10, 1.68) | 0.005 | | |
| Up and about >50% | 2.36 (1.75, 3.19) | <0.001 | | |
| Confined to bed/chair >50% | 2.59 (1.74, 3.85) | <0.001 | | |
| Not recorded | 1.53 (1.20, 1.94) | <0.001 | | |
| **Anatomical site** | | | <0.001 | 32.31 |
| Larynx | 0.77 (0.59, 0.99) | 0.043 | | |
| Oral cavity | 1.16 (0.90, 1.50) | 0.253 | | |
| Oropharynx | 1.00 (Ref.) | - | | |
| Hypopharynx | 1.53 (1.12, 2.08) | 0.008 | | |
| Nasal cavity | 1.09 (0.73, 1.63) | 0.678 | | |
| Lip | 0.31 (0.13, 0.72) | 0.007 | | |
| Other/salivary gland | 0.87 (0.58, 1.30) | 0.489 | | |
| **Stage** | | | <0.001 | 101.33 |
| I | 1.00 (Ref.) | - | | |
| II | 2.16 (1.53, 3.05) | <0.001 | | |
| III | 3.05 (2.13, 4.37) | <0.001 | | |
| IV | 5.24 (3.72, 7.38) | <0.001 | | |
| Unknown | 3.41 (2.15, 5.41) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 82.17 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.63 (1.23, 2.16) | <0.001 | | |
| Surgery and radiotherapy | 1.11 (0.85, 1.45) | 0.456 | | |
| Surgery, radiotherapy and chemotherapy | 1.47 (0.96, 2.26) | 0.079 | | |
| Radiotherapy and chemotherapy | 1.71 (1.22, 2.39) | 0.002 | | |
| Chemotherapy +/- surgery | 7.28 (4.55, 11.65) | <0.001 | | |

**Table 3.29 – Mutually adjusted hazard ratios for disease-specific mortality after one year for each patient, tumour, and treatment factor following the exclusion of people who had oropharynx cancer (n = 1,497)**

| Variable | One-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.019 | 11.81 |
| Less than 45 | 0.59 (0.29, 1.23) | 0.160 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.78 (0.55, 1.10) | 0.157 | | |
| 65 to 74 | 0.87 (0.61, 1.24) | 0.450 | | |
| 75 and over | 1.30 (0.87, 1.93) | 0.202 | | |
| **Smoking status** | | | 0.054 | 7.65 |
| Never smoked | 1.00 (Ref.) | - | | |
| Previous smoker | 0.67 (0.44, 1.03) | 0.066 | | |
| Current smoker | 0.86 (0.58, 1.28) | 0.459 | | |
| Unknown | 0.35 (0.13, 0.91) | 0.031 | | |
| **Alcohol consumption** | | | 0.012 | 11.05 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.61 (1.14, 2.25) | 0.006 | | |
| Current problem drinker | 1.38 (1.05, 1.81) | 0.023 | | |
| Not recorded | 0.89 (0.58, 1.37) | 0.596 | | |
| **WHO Performance Status** | | | <0.001 | 29.48 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.43 (1.06, 1.94) | 0.021 | | |
| Up and about >50% | 2.48 (1.69, 3.65) | <0.001 | | |
| Confined to bed/chair >50% | 2.62 (1.70, 4.05) | <0.001 | | |
| Not recorded | 1.48 (1.06, 2.09) | 0.0234 | | |
| **Stage** | | | <0.001 | 65.94 |
| I | 1.00 (Ref.) | - | | |
| II | 5.48 (2.78, 10.81) | <0.001 | | |
| III | 7.43 (3.71, 14.87) | <0.001 | | |
| IV | 12.84 (6.57, 25.10) | <0.001 | | |
| Unknown | 7.62 (3.62, 16.01) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 170.84 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.59 (1.09, 2.30) | 0.015 | | |
| Surgery and radiotherapy | 1.10 (0.75, 1.61) | 0.630 | | |
| Surgery, radiotherapy and chemotherapy | 2.00 (1.07, 3.71) | 0.029 | | |
| Radiotherapy and chemotherapy | 2.97 (1.89, 4.66) | <0.001 | | |
| Chemotherapy +/- surgery | 8.28 (4.65, 14.74) | <0.001 | | |
| No treatment | 9.10 (5.92, 13.98) | <0.001 | | |
| **Network/region** | | | 0.007 | 9.84 |
| WoSCAN (West Scotland) | 1.04 (0.78, 1.40) | 0.770 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.60 (1.14, 2.24) | 0.006 | | |

**Table 3.30 – Mutually adjusted hazard ratios for disease-specific mortality after five years for each patient, tumour, and treatment factor following the exclusion of people who had oropharynx cancer (n = 1,497)**

| Variable | Five-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.011 | 12.98 |
| Less than 45 | 0.54 (0.28, 1.04) | 0.065 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.85 (0.63, 1.15) | 0.297 | | |
| 65 to 74 | 0.99 (0.73, 1.35) | 0.961 | | |
| 75 and over | 1.33 (0.94, 1.87) | 0.106 | | |
| **Alcohol consumption** | | | <0.001 | 19.50 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.57 (1.18, 2.09) | 0.002 | | |
| Current problem drinker | 1.36 (1.08, 1.70) | 0.009 | | |
| Not recorded | 0.74 (0.52, 1.03) | 0.077 | | |
| **WHO Performance Status** | | | <0.001 | 46.04 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.33 (1.03, 1.71) | 0.031 | | |
| Up and about >50% | 2.63 (1.87, 3.68) | <0.001 | | |
| Confined to bed/chair >50% | 2.88 (1.97, 4.22) | <0.001 | | |
| Not recorded | 1.51 (1.14, 2.01) | 0.005 | | |
| **Anatomical site** | | | 0.013 | 14.37 |
| Larynx | 1.00 (Ref.) | - | | |
| Oral cavity | 1.27 (0.99, 1.63) | 0.058 | | |
| Hypopharynx | 1.29 (0.94, 1.76) | 0.117 | | |
| Nasal cavity | 0.98 (0.65, 1.49) | 0.934 | | |
| Lip | 0.20 (0.06, 0.66) | 0.008 | | |
| Other/salivary gland | 1.04 (0.70, 1.56) | 0.840 | | |
| **Stage** | | | <0.001 | 86.15 |
| I | 1.00 (Ref.) | - | | |
| II | 2.66 (1.72, 4.11) | <0.001 | | |
| III | 3.77 (2.41, 5.91) | <0.001 | | |
| IV | 6.64 (4.34, 10.17) | <0.001 | | |
| Unknown | 4.51 (2.70, 7.55) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 144.38 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.42 (1.03, 1.97) | 0.032 | | |
| Surgery and radiotherapy | 1.03 (0.75, 1.42) | 0.834 | | |
| Surgery, radiotherapy and chemotherapy | 1.59 (0.91, 2.76) | 0.103 | | |
| Radiotherapy and chemotherapy | 2.43 (1.63, 3.61) | <0.001 | | |
| Chemotherapy +/- surgery | 6.68 (3.94, 11.33) | <0.001 | | |
| No treatment | 6.71 (4.55, 9.90) | <0.001 | | |
| **Network/region** | | | 0.019 | 7.97 |
| WoSCAN (West Scotland) | 1.05 (0.82, 1.34) | 0.712 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.45 (1.09, 1.93) | 0.012 | | |

**Table 3.31 – Mutually adjusted hazard ratios for disease-specific mortality after 12 years for each patient, tumour, and treatment factor following the exclusion of people who had oropharynx cancer (n = 1,497)**

| Variable | 12-year HR (95% CI) | HR p-value | p-value | Chi-sq. |
|---|---|---|---|---|
| **Age at diagnosis** | | | 0.005 | 15.01 |
| Less than 45 | 0.71 (0.42, 1.19) | 0.194 | | |
| 45 to 54 | 1.00 (Ref.) | - | | |
| 55 to 64 | 0.86 (0.65, 1.13) | 0.281 | | |
| 65 to 74 | 1.06 (0.80, 1.40) | 0.694 | | |
| 75 and over | 1.41 (1.02, 1.94) | 0.035 | | |
| **Alcohol consumption** | | | <0.001 | 23.77 |
| Never/occasionally drank | 1.00 (Ref.) | - | | |
| Previous problem drinker | 1.58 (1.20, 2.07) | 0.001 | | |
| Current problem drinker | 1.46 (1.18, 1.81) | <0.001 | | |
| Not recorded | 0.79 (0.58, 1.08) | 0.135 | | |
| **WHO Performance Status** | | | <0.001 | 45.09 |
| Normal activity | 1.00 (Ref.) | - | | |
| Strenuous restricted | 1.28 (1.01, 1.62) | 0.041 | | |
| Up and about >50% | 2.44 (1.76, 3.38) | <0.001 | | |
| Confined to bed/chair >50% | 2.80 (1.94, 4.04) | <0.001 | | |
| Not recorded | 1.45 (1.11, 1.88) | 0.006 | | |
| **Anatomical site** | | | 0.004 | 17.34 |
| Larynx | 1.00 (Ref.) | - | | |
| Oral cavity | 1.27 (1.00, 1.60) | 0.046 | | |
| Hypopharynx | 1.37 (1.01, 1.85) | 0.041 | | |
| Nasal cavity | 0.96 (0.65, 1.42) | 0.825 | | |
| Lip | 0.32 (0.14, 0.74) | 0.008 | | |
| Other/salivary gland | 1.02 (0.70, 1.50) | 0.904 | | |
| **Stage** | | | <0.001 | 90.20 |
| I | 1.00 (Ref.) | - | | |
| II | 2.27 (1.58, 3.28) | <0.001 | | |
| III | 3.19 (2.18, 4.68) | <0.001 | | |
| IV | 5.40 (3.76, 7.76) | <0.001 | | |
| Unknown | 3.74 (2.37, 5.90) | <0.001 | | |
| **Treatment modality** | | | <0.001 | 90.20 |
| Surgery only | 1.00 (Ref.) | - | | |
| Radiotherapy only | 1.45 (1.07, 1.96) | 0.017 | | |
| Surgery and radiotherapy | 1.07 (0.80, 1.44) | 0.632 | | |
| Surgery, radiotherapy and chemotherapy | 1.51 (0.90, 2.55) | 0.119 | | |
| Radiotherapy and chemotherapy | 2.31 (1.59, 3.36) | <0.001 | | |
| Chemotherapy +/- surgery | 6.59 (3.92, 11.08) | <0.001 | | |
| No treatment | 6.57 (4.51, 9.58) | <0.001 | | |
| **Network/region** | | | 0.049 | 6.03 |
| WoSCAN (West Scotland) | 1.13 (0.89, 1.42) | 0.312 | | |
| SCAN (East Scotland) | 1.00 (Ref.) | - | | |
| NOSCAN (North Scotland) | 1.40 (1.07, 1.84) | 0.016 | | |

## 3.4 Discussion

Overall survival estimates after one year, five years, and 12 years were 76.0% (95% CI 74.0% to 77.9%), 46.1% (95% CI 43.8% to 48.4%), and 26.3% (95% CI 24.3% to 28.3%), respectively, while disease-specific survival was higher at all three time points at 82.3% (95% CI 80.4% to 84.0%), 64.1% (95% CI 61.7% to 66.4%), and 56.9% (95% CI 54.3% to 59.4%), respectively. Net survival estimates after one year, five years, and 12 years were 78.3% (95% CI 76.2% to 80.3%), 53.8% (95% CI 51.1% to 56.5%), and 41.4% (95% CI 37.6% to 45.1%), respectively.

Poor overall survival, disease-specific survival, and net survival estimates were strongly associated with older age, but interestingly, there was not an obvious difference in survival between males and females. Poor survival was also associated with residing in areas of lower deprivation status, current or previous smoking, current or previous levels of alcohol consumption, and worse WHO Performance Status. In addition, patients who were diagnosed with tumours of the hypopharynx, or tumours of higher stage experienced poorer survival outcomes. People who were treated with a form of therapy which involved chemotherapy were also more likely to have worse survival outcomes. There was no obvious difference between the survival results across the three Scottish Cancer Networks.

Following minimal adjustment for age and sex, the patients who were from the least deprived regions still had a higher risk of mortality, particularly for disease-specific mortality in the short-term. Individuals who were reported as being current or previous smokers or alcohol drinkers at the time of their diagnosis also exhibited a higher risk of all-cause mortality and disease-specific mortality. Following minimal adjustment for age and sex, WHO Performance Status remained associated with all-cause mortality and disease-specific mortality, with a substantial difference in the excess risk of mortality between the people who presented with a normal WHO Performance Status and those who were restricted in their levels of strenuous activity at the time of their diagnosis. Minimal adjustment by age and sex did not explain the differences that were observed between the people with tumours in different anatomical sites of the head and neck, nor did it explain the difference exhibited between the those with cancer of higher tumour stages. Following minimal adjustment for age and sex, patients who were treated with surgery only continued to have the lowest risk of all-cause mortality and disease-specific mortality, while those who were treated with any form of therapy that involved chemotherapy had the highest risk of mortality, along with those who did not receive any treatment. Interestingly, there was no obvious difference across the three Scottish Cancer Networks following adjustment for age and sex, until 12 years by which time those who were being

treated in the WoSCAN region had a slightly higher risk of all-cause mortality than those in other regions. However, these results were not reflected in the minimally adjusted models for disease-specific mortality, suggesting that the people in the WoSCAN area were more likely to have died as a result of other causes of death in the long-term.

In the mutually adjusted models, the patient, tumour, and treatment factors that were independently associated with one-year, five-year, and 12-year all-cause mortality following the forced inclusion of age at diagnosis, tumour stage, and treatment modality, included WHO Performance Status, alcohol consumption, anatomical site, and smoking status. The results for the mutually adjusted models for disease-specific mortality differed slightly, in that after one year the factors with an independent association with disease-specific mortality after the forced inclusion of age at diagnosis, tumour stage, and treatment modality included WHO Performance Status, alcohol consumption, and Scottish Cancer Network. However, by five years and 12 years, the factors that had an independent association with disease-specific mortality after the forced inclusion of age at diagnosis, tumour stage, and treatment modality included WHO Performance Status, alcohol consumption, and anatomical site, which was the same as the results for all-cause mortality.

The strong association of patients with higher tumour stage and survival reflects the high prevalence of disease-specific deaths in this population. Likewise, the relationship between WHO Performance Status and survival could be an indicator of the severity of their cancer, or additionally, WHO Performance Status could be a representation of the person's comorbidities, which have been previously described to have a negative impact on survival of people with head and neck cancer (Piccirillo, 2000). Similarly, the association of prior smoking and alcohol consumption are likely to be linked to other comorbidities such as chronic obstructive pulmonary disease, heart disease, liver disease and other cancers (Boje *et al.*, 2013). The strong relationship between the differing treatment modalities and survival is likely to be a reflection for the people who received palliative or supportive care as opposed to curative treatment. This would particularly be the case for those who received no treatment for their cancer, however in a sensitivity analysis excluding these people, the same results were observed. There was a significant variance in survival of people by anatomical site, which is likely to be influenced by the inclusion of people with cancer of the lip, who had a considerably higher overall survival, disease-specific survival, and net survival results compared to the people with tumours that were in other sites of the head and neck.

There was a substantial difference between overall survival, disease-specific survival, and net survival estimates in this study, particularly in the long-term follow-up period. This study demonstrates that overall survival overestimates death as a result of head and neck

cancer since the specific cause of the patients' death is not considered in this measurement of survival. Contrary to this, disease-specific survival may also be an unreliable estimate in long-term follow-up studies because the measurement relies on cause of death information from a death certificate, which is often not accurate. The difference between the overall and the disease-specific results in this study suggest that people are dying of other head and neck cancer related causes that are not a direct result of the person's head and neck cancer and are therefore not documented clearly on their death certificates.

Net survival estimates survival using the background mortality of a group of people with the same demographics as the patient in the study (in this case, calendar year, age, sex, and Carstairs 2001 Category), and calculates the excess death that has occurred as a result of the patients' disease. There is no need to use death certificates to compute net survival and as thus there is little inaccuracy as to the survival of the SAHNC cohort from head and neck cancer. Therefore, we feel that the use of net survival provides a good compromise to the traditional method of overall and disease-specific survival in long-term studies to estimate the true burden of head and neck cancer deaths.

One limitation of this study is the absence of HPV status of the people in the cohort. Over the last two decades, there has been an increase in the association in the rising incidence of head and neck cancer with HPV (Junor *et al.*, 2010; Chaturvedi *et al.*, 2013; Purkayastha *et al.*, 2016). This trend is particularly common for people with cancer of the oropharynx for whom around one to two thirds of tumours may be HPV-driven (Kreimer *et al.*, 2005). People with HPV-positive tumours have a considerably better prognosis than people with HPV-negative tumours, even following adjustment for other baseline covariates (Ragin and Taioli, 2007; Wang *et al.*, 2015). However, the primary focus of this analysis with the SAHNC cohort was to investigate the long-term survival of people with head and neck cancer in Scotland diagnosed between the years of 1999 and 2001. As a result, the baseline data collection for this study was ahead of the discovery of the association of HPV with head and neck cancer (D'Souza *et al.*, 2007) and therefore HPV data were not routinely collected or available. However, aside from patients with cancer of the oropharynx, the majority of head and neck cancers that are diagnosed today are HPV-negative and it is likely that these tumours are associated with tobacco and alcohol consumption (Herrero *et al.*, 2003; Hashibe *et al.*, 2009). Previous studies have suggested that smoking status, alcohol consumption, and HPV status are three independent risk factors of incidence and survival of people with head and neck cancer (Gillison *et al.*, 2008; Smith *et al.*, 2012). Furthermore, the oropharyngeal patients in this study did not exhibit the well-documented survival advantage that is usually observed for HPV-associated oropharyngeal cancer (Wang *et al.*, 2015). A sensitivity analysis involving the

exclusion of people with oropharynx cancer for this study demonstrated similar results to the whole cohort. Therefore, the SAHNC patients' cancers are likely to be predominantly related to smoking and alcohol behaviours and as a result, we propose that our findings remain relevant to clinicians, researchers, and other health professionals in gaining an understanding of the long-term prognosis of people with non-HPV driven head and neck cancer, particularly since the prevalence of smoking and problem alcohol consumption was very high in this study.

The SAHNC cohort also pre-dates the use of organ preservation strategies that were introduced in Scotland in 2006 (Scottish Intercollegiate Guidelines Network, 2001-2014). However, studies following the introduction of these practices outline the importance of ensuring clear margins in surgery in the treatment of head and neck cancer (Gourin and Johnson, 2009; Hormann and Sadick, 2013). Therefore, due to the high proportion of people being treated with surgery in the SAHNC cohort, this study also remains relevant, and this study may be used in treatment planning decisions for people with head and neck cancer. Moreover, these analyses were based on historical cases (1999 to 2001), which is a prerequisite for estimating long-term follow-up, and so could be argued as a strength of the SAHNC cohort.

The SAHNC cohort represented 77% of all head and neck cancer cases that were recorded on the Scottish Cancer Registry over the two-year study period and therefore, was representative of head and neck cancer cases in Scotland. This study adds to the worldwide literature on the long-term survival of people with head and neck cancer, and provides an in-depth analysis of overall survival, disease-specific survival, and net survival of people with head and neck cancer using a national clinical cohort. This study also supports the use of net survival, particularly in analyses with long-term follow-up.

### 3.4.1 Conclusion

Overall survival estimates after one year, five years, and 12 years were 76.0% (95% CI 74.0% to 77.9%), 46.1% (95% CI 43.8% to 48.4%), and 26.3% (95% CI 24.3% to 28.3%), respectively, while disease-specific survival was higher at all three time points at 82.3% (95% CI 80.4% to 84.0%), 64.1% (95% CI 61.7% to 66.4%), and 56.9% (95% CI 54.3% to 59.4%), respectively. Net survival estimates after one year, five years, and 12 years were 78.3% (95% CI 76.2% to 80.3%), 53.8% (95% CI 51.1% to 56.5%), and 41.4% (95% CI 37.6% to 45.1%), respectively. Following mutual adjustment, overall and disease-specific survival for people with head and neck cancer was associated with age at diagnosis, cancer stage, treatment modality, WHO Performance Status, alcohol consumption, anatomical site, smoking status, and cancer network.

The substantial difference between overall survival, disease-specific survival and net survival demonstrates the overestimation of deaths that are specific to head and neck cancer when using overall survival, and the underestimation of disease-specific mortality when using death certificates where people have died only from head and neck cancer. These results suggest that people are dying of other causes that are related to their head and neck cancer but are not as a direct result of their cancer. Therefore, the use of net survival seems to provide a good compromise to traditional methods to estimate the true burden of head and neck cancer in long-term follow-up studies.

# 4 Inequality in survival of a population-based cohort study of people with head and neck cancer in Scotland (SAHNC)

## 4.1 Introduction

Chapter 3 investigated which patient, tumour, and treatment factors had an independent association with one-year, five-year, and 12-year survival for the SAHNC cohort. It was observed that there was inequality in survival by Carstairs 2001 Category, however when a forward-stepwise multivariate Cox proportional hazards model was performed, socioeconomic status was no longer a predictor of one-year, five-year, or 12-year all-cause mortality or disease-specific mortality.

### 4.1.1 Aims and objectives

Following on from the research of Chapter 3, and by also using the SAHNC cohort, the aims of Chapter 4 are to explore the drivers of inequality in survival of people with head and neck cancer by using an area-based measurement of socioeconomic status (Scottish Audit of Head and Neck Cancers Steering Group, 2004). This chapter explores socioeconomic inequality in Scotland one year, five years, and 12 years after a diagnosis of head and neck cancer. The objectives of this chapter are to:

1. Explore the underlying patient, tumour and treatment factors that are associated with socioeconomic inequality in survival of people with head and neck cancer.
2. Examine the differences in socioeconomic inequality in survival of people with head and neck cancer via the use of overall survival, disease-specific survival, and net survival estimates.

## 4.2 Methods

### 4.2.1 Data included

This chapter utilises the same data that was used in the study that investigated the determinants of survival using the SAHNC cohort, including the number of patients, and all of the patient, tumour, and treatment factors that were defined in Chapter 3.

### 4.2.2 Statistical analyses

The statistical methods used throughout this chapter were the same as the methods that were used throughout Chapter 3 for determining overall survival, disease-specific survival, and net survival and the same statistical software programmed that were used in Chapter 3 were also used in this chapter. In addition to the analyses performed in Chapter 3, frequency tables that displayed cross-tabulations of each of the patient, tumour, and treatment factors with Carstairs 2001 Category were generated, and the proportions across each of the groups were compared using the Pearson's chi-square test. The primary and secondary causes of deaths of the participants within each of the Carstairs 2001 Category were also investigated.

Cox proportional hazards models for all-cause mortality and disease-specific mortality were used to determine the magnitude of and the explanations for socioeconomic inequality observed. Several models were produced by adjusting for: (a) age and sex; (b) age, sex, and smoking status; (c) age, sex, and alcohol consumption; (d) age, sex, and WHO Performance Status; (e) age, sex, and anatomical site; (f) age, sex, and tumour stage; (g) age, sex, and treatment modality; (h) age, sex, and Scottish Cancer Network; (i) age, sex, and all participant factors (including smoking status, alcohol consumption, and WHO Performance Status); (j) age, sex, and all tumour and treatment factors (including anatomical site, tumour stage, treatment modality, and Scottish Cancer Network); and (k) age, sex, and all patient, tumour, and treatment (full adjustment). A sensitivity analysis was performed which excluded WHO Performance Status from all of the models since it was such a strong predictor of survival in Chapter 3. Therefore, WHO Performance Status may be an indicator of death and as thus, including it in models to estimate mortality may be an over-adjustment.

In addition, the SII was also calculated for each of the models that were produced to compare inequality over time. The SII is based on the regression of the mid-point of survival or mortality for each Carstairs 2001 Category (Regidor, 2004).

## 4.3 Results

### 4.3.1 Cross-tabulations of Carstairs 1991 Category by each baseline characteristic

The numbers and proportions of all of the patient, tumour, and treatment factors that were cross-tabulated with Carstairs 2001 Category are displayed in Table 4.1 to Table 4.3 on Page 165 to Page 167.

#### 4.3.1.1 Description of the participant factors by Carstairs 2001 Category

A total of 528 (29.0%) participants of the SAHNC cohort resided in areas that were of the most deprived in Scotland (group five), whereas only 241 (13.2%) of the participants resided in the least deprived areas of Scotland (group one). There were no obvious differences across the Carstairs 2001 Category by age or sex, however there was a slightly higher proportion of males who were from the most deprived regions compared to those from the least deprived regions (n = 387 (73.3%) compared with n = 161 (66.8%)). As the deprivation category increased from group one (least deprived) to group five (most deprived) the proportion of current smokers increased from 49.0% (n = 118) to 75.0% (n = 396). However, it can be observed that even among the least deprived groups, the prevalence of smoking was high, which is not surprising for a cohort of people with head and neck cancer. The increase in proportions across the Carstairs 2001 Category could also be observed for alcohol consumption where a proportion of 31.6% (n = 76) of participants were current or previous problem drinkers within the least deprived group, compared to a proportion of 45.8% (n = 242) in the most deprived group. The levels of normal WHO Performance Status decreased across the Carstairs 2001 Category from 56.9% (n = 137) in the least deprived group to 38.8% (n = 205) in the most deprived group.

#### 4.3.1.2 Description of the tumour factors by Carstairs 2001 Category

There were no obvious differences in the proportions of the anatomical site of the patients' tumours across the Carstairs 2001 Category. However, the participants who resided in the most deprived areas were more likely to have tumours that were stage IV at 40.0% (n = 211) compared to the participants who resided in the least deprived areas at 32.8% (n = 79). Similarly, the participants who were in the least deprived group had a greater proportion of stage I cancers at 24.1% (n = 58) compared to the participants who were in the most deprived group at 17.4% (n = 92). There were no clear differences across the Carstairs 2001 Category by the histology of the participants' tumours.

#### 4.3.1.3 Description of the treatment factors by Carstairs 2001 Category

The participants who lived in the least deprived areas were more likely to be treated using single modality treatments such as surgery only or radiotherapy only at 29.9% (n = 72) and 30.7% (n = 74), respectively, compared to the participants who lived in the most deprived regions at 24.6% (n = 130) and 22.5% (n = 119), respectively. The participants who resided in the most deprived regions of Scotland were more likely to have been treated with a combination of chemotherapy, radiotherapy, and surgery at 16.7% (n = 88)

compared to the participants who resided in the least deprived areas at 9.5% (n = 23). The participants who were in the most deprived group also had a higher proportion of participants who received no treatment at 9.1% (n = 48) compared to the participants who were in the least deprived group at 5.4% (n = 13). However, these differences are more likely to reflect the stage of the patients' tumours, given the higher proportion of people from the most deprived regions with a stage IV tumour. The people from the most deprived area were more likely to have been treated in the West of Scotland Cancer Network at 78.2% (n = 413) while those from the least deprived area were more likely to be treated in either the East of Scotland Cancer Network or the North of Scotland Cancer Network at 34.4% (n = 83) and 30.3% (n = 73).

**Table 4.1 – Baseline characteristics by Carstairs 2001 Category for each participant factor**

| Variable | Frequencies of Carstairs 2001 Category (Col. %) | | | | | Chi-square p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Whole cohort (Row %)** | 241 (13.2%) | 317 (17.4%) | 325 (17.9%) | 409 (22.5%) | 528 (29.0%) | - |
| **Age at diagnosis** | | | | | | 0.470 |
| Less than 45 | 16 (6.6%) | 23 (7.3%) | 16 (4.9%) | 21 (5.1%) | 23 (4.4%) | |
| 45 to 54 | 35 (14.5%) | 44 (13.9%) | 45 (13.9%) | 68 (16.6%) | 96 (18.2%) | |
| 55 to 64 | 70 (29.1%) | 105 (33.1%) | 108 (33.2%) | 140 (34.2%) | 169 (32.0%) | |
| 65 to 74 | 72 (29.9%) | 90 (28.4%) | 111 (34.2%) | 108 (26.4%) | 170 (32.2%) | |
| 75 and over | 48 (19.9%) | 55 (17.4%) | 45 (13.9%) | 72 (17.6%) | 70 (13.3%) | |
| **Sex** | | | | | | 0.440 |
| Male | 161 (66.8%) | 227 (71.6%) | 236 (72.6%) | 289 (70.7%) | 387 (73.3%) | |
| Female | 80 (33.2%) | 90 (28.4%) | 89 (27.4%) | 120 (29.3%) | 141 (26.7%) | |
| **Smoking status** | | | | | | <0.001 |
| Current smoker | 118 (49.0%) | 173 (54.6%) | 191 (58.8%) | 256 (62.6%) | 396 (75.0%) | |
| Previous smoker | 60 (24.9%) | 86 (27.1%) | 68 (20.9%) | 100 (24.5%) | 91 (17.2%) | |
| Never smoked | 56 (23.2%) | 45 (14.2%) | 50 (15.4%) | 41 (10.0%) | 29 (5.5%) | |
| Not recorded | 7 (2.9%) | 13 (4.1%) | 16 (4.9%) | 12 (2.9%) | 12 (2.3%) | |
| **Alcohol consumption** | | | | | | <0.001 |
| Current (problem) drinker | 51 (21.2%) | 77 (24.3%) | 80 (24.6%) | 108 (26.4%) | 180 (34.1%) | |
| Previous (problem) drinker | 25 (10.4%) | 29 (9.2%) | 49 (15.1%) | 47 (11.5%) | 62 (11.7%) | |
| Occasional/never drank | 138 (57.3%) | 164 (51.7%) | 150 (46.2%) | 198 (48.4%) | 241 (45.6%) | |
| Not recorded | 27 (11.2%) | 47 (14.8%) | 46 (14.2%) | 56 (13.7%) | 45 (8.5%) | |
| **WHO Performance Status** | | | | | | 0.003 |
| Normal activity | 137 (56.9%) | 169 (53.3%) | 137 (42.3%) | 177 (43.3%) | 205 (38.8%) | |
| Strenuous activity restricted | 54 (22.4%) | 66 (20.8%) | 94 (28.9%) | 102 (24.9%) | 149 (28.2%) | |
| Up and about > 50% | 18 (7.5%) | 23 (7.3%) | 17 (5.2%) | 33 (8.1%) | 46 (8.7%) | |
| Confined to bed/chair >50% | 8 (3.3%) | 18 (5.7%) | 22 (6.8%) | 26 (6.4%) | 23 (4.4%) | |
| Not recorded | 24 (10.0%) | 41 (12.9%) | 55 (16.9%) | 71 (17.4%) | 105 (19.9%) | |

**Table 4.2 – Baseline characteristics by Carstairs 2001 Category for each tumour factor**

| Variable | Frequencies of Carstairs 2001 Category (Col. %) | | | | | Chi-square p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Anatomical site** | | | | | | 0.470 |
| Lip | 11 (4.6%) | 17 (5.4%) | 18 (5.5%) | 23 (5.6%) | 16 (3.0%) | |
| Larynx | 71 (29.5%) | 102 (32.2%) | 103 (31.7%) | 143 (35.0%) | 165 (31.3%) | |
| Nasal cavity | 12 (5.0%) | 14 (4.4%) | 22 (6.8%) | 15 (3.7%) | 22 (4.2%) | |
| Oral cavity | 76 (31.5%) | 93 (29.3%) | 78 (24.0%) | 97 (23.7%) | 162 (30.7%) | |
| Oropharynx | 40 (16.6%) | 53 (16.7%) | 63 (19.4%) | 69 (16.9%) | 98 (18.6%) | |
| Hypopharynx | 12 (5.0%) | 19 (6.0%) | 20 (6.2%) | 35 (8.6%) | 33 (6.3%) | |
| Other/salivary gland | 19 (7.9%) | 19 (6.0%) | 21 (6.5%) | 27 (6.6%) | 32 (6.1%) | |
| **Stage** | | | | | | 0.023 |
| I | 58 (24.1%) | 85 (26.8%) | 75 (23.1%) | 73 (17.9%) | 92 (17.4%) | |
| II | 48 (19.9%) | 62 (19.6%) | 65 (20.0%) | 88 (21.5%) | 106 (20.1%) | |
| III | 37 (15.4%) | 42 (13.3%) | 40 (12.3%) | 80 (19.6%) | 74 (14.0%) | |
| IV | 79 (32.8%) | 102 (32.2%) | 125 (38.5%) | 145 (35.5%) | 211 (40.0%) | |
| Unknown | 19 (7.9%) | 26 (8.2%) | 20 (6.2%) | 23 (5.6%) | 45 (8.5%) | |
| **Histology** | | | | | | 0.621 |
| SCC | 211 (87.6%) | 269 (84.9%) | 282 (86.8%) | 355 (86.8%) | 468 (88.6%) | |
| Non-SCC | 30 (12.5%) | 48 (15.1%) | 43 (13.2%) | 54 (13.2%) | 60 (11.4%) | |

**Table 4.3 – Baseline characteristics by Carstairs 2001 Category for each treatment factor**

| Variable | Frequencies of Carstairs 2001 Category (Col. %) | | | | | Chi-square p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Treatment modality** | | | | | | 0.064 |
| Surgery only | 72 (29.9%) | 83 (26.2%) | 86 (26.5%) | 106 (25.9%) | 130 (24.6%) | |
| Radiotherapy only | 74 (30.7%) | 99 (31.2%) | 98 (30.2%) | 117 (28.6%) | 119 (22.5%) | |
| Surgery + radiotherapy | 59 (24.5%) | 82 (25.9%) | 73 (22.5%) | 101 (24.7%) | 143 (27.1%) | |
| Chemo +/- radio +/- surgery | 23 (9.5%) | 34 (10.7%) | 48 (14.8%) | 56 (13.7%) | 88 (16.7%) | |
| No treatment | 13 (5.4%) | 19 (6.0%) | 20 (6.2%) | 29 (7.1%) | 48 (9.1%) | |
| **Network** | | | | | | <0.001 |
| WoSCAN (West Scotland) | 85 (35.3%) | 110 (34.7%) | 149 (45.9%) | 244 (59.7%) | 413 (78.2%) | |
| SCAN (East Scotland) | 83 (34.4%) | 85 (26.8%) | 108 (33.2%) | 108 (26.4%) | 56 (10.6%) | |
| NOSCAN (North Scotland) | 73 (30.3%) | 122 (38.5%) | 68 (20.9%) | 68 (20.9%) | 59 (11.2%) | |

#### 4.3.1.4 Death rates by September 2013 by Carstairs 2001 Category

The number and proportions of deaths by Carstairs 2001 Category are displayed in Table 4.4. As the Carstairs 2001 Category increased from group one (least deprived) to five (most deprived), the proportion of patients dying as a result of head and neck cancer as their primary cause of death increased from 42.6% (n = 78) to 51.9% (n = 216). This trend was also observed for the patients' secondary causes of death which increased from 51.9% (n = 95) to 61.5% (n = 256) for those head and neck cancer deaths.

### 4.3.2 Cause of death by Carstairs 2001 Category

The proportions of head and neck cancer related deaths during each time period following diagnosis are also displayed in Table 4.4. Compared to the participants who were in the least deprived group, the participants who were in the most deprived group had a higher proportion of head and neck cancer deaths in the first year after their diagnosis (33.3% versus 48.1%, respectively). However, the patients who were in the second Carstairs 2001 Category had the highest proportion of head and neck cancer deaths after the first year of diagnosis at 52.5%. After one year and before five years, the participants who were in the least deprived Carstairs 2001 Category had the highest proportion of head and neck cancer deaths at 51.3%, which was followed by the participants who were in Carstairs 2001 Category three at 46.5%. After five years, there were no differences in the proportions of head and neck cancer deaths across the Carstairs 2001 Category.

**Table 4.4 – Primary and secondary cause of death by September 2013 by Carstairs 2001 Category**

| | Frequencies of Carstairs 2001 Category (Col. %) | | | | | |
|---|---|---|---|---|---|---|
| | **1 – Least deprived** | **2** | **3** | **4** | **5 – Most deprived** | **Chi-square** |
| **Primary cause of death** | | | | | | 0.080 |
| Cancer – Head and neck | 78 (42.6%) | 99 (43.8%) | 127 (51.4%) | 157 (50.5%) | 216 (51.9%) | |
| Cancer – Other | 46 (25.1%) | 54 (23.9%) | 61 (24.7%) | 73 (23.5%) | 74 (17.8%) | |
| Other | 59 (32.2%) | 73 (32.3%) | 59 (23.9%) | 81 (26.1%) | 126 (30.3%) | |
| **Secondary cause of death** | | | | | | 0.066 |
| Cancer – Head and neck | 95 (51.9%) | 127 (56.2%) | 152 (61.5%) | 190 (61.1%) | 256 (61.5%) | |
| Cancer – Other | 40 (21.9%) | 35 (15.5%) | 46 (18.6%) | 59 (19.0%) | 58 (13.9%) | |
| Other | 48 (26.2%) | 64 (28.3%) | 49 (19.8%) | 62 (19.9%) | 102 (24.5%) | |
| **Head and Neck cancer deaths** | | | | | | 0.240 |
| Up to one year | 26 (33.3%) | 52 (52.5%) | 55 (43.3%) | 71 (45.2%) | 104 (48.1%) | |
| Between one and five years | 40 (51.3%) | 37 (37.4%) | 59 (46.5%) | 61 (38.9%) | 85 (39.4%) | |
| More than five years | 12 (15.4%) | 10 (10.1%) | 13 (10.2%) | 25 (15.9%) | 27 (12.5%) | |

### 4.3.3 Overall survival, disease-specific survival, and net survival results by Carstairs 2001 Category

One-year, five-year, and 12-year overall survival, disease-specific survival, and net survival results by each Carstairs 2001 Category along with the SII for each measurement are displayed in Table 4.5. These estimates are the same as the figures that are outlined in Table 3.5 to Table 3.7 on Page 116 to Page 118 of Chapter 3. However, this chapter provides a more detailed review, including comparisons of the SII estimates.

There was clear inequality in overall survival, disease-specific survival, and net survival across Carstairs 2001 Category after one year of follow-up. One-year overall survival for the participants who resided in the least deprived areas was 83.4% (95% CI 78.1% to 87.5%), whereas the participants who resided in the most deprived areas had a considerably lower one-year overall survival of 71.8% (95% CI 67.7% to 75.4%). Similarly, one-year disease-specific survival was also substantially lower for the participants who were from the most deprived regions at 71.9% (95% CI 75.2% to 82.4%), compared to 88.8% (95% CI 83.9% to 92.9%) for the participants who were from the least deprived regions. One-year net survival also demonstrated the same difference, and the participants who were in the least deprived group had one-year net survival of 86.1% (95% CI 81.3% to 91.0%), while the participants who were in the most deprived group had a considerably lower one-year net survival result of 73.7% (95% CI 69.7% to 77.6%). One year after the patient's diagnosis of head and neck cancer, the SII across Carstairs 2001 Category was highest for net survival at 13.6 (95% CI 7.1 to 20.1), and lowest for disease-specific survival at 9.5 (95% CI 1.4 to 17.7). This result for the SII suggests that within the first year after their diagnosis the participants who are from more deprived regions are more likely to die as a result of underlying causes of their head and neck cancer that may not necessarily be considered in disease-specific survival.

After five years, the inequality by overall survival, disease-specific survival, and net survival remained and those who were from the least deprived and most deprived areas had five-year overall survival of 49.8% (95% CI 43.3% to 55.9%) and 40.5% (95% CI 36.3% to 44.7%), respectively. Similarly, the participants who were from the least deprived regions still had a considerably higher disease-specific and net survival result of 69.6% (95% CI 62.9% to 75.3%) and 58.1% (95% CI 50.4% to 65.8%), respectively, compared to the participants who were from the most deprived regions at 59.6% (95% CI 54.9% to 63.9%) and 46.6% (95% CI 41.7% to 51.5%), respectively. Similar to the results for one-year survival, the SII was the strongest for net survival at 16.1 (95% CI -1.0 to 33.3), and inequality had increased for all three measurements of survival. However, the results were

not clear cut since the confidence intervals for all three of the SIIs were crossing over zero.

After 12 years, inequality in overall survival by Carstairs 2001 Category had attenuated, and patients who were from the least deprived and most deprived regions had 12-year overall survival of 27.0% (95% CI 21.5% to 32.7%) and 22.9% (95% CI 19.4% to 26.6%), respectively. This attenuation can also be demonstrated by the lower SII of 7.4 (95% CI -2.7 to 17.5) after 12 years for overall survival. Similar results were observed for net survival, and the participants who were from the least deprived and most deprived areas had 12-year net survival of 40.4% (95% CI 30.7% to 50.0%) and 35.7% (95% CI 29.6% to 41.8%), respectively, with an SII of 6.6 (95% CI -17.2 to 30.3). Contrastingly, the inequality by disease-specific survival was at its strongest after 12 years with an SII of 16.5 (95% CI 1.5 to 31.5). The participants who were from the least deprived and most deprived regions had 12-year disease-specific survival of 61.8% (95% CI 54.4% to 68.4%) and 51.1% (95% CI 46.0% to 55.9%), respectively.

**Table 4.5 – One-year, five-year, and 12-year overall survival, disease-specific survival, and net survival results for each Carstairs 2001 Category**

| Carstairs 2001 Category | Overall survival % (95% CI) | Disease-specific survival % (95% CI) | Net survival % (95% CI) |
|---|---|---|---|
| **One-year** | | | |
| 1 (Least deprived) | 83.4 (78.1, 87.5) | 88.8 (83.9, 92.2) | 86.1 (81.3, 91.0) |
| 2 | 78.6 (73.6, 82.7) | 83.2 (78.5, 86.9) | 80.9 (76.2, 85.5) |
| 3 | 76.3 (71.3, 80.6) | 82.2 (77.5, 86.1) | 78.6 (73.8, 83.3) |
| 4 | 75.1 (70.6, 79.0) | 81.8 (77.5, 85.3) | 77.2 (72.8, 81.5) |
| 5 (Most deprived) | 71.8 (67.7, 75.4) | 79.1 (75.2, 82.4) | 73.7 (69.7, 77.6) |
| *SII (95% CI)* | *12.7 (6.7, 18.8)* | *9.5 (1.4, 17.7)* | *13.6 (7.1, 20.1)* |
| **Five-year** | | | |
| 1 (Least deprived) | 49.8 (43.3, 55.9) | 69.6 (62.9, 75.3) | 58.1 (50.4, 65.8) |
| 2 | 52.1 (46.4, 57.4) | 69.8 (64.2, 74.8) | 61.0 (54.4, 67.6) |
| 3 | 44.6 (39.2, 49.9) | 61.0 (55.1, 66.4) | 52.9 (46.4, 59.3) |
| 4 | 47.7 (42.8, 52.4) | 64.4 (59.2, 69.1) | 55.8 (50.1, 61.6) |
| 5 (Most deprived) | 40.5 (36.3, 44.7) | 59.6 (54.9, 63.9) | 46.6 (41.7, 51.5) |
| *SII (95% CI)* | *12.9 (-1.8, 27.5)* | *12.5 (-1.8, 26.9)* | *16.1 (-1.0, 33.3)* |
| **12-year** | | | |
| 1 (Least deprived) | 27.0 (21.5, 32.7) | 61.8 (54.4, 68.4) | 40.4 (30.7, 50.0) |
| 2 | 30.6 (25.6, 35.7) | 65.6 (59.6, 70.9) | 43.8 (35.0, 52.6) |
| 3 | 26.2 (21.5, 31.0) | 55.5 (49.2, 61.3) | 40.7 (31.5, 49.9) |
| 4 | 26.9 (22.7, 31.3) | 55.5 (49.9, 60.8) | 46.6 (38.4, 54.7) |
| 5 (Most deprived) | 22.9 (19.4, 26.6) | 51.1 (46.0, 55.9) | 35.7 (29.6, 41.8) |
| *SII (95% CI)* | *7.4 (-2.7, 17.5)* | *16.5 (1.5, 31.5)* | *6.6 (-17.2, 30.3)* |

### 4.3.4 Adjusted Cox proportional hazards models for all-cause mortality by Carstairs 2001 Category

The adjusted Cox Proportional hazards models for all-cause mortality by Carstairs 2001 Category along with the SIIs for each model are displayed in Table 4.6 to Table 4.9 on Page 175 to Page 178.

#### 4.3.4.1 Adjusted Cox proportional hazards models by age and sex for all-cause mortality by Carstairs 2001 Category

Trends were observed following minimal adjustment for age and sex in the models for all-cause mortality at all three time points (Table 4.6). After one year, five years, and 12 years, the participants who resided in the most deprived areas of Scotland were 96% (HR = 1.96, 95% CI 1.38 to 2.77), 43% (HR = 1.43, 95% CI 1.15 to 1.76) and 27% (HR = 1.27, 95% CI 1.06 to 1.52) more at risk of all-cause mortality following adjustment for age and sex, respectively. Inequality in survival following adjustment for age and sex was strongest after one year of follow-up and attenuated over time. This can be demonstrated from both the reduction in the hazard ratios for those in the most deprived group, and the reduction in the SIIs from 1.1 (95% CI 0.7 to 1.5) after one year to 0.4 (95% CI 0.1 to 0.7) after 12 years.

#### 4.3.4.2 Adjusted Cox proportional hazards models by individual patient, tumour, and treatment factors for all-cause mortality by Carstairs 2001 Category

In minimally adjusted models that were adjusted by each of the individual patient, tumour, and treatment factors (Table 4.6 and Table 4.7), there were no variables that fully explained the inequality in all-cause mortality after one or five years. Although inequality remained strong, there was a slight attenuation across Carstairs 2001 Category after one year following adjustment for WHO Performance Status, smoking status, tumour stage, and treatment modality, which can be observed by the reduction in the SII and the attenuation of the hazard ratios. Similarly, after 12 years, the people from the most deprived areas continued to be at an increased risk of all-cause mortality compared to the people from the least deprived area in each of the minimally adjusted models that were adjusted by the individual patient, tumour, and treatment factors. However, smoking status fully explained the inequality in all-cause mortality observed across Carstairs 2001 Category after 12 years, which can be demonstrated in the attenuation of the hazard ratios and the reduction in the SII to 0.2 (95% CI -0.1 to 0.4).

#### 4.3.4.3 Adjusted Cox proportional hazards models by all patient, tumour, and treatment factors for all-cause mortality by Carstairs 2001 Category

Following adjustment for age, sex and, a) all participant factors, b) all tumour factors, and c) all treatment factors, inequality had reduced, but remained clear after one year in all of the models (Table 4.8). However, after five years and 12 years, inequality was no longer apparent following adjustment for age, sex, and participant factors, which can be demonstrated by the attenuation in the hazard ratios and the reduction of the SIIs to 0.2 (95% CI -0.2 to 0.6) and 0.1 (95% CI -0.3 to 0.4), respectively. Inequality remained after five years following adjustment for age, sex, and a) tumour factors, and b) treatment factors. However, after 12 years, there was no longer inequality when adjusting by these factors. Interestingly, following adjustment for age, sex, tumour, and treatment factors combined, there was no longer a difference between the participants who were most deprived and the participants in other Carstairs 2001 Category at any time point.

#### 4.3.4.4 Fully adjusted Cox proportional hazards models for all-cause mortality by Carstairs 2001 Category

Following full adjustment for age, sex, patient, tumour, and treatment factors, there was no longer inequality across the Carstairs 2001 Category (one-year HR = 1.16, 95% CI 0.80 to 1.68, five-year HR = 0.97, 95% CI 0.78 to 1.22, 12-year HR = 0.87, 95% CI 0.72 to 1.05) (Table 4.8). The attenuation of inequality was also demonstrated by the SIIs which had reduced from 1.1 (95% CI 0.7 to 1.5) to 0.2 (95% CI -0.4 to 0.7) after one-year, 0.6 (95% CI 0.1 to 1.0) to 0.03 (95% CI -0.6 to 0.6) after five-years, and 0.4 (95% CI 0.1 to 0.7) to -0.1 (95% CI -0.5 to 0.4) after 12-years in the minimally adjusted models by age and sex and the fully adjusted models, respectively.

#### 4.3.4.5 Fully adjusted Cox proportional hazards models for all-cause mortality by Carstairs 2001 Category by removing WHO Performance Status

In a sensitivity analysis which excluded WHO Performance Status as an adjustment variable, the results were similar to the models that included WHO Performance Status as an adjustment variable (Table 4.9). Following adjustment for age, sex and participant factors, inequality in survival was stronger after one and five years. After one year, the participants who were from the most deprived areas were 66% (HR = 1.66, 95% CI 1.17 to 2.37) more at risk of all-cause mortality than the people who were from the least deprived areas, compared to 46% (HR = 1.46, 95% CI 1.02 to 2.09) more at risk in the model which included WHO Performance Status too. However, after five years, the

participants who were from the most deprived regions were 25% (HR = 1.25, 95% CI 1.01 to 1.55) more at risk of all-cause mortality than the participants who were from the least deprived regions, compared to no excess risk (HR = 1.11, 95% CI 0.89 to 1.38) in the model which include WHO Performance Status. When WHO Performance Status was removed as an adjustment variable in the model that was fully adjusted by age, sex, patient, tumour, and treatment factors, the results were the same, and the participants who were from the most deprived areas were at no extra risk than those who were from the least deprived areas.

**Table 4.6 – Minimally adjusted hazard ratios by participant factors for all-cause mortality (ACM) after one year, five years, and 12 years for Carstairs 2001 Category**

| | Adjusted by age and sex | | Adjusted by WHO* | | Adjusted by Smoking^ | | Adjusted by Alcohol+ | |
|---|---|---|---|---|---|---|---|---|
| **Variable** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| **One-year ACM** | | <0.001 | | 0.003 | | 0.003 | | <0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.35 (0.92, 2.00) | | 1.22 (0.83, 1.81) | | 1.31 (0.88, 1.93) | | 1.36 (0.92, 2.01) | |
| 3 | 1.53 (1.05, 2.25) | | 1.38 (0.94, 2.03) | | 1.47 (1.00, 2.15) | | 1.51 (1.03, 2.22) | |
| 4 | 1.62 (1.12, 2.33) | | 1.37 (0.95, 1.98) | | 1.49 (1.03, 2.15) | | 1.57 (1.09, 2.27) | |
| 5 (Most deprived) | 1.96 (1.38, 2.77) | | 1.66 (1.16, 2.35) | | 1.68 (1.18, 2.40) | | 1.85 (1.30, 2.63) | |
| *SII (95% CI)* | *1.1 (0.7, 1.5)* | | *0.7 (0.3, 1.1)* | | *0.7 (0.2, 1.2)* | | *0.9 (0.4, 1.4)* | |
| **Five-year ACM** | | <0.001 | | 0.008 | | 0.012 | | 0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.99 (0.78, 1.26) | | 0.90 (0.71, 1.14) | | 0.97 (0.76, 1.23) | | 1.00 (0.79, 1.27) | |
| 3 | 1.22 (0.97, 1.54) | | 1.12 (0.89, 1.41) | | 1.19 (0.94, 1.49) | | 1.21 (0.96, 1.52) | |
| 4 | 1.14 (0.91, 1.43) | | 1.00 (0.80, 1.25) | | 1.07 (0.85, 1.34) | | 1.10 (0.88, 1.38) | |
| 5 (Most deprived) | 1.43 (1.15, 1.76) | | 1.24 (1.00, 1.53) | | 1.26 (1.02, 1.56) | | 1.35 (1.09, 1.67) | |
| *SII (95% CI)* | *0.6 (0.1, 1.0)* | | *0.3 (-0.2, 0.9)* | | *0.3 (-0.1, 0.8)* | | *0.4 (0.0, 0.9)* | |
| **12-year ACM** | | <0.001 | | 0.029 | | 0.102 | | 0.009 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.94 (0.77, 1.15) | | 0.87 (0.71, 1.06) | | 0.92 (0.75, 1.12) | | 0.95 (0.78, 1.16) | |
| 3 | 1.09 (0.89, 1.32) | | 1.01 (0.83, 1.23) | | 1.05 (0.87, 1.28) | | 1.06 (0.88, 1.29) | |
| 4 | 1.08 (0.89, 1.30) | | 0.96 (0.79, 1.16) | | 1.00 (0.83, 1.20) | | 1.04 (0.86, 1.25) | |
| 5 (Most deprived) | 1.27 (1.06, 1.52) | | 1.13 (0.94, 1.35) | | 1.10 (0.92, 1.32) | | 1.20 (1.01, 1.44) | |
| *SII (95% CI)* | *0.4 (0.1, 0.7)* | | *0.2 (-0.2, 0.6)* | | *0.2 (-0.1, 0.4)* | | *0.3 (0.0, 0.6)* | |

*Adjusted by age, sex and WHO Performance Status
^Adjusted by age, sex and smoking status
+Adjusted by age, sex and alcohol consumption

**Table 4.7 – Minimally adjusted hazard ratios by tumour and treatment factors for all-cause mortality (ACM) after one year, five years, and 12 years for Carstairs 2001 Category**

| Variable | Adjusted by Site* HR (95% CI) | p-value | Adjusted by Stage^ HR (95% CI) | p-value | Adjusted by Treatment+ HR (95% CI) | p-value | Adjusted by Network& HR (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|
| **One-year ACM** | | <0.001 | | 0.002 | | 0.007 | | <0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.38 (0.93, 2.03) | | 1.32 (1.89, 1.95) | | 1.21 (0.81, 1.78) | | 1.36 (0.92, 2.01) | |
| 3 | 1.54 (1.05, 2.25) | | 1.51 (1.03, 2.21) | | 1.53 (1.04, 2.25) | | 1.53 (1.04, 2.25) | |
| 4 | 1.63 (1.13, 2.35) | | 1.52 (1.05, 2.20) | | 1.48 (1.03, 2.14) | | 1.61 (1.12, 2.33) | |
| 5 (Most deprived) | 1.91 (1.35, 2.71) | | 1.73 (1.22, 2.46) | | 1.58 (1.11, 2.25) | | 1.96 (1.37, 2.80) | |
| *SII (95% CI)* | *1.0 (0.5, 1.5)* | | *0.8 (0.3, 1.3)* | | *0.6 (0.0, 1.3)* | | *1.7 (0.6, 1.5)* | |
| **Five-year ACM** | | <0.001 | | 0.004 | | 0.005 | | <0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.03 (0.81, 1.31) | | 1.00 (0.79, 1.27) | | 0.91 (0.72, 1.16) | | 0.99 (0.78, 1.26) | |
| 3 | 1.28 (1.02, 1.61) | | 1.25 (0.99, 1.57) | | 1.23 (0.97, 1.55) | | 1.22 (0.96, 1.53) | |
| 4 | 1.19 (0.95, 1.49) | | 1.10 (0.88, 1.37) | | 1.12 (0.89, 1.40) | | 1.13 (0.90, 1.42) | |
| 5 (Most deprived) | 1.41 (1.15, 1.75) | | 1.32 (1.07, 1.63) | | 1.24 (1.00, 1.53) | | 1.40 (1.13, 1.74) | |
| *SII (95% CI)* | *0.5 (0.1, 0.9)* | | *0.4 (-0.1, 0.9)* | | *0.3 (-0.2, 0.9)* | | *0.5 (0.1, 1.0)* | |
| **12-year ACM** | | 0.001 | | 0.012 | | 0.010 | | 0.006 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.96 (0.79, 1.18) | | 0.94 (0.77, 1.15) | | 0.88 (0.72, 1.07) | | 0.93 (0.77, 1.14) | |
| 3 | 1.14 (0.94, 1.39) | | 1.09 (0.90, 1.33) | | 1.10 (0.90, 1.33) | | 1.08 (0.89, 1.31) | |
| 4 | 1.12 (0.93, 1.35) | | 1.04 (0.86, 1.25) | | 1.07 (0.89, 1.29) | | 1.05 (1.05, 1.27) | |
| 5 (Most deprived) | 1.25 (1.05, 1.50) | | 1.19 (1.00, 1.42) | | 1.14 (0.96, 1.37) | | 1.22 (1.02, 1.47) | |
| *SII (95% CI)* | *0.3 (0.1, 0.6)* | | *0.3 (0.0, 0.6)* | | *0.3 (-0.1, 0.6)* | | *0.3 (0.0, 0.6)* | |

*Adjusted by age, sex and anatomical site
^Adjusted by age, sex and tumour stage
+Adjusted by age, sex and treatment modality
&Adjusted by age, sex and Scottish Cancer Network

**Table 4.8 – Adjusted hazard ratios by a combination of patient, tumour, and treatment factors for all-cause mortality (ACM) after one year, five years, and 12 years for Carstairs 2001 Category**

| Variable | Adjusted by all participant factors* HR (95% CI) | p-value | Adjusted by all tumour factors^ HR (95% CI) | p-value | Adjusted by all treatment factors+ HR (95% CI) | p-value | Adjusted by tumour and treatment factors combined& HR (95% CI) | p-value | Adjusted by all patient, tumour, and treatment factors combined% HR (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|---|---|
| **One-year ACM** | | 0.037 | | 0.002 | | 0.006 | | 0.113 | | 0.351 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.20 (0.81, 1.78) | | 1.32 (0.89, 2.95) | | 1.18 (0.79, 1.74) | | 1.09 (0.74, 1.62) | | 0.99 (0.67, 1.47) | |
| 3 | 1.31 (0.89, 1.92) | | 1.53 (1.04, 2.25) | | 1.55 (1.06, 2.29) | | 1.42 (0.96, 2.09) | | 1.28 (0.86, 1.89) | |
| 4 | 1.30 (0.90, 1.89) | | 1.53 (1.06, 2.21) | | 1.51 (1.04, 2.18) | | 1.29 (0.89, 1.88) | | 1.16 (0.79, 1.69) | |
| 5 (Most deprived) | 1.46 (1.02, 2.09) | | 1.73 (1.22, 2.46) | | 1.59 (1.11, 2.29) | | 1.32 (0.92, 1.91) | | 1.16 (0.80, 1.68) | |
| *SII (95% CI)* | *0.5 (0.2, 0.8)* | | *0.8 (0.2, 1.3)* | | *0.7 (0.0, 1.4)* | | *0.3 (-0.3, 1.0)* | | *0.2 (-0.4, 0.7)* | |
| **Five-year ACM** | | 0.157 | | 0.004 | | 0.003 | | 0.065 | | 0.715 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.89 (0.70, 1.13) | | 1.03 (0.81, 1.31) | | 0.90 (0.71, 1.15) | | 0.91 (0.72, 1.16) | | 0.80 (0.63, 1.02) | |
| 3 | 1.07 (0.85, 1.35) | | 1.32 (1.04, 1.66) | | 1.24 (0.98, 1.57) | | 1.29 (1.02, 1.63) | | 1.11 (0.88, 1.41) | |
| 4 | 0.95 (0.76, 1.19) | | 1.13 (0.90, 1.42) | | 1.14 (0.91, 1.43) | | 1.07 (0.85, 1.34) | | 0.90 (0.72, 1.14) | |
| 5 (Most deprived) | 1.11 (0.89, 1.38) | | 1.33 (1.08, 1.65) | | 1.28 (1.03, 1.59) | | 1.17 (0.94, 1.46) | | 0.97 (0.78, 1.22) | |
| *SII (95% CI)* | *0.2 (-0.2, 0.6)* | | *0.4 (-0.2, 0.9)* | | *0.4 (-0.1, 1.0)* | | *0.2 (-0.5, 0.9)* | | *0.03 (-0.6, 0.6)* | |
| **12-year ACM** | | 0.624 | | 0.015 | | 0.015 | | 0.197 | | 0.465 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.86 (0.70, 1.04) | | 0.95 (0.78, 1.16) | | 0.87 (0.71, 1.06) | | 0.87 (0.71, 1.06) | | 0.79 (0.64, 0.96) | |
| 3 | 0.95 (0.78, 1.16) | | 1.15 (0.94, 1.40) | | 1.10 (0.91, 1.34) | | 1.14 (0.94, 1.39) | | 0.99 (0.81, 1.21) | |
| 4 | 0.89 (0.74, 1.08) | | 1.07 (0.88, 1.29) | | 1.07 (0.89, 1.30) | | 1.02 (0.84, 1.23) | | 0.86 (0.71, 1.05) | |
| 5 (Most deprived) | 0.99 (0.82, 1.19) | | 1.19 (0.99, 1.42) | | 1.14 (0.95, 1.37) | | 1.06 (0.88, 1.27) | | 0.87 (0.72, 1.05) | |
| *SII (95% CI)* | *0.1 (-0.3, 0.4)* | | *0.3 (-0.1, 0.6)* | | *0.3 (-0.1, 0.6)* | | *0.1 (-0.4, 0.6)* | | *-0.1 (-0.5, 0.4)* | |

*Adjusted by age, sex and all participant factors including smoking status, alcohol consumption and WHO Performance Status
^Adjusted by age, sex and all tumour factors including anatomical site and tumour stage
+Adjusted by age, sex and all treatment modality and network
&Adjusted by age, sex and both tumour and treatment factors including stage, anatomical site, treatment modality and network of treatment
%Adjusted by all factors including age, sex, smoking status, alcohol consumption, WHO Performance status, stage, anatomical site, treatment modality and network of treatment

**Table 4.9 – Sensitivity analysis - adjusted hazard ratios by a combination of patient, tumour, and treatment factors for all-cause mortality (ACM) after one year, five years, and 12 years for Carstairs 2001 Category excluding WHO Performance Status**

| | Adjusted by all participant factors excluding WHO* | | Adjusted by all patient, tumour, and treatment factors combined excluding WHO^ | |
|---|---|---|---|---|
| **Variable** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| **One-year ACM** | | 0.005 | | 0.222 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.32 (0.89, 1.95) | | 1.16 (0.78, 1.73) | |
| 3 | 1.46 (1.00, 2.14) | | 1.37 (0.93, 2.02) | |
| 4 | 1.49 (1.03, 2.15) | | 1.28 (0.88, 1.85) | |
| 5 (Most deprived) | 1.66 (1.17, 2.37) | | 1.29 (0.89, 1.89) | |
| *SII (95% CI)* | *0.7 (0.2, 1.2)* | | *0.3 (-0.3, 0.8)* | |
| **Five-year ACM** | | 0.021 | | 0.428 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.98 (0.77, 1.25) | | 0.95 (0.75, 1.21) | |
| 3 | 1.18 (0.94, 1.49) | | 1.21 (0.96, 1.53) | |
| 4 | 1.06 (0.84, 1.33) | | 1.01 (0.80, 1.27) | |
| 5 (Most deprived) | 1.25 (1.01, 1.55) | | 1.09 (0.87, 1.36) | |
| *SII (95% CI)* | *0.3 (-0.1, 0.7)* | | *0.1 (-0.4, 0.6)* | |
| **12-year ACM** | | 0.160 | | 0.752 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.93 (0.76, 1.14) | | 0.91 (0.74, 1.11) | |
| 3 | 1.04 (0.86, 1.27) | | 1.07 (0.88, 1.31) | |
| 4 | 0.99 (0.82, 1.19) | | 0.95 (0.79, 1.16) | |
| 5 (Most deprived) | 1.10 (0.91, 1.31) | | 0.95 (0.79, 1.15) | |
| *SII (95% CI)* | *0.2 (-0.1, 0.4)* | | *0.0 (-0.4, 0.3)* | |

*Adjusted by age, sex and all participant factors including smoking status and alcohol consumption
^Adjusted by all factors including age, sex, smoking status, alcohol consumption, WHO Performance status, stage, anatomical site, treatment modality and network of treatment

### 4.3.5 Adjusted Cox proportional hazards models for disease-specific mortality by Carstairs 2001 Category

Minimally adjusted Cox Proportional hazards models for disease-specific mortality by Carstairs 2001 Category along with the SII for each model are displayed in Table 4.10 to Table 4.13 on Page 182 to Page 185.

#### 4.3.5.1 Adjusted Cox proportional hazards models by age and sex for disease-specific mortality by Carstairs 2001 Category

Similar to the models for all-cause mortality, there was clear inequality by disease-specific mortality following minimal adjustment by age and sex at all three time points. (Table 4.10). After one year, five years, and 12 years the participants who resided in the most deprived areas of Scotland were two-fold (HR = 2.09, 95% CI 1.36 to 3.22), 55% (HR = 1.55, 95% CI 1.17 to 2.06) and 51% (HR = 1.51, 95% CI 1.16 to 1.96) more at risk of disease-specific mortality following adjustment for age and sex, respectively. Inequality in survival following adjustment for age and sex was strongest after one-year of follow-up and attenuated over time which can be demonstrated in the reduction in the SII from 1.1 (95% CI 0.2 to 1.9) at one-year to 0.7 (95% CI 0.2 to 1.2) at 12-years. In addition, the magnitude of the inequality by disease-specific mortality was stronger than it was for all-cause mortality at all three time points.

#### 4.3.5.2 Adjusted Cox proportional hazards models by individual patient, tumour, and treatment factors for disease-specific mortality by Carstairs 2001 Category

In the minimally adjusted models by each individual patient, tumour, and treatment factor (Table 4.10 and Table 4.11), there was no adjustment variable that fully explained the inequality in disease-specific mortality after one year, five years, or 12 years. However, when the models were adjusted by age, sex and, a) WHO Performance Status, b) smoking status, c) tumour stage, or e) treatment modality, inequality attenuated which can be demonstrated by the reduction in the hazard ratios and the reduction in the SIIs.

#### 4.3.5.3 Fully adjusted Cox proportional hazards models for disease-specific mortality by Carstairs 2001 Category

In contrast to the model for all-cause mortality, following adjustment for age, sex, and participant factors, there was no longer a difference between the participants who were from the most deprived regions and the participants in other Carstairs 2001 Categories

(one-year HR = 1.51, 95% CI 0.97 to 2.34, five-year HR = 1.21, 95% CI 0.91 to 1.62, 12-year HR = 1.18, 95% CI 0.90 to 1.55) (Table 4.12). The reduction in the inequality following adjustment for age, sex, and participant factors could also be observed from the SIIs which were 0.7 (95% CI -0.1 to 3.5), 0.3 (95% CI -0.3 to 0.8) and 0.3 (95% CI -0.2 to 0.7) after one year, five years, and 12 years, respectively.

Similar to the models for all-cause mortality, in the models adjusting for age, sex, and tumour factors, inequality by disease-specific survival remained strong after one year and five years, and the participants who were from the most deprived areas were 85% (HR = 1.85, 95% CI 1.20 to 2.86) and 42% (HR = 1.42, 95% CI 1.07 to 1.88) more at risk of disease-specific mortality compared to the participants who were from the least deprived areas (Table 4.12). However, unlike the model for all-cause mortality, after 12 years the participants in the most deprived group remained 38% (HR = 1.38, 95% CI 1.06 to 1.79) more at risk of disease-specific mortality compared to the participants who were least deprived. Interestingly, the SII did not display inequality in disease-specific survival following adjustment by age, sex, and tumour factors at one, five or 12 years at 0.8 (95% CI -0.1 to 1.7), 0.4 (95% CI -0.4 to 1.3), and 0.5 (95% CI -0.2 to 1.1) respectively.

Following adjustment for age, sex, and treatment factors, similar results were observed to the models for all-cause mortality (Table 4.12). After one year, the participants in the most deprived group were 79% (HR = 1.79, 95% CI 1.15 to 2.80) more at risk of disease-specific mortality compared to the participants who were in the least deprived group. Inequality had attenuated slightly by five-years and the participants who were from the most deprived areas were 46% (HR = 1.46, 95% CI 1.09 to 1.95) more at risk of disease-specific mortality than the participants who were from the least deprived areas. However, unlike the results for all-cause mortality, after 12 years, the participants who lived in the most deprived regions were 38% (HR = 1.38, 95% CI 1.05 to 1.82) more at risk of disease-specific mortality. Similar to the model adjusting by age, sex, and tumour factors, the SII did not display the inequality in disease-specific survival following adjustment by age, sex, and treatment factors after one year, five years or 12 years at 1.1 (95% CI -0.2 to 2.4), 0.6 (95% CI -0.2 to 1.4), and 0.6 (95% CI -0.2 to 1.3) respectively.

Similar to the results for all-cause mortality, following adjustment for age, sex, tumour, and treatment factors, there was no longer a difference between the participants who were from the most deprived regions and the participants in other Carstairs 2001 Categories (one-year HR = 1.45, 95% CI 0.92 to 2.29, five-year HR = 1.27, 95% CI 0.95 to 1.71, 12-year HR = 1.22, 95% CI 0.92 to 1.60) for disease-specific mortality (Table 4.12). The reduction in inequality following adjustment for age, sex, tumour, and treatment factors could also be observed from the SIIs which were 0.4 (95% CI -0.4 to 1.3), 0.3 (95% CI -0.7 to 1.4) and 0.3 (95% CI -0.6 to 1.2) at one-year, five-year, and 12-years, respectively.

Similar to the results for all-cause mortality, following full adjustment for age, sex, patient, tumour, and treatment factors, there was also no longer a clear inequality across Carstairs 2001 Category, suggesting that the participants who were from the most deprived areas were no longer at an increased risk of disease-specific mortality (one-year HR = 1.23, 95% CI 0.78 to 1.96, five-year HR = 1.07, 95% CI 0.79 to 1.45, 12-year HR = 1.02, 95% CI 0.77 to 1.35) (Table 4.11). The attenuation of inequality was also demonstrated by the SIIs which had reduced from 1.1 (95% CI 0.2 to 1.9) to 0.2 (95% CI -0.5 to 0.9) after one year, 0.7 (95% CI 0.1 to 1.2) to 0.1 (95% CI -0.7 to 1.0) after five years, and 0.7 (95% CI 0.2 to 1.2) to 0.1 (95% CI -0.7 to 0.9) after 12 years in the minimally adjusted models by age and sex and the fully adjusted models, respectively.

#### 4.3.5.4 Fully adjusted Cox proportional hazards models for disease-specific mortality by Carstairs 2001 Category by removing WHO Performance Status

In a sensitivity analysis which excluded WHO Performance Status as an adjustment variable, the results were similar to the models that included WHO Performance Status as an adjustment variable (Table 4.13). Following adjustment for age, sex, and participant factors, inequality in survival was stronger after one year, five years, and 12 years. When WHO Performance Status was removed as an adjustment variable in the model that was fully adjusted by age, sex, patient, tumour, and treatment factors, the results were the same, and the participants who were from the most deprived areas were at no extra risk than those who were from the least deprived areas.

**Table 4.10 – Minimally adjusted hazard ratios by participant factors for disease-specific mortality (DSM) after one year, five years, and 12 years for Carstairs 2001 Category**

| Variable | Adjusted by age and sex HR (95% CI) | p-value | Adjusted by WHO* HR (95% CI) | p-value | Adjusted by Smoking^ HR (95% CI) | p-value | Adjusted by Alcohol+ HR (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|
| **One-year DSM** | | 0.001 | | 0.025 | | 0.026 | | 0.005 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.59 (0.99, 2.54) | | 1.42 (0.88, 2.28) | | 1.54 (0.96, 2.47) | | 1.60 (1.00, 2.56) | |
| 3 | 1.69 (1.06, 2.69) | | 1.50 (0.94, 2.39) | | 1.62 (1.01, 2.59) | | 1.67 (1.05, 2.67) | |
| 4 | 1.72 (1.10, 2.69) | | 1.43 (0.91, 2.25) | | 1.59 (1.01, 2.49) | | 1.67 (1.07, 2.62) | |
| 5 (Most deprived) | 2.09 (1.36, 3.22) | | 1.73 (1.12, 2.67) | | 1.78 (1.15, 2.75) | | 1.98 (1.28, 3.05) | |
| *SII (95% CI)* | *1.1 (0.2, 1.9)* | | *0.7 (0.0, 1.4)* | | *0.7 (-0.2, 1.6)* | | *0.9 (0.0, 1.8)* | |
| **Five-year DSM** | | <0.001 | | 0.018 | | 0.012 | | 0.003 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.06 (0.77, 1.46) | | 0.96 (0.69, 1.32) | | 1.05 (0.76, 1.44) | | 1.08 (0.78, 1.48) | |
| 3 | 1.41 (1.04, 1.92) | | 1.28 (0.95, 1.74) | | 1.38 (1.02, 1.87) | | 1.40 (1.03, 1.90) | |
| 4 | 1.28 (0.95, 1.72) | | 1.11 (0.82, 1.50) | | 1.21 (0.90, 1.63) | | 1.25 (0.93, 1.68) | |
| 5 (Most deprived) | 1.55 (1.17, 2.06) | | 1.32 (1.00, 1.76) | | 1.39 (1.05, 1.85) | | 1.48 (1.11, 1.96) | |
| *SII (95% CI)* | *0.7 (0.1, 1.2)* | | *0.4 (-0.2, 1.0)* | | *0.4 (-0.2, 1.0)* | | *0.5 (0.0, 1.1)* | |
| **12-year DSM** | | <0.001 | | 0.005 | | 0.005 | | 0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.98 (0.73, 1.33) | | 0.89 (0.66, 1.20) | | 0.97 (0.72, 1.30) | | 1.00 (0.74, 1.35) | |
| 3 | 1.32 (0.99, 1.75) | | 1.21 (0.91, 1.60) | | 1.29 (0.97, 1.72) | | 1.30 (0.98, 1.73) | |
| 4 | 1.27 (0.97, 1.68) | | 1.11 (0.84, 1.46) | | 1.20 (0.91, 1.58) | | 1.23 (0.94, 1.62) | |
| 5 (Most deprived) | 1.51 (1.16, 1.96) | | 1.30 (1.00, 1.70) | | 1.35 (1.03, 1.76) | | 1.43 (1.10, 1.86) | |
| *SII (95% CI)* | *0.7 (0.2, 1.2)* | | *0.4 (-0.1, 1.0)* | | *0.3 (-0.2, 0.9)* | | *0.6 (0.1, 1.0)* | |

*Adjusted by age, sex and WHO Performance Status
^Adjusted by age, sex and smoking status
+Adjusted by age, sex and alcohol consumption

**Table 4.11 – Minimally adjusted hazard ratios by tumour and treatment factors for disease-specific mortality (DSM) after one year, five years, and 12 years for Carstairs 2001 Category**

| Variable | Adjusted by Site* HR (95% CI) | p-value | Adjusted by Stage^ HR (95% CI) | p-value | Adjusted by Treatment+ HR (95% CI) | p-value | Adjusted by Network& HR (95% CI) | p-value |
|---|---|---|---|---|---|---|---|---|
| **One-year DSM** | | 0.002 | | 0.012 | | 0.039 | | <0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.61 (1.01, 2.59) | | 1.55 (0.97, 2.49) | | 1.42 (0.88, 2.27) | | 1.58 (0.98, 2.53) | |
| 3 | 1.69 (1.06, 2.70) | | 1.68 (1.05, 2.69) | | 1.73 (1.08, 2.77) | | 1.71 (1.07, 2.72) | |
| 4 | 1.74 (1.11, 2.72) | | 1.63 (1.04, 2.56) | | 1.60 (1.02, 2.51) | | 1.77 (1.13, 2.79) | |
| 5 (Most deprived) | 2.05 (1.33, 3.15) | | 1.86 (1.21, 2.87) | | 1.68 (1.08, 2.59) | | 2.21 (1.42, 3.44) | |
| *SII (95% CI)* | *1.0 (0.2, 1.9)* | | *0.8 (-0.1, 1.7)* | | *0.6 (-0.4, 1.6)* | | *1.3 (0.5, 2.1)* | |
| **Five-year DSM** | | 0.002 | | 0.010 | | 0.019 | | <0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.12 (0.81, 1.54) | | 1.08 (0.78, 1.49) | | 0.98 (0.71, 1.35) | | 1.06 (0.77, 1.45) | |
| 3 | 1.48 (1.09, 2.01) | | 1.46 (1.08, 1.98) | | 1.44 (1.06, 1.95) | | 1.43 (1.05, 1.94) | |
| 4 | 1.33 (0.99, 1.78) | | 1.24 (0.92, 1.66) | | 1.25 (0.93, 1.69) | | 1.31 (0.97, 1.77) | |
| 5 (Most deprived) | 1.53 (1.15, 2.03) | | 1.42 (1.07, 1.89) | | 1.31 (0.99, 1.74) | | 1.61 (1.20, 2.15) | |
| *SII (95% CI)* | *0.6 (-0.1, 1.2)* | | *0.5 (-0.3, 1.2)* | | *0.4 (-0.4, 1.2)* | | *0.7 (0.1, 1.3)* | |
| **12-year DSM** | | <0.001 | | 0.003 | | 0.005 | | <0.001 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.02 (0.76, 1.38) | | 1.00 (0.74, 1.35) | | 0.91 (0.67, 1.23) | | 0.98 (0.72, 1.32) | |
| 3 | 1.39 (1.04, 1.85) | | 1.35 (1.02, 1.80) | | 1.34 (1.01, 1.78) | | 1.32 (1.00, 1.76) | |
| 4 | 1.32 (1.00, 1.73) | | 1.23 (0.93, 1.62) | | 1.26 (0.96, 1.66) | | 1.28 (0.97, 1.69) | |
| 5 (Most deprived) | 1.48 (1.14, 1.92) | | 1.39 (1.07, 1.81) | | 1.30 (1.00, 1.69) | | 1.51 (1.16, 1.98) | |
| *SII (95% CI)* | *0.6 (0.1, 1.2)* | | *0.5 (-0.1, 1.0)* | | *0.4 (-0.3, 1.1)* | | *0.7 (0.2, 1.1)* | |

*Adjusted by age, sex and anatomical site
^Adjusted by age, sex and tumour stage
+Adjusted by age, sex and treatment modality
&Adjusted by age, sex and Scottish Cancer Network

**Table 4.12 – Adjusted hazard ratios by a combination of patient, tumour, and treatment factors for disease-specific mortality (DSM) after one year, five years, and 12 years for Carstairs 2001 Category**

| | Adjusted by all participant factors* | | Adjusted by all tumour factors^ | | Adjusted by all treatment factors+ | | Adjusted by tumour and treatment factors combined& | | Adjusted by all patient, tumour, and treatment factors combined% | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| **One-year DSM** | | 0.162 | | 0.013 | | 0.012 | | 0.129 | | 0.431 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.41 (0.88, 2.27) | | 1.54 (0.96, 2.48) | | 1.36 (0.85, 2.18) | | 1.23 (0.76, 1.97) | | 1.11 (0.69, 1.80) | |
| 3 | 1.42 (0.88, 2.27) | | 1.69 (1.06, 2.71) | | 1.77 (1.11, 2.84) | | 1.57 (0.98, 2.52) | | 1.40 (0.87, 2.26) | |
| 4 | 1.37 (0.87, 2.16) | | 1.64 (1.04, 2.58) | | 1.67 (1.06, 2.63) | | 1.42 (0.90, 2.25) | | 1.24 (0.78, 1.98) | |
| 5 (Most deprived) | 1.51 (0.97, 2.34) | | 1.85 (1.20, 2.86) | | 1.79 (1.15, 2.80) | | 1.45 (0.92, 2.29) | | 1.23 (0.78, 1.96) | |
| *SII (95% CI)* | *0.7 (-0.1, 3.5)* | | *0.8 (-0.1, 1.7)* | | *1.1 (-0.2, 2.4)* | | *0.4 (-0.4, 1.3)* | | *0.2 (-0.5, 0.9)* | |
| **Five-year DSM** | | 0.117 | | 0.014 | | 0.001 | | 0.046 | | 0.343 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.96 (0.70, 1.33) | | 1.10 (0.80, 1.51) | | 0.96 (0.69, 1.32) | | 0.94 (0.68, 1.29) | | 0.82 (0.59, 1.14) | |
| 3 | 1.24 (0.91, 1.68) | | 1.52 (1.12, 2.06) | | 1.47 (1.09, 2.02) | | 1.49 (1.10, 2.03) | | 1.29 (0.95, 1.77) | |
| 4 | 1.07 (0.79, 1.45) | | 1.26 (0.93, 1.70) | | 1.34 (0.99, 1.80) | | 1.21 (0.89, 1.63) | | 1.03 (0.75, 1.40) | |
| 5 (Most deprived) | 1.21 (0.91, 1.62) | | 1.42 (1.07, 1.88) | | 1.46 (1.09, 1.95) | | 1.27 (0.95, 1.71) | | 1.07 (0.79, 1.45) | |
| *SII (95% CI)* | *0.3 (-0.3, 0.8)* | | *0.4 (-0.4, 1.3)* | | *0.6 (-0.2, 1.4)* | | *0.3 (-0.7, 1.4)* | | *0.1 (-0.7, 1.0)* | |
| **12-year DSM** | | 0.066 | | 0.005 | | <0.001 | | 0.036 | | 0.359 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 0.89 (0.66, 1.20) | | 1.01 (0.75, 1.36) | | 0.89 (0.66, 1.21) | | 0.88 (0.65, 1.19) | | 0.78 (0.58, 1.06) | |
| 3 | 1.16 (0.87, 1.54) | | 1.40 (1.05, 1.87) | | 1.37 (1.03, 1.83) | | 1.38 (1.04, 1.85) | | 1.20 (0.90, 1.61) | |
| 4 | 1.06 (0.80, 1.40) | | 1.25 (0.94, 1.64) | | 1.32 (1.00, 1.74) | | 1.19 (0.90, 1.58) | | 1.02 (0.77, 1.35) | |
| 5 (Most deprived) | 1.18 (0.90, 1.55) | | 1.38 (1.06, 1.79) | | 1.38 (1.05, 1.82) | | 1.22 (0.92, 1.60) | | 1.02 (0.77, 1.35) | |
| *SII (95% CI)* | *0.3 (-0.2, 0.7)* | | *0.5 (-0.2, 1.1)* | | *0.6 (-0.2, 1.3)* | | *0.3 (-0.6, 1.2)* | | *0.1 (-0.7, 0.9)* | |

*Adjusted by age, sex and all participant factors including smoking status, alcohol consumption and WHO Performance Status
^Adjusted by age, sex and all tumour factors including anatomical site and tumour stage
+Adjusted by age, sex and all treatment modality and network
&Adjusted by age, sex and both tumour and treatment factors including stage, anatomical site, treatment modality and network of treatment
%Adjusted by all factors including age, sex, smoking status, alcohol consumption, WHO Performance status, stage, anatomical site, treatment modality and network of treatment

**Table 4.13 – Sensitivity analysis - adjusted hazard ratios by a combination of patient, tumour, and treatment factors for disease-specific mortality (DSM) after one year, five years, and 12 years for Carstairs 2001 Category excluding WHO Performance Status**

| | Adjusted by all participant factors* | | Adjusted by all patient, tumour, and treatment factors combined^ | |
|---|---|---|---|---|
| **Variable** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| **One-year DSM** | | 0.032 | | 0.274 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.57 (0.98, 2.52) | | 1.33 (0.82, 2.15) | |
| 3 | 1.62 (1.01, 2.59) | | 1.53 (0.95, 2.47) | |
| 4 | 1.59 (1.01, 2.50) | | 1.40 (0.88, 2.21) | |
| 5 (Most deprived) | 1.77 (1.14, 2.73) | | 1.41 (0.89, 2.23) | |
| *SII (95% CI)* | *0.7 (-0.3, 1.6)* | | *0.3 (-0.5, 1.1)* | |
| **Five-year DSM** | | 0.018 | | 0.163 |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | |
| 2 | 1.07 (0.78, 1.47) | | 1.01 (0.73, 1.39) | |
| 3 | 1.38 (1.02, 1.87) | | 1.41 (1.04, 1.92) | |
| 4 | 1.21 (0.90, 1.63) | | 1.18 (0.87, 1.60) | |
| 5 (Most deprived) | 1.38 (1.04, 1.84) | | 1.22 (0.90, 1.65) | |
| *SII (95% CI)* | *0.4 (-0.2, 1.0)* | | *0.2 (-0.6, 1.0)* | |
| **12-year DSM** | | 0.009 | | |
| 1 (Least deprived) | 1.00 (Ref.) | | 1.00 (Ref.) | 0.174 |
| 2 | 0.99 (0.73, 1.33) | | 0.95 (0.70, 1.28) | |
| 3 | 1.28 (0.96, 1.70) | | 1.31 (0.98, 1.75) | |
| 4 | 1.19 (0.90, 1.57) | | 1.16 (0.88, 1.54) | |
| 5 (Most deprived) | 1.33 (1.02, 1.74) | | 1.15 (0.87, 1.53) | |
| *SII (95% CI)* | *0.4 (0.0, 0.9)* | | *0.2 (-0.5, 0.9)* | |

*Adjusted by age, sex and all participant factors including smoking status and alcohol consumption
^Adjusted by all factors including age, sex, smoking status, alcohol consumption, WHO Performance status, stage, anatomical site, treatment modality and network of treatment

## 4.4 Discussion

This study demonstrates that there was a clear gradient across Carstairs 2001 Category for overall survival and disease-specific survival after one year, five years, and 12 years for people with a diagnosis of head and neck cancer between the years of 1999 and 2001 in Scotland. Inequality in disease-specific survival became worse over the follow-up time from one years, five years, and 12 years after diagnosis, but the same trend was not apparent for overall survival and net survival estimates. However, following adjustment for age and sex, this trend for disease-specific survival was no longer apparent. In addition, the results for the net survival analysis demonstrated a gradient across the Carstairs 2001 Categories after one year and five years, but this gradient disappeared by 12 years, suggesting that some of the inequality in long-term survival was partly attributable to background mortality.

Following full adjustment after one year, five years, and 12 years, inequality was no longer apparent, suggesting that inequality in survival of patients with head and neck cancer can be explained by multiple patient, tumour, and treatment factors. Following multiple individual adjustments of various participants, tumour, and treatment factors, none of the models were fully explained which suggests that inequality in survival of participants with head and neck cancer is not straightforward, and that many factors play a combined effect in the role of the explanation of inequality in head and neck cancer survival. In addition, the results for the net survival analysis demonstrated a gradient across the Carstairs 2001 Category after one year and five years, but this gradient disappears by 12 years, suggesting that some of the inequality in long-term survival is partly attributable to background mortality, and since this cohort has such long follow-up, influence from background mortality is to be expected.

There are limitations to this study, several of which were discussed in Chapter 3. In addition to these, socioeconomic status was measured using the area based Carstairs 2001 Index (Carstairs and Morris, 1989; McLoone, 2000), which is derived from the 2001 Census and considers the proportion of male unemployment, those in social classes IV and V, lack of car ownership, and overcrowding in a dwelling. Since this was a clinical cohort study, further data on socioeconomic status indexes (including education level and levels of income) was not collected as part of this study. The Carstairs 2001 Category may not accurately represent rural and urban populations as it may be essential for people in these areas to own a car (Valentova, 2011), and as other indices such as education level of income were not available for this analysis, Carstairs 2001 Category was the best measurement available.

### 4.4.1 Conclusion

This study adds to the understanding of inequality in survival for people with head and neck cancer. The SAHNC cohort represented 77% of all head and neck cancer cases on the Scottish Cancer Registry over a two-year period and is therefore a good representation of head and neck cancer in Scotland. In unadjusted models, a clear gradient across Carstairs 2001 Category for overall survival, disease-specific survival, and net survival was observed after one year, five years, and 12 years for this cohort of people with head and neck cancer. Following adjustment for multiple patient, tumour, and treatment factors, inequality was no longer present for all-cause mortality and disease-specific mortality. This study concludes that explanations for inequality in survival of participants with head and neck cancer are not straightforward, and that many factors including various patient, tumour, and treatment factors play a part in inequality in survival of participants with head and neck cancer.

# 5 Inequality in survival of people with head and neck cancer in England: Results from the Head and Neck 5000 prospective clinical cohort study (HN5000)

## 5.1 Introduction

This chapter aims to undertake an in-depth exploration into the nature and extent of socioeconomic inequality in survival of people with head and neck cancer by considering both area-based and individual dimensions of socioeconomic circumstances. The explanations for inequality will be explored via multiple demographic data, health status, behavioural factors, tumour factors, and treatment factors.

The HN5000 is a population-based prospective clinical cohort study of people with head and neck cancer. Those with a new primary head and neck tumour who had been diagnosed on the NHS in England, Scotland, or Wales were eligible to be recruited to the study between April 2011 and December 2014 (Ness *et al.*, 2014). The study was funded by the National Institute of Health Research (NIHR) and was conducted by the University of Bristol. Full ethical approval was granted by the National Research Ethics Committee (South West Frenchay Ethics Committee, reference 10/H0107/57, 5th November 2010) and the study was approved by the Research and Development departments for the participating NHS trusts. The primary aim of the HN5000 was to "*evaluate the impact of centralisation of care for people with head and neck cancer"* (Ness *et al.,* 2014). However, in addition to this, the study team aimed to develop a *"well-phenotyped clinical cohort that will provide a biomedical resource for translational and prognostic research in head and neck cancer"* and welcomed collaboration from other head and neck cancer researchers (Ness *et al.*, 2014).

Previous studies have relied on either area-based or individual measurements of socioeconomic status to document and explain potential explanatory factors of inequality in survival of people with head and neck cancer. No prior study has investigated both forms of measurements of socioeconomic status. In this thesis, the HN5000 provides the unique opportunity to thoroughly explore inequality in survival of people with head and neck cancer via the use of both area-based and individual measurements of socioeconomic status, which were not both available in any of the previous chapters throughout this thesis. Although this study does not contain long-term follow-up data due

to the recency of the recruitment of the cohort, the database contains detailed information on patient demographics, health status, behavioural data, tumour factors, and treatment information to explore as potential confounders for inequality in survival of people with head and neck cancer.

### 5.1.1 Aims and objectives

The aim of Chapter 5 is to explore the underlying determinants of both area-based and individual measurements of socioeconomic status of people diagnosed with head and neck cancer on the HN5000 cohort study (Ness *et al.*, 2014; Ness *et al.*, 2015). The objectives of this chapter are to:

1. Explore the underlying demographic, health, behavioural, tumour, and treatment factors that are associated with socioeconomic inequality in survival of people with head and neck cancer.
2. Compare socioeconomic inequality in both area-based and induvial measurements of socioeconomic status.

## 5.2 Methods

### 5.2.1 Data collection

The HN5000 baseline data collection was undertaken between 1st April 2011 and 31st December 2014. A total of 76 UK centres contributed to the study throughout England, Scotland, and Wales. Information was gathered from clinical records using data capture forms which were completed by research nurses on the participants' diagnosis of head and neck cancer and the treatment modality that they received. In addition, the participants were asked to self-complete three questionnaires at baseline prior to the start of treatment, at four months after their diagnosis, and at 12 months after their diagnosis. At each time point, the cohort was asked about their demographics, general health, behaviours, and a variety of information relating to their socioeconomic position (described in detail below). In addition, there were also separate questionnaire sheets enquiring about the participants' outlook and feelings, and about their sexual behaviours, however these results will not be used as part of this study.

#### 5.2.1.1 SES factors

**Area-based measurement of socioeconomic status**

Due to the nature of this work and the need to utilise an area-based measurement of socioeconomic status to compare with individual measurements of socioeconomic status, only those recruited from England were included in this study. Therefore, the area-based measurement of socioeconomic status was derived from the English IMD 2010 score (English Indices of Deprivation, 2011) which were linked to the HN5000 using the participants' home postcodes and Lower Layer Super Output Area (LLSOA) codes (NHS, 2019). The IMD 2010 categorises geographical areas in England using information from seven domains: (a) Income Deprivation, (b) Employment Deprivation, (c) Health Deprivation and Disability, (d) Education Skills and Training Deprivation, (e) Barriers to Housing and Services, (f) Living Environment Deprivation, and (g) Crime. The IMD 2010 score has five categories – group one represents the people from the most deprived areas and group five represents the people from the least deprived areas.

**Individual measurements of socioeconomic status**

The individual measurements of socioeconomic status were obtained from the participants' questionnaire responses at baseline prior to the start of treatment. This included: highest education level attained, number of years spent in full-time education, total annual household income, proportion of income from benefits, and whether the participants had any financial concerns of living with or after cancer. The highest education level that the participants had attained was grouped as: (a) up to secondary school (primary school or secondary school, which usually includes students up to the age of 16), (b) further education (school/college sixth form or further education college, which usually includes students between the ages of 16 to 18), and (c) higher education or university (which usually includes students aged 18 and over). The number of years that the participants had spent in education was categorised as: a) less than £11,999 a year, b) between £12,000 (approximately 18,826 US$ in August 2012) and £28,999 a year, or c) more than £29,000 a year (approximately 45,497 US$ in August 2012). Note that in the financial year 2012/2013 the median disposable income in the UK was approximately £24,200. The total proportion of a patient's income that they received from benefits was recorded on the questionnaire as: (a) all, (b) about three quarters, (c) about half, (d) about a quarter, (e) very little, and (f) none, but for the purpose of this analysis, this was grouped as: (a) all, (b) some (groups b to e), and (c) none. Whether the participants had any financial concerns of living with or after cancer or not was recorded as: (a) yes, or (b) no.

#### 5.2.1.2 Demographic data

The participants' demographic data were recorded on the age of the participants when they provided informed consent to the study and the participants' sex which was obtained from the baseline data capture form. Marital status was recorded on the baseline questionnaire as: (a) single, (b) widowed, (c) separated, (d) married, (e) divorced, and (f) living with a partner, and for the purpose of this analysis, this was grouped as: (a) single; (b) married or living with a partner; and (c) separated, divorced, or widowed.

#### 5.2.1.3 Health status data

The health status of the participants was recorded via comorbidity and WHO Performance Status (Oken *et al.*, 1982) from the baseline data prior to the start of the participants' treatment. Comorbidity was recorded on the baseline data capture form using the Adult Comorbidity Evaluation (ACE-27) (Piccirillo and Feinstein, 1996), which categorises people as having: (a) no comorbidity, (b) mild comorbidity, c) moderate comorbidity, and (d) severe comorbidity. For the purpose of this analysis the two worst comorbidities were grouped into a "moderate/severe" category due to low numbers. WHO Performance Status was measured on the participants' baseline questionnaire and was recorded as: (a) normal activity, (b) strenuous activity restricted, (c) up and about for more than 50% of their waking hours, (d) confined to a bed or chair for more than 50%, and (e) confined to a bed or chair for 100% of their waking hours. Due to small numbers, the worst two WHO Performance Status categories were combined into a "confined to a bed or chair for more than 50% of their waking hours" category.

#### 5.2.1.4 Behavioural factor data

The participants' behavioural data were recorded on smoking status and alcohol consumption. Smoking status was recorded on the baseline questionnaire and was defined as: (a) current smoker, (b) previous smoker, and (c) never smoked. The number of units of alcohol per week that the participants drank was calculated from the baseline questionnaire responses to how many days per week they drank alcohol, and how many bottles of wine, spirits, or pints of beers/lager/cider they drank each week before they were diagnosed with cancer. Using the responses to these questions, the participants' alcohol consumption was calculated in units and subsequently grouped as: (a) none, (b) moderate (more than zero and less than 14 units per week for men and women), (c) hazardous (between 14 and 50 units per week for men, and between 14 and 35 units per week for women), and (d) harmful (more than 50 units per week for men, and more than 35 units per week for women) (NICE, 2011b).

#### 5.2.1.5 Tumour factors

The tumour factors were recorded on the anatomical site of the tumour, tumour stage, and HPV status. Anatomical site was determined using ICD-10 codes (World Health Organization, 2016). Tumours of the (a) lip and oral cavity (C00, C02-C04, C05.0, C06), (b) oropharynx (C01, C05.1, C05.2, C09, C10), (c) nasopharynx (C11), (d) hypopharynx (C12, C13), (e) larynx (C32, C10.1), (f) nasal cavity (C30.0), (g) sinuses (C31), (h) major salivary glands (C07, C08), (i) minor salivary glands (any ICD-10 code with histology recorded as "salivary gland"), and (j) other sites of the head and neck (C14.0, C30.1, C41.1, C69.5) were included. Due to small numbers, the participants with cancers of the nasopharynx, nasal cavity, sinuses, and other sites of the head and neck were combined into one group for this study which has been labelled as "Other". Tumour stage was classified using the TNM Classification of Malignant Tumours from the UICC, Seventh Edition, which divides tumours into four categories from stage I to stage IV (Sobin *et al.*, 2009). HPV status was determined by the German Cancer Research Center (DKFZ) in Heidelberg. An HPV-positive result was determined from a serological response to HPV16 E6 antibodies using a glutathione S-transferase multiplex assay with a cut-off value of more than 1000 Median Fluorescence Intensity (MFI) units (Waterboer *et al.*, 2005).

#### 5.2.1.6 Treatment factors

The treatment modality that the participants received was extracted from the data capture forms at four-months and was grouped as: (a) surgery only; (b) chemoradiotherapy only, (c) radiotherapy only, (d) surgery combined with chemotherapy, chemoradiotherapy or radiotherapy; (e) chemotherapy only; and (f) no treatment.

### 5.2.2 Data verification

The HN5000 data was entered onto a central database which contained automatic range and logic checks with the aim of reducing data entry issues. In addition, missing, inconsistent and text fields were identified and checked against pathology reports, particularly for the tumour diagnosis and the stage of the tumour. Where data were not clear, the HN5000 study team at the University of Bristol contacted the study centres for additional information. Finally, double data entry was complete on a random sample of 10% of the questionnaire data to determine an error rate and to highlight sections within the questionnaires that may require double data entry for the whole cohort of people.

### 5.2.3 Data linkage

On 11th October 2018, the cohort was linked to mortality data by the National Office of Statistics from the UK Health and Social Care Information Centre. The number of days between the date of consent and the date of death or the most recent follow-up date was calculated.

### 5.2.4 Eligible cases

All of these analyses were performed using the HN5000 data release V2.4 (October 2018). Participants were excluded from the HN5000 if they had withdrawn or were found to be ineligible because a biopsy result confirmed that they did not have head and neck cancer or had a carcinoma in situ. In addition, for this analysis, people who had thyroid cancer, cancer of unknown primary (CUP), or did not live in England (and therefore could not be linked to IMD data) were also excluded. Participants were also removed if they had not returned any of their questionnaire pack.

### 5.2.5 Statistical analyses

Frequency tables of each of the participant, demographic, health, behavioural, tumour, treatment, and socioeconomic status factors are displayed along with the proportion of deaths that had occurred by October 2018. Frequency tables that displayed the cross-tabulation of the socioeconomic status factors with each participant, demographic, health, behavioural, tumour, and treatment factors were generated without the “unknown” categories and the proportions across each of the groups were compared using the Pearson’s chi-square test.

Three-year overall survival was determined using the Kaplan-Meier method with 95% confidence intervals. The differences between the results of the Kaplan-Meier curves were determined using the long-rank test.

Adjusted Cox Proportional Hazard models for all-cause mortality were displayed to identify the potential explanatory factors of the inequality in survival. Hazard ratios (HR) with confidence intervals (CI) and p-values for each socioeconomic status variable were produced to measure the differences in all-cause mortality between various groups of people. To explore the potential explanatory factors of inequality, these models were adjusted by: (a) age and sex; (b) age, sex, and each individual factor separately (including comorbidity, smoking status, alcohol consumption, anatomical site, stage, HPV status, and treatment modality); (c) age, sex, and health and behavioural factors combined (including comorbidity, smoking status, and alcohol consumption); (d) age, sex, tumour,

and treatment factors combined (including anatomical site, stage, HPV status and treatment modality); or (e) age, sex, and all of the potential explanatory factors combined (including comorbidity, smoking status, alcohol consumption, anatomical site, stage, HPV status, and treatment modality).

All of the statistical analyses were performed using Stata Version 16.0 (StataCorp., 2019).

### 5.2.6 Missing data

Patterns of missing data were checked and reviewed for the whole cohorts' data. The risk of bias from levels of missing data was investigated by cross-tabulating the data from the participants who did and did not return their questionnaire with each of the demographic, health, behavioural, tumour, treatment, and socioeconomic status factors.

#### 5.2.6.1 Multiple imputation

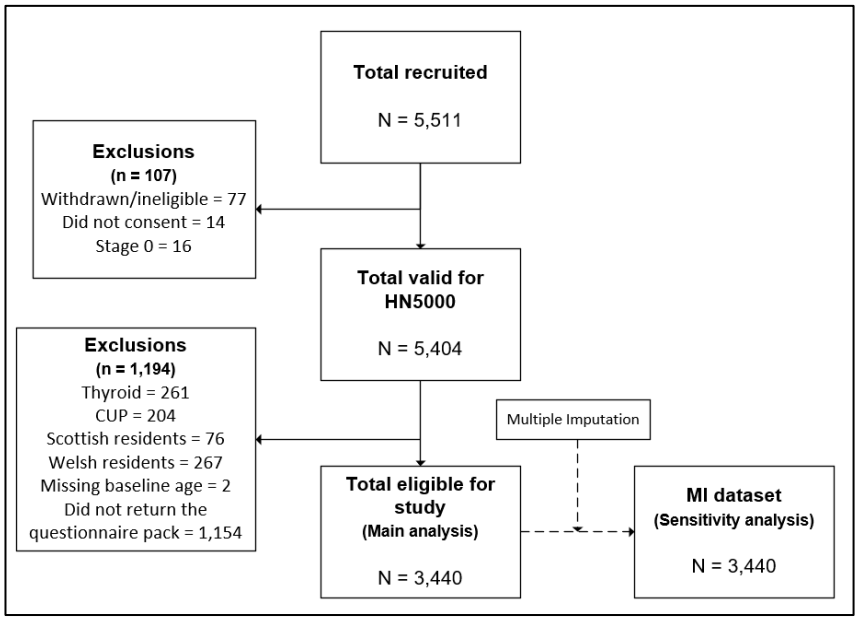
As a result of the high levels of missing data in the HN5000 cohort, multiple imputation (MI) was performed to impute values for missing data (Little and Rubin, 2019). The *ICE* package for the multiple Imputation of Chained Equations in Stata 16.0 was used (Royston, 2009). Twenty imputed datasets were generated using a model which included the event indicator for death, the Nelson-Aalen estimator of the cumulative hazard (White and Royston, 2009), all of the socioeconomic status variables, and all of the potential explanatory factors. The results of the minimally and mutually adjusted Cox Proportional Hazards models following multiple imputation were computed using the *mim* command in Stata 16.0 (Galati *et al.*, 2007), which combines the results from each imputed dataset using Rubin's Rules (Rubin, 1987).

## 5.3 Results

### 5.3.1 Eligible cases

A total of 5,511 participants were recruited for the HN5000, however 107 (1.9%) participants were excluded from the cohort due to either withdrawing, being ineligible due to not having a primary head and neck cancer, not consenting to the study, or having a tumour of stage 0 (Figure 5.1). In addition, a total of 1,964 (36.3%) participants were excluded from this analysis due to having thyroid cancer, CUP, residing in Scotland or Wales, or for not returning their baseline questionnaire pack. Thus, a total of 3,440 were eligible for this analysis – 62.4% of the original 5,511 people that were recruited.

**Figure 5.1 – Flow chart of eligible cases included in the HN5000 cohort study**




### 5.3.2 Missing data

Following the exclusion of the participants who did not return their questionnaire, data were still missing for marital status (n = 44/1.3%), comorbidity (n = 75/2.2%), WHO Performance Status (n = 162/4.7%), smoking status (n = 173/5.0%) and alcohol consumption (n = 111/3.2%). In addition, some data were also missing for tumour stage (n = 31/0.9%) and HPV status (n = 459/13.3%). For the socioeconomic status factors, some data were missing for IMD Category (n = 85/2.5%), highest education level obtained (n = n = 208/6.0%), time spent in education (n = 329/9.6%), total annual household income (n = 517/15.0%), proportion of income from benefits (n = 214/6.2%), and whether the people were having financial concerns of living with or after cancer (n = 208/6.0%).

### 5.3.3 Baseline characteristics

The numbers and proportions of the participant characteristics, demographic factors, health status, behavioural factors, tumour and treatment factors, and socioeconomic factors along with the proportion of deaths observed by October 2018 for each variable are displayed in Table 5.1 and Table 5.2.

The age at date of consent of the participants ranged from 22 to 95 (median = 62 years), and nearly three quarters (n = 2,526/73.4%) of the cohort was male. Most of the people were either married or living with a partner (n = 2,283/66.4%). More than a half (n = 1,881/54.7%) of the participants had at least a mild comorbidity, however 52.3% (n = 1,799) of the cohort were of normal WHO Performance Status at the time of their diagnosis. Approximately three quarters (n = 2,527/73.5%) of the cohort were either

current or former smokers, and 70.3% (n = 2,418) of the participants were moderate to harmful drinkers. A proportion of 38.8% (n = 1,334) of people had tumours of the oropharynx, while 45.2% (n = 1,555) of the cohort had stage IV tumours, and 61.5% (n = 2,114) of the participants were diagnosed with HPV negative tumours. The participants were most likely to be treated with chemoradiotherapy or a combination of surgery and chemoradiotherapy (n = 1,936/56.2%). There was an even spread of participants across the IMD Categories ranging from 17.9% (n = 616) to 21.7% (n = 746). Nearly half (n = 1,556/45.2%) of the cohort had attained an education level of up to secondary school, and nearly one third (n = 1,007/29.3%) of participants had spent 10 years or less in full-time education. More than half (n = 1,988/57.8%) of the cohort earned less than £29,000 per year, one third (n = 1,100/32.0%) earned at least some of their income from benefits, and 34.3% (n = 1,181) of people had financial concerns of living with cancer.

**Table 5.1 – Frequency and number of people who had died by October 2018 for the participant characteristics, demographic factors, health and behavioural factors, and tumour and treatment factors**

| Variable | Frequency (col. %) | Died by October 2018 (row %) |
|---|---|---|
| **Whole cohort** | 3,440 | 1,068 (31.1%) |
| **Age group** | | |
| Less than 44 | 210 (6.1%) | 37 (17.6%) |
| 45 to 54 | 676 (19.7%) | 156 (23.1%) |
| 55 to 64 | 1,192 (34.7%) | 356 (29.9%) |
| 65 to 74 | 940 (27.3%) | 313 (33.3%) |
| 75 and over | 422 (12.3%) | 206 (48.8%) |
| **Sex** | | |
| Male | 2,526 (73.4%) | 820 (32.5%) |
| Female | 914 (26.6%) | 248 (27.1%) |
| **Marital status** | | |
| Single | 427 (12.4%) | 153 (35.8%) |
| Separated/divorced/widowed | 686 (19.9%) | 280 (40.8%) |
| Married/living with partner | 2,283 (66.4%) | 620 (27.2%) |
| Unknown | 44 (1.3%) | 15 (34.1%) |
| **Comorbidity** | | |
| No comorbidity | 1,484 (43.1%) | 321 (21.6%) |
| Mild comorbidity | 1,149 (33.4%) | 372 (32.4%) |
| Moderate/severe comorbidity | 732 (21.3%) | 352 (48.1%) |
| Unknown | 75 (2.2%) | 23 (30.7%) |
| **WHO Performance Status** | | |
| Normal activity | 1,799 (52.3%) | 377 (21.0%) |
| Strenuous activity restricted | 843 (24.5%) | 306 (36.3%) |
| Up and about > 50% | 470 (13.7%) | 207 (44.0%) |
| Confined > 50% or 100% | 166 (4.8%) | 105 (63.3%) |
| Unknown | 162 (4.7%) | 73 (45.1%) |
| **Smoking status** | | |
| Current smoker | 664 (19.3%) | 301 (45.3%) |
| Former smoker | 1,863 (54.2%) | 573 (30.8%) |
| Never smoked | 740 (21.5%) | 150 (20.3%) |
| Unknown | 173 (5.0%) | 44 (25.4%) |
| **Alcohol consumption** | | |
| Non-drinker | 911 (26.5%) | 297 (32.6%) |
| Moderate | 729 (21.2%) | 179 (24.6%) |
| Hazardous | 1,210 (35.2%) | 359 (29.7%) |
| Harmful | 479 (13.9%) | 182 (38.0%) |
| Unknown | 111 (3.2%) | 51 (46.0%) |
| **Anatomical Site** | | |
| Oropharynx | 1,334 (38.8%) | 332 (24.9%) |
| Lip and oral cavity | 900 (26.2%) | 318 (35.3%) |
| Larynx | 728 (21.2%) | 214 (29.4%) |
| Hypopharynx | 160 (4.7%) | 96 (60.0%) |
| Salivary glands | 147 (4.3%) | 34 (23.1%) |
| Other | 171 (5.0%) | 74 (43.3%) |
| **Stage** | | |
| I | 788 (22.9%) | 131 (16.6%) |
| II | 593 (17.2%) | 176 (29.7%) |
| III | 473 (13.8%) | 155 (32.8%) |
| IV | 1,555 (45.2%) | 590 (37.9%) |
| Unknown | 31 (0.9%) | 16 (51.6%) |
| **HPV status** | | |
| Negative | 2,114 (61.5%) | 760 (36.0%) |
| Positive | 867 (25.2%) | 150 (17.3%) |
| Unknown | 459 (13.3%) | 158 (34.4%) |
| **Treatment** | | |
| Surgery only | 765 (22.2%) | 167 (21.8%) |
| Chemoradiotherapy only | 1,064 (30.9%) | 311 (29.2%) |
| Radiotherapy only | 702 (20.4%) | 255 (36.3%) |
| Surgery and chemo/radio | 872 (25.3%) | 302 (34.6%) |
| Chemotherapy only | 15 (0.4%) | 14 (93.3%) |
| No treatment | 22 (0.6%) | 19 (86.4%) |

**Table 5.2 – Frequency and number of people who had died by October 2018 for all of the socioeconomic status factors**

| Variable | Frequency (col. %) | Died by October 2018 (row %) |
|---|---|---|
| **IMD Category** | | |
| 1 – Most deprived | 674 (19.6%) | 257 (38.1%) |
| 2 | 616 (17.9%) | 188 (30.5%) |
| 3 | 746 (21.7%) | 227 (30.4%) |
| 4 | 664 (19.3%) | 186 (28.0%) |
| 5 – Least deprived | 655 (19.0%) | 182 (27.8%) |
| Unknown | 85 (2.5%) | 28 (32.9%) |
| **Highest education level** | | |
| Up to secondary school | 1,556 (45.2%) | 535 (34.4%) |
| Further education | 827 (24.0%) | 229 (27.7%) |
| Higher education/degree | 849 (24.7%) | 229 (27.0%) |
| Unknown | 208 (6.0%) | 75 (36.1%) |
| **Time in education** | | |
| 10 years or less | 1,007 (29.3%) | 358 (35.6%) |
| 11 to 13 years | 1,200 (34.9%) | 334 (27.8%) |
| 14 years or more | 904 (26.3%) | 263 (29.1%) |
| Unknown | 329 (9.6%) | 113 (34.4%) |
| **Household income** | | |
| £11,999 or less | 884 (25.7%) | 344 (38.9%) |
| £12,000 to £28,999 | 1,104 (32.1%) | 336 (30.4%) |
| £29,000 or more | 935 (27.2%) | 187 (20.0%) |
| Unknown | 517 (15.0%) | 201 (38.9%) |
| **Income from benefits** | | |
| All | 487 (14.2%) | 213 (43.7%) |
| Some | 613 (17.8%) | 231 (27.7%) |
| None | 2,126 (61.8%) | 548 (25.8%) |
| Unknown | 214 (6.2%) | 76 (35.5%) |
| **Financial concerns** | | |
| Yes | 1,181 (34.3%) | 358 (30.3%) |
| No | 2,051 (59.6%) | 631 (30.8%) |
| Unknown | 208 (6.0%) | 79 (38.0%) |

### 5.3.4 Cross-tabulations of each of the socioeconomic status factors with the potential explanatory factors

#### 5.3.4.1 Cross-tabulation of IMD Category with potential explanatory factors

The cross-tabulation of each IMD Category with all of the potential explanatory factors is displayed in Table 5.3 to Table 5.5. In addition, the cross-tabulation of each IMD Category with the individual measurements of socioeconomic status is displayed in Table 5.6. People who resided in areas of the least deprived IMD Category were more likely to be younger, have moderate or severe comorbidities, have worse WHO Performance Status and be current smokers or be harmful drinkers. In addition, the participants from the most deprived regions were slightly more likely to be males and were increasingly more likely to be single, separated, divorced, or widowed. Those who were from the least deprived areas were also more likely to have tumours of the larynx, tumours that were HPV negative, and be treated with radiotherapy only. There was no difference across the IMD Categories by tumour stage. People who resided in the most deprived areas were more likely to have obtained an education level of up to secondary school, have spent less time

in education, earn £11,999 or less per year, earn all of their income from benefits, or have financial concerns of living with or after cancer.

#### 5.3.4.2 Cross-tabulation of highest education level with potential explanatory factors

The cross-tabulation of highest education level attained with all of the potential explanatory factors for inequality is displayed in Table 5.7. The participants who had attained an education level of up to secondary school were more likely to be older, have moderate or severe comorbidities, have worse WHO Performance Status, and be current or former smokers. Interestingly, these people were also more likely to be married or living with a partner, be non-drinkers of alcohol, and there was a slightly higher proportion of females who had attained an education level of up to secondary school. In addition, those who had attained an education level of up to secondary school were more likely to have tumours of the larynx, tumours that were HPV negative, and be treated with radiotherapy only. There was no difference between the tumour staging across the groups for the highest level of education the participants had attained.

#### 5.3.4.3 Cross-tabulation of the number of years spent in education with potential explanatory factors

The cross-tabulation of the number of years spent in education with all of the potential explanatory factors is displayed in Table 5.8. The participants who had spent 10 years or less in education were more likely to be older and male. In addition, these people were also more likely to have mild to severe comorbidities, have worse WHO Performance Status, and be current or former smokers. Those who had spent 10 years or less in education were also more likely to have tumours of the larynx, tumours that were HPV negative, and be treated with radiotherapy only. There was no difference between the proportion of participants across the groups for the number of years the people spent in education by marital status, alcohol consumption, or tumour stage.

#### 5.3.4.4 Cross-tabulation of annual household income with potential explanatory factors

The cross-tabulation of annual household income with all of the potential explanatory factors is displayed in Table 5.9. The participants who had earned £11,000 or less per year were more likely to be older, male, and be single, separated, divorced, or widowed. In addition, these people were also more likely to have mild to severe comorbidities, have worse WHO Performance Status, or be current smokers and non-drinkers. Those who

had spent 10 years or less in education were also more likely to have tumours of the lip and oral cavity or the larynx, have tumours that were stage II, be HPV negative, and have treatment with surgery only or radiotherapy only.

#### 5.3.4.5 Cross-tabulation of proportion of income from benefits with potential explanatory factors

The cross-tabulation of proportion of income from benefits with all of the potential explanatory factors is displayed in Table 5.10. The participants who earned all of their income from benefits were more likely to be between the ages of 45 and 64 and be male, single, separated, divorced, or widowed. In addition, these people were also more likely to have mild to severe comorbidities, have worse WHO Performance Status, be current smokers and be either non-drinkers or harmful drinkers. Those who earned all of their income from benefits were also more likely to have tumours of the larynx, have tumours that were stage II, be HPV negative, and be treated with radiotherapy only.

#### 5.3.4.6 Cross-tabulation of proportion of financial concerns with potential explanatory factors

The cross-tabulation of the proportion of income from benefits that the participants received with all of the potential explanatory factors is displayed in Table 5.11. The participants who were having financial concerns of living with or after cancer were more likely to be younger and male, single, separated, divorced, or widowed. In addition, these people were also more likely have worse WHO Performance Status, be current smokers and be harmful drinkers. Those who earned all of their income from benefits were also more likely to have tumours of the oropharynx, have tumours that were stage IV, be HPV positive, and be treated with chemoradiotherapy only or surgery combined with chemoradiotherapy.

#### 5.3.4.7 Summary of findings from cross-tabulations of socioeconomic status factors with potential explanatory factors

Generally, those with lower socioeconomic status were more likely to have comorbidities, worse WHO Performance Status, be current or former smokers, and have tumours of the larynx and be HPV negative. There were no clear similarities across the socioeconomic status factors by age, sex, marital status, alcohol consumption, tumour stage or the treatment modality the participants received.

**Table 5.3 – Cross-tabulation of IMD Category with participant characteristics and demographic factors**

| Variable | IMD Category | | | | | |
|---|---|---|---|---|---|---|
| | 1 – Most deprived | 2 | 3 | 4 | 5 – Least deprived | p-value |
| **Age group** | | | | | | <0.001 |
| Less than 44 | 44 (6.5%) | 39 (6.3%) | 37 (5.0%) | 46 (6.9%) | 41 (6.3%) | |
| 45 to 54 | 160 (23.7%) | 136 (22.1%) | 150 (20.1%) | 114 (17.2%) | 101 (15.4%) | |
| 55 to 64 | 252 (37.4%) | 198 (32.1%) | 262 (35.1%) | 216 (32.5%) | 232 (35.4%) | |
| 65 to 74 | 158 (23.4%) | 175 (28.4%) | 209 (28.0%) | 177 (26.7%) | 197 (30.1%) | |
| 75 and over | 60 (8.9%) | 68 (11.0%) | 88 (11.8%) | 111 (16.7%) | 84 (12.8%) | |
| **Sex** | | | | | | 0.047 |
| Male | 515 (76.4%) | 432 (70.1%) | 549 (73.6%) | 502 (75.6%) | 467 (71.3%) | |
| Female | 159 (23.6%) | 184 (29.9%) | 197 (26.4%) | 162 (24.4%) | 188 (28.7%) | |
| **Marital status** | | | | | | <0.001 |
| Single | 144 (21.8%) | 73 (12.0%) | 113 (15.3%) | 49 (7.4%) | 39 (6.0%) | |
| Separated, divorced, or widowed. | 167 (25.3%) | 149 (24.5%) | 148 (20.1%) | 101 (15.3%) | 99 (15.3%) | |
| Married or living with partner | 349 (52.9%) | 387 (63.5%) | 476 (64.6%) | 511 (77.3%) | 507 (78.6%) | |

**Table 5.4 – Cross-tabulation of IMD Category with all of the health and behavioural factors**

| Variable | IMD Category | | | | | |
|---|---|---|---|---|---|---|
| | 1 – Most deprived | 2 | 3 | 4 | 5 – Least deprived | p-value |
| **Comorbidity** | | | | | | <0.001 |
| No comorbidity | 252 (38.0%) | 255 (42.9%) | 334 (45.8%) | 298 (45.6%) | 315 (49.2%) | |
| Mild comorbidity | 220 (33.2%) | 210 (35.3%) | 234 (32.1%) | 228 (34.9%) | 222 (34.7%) | |
| Moderate/severe comorbidity | 191 (28.8%) | 130 (21.8%) | 161 (22.1%) | 127 (19.4%) | 103 (16.1%) | |
| **WHO Performance Status** | | | | | | <0.001 |
| Normal activity | 246 (39.7%) | 293 (50.3%) | 384 (53.6%) | 418 (64.6%) | 410 (65.3%) | |
| Strenuous activity restricted | 173 (27.9%) | 165 (28.3%) | 191 (26.7%) | 149 (23.0%) | 146 (23.2%) | |
| Up and about > 50% | 131 (21.2%) | 107 (18.4%) | 98 (13.7%) | 64 (9.9%) | 54 (8.6%) | |
| Confined > 50% or 100% | 69 (11.1%) | 18 (3.1%) | 43 (6.0%) | 16 (2.5%) | 18 (2.9%) | |
| **Smoking status** | | | | | | <0.001 |
| Current smoker | 218 (34.4%) | 141 (23.9%) | 126 (17.8%) | 99 (15.5%) | 61 (9.8%) | |
| Former smoker | 349 (55.1%) | 339 (57.5%) | 418 (59.2%) | 360 (56.5%) | 347 (56.0%) | |
| Never smoked | 66 (10.4%) | 110 (18.6%) | 162 (22.9%) | 178 (27.9%) | 212 (34.2%) | |
| **Alcohol consumption** | | | | | | <0.001 |
| Non-drinker | 182 (28.4%) | 187 (31.2%) | 190 (26.3%) | 174 (27.0%) | 154 (24.0%) | |
| Moderate | 111 (17.3%) | 120 (20.0%) | 173 (24.0%) | 149 (23.1%) | 166 (25.9%) | |
| Hazardous | 219 (34.2%) | 209 (34.9%) | 255 (35.3%) | 239 (37.1%) | 259 (40.3%) | |
| Harmful | 129 (20.1%) | 83 (13.9%) | 104 (14.4%) | 83 (12.9%) | 63 (9.8%) | |

**Table 5.5 – Cross-tabulation of IMD Category with all of the tumour and treatment factors**

| Variable | IMD Category | | | | | |
|---|---|---|---|---|---|---|
| | 1 – Most deprived | 2 | 3 | 4 | 5 – Least deprived | p-value |
| **Anatomical Site** | | | | | | <0.001 |
| Oropharynx | 208 (30.9%) | 259 (42.0%) | 300 (40.2%) | 282 (42.5%) | 252 (38.5%) | |
| Lip and oral cavity | 191 (28.3%) | 133 (21.6%) | 190 (25.5%) | 168 (25.3%) | 195 (29.8%) | |
| Larynx | 171 (25.4%) | 142 (23.1%) | 148 (19.8%) | 133 (20.0%) | 116 (17.7%) | |
| Hypopharynx | 44 (6.5%) | 29 (4.7%) | 37 (5.0%) | 20 (3.0%) | 26 (4.0%) | |
| Salivary glands | 17 (2.5%) | 23 (3.7%) | 40 (5.4%) | 31 (4.7%) | 32 (4.9%) | |
| Other | 43 (6.4%) | 30 (4.9%) | 31 (4.2%) | 30 (4.5%) | 34 (5.2%) | |
| **Stage** | | | | | | 0.25 |
| I | 153 (22.9%) | 135 (22.1%) | 176 (23.8%) | 148 (22.6%) | 160 (24.6%) | |
| II | 139 (20.8%) | 109 (17.8%) | 122 (16.5%) | 110 (16.8%) | 98 (15.1%) | |
| III | 100 (15.0%) | 79 (12.9%) | 113 (15.3%) | 84 (12.8%) | 87 (13.4%) | |
| IV | 276 (41.3%) | 289 (47.2%) | 329 (44.5%) | 312 (47.7%) | 305 (46.9%) | |
| **HPV status** | | | | | | 0.003 |
| Negative | 446 (77.6%) | 375 (69.7%) | 451 (69.9%) | 395 (68.9%) | 398 (68.4%) | |
| Positive | 129 (22.4%) | 163 (30.3%) | 194 (30.1%) | 178 (31.1%) | 184 (31.6%) | |
| **Treatment** | | | | | | 0.014 |
| Surgery only | 148 (22.0%) | 118 (19.2%) | 159 (21.3%) | 144 (21.7%) | 180 (27.5%) | |
| Chemoradiotherapy only | 197 (29.2%) | 191 (31.0%) | 235 (31.5%) | 219 (33.0%) | 194 (29.6%) | |
| Radiotherapy only | 167 (24.8%) | 133 (21.6%) | 154 (20.6%) | 128 (19.3%) | 102 (15.6%) | |
| Surgery and chemo/radio | 152 (22.6%) | 167 (27.1%) | 190 (25.5%) | 168 (25.3%) | 174 (26.6%) | |
| Chemotherapy only | 5 (0.7%) | 2 (0.3%) | 5 (0.7%) | 1 (0.2%) | 2 (0.3%) | |
| No treatment | 5 (0.7%) | 5 (0.8%) | 3 (0.4%) | 4 (0.6%) | 3 (0.5%) | |

**Table 5.6 – Cross-tabulation of IMD Category with all of the other socioeconomic status factors**

| Variable | IMD Category | | | | | p-value |
|---|---|---|---|---|---|---|
| | 1 – Most deprived | 2 | 3 | 4 | 5 – Least deprived | |
| **Highest education level** | | | | | | <0.001 |
| Up to secondary school | 395 (64.5%) | 334 (57.1%) | 307 (43.6%) | 260 (41.5%) | 221 (35.5%) | |
| Further education | 138 (22.5%) | 139 (23.8%) | 194 (27.6%) | 172 (27.4%) | 168 (27.0%) | |
| Higher education/degree | 79 (12.9%) | 112 (19.1%) | 203 (28.8%) | 195 (31.1%) | 234 (37.6%) | |
| **Time spent in education** | | | | | | <0.001 |
| 10 years or less | 250 (42.5%) | 208 (38.3%) | 209 (30.5%) | 172 (28.0%) | 148 (24.5%) | |
| 11 to 13 years | 209 (35.5%) | 196 (36.1%) | 279 (40.7%) | 252 (41.0%) | 233 (38.6%) | |
| 14 years or more | 129 (21.9%) | 139 (25.6%) | 197 (28.8%) | 191 (31.1%) | 222 (36.8%) | |
| **Annual household income** | | | | | | <0.001 |
| £11,999 or less | 294 (53.3%) | 193 (37.0%) | 175 (27.6%) | 106 (18.7%) | 94 (16.4%) | |
| £12,000 to £28,999 | 194 (35.1%) | 206 (39.5%) | 245 (38.6%) | 211 (37.3%) | 211 (36.9%) | |
| £29,000 or more | 64 (11.6%) | 123 (23.6%) | 215 (33.9%) | 249 (44.0%) | 267 (46.7%) | |
| **Income from benefits** | | | | | | <0.001 |
| All | 233 (37.5%) | 98 (16.8%) | 84 (11.9%) | 32 (5.2%) | 28 (4.5%) | |
| Some | 114 (18.3%) | 120 (20.5%) | 136 (19.3%) | 118 (19.1%) | 107 (17.3%) | |
| None | 275 (44.2%) | 366 (62.7%) | 483 (68.7%) | 468 (75.7%) | 482 (78.1%) | |
| **Financial concerns** | | | | | | <0.001 |
| Yes | 299 (47.6%) | 226 (39.2%) | 263 (37.4%) | 193 (30.7%) | 170 (27.8%) | |
| No | 329 (52.4%) | 351 (60.8%) | 440 (62.6%) | 436 (69.3%) | 442 (72.2%) | |

**Table 5.7 – Cross-tabulation of highest education level with the participant characteristics, demographic, health, behavioural, tumour and treatment factors**

| Variable | Education level obtained | | | |
|---|---|---|---|---|
| | Up to secondary school | Further education | Higher education or university | p-value |
| **Age group** | | | | <0.001 |
| Less than 44 | 55 (3.5%) | 81 (9.8%) | 69 (8.1%) | |
| 45 to 54 | 275 (17.7%) | 201 (24.3%) | 162 (19.1%) | |
| 55 to 64 | 526 (33.8%) | 299 (36.2%) | 304 (35.8%) | |
| 65 to 74 | 491 (31.6%) | 171 (20.7%) | 225 (26.5%) | |
| 75 and over | 209 (13.4%) | 75 (9.1%) | 89 (10.5%) | |
| **Sex** | | | | 0.31 |
| Male | 1130 (72.6%) | 607 (73.4%) | 641 (75.5%) | |
| Female | 426 (27.4%) | 220 (26.6%) | 208 (24.5%) | |
| **Marital status** | | | | 0.025 |
| Single | 194 (12.5%) | 111 (13.5%) | 98 (11.6%) | |
| Separated/divorced/widowed | 344 (22.2%) | 149 (18.1%) | 150 (17.7%) | |
| Married/living with partner | 1015 (65.4%) | 565 (68.5%) | 600 (70.8%) | |
| **Comorbidity** | | | | <0.001 |
| No comorbidity | 601 (39.6%) | 403 (49.8%) | 410 (49.2%) | |
| Mild comorbidity | 547 (36.1%) | 247 (30.5%) | 266 (31.9%) | |
| Moderate/severe comorbidity | 369 (24.3%) | 159 (19.7%) | 157 (18.8%) | |
| **WHO Performance Status** | | | | <0.001 |
| Normal activity | 702 (47.8%) | 459 (57.1%) | 554 (66.3%) | |
| Strenuous activity restricted | 427 (29.1%) | 209 (26.0%) | 173 (20.7%) | |
| Up and about > 50% | 252 (17.2%) | 103 (12.8%) | 84 (10.0%) | |
| Confined > 50% or 100% | 88 (6.0%) | 33 (4.1%) | 25 (3.0%) | |
| **Smoking status** | | | | <0.001 |
| Current smoker | 363 (24.4%) | 139 (17.6%) | 124 (15.1%) | |
| Former smoker | 869 (58.5%) | 456 (57.6%) | 439 (53.4%) | |
| Never smoked | 254 (17.1%) | 197 (24.9%) | 259 (31.5%) | |
| **Alcohol consumption** | | | | <0.001 |
| Non-drinker | 462 (30.8%) | 200 (24.8%) | 184 (22.1%) | |
| Moderate | 317 (21.1%) | 179 (22.2%) | 201 (24.2%) | |
| Hazardous | 512 (34.1%) | 307 (38.1%) | 328 (39.4%) | |
| Harmful | 211 (14.0%) | 119 (14.8%) | 119 (14.3%) | |
| **Anatomical Site** | | | | |
| Oropharynx | 557 (35.8%) | 362 (43.8%) | 353 (41.6%) | |
| Lip and oral cavity | 389 (25.0%) | 224 (27.1%) | 232 (27.3%) | |
| Larynx | 379 (24.4%) | 144 (17.4%) | 144 (17.0%) | |
| Hypopharynx | 86 (5.5%) | 28 (3.4%) | 34 (4.0%) | |
| Salivary glands | 65 (4.2%) | 36 (4.4%) | 42 (4.9%) | |
| Other | 80 (5.1%) | 33 (4.0%) | 44 (5.2%) | |
| **Stage** | | | | |
| I | 341 (22.2%) | 188 (22.9%) | 202 (23.9%) | |
| II | 280 (18.2%) | 139 (17.0%) | 142 (16.8%) | |
| III | 229 (14.9%) | 101 (12.3%) | 106 (12.6%) | |
| IV | 689 (44.8%) | 392 (47.8%) | 394 (46.7%) | |
| **HPV status** | | | | |
| Negative | 989 (73.5%) | 488 (66.9%) | 498 (68.2%) | |
| Positive | 356 (26.5%) | 241 (33.1%) | 232 (31.8%) | |
| **Treatment** | | | | |
| Surgery only | 327 (21.0%) | 192 (23.2%) | 197 (23.2%) | |
| Chemoradiotherapy only | 463 (29.8%) | 275 (33.3%) | 275 (32.4%) | |
| Radiotherapy only | 358 (23.0%) | 143 (17.3%) | 143 (16.8%) | |
| Surgery and chemo/radio | 389 (25.0%) | 205 (24.8%) | 230 (27.1%) | |
| Chemotherapy only | 7 (0.4%) | 6 (0.7%) | 1 (0.1%) | |
| No treatment | 12 (0.8%) | 6 (0.7%) | 3 (0.4%) | |

**Table 5.8 – Cross-tabulation of time spent in education with the participant characteristics, demographic, health, behavioural, tumour and treatment factors**

| Variable | Time spent in education | | | |
|---|---|---|---|---|
| | 10 years or less | 11 to 13 years | 14 years or more | p-value |
| **Age group** | | | | <0.001 |
| Less than 44 | 24 (2.4%) | 76 (6.3%) | 85 (9.4%) | |
| 45 to 54 | 104 (10.3%) | 311 (25.9%) | 170 (18.8%) | |
| 55 to 64 | 333 (33.1%) | 441 (36.8%) | 306 (33.8%) | |
| 65 to 74 | 367 (36.4%) | 275 (22.9%) | 237 (26.2%) | |
| 75 and over | 179 (17.8%) | 97 (8.1%) | 106 (11.7%) | |
| **Sex** | | | | <0.001 |
| Male | 806 (80.0%) | 866 (72.2%) | 625 (69.1%) | |
| Female | 201 (20.0%) | 334 (27.8%) | 279 (30.9%) | |
| **Marital status** | | | | 0.12 |
| Single | 124 (12.3%) | 125 (10.4%) | 124 (13.7%) | |
| Separated/divorced/widowed | 216 (21.5%) | 237 (19.8%) | 173 (19.2%) | |
| Married/living with partner | 665 (66.2%) | 836 (69.8%) | 606 (67.1%) | |
| **Comorbidity** | | | | <0.001 |
| No comorbidity | 352 (35.7%) | 559 (47.6%) | 426 (48.4%) | |
| Mild comorbidity | 373 (37.9%) | 370 (31.5%) | 296 (33.6%) | |
| Moderate/severe comorbidity | 260 (26.4%) | 245 (20.9%) | 159 (18.0%) | |
| **WHO Performance Status** | | | | <0.001 |
| Normal activity | 421 (44.3%) | 715 (61.2%) | 525 (59.7%) | |
| Strenuous activity restricted | 297 (31.3%) | 263 (22.5%) | 209 (23.8%) | |
| Up and about > 50% | 166 (17.5%) | 146 (12.5%) | 106 (12.0%) | |
| Confined > 50% or 100% | 66 (6.9%) | 44 (3.8%) | 40 (4.5%) | |
| **Smoking status** | | | | <0.001 |
| Current smoker | 205 (21.2%) | 225 (19.6%) | 167 (19.1%) | |
| Former smoker | 601 (62.2%) | 642 (55.9%) | 462 (52.9%) | |
| Never smoked | 161 (16.6%) | 281 (24.5%) | 245 (28.0%) | |
| **Alcohol consumption** | | | | 0.56 |
| Non-drinker | 289 (29.6%) | 298 (25.5%) | 234 (26.6%) | |
| Moderate | 205 (21.0%) | 263 (22.5%) | 198 (22.5%) | |
| Hazardous | 350 (35.8%) | 435 (37.2%) | 325 (37.0%) | |
| Harmful | 134 (13.7%) | 172 (14.7%) | 122 (13.9%) | |
| **Anatomical Site** | | | | <0.001 |
| Oropharynx | 343 (34.1%) | 514 (42.8%) | 356 (39.4%) | |
| Lip and oral cavity | 254 (25.2%) | 297 (24.8%) | 264 (29.2%) | |
| Larynx | 268 (26.6%) | 238 (19.8%) | 148 (16.4%) | |
| Hypopharynx | 58 (5.8%) | 42 (3.5%) | 42 (4.6%) | |
| Salivary glands | 37 (3.7%) | 49 (4.1%) | 48 (5.3%) | |
| Other | 47 (4.7%) | 60 (5.0%) | 46 (5.1%) | |
| **Stage** | | | | 0.49 |
| I | 215 (21.5%) | 274 (23.0%) | 210 (23.5%) | |
| II | 183 (18.3%) | 199 (16.7%) | 165 (18.5%) | |
| III | 154 (15.4%) | 156 (13.1%) | 118 (13.2%) | |
| IV | 447 (44.7%) | 561 (47.1%) | 401 (44.9%) | |
| **HPV status** | | | | <0.001 |
| Negative | 652 (75.6%) | 702 (66.7%) | 544 (70.0%) | |
| Positive | 211 (24.4%) | 350 (33.3%) | 233 (30.0%) | |
| **Treatment** | | | | <0.001 |
| Surgery only | 213 (21.2%) | 254 (21.2%) | 224 (24.8%) | |
| Chemoradiotherapy only | 273 (27.1%) | 411 (34.3%) | 285 (31.5%) | |
| Radiotherapy only | 259 (25.7%) | 205 (17.1%) | 163 (18.0%) | |
| Surgery and chemo/radio | 247 (24.5%) | 319 (26.6%) | 225 (24.9%) | |
| Chemotherapy only | 8 (0.8%) | 3 (0.3%) | 3 (0.3%) | |
| No treatment | 7 (0.7%) | 8 (0.7%) | 4 (0.4%) | |

**Table 5.9 – Cross-tabulation of annual household income with the participant characteristics, demographic, health, behavioural, tumour and treatment factors**

| Variable | Total annual household income | | | |
|---|---|---|---|---|
| | £11,999 or less | £12,000 to £28,999 | £29,000 or more | p-value |
| **Age group** | | | | <0.001 |
| Less than 44 | 39 (4.4%) | 61 (5.5%) | 94 (10.1%) | |
| 45 to 54 | 174 (19.7%) | 175 (15.9%) | 263 (28.1%) | |
| 55 to 64 | 298 (33.7%) | 394 (35.7%) | 358 (38.3%) | |
| 65 to 74 | 260 (29.4%) | 344 (31.2%) | 168 (18.0%) | |
| 75 and over | 113 (12.8%) | 130 (11.8%) | 52 (5.6%) | |
| **Sex** | | | | <0.001 |
| Male | 620 (70.1%) | 824 (74.6%) | 752 (80.4%) | |
| Female | 264 (29.9%) | 280 (25.4%) | 183 (19.6%) | |
| **Marital status** | | | | <0.001 |
| Single | 203 (23.3%) | 121 (11.1%) | 49 (5.3%) | |
| Separated/divorced/widowed | 310 (35.5%) | 197 (18.0%) | 72 (7.8%) | |
| Married/living with partner | 360 (41.2%) | 774 (70.9%) | 808 (87.0%) | |
| **Comorbidity** | | | | <0.001 |
| No comorbidity | 285 (32.7%) | 507 (47.0%) | 543 (59.2%) | |
| Mild comorbidity | 345 (39.6%) | 334 (31.0%) | 256 (27.9%) | |
| Moderate/severe comorbidity | 241 (27.7%) | 237 (22.0%) | 118 (12.9%) | |
| **WHO Performance Status** | | | | <0.001 |
| Normal activity | 322 (38.2%) | 611 (56.6%) | 689 (74.4%) | |
| Strenuous activity restricted | 262 (31.0%) | 273 (25.3%) | 175 (18.9%) | |
| Up and about > 50% | 187 (22.2%) | 151 (14.0%) | 55 (5.9%) | |
| Confined > 50% or 100% | 73 (8.6%) | 45 (4.2%) | 7 (0.8%) | |
| **Smoking status** | | | | <0.001 |
| Current smoker | 273 (32.3%) | 199 (18.7%) | 89 (10.0%) | |
| Former smoker | 460 (54.5%) | 619 (58.2%) | 508 (56.9%) | |
| Never smoked | 111 (13.2%) | 245 (23.0%) | 296 (33.1%) | |
| **Alcohol consumption** | | | | <0.001 |
| Non-drinker | 279 (32.6%) | 299 (27.5%) | 165 (17.9%) | |
| Moderate | 159 (18.6%) | 254 (23.3%) | 219 (23.8%) | |
| Hazardous | 261 (30.5%) | 398 (36.5%) | 416 (45.2%) | |
| Harmful | 157 (18.3%) | 138 (12.7%) | 120 (13.0%) | |
| **Anatomical Site** | | | | <0.001 |
| Oropharynx | 275 (31.1%) | 436 (39.5%) | 469 (50.2%) | |
| Lip and oral cavity | 248 (28.1%) | 286 (25.9%) | 199 (21.3%) | |
| Larynx | 228 (25.8%) | 239 (21.6%) | 141 (15.1%) | |
| Hypopharynx | 68 (7.7%) | 37 (3.4%) | 21 (2.2%) | |
| Salivary glands | 24 (2.7%) | 54 (4.9%) | 52 (5.6%) | |
| Other | 41 (4.6%) | 52 (4.7%) | 53 (5.7%) | |
| **Stage** | | | | <0.001 |
| I | 208 (23.7%) | 258 (23.5%) | 206 (22.2%) | |
| II | 189 (21.5%) | 172 (15.7%) | 131 (14.1%) | |
| III | 132 (15.0%) | 146 (13.3%) | 124 (13.4%) | |
| IV | 349 (39.7%) | 521 (47.5%) | 465 (50.2%) | |
| **HPV status** | | | | <0.001 |
| Negative | 618 (83.1%) | 665 (69.5%) | 478 (57.7%) | |
| Positive | 126 (16.9%) | 292 (30.5%) | 350 (42.3%) | |
| **Treatment** | | | | <0.001 |
| Surgery only | 208 (23.5%) | 257 (23.3%) | 172 (18.4%) | |
| Chemoradiotherapy only | 245 (27.7%) | 351 (31.8%) | 362 (38.7%) | |
| Radiotherapy only | 221 (25.0%) | 219 (19.8%) | 128 (13.7%) | |
| Surgery and chemo/radio | 198 (22.4%) | 265 (24.0%) | 270 (28.9%) | |
| Chemotherapy only | 7 (0.8%) | 5 (0.5%) | 2 (0.2%) | |
| No treatment | 5 (0.6%) | 7 (0.6%) | 1 (0.1%) | |

**Table 5.10 – Cross-tabulation of income from benefits with the participant characteristics, demographic, health, behavioural, tumour and treatment factors**

| Variable | Income from benefits | | | |
|---|---|---|---|---|
| | All | Some | None | p-value |
| **Age group** | | | | <0.001 |
| Less than 44 | 20 (4.1%) | 55 (9.0%) | 128 (6.0%) | |
| 45 to 54 | 119 (24.4%) | 101 (16.5%) | 437 (20.6%) | |
| 55 to 64 | 194 (39.8%) | 183 (29.9%) | 762 (35.8%) | |
| 65 to 74 | 123 (25.3%) | 164 (26.8%) | 578 (27.2%) | |
| 75 and over | 31 (6.4%) | 110 (17.9%) | 221 (10.4%) | |
| **Sex** | | | | 0.017 |
| Male | 378 (77.6%) | 430 (70.1%) | 1581 (74.4%) | |
| Female | 109 (22.4%) | 183 (29.9%) | 545 (25.6%) | |
| **Marital status** | | | | <0.001 |
| Single | 150 (31.0%) | 56 (9.2%) | 199 (9.4%) | |
| Separated/divorced/widowed | 171 (35.3%) | 147 (24.2%) | 312 (14.8%) | |
| Married/living with partner | 163 (33.7%) | 405 (66.6%) | 1595 (75.7%) | |
| **Comorbidity** | | | | <0.001 |
| No comorbidity | 120 (25.2%) | 231 (38.4%) | 1074 (51.7%) | |
| Mild comorbidity | 193 (40.5%) | 188 (31.2%) | 686 (33.0%) | |
| Moderate/severe comorbidity | 164 (34.4%) | 183 (30.4%) | 317 (15.3%) | |
| **WHO Performance Status** | | | | <0.001 |
| Normal activity | 120 (26.3%) | 251 (42.0%) | 1377 (65.7%) | |
| Strenuous activity restricted | 138 (30.3%) | 174 (29.1%) | 492 (23.5%) | |
| Up and about > 50% | 123 (27.0%) | 126 (21.1%) | 195 (9.3%) | |
| Confined > 50% or 100% | 75 (16.4%) | 46 (7.7%) | 31 (1.5%) | |
| **Smoking status** | | | | <0.001 |
| Current smoker | 194 (40.9%) | 116 (19.9%) | 317 (15.6%) | |
| Former smoker | 248 (52.3%) | 343 (58.7%) | 1162 (57.3%) | |
| Never smoked | 32 (6.8%) | 125 (21.4%) | 549 (27.1%) | |
| **Alcohol consumption** | | | | <0.001 |
| Non-drinker | 144 (31.0%) | 194 (32.7%) | 502 (24.1%) | |
| Moderate | 69 (14.8%) | 123 (20.7%) | 489 (23.4%) | |
| Hazardous | 141 (30.3%) | 202 (34.0%) | 823 (39.5%) | |
| Harmful | 111 (23.9%) | 75 (12.6%) | 272 (13.0%) | |
| **Anatomical Site** | | | | <0.001 |
| Oropharynx | 159 (32.6%) | 221 (36.1%) | 893 (42.0%) | |
| Lip and oral cavity | 134 (27.5%) | 162 (26.4%) | 531 (25.0%) | |
| Larynx | 128 (26.3%) | 138 (22.5%) | 417 (19.6%) | |
| Hypopharynx | 45 (9.2%) | 31 (5.1%) | 66 (3.1%) | |
| Salivary glands | 8 (1.6%) | 25 (4.1%) | 109 (5.1%) | |
| Other | 13 (2.7%) | 36 (5.9%) | 110 (5.2%) | |
| **Stage** | | | | 0.033 |
| I | 98 (20.2%) | 149 (24.4%) | 480 (22.8%) | |
| II | 104 (21.4%) | 111 (18.2%) | 344 (16.4%) | |
| III | 77 (15.8%) | 90 (14.7%) | 281 (13.4%) | |
| IV | 207 (42.6%) | 261 (42.7%) | 997 (47.4%) | |
| **HPV status** | | | | <0.001 |
| Negative | 341 (84.0%) | 392 (75.1%) | 1234 (66.1%) | |
| Positive | 65 (16.0%) | 130 (24.9%) | 634 (33.9%) | |
| **Treatment** | | | | <0.001 |
| Surgery only | 110 (22.6%) | 138 (22.5%) | 464 (21.8%) | |
| Chemoradiotherapy only | 139 (28.5%) | 170 (27.7%) | 710 (33.4%) | |
| Radiotherapy only | 122 (25.1%) | 156 (25.4%) | 357 (16.8%) | |
| Surgery and chemo/radio | 108 (22.2%) | 144 (23.5%) | 573 (27.0%) | |
| Chemotherapy only | 4 (0.8%) | 2 (0.3%) | 8 (0.4%) | |
| No treatment | 4 (0.8%) | 3 (0.5%) | 14 (0.7%) | |

**Table 5.11 – Cross-tabulation of financial concerns with the participant characteristics, demographic, health, behavioural, tumour and treatment factors**

| Variable | Financial concerns | | p-value |
|---|---|---|---|
| | Yes | No | |
| **Age group** | | | <0.001 |
| Less than 44 | 115 (9.7%) | 91 (4.4%) | |
| 45 to 54 | 376 (31.8%) | 271 (13.2%) | |
| 55 to 64 | 500 (42.3%) | 643 (31.4%) | |
| 65 to 74 | 150 (12.7%) | 724 (35.3%) | |
| 75 and over | 40 (3.4%) | 322 (15.7%) | |
| **Sex** | | | 0.002 |
| Male | 912 (77.2%) | 1484 (72.4%) | |
| Female | 269 (22.8%) | 567 (27.6%) | |
| **Marital status** | | | <0.001 |
| Single | 186 (16.0%) | 221 (10.8%) | |
| Separated/divorced/widowed | 236 (20.2%) | 401 (19.7%) | |
| Married/living with partner | 744 (63.8%) | 1417 (69.5%) | |
| **Comorbidity** | | | 0.005 |
| No comorbidity | 559 (48.7%) | 861 (42.8%) | |
| Mild comorbidity | 357 (31.1%) | 708 (35.2%) | |
| Moderate/severe comorbidity | 231 (20.1%) | 444 (22.1%) | |
| **WHO Performance Status** | | | <0.001 |
| Normal activity | 554 (48.0%) | 1192 (59.3%) | |
| Strenuous activity restricted | 328 (28.4%) | 486 (24.2%) | |
| Up and about > 50% | 208 (18.0%) | 241 (12.0%) | |
| Confined > 50% or 100% | 64 (5.5%) | 91 (4.5%) | |
| **Smoking status** | | | <0.001 |
| Current smoker | 299 (26.4%) | 330 (16.8%) | |
| Former smoker | 615 (54.2%) | 1140 (58.2%) | |
| Never smoked | 220 (19.4%) | 489 (25.0%) | |
| **Alcohol consumption** | | | 0.004 |
| Non-drinker | 305 (26.4%) | 546 (27.3%) | |
| Moderate | 231 (20.0%) | 452 (22.6%) | |
| Hazardous | 418 (36.2%) | 746 (37.3%) | |
| Harmful | 200 (17.3%) | 254 (12.7%) | |
| **Anatomical Site** | | | <0.001 |
| Oropharynx | 546 (46.2%) | 728 (35.5%) | |
| Lip and oral cavity | 268 (22.7%) | 562 (27.4%) | |
| Larynx | 187 (15.8%) | 496 (24.2%) | |
| Hypopharynx | 60 (5.1%) | 80 (3.9%) | |
| Salivary glands | 49 (4.1%) | 94 (4.6%) | |
| Other | 71 (6.0%) | 91 (4.4%) | |
| **Stage** | | | <0.001 |
| I | 185 (15.8%) | 548 (27.0%) | |
| II | 186 (15.8%) | 371 (18.3%) | |
| III | 179 (15.2%) | 268 (13.2%) | |
| IV | 624 (53.2%) | 844 (41.6%) | |
| **HPV status** | | | <0.001 |
| Negative | 665 (65.5%) | 1306 (73.0%) | |
| Positive | 351 (34.5%) | 483 (27.0%) | |
| **Treatment** | | | <0.001 |
| Surgery only | 193 (16.3%) | 515 (25.1%) | |
| Chemoradiotherapy only | 460 (39.0%) | 561 (27.4%) | |
| Radiotherapy only | 184 (15.6%) | 457 (22.3%) | |
| Surgery and chemo/radio | 330 (27.9%) | 496 (24.2%) | |
| Chemotherapy only | 5 (0.4%) | 10 (0.5%) | |
| No treatment | 9 (0.8%) | 12 (0.6%) | |

### 5.3.5 Overall survival results

#### 5.3.5.1 Follow-up

The median follow-up time of the whole cohort was 4.8 years (IQR = 4.3 to 5.9 years) and 1.6 years (IQR = 0.8 to 2.9 years) for those who were alive and for those who had died by the end of the follow-up period, respectively.

#### 5.3.5.2 Three-year overall survival for the whole cohort and by the participant characteristics and demographic factors

Three-year overall survival for the whole cohort, participant characteristics, and patient demographics are displayed in Table 5.12. The Kaplan-Meier results for the probability of death over time since the participants' diagnosis for the whole cohort, participant characteristics, and demographic data are displayed in Figure 5.2 to Figure 5.5. Three-year survival for the cohort was 76.3% (95% CI = 74.9% to 77.7%). Those who were aged 75 and over had the lowest three-year overall survival at 64.7% (95% CI = 59.9% to 69.0%) compared to those who were less than 44 who had three-year overall survival of 85.2% (95% CI = 79.7% to 89.4%). Males had lower three-year overall survival than females at 75.5% (95% CI = 73.7% to 77.1%) and 78.8% (95% CI = 76.0% to 81.3%), respectively. The people who were separated, divorced, or widowed had the lowest three-year overall survival at 67.8% (95% CI = 64.2% to 71.1%) compared to the people who were married or living with a partner who had the highest three-year overall survival at 79.5% (95% CI = 77.7% to 81.1%).

**Table 5.12 – Three-year survival for all of the participant characteristics and demographic factors**

| Variable | Three-year survival (95% CI) | p-value |
|---|---|---|
| **Whole cohort** | 76.3 (74.9, 77.7) | - |
| **Age group** | | <0.001 |
| Less than 44 | 85.2 (79.7, 89.4) | |
| 45 to 54 | 82.0 (78.8, 84.7) | |
| 55 to 64 | 77.8 (75.3, 80.0) | |
| 65 to 74 | 73.7 (70.8, 76.4) | |
| 75 and over | 64.7 (59.9, 69.0) | |
| **Sex** | | 0.006 |
| Male | 75.5 (73.7, 77.1) | |
| Female | 78.8 (76.0, 81.3) | |
| **Marital status** | | <0.001 |
| Single | 73.8 (69.3, 77.7) | |
| Separated/divorced/widowed | 67.8 (64.2, 71.1) | |
| Married/living with partner | 79.5 (77.7, 81.1) | |
| Unknown | 72.7 (57.0, 83.5) | |

**Figure 5.2 – Kaplan-Meier plot for overall survival for the whole cohort**

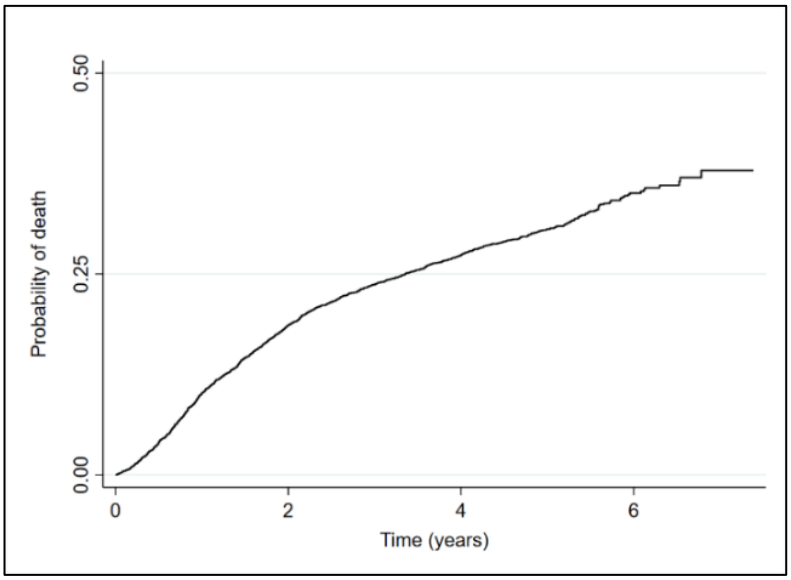



**Figure 5.3 – Kaplan-Meier plot for overall survival for age group**

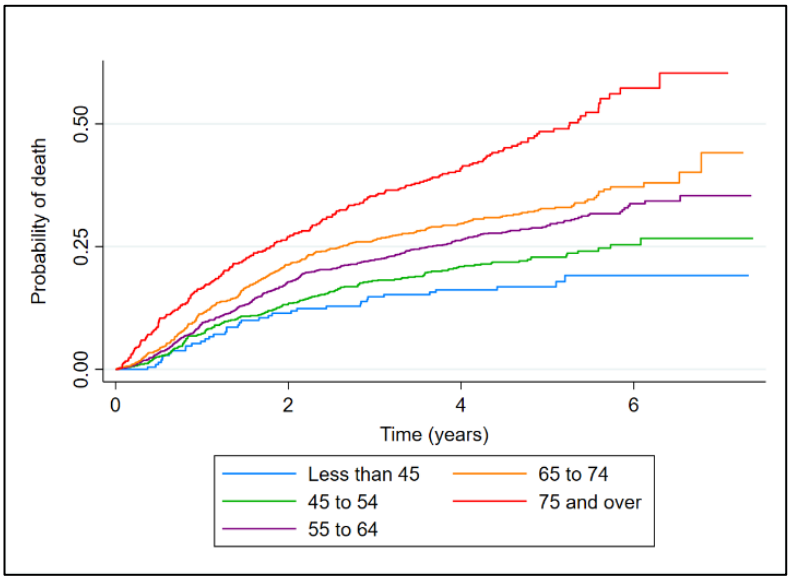



**Figure 5.4 – Kaplan-Meier plot for overall survival for sex**

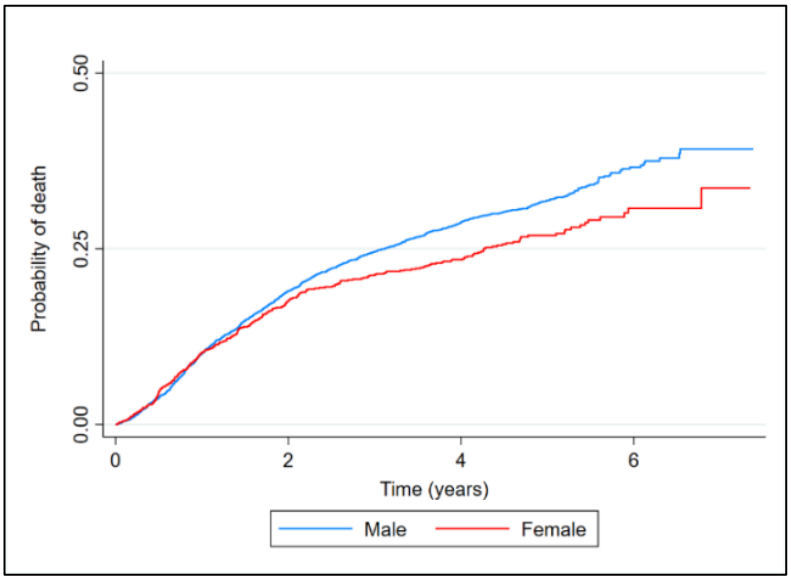
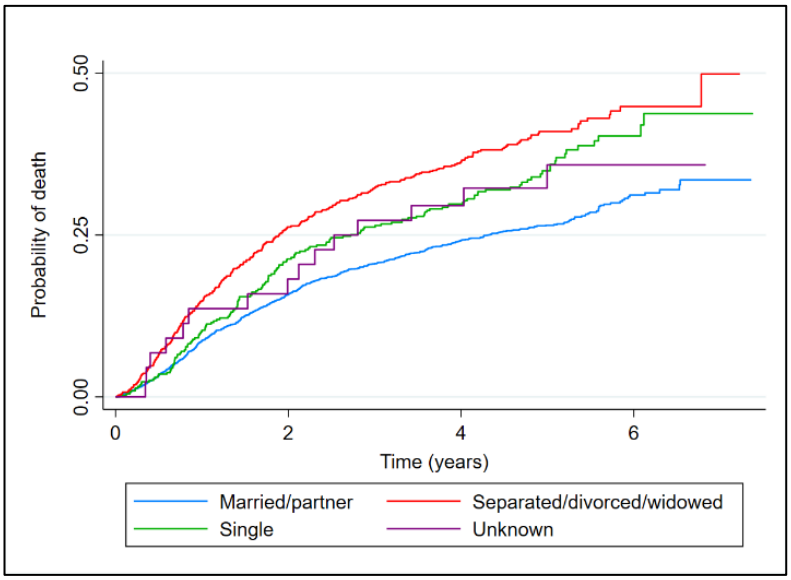


**Figure 5.5 – Kaplan-Meier plot for overall survival for marital status**




### 5.3.5.3 Three-year overall survival by the health and behavioural factors

The results for three-year overall survival for the health and behavioural factors are displayed in Table 5.13. The Kaplan-Meier plots for overall survival by the health and behavioural factors are displayed in Figure 5.6 to Figure 5.9. Those who had moderate to severe comorbidities had the lowest three-year overall survival at 62.4% (95% CI = 58.8% to 83.0%) compared to those who had no comorbidity who had three-year overall survival of 83.8% (95% CI = 81.9% to 85.6%). As WHO Performance Status reduced, the three-year overall survival results also reduced from 84.1% (95% CI = 82.3% to 85.7%) for those who were of normal activity at the time of their diagnosis, to 50.6% (95% CI = 42.8% to 57.9%) for those who were confined to a bed or chair for at least 50% of their waking hours. Those who were current smokers at the time of their diagnosis had the lowest three-year overall survival of 65.5% (95% CI = 61.9% to 69.0%), compared to those who were former smokers at 76.6% (95% CI = 74.6% to 78.5%). Those who had never smoked in their lifetime had the highest three-year overall survival of 84.6% (95% CI = 81.8% to 87.0%). There was not a trend in three-year overall survival by alcohol consumption for those who were non-drinkers to those who were hazardous drinkers, with non-drinkers having the lowest three-year overall survival at 75.9% (95% CI = 72.9% to 78.5%), compared to hazardous drinkers at 77.2% (95% CI = 74.7% to 79.5%). However, those who drank to harmful levels had the lowest three-year overall survival at 69.9% (95% CI = 65.6% to 73.8%).

**Table 5.13 – Three-year survival for all of the health and behavioural factors**

| Variable | Three-year survival (95% CI) | p-value |
|---|---|---|
| **Comorbidity** | | <0.001 |
| No comorbidity | 83.8 (81.9, 85.6) | |
| Mild comorbidity | 75.6 (73.0, 78.0) | |
| Moderate/severe comorbidity | 62.4 (58.8, 65.8) | |
| Unknown | 74.7 (63.2, 83.0) | |
| **WHO Performance Status** | | <0.001 |
| Normal activity | 84.1 (82.3, 85.7) | |
| Strenuous activity restricted | 72.2 (69.1, 75.1) | |
| Up and about > 50% | 67.5 (63.0, 71.5) | |
| Confined > 50% or 100% | 50.6 (42.8, 57.9) | |
| Unknown | 64.2 (56.3, 71.0) | |
| **Smoking status** | | <0.001 |
| Current smoker | 65.5 (61.8, 69.0) | |
| Former smoker | 76.6 (74.6, 78.5) | |
| Never smoked | 84.6 (81.8, 87.0) | |
| Unknown | 79.8 (73.0, 85.0) | |
| **Alcohol consumption** | | <0.001 |
| Non-drinker | 75.9 (72.9, 78.5) | |
| Moderate | 81.5 (78.5, 84.1) | |
| Hazardous | 77.2 (74.7, 79.5) | |
| Harmful | 69.9 (65.6, 73.8) | |
| Unknown | 64.9 (55.2, 72.9) | |

**Figure 5.6 – Kaplan-Meier plot for overall survival for comorbidity**

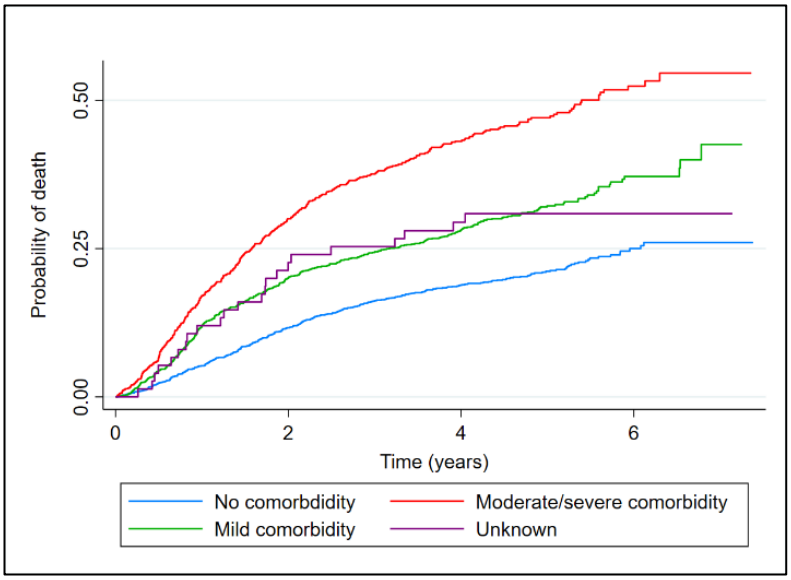


**Figure 5.7 – Kaplan-Meier plot for overall survival for WHO Performance Status**

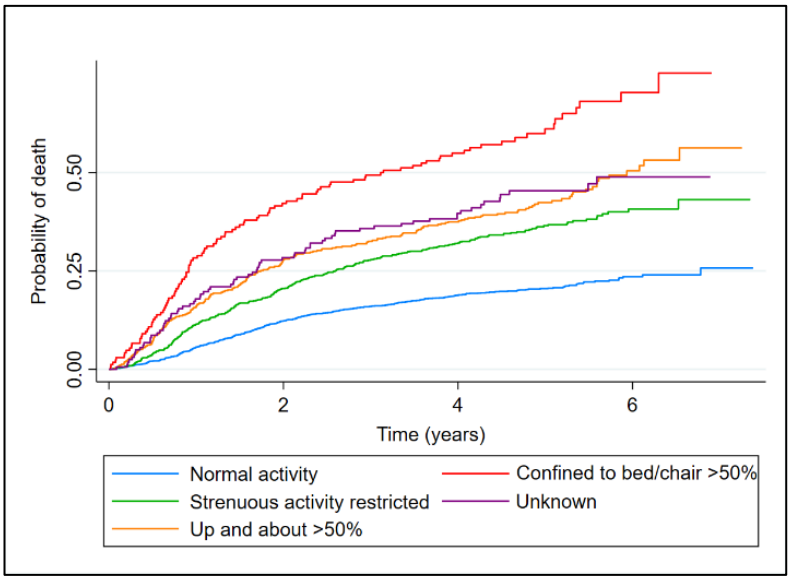



**Figure 5.8 – Kaplan-Meier plot for overall survival for smoking status**

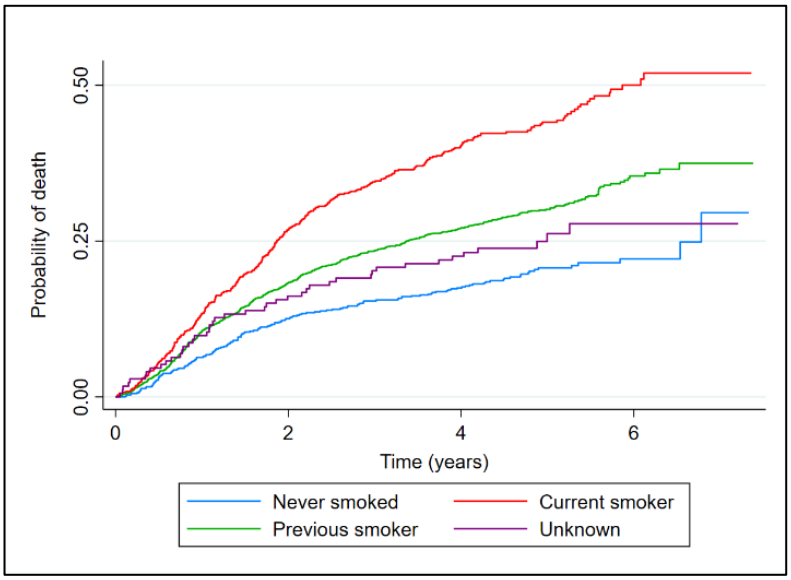
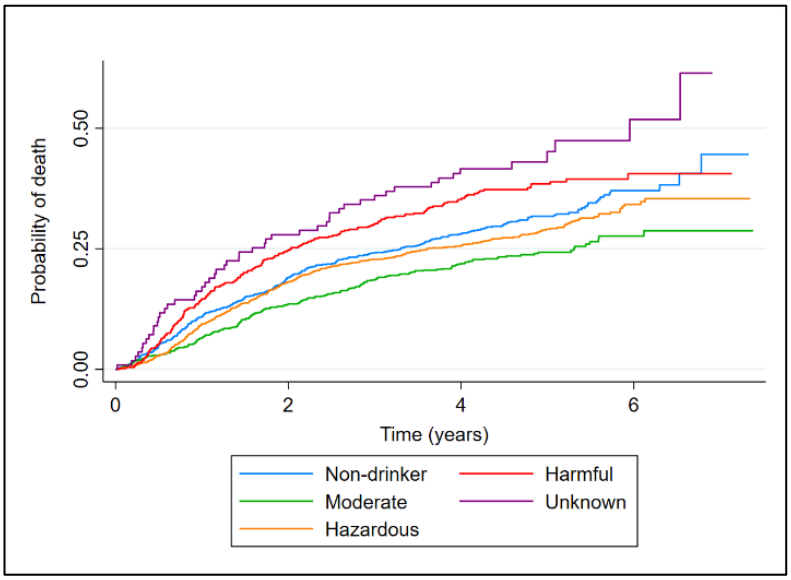



**Figure 5.9 – Kaplan-Meier plot for overall survival for alcohol consumption**



#### 5.3.5.4 Three-year overall survival by the tumour and treatment factors

The results for three-year overall survival for the tumour and treatment factors are displayed in Table 5.14. The Kaplan-Meier plots for overall survival by the health and behavioural factors are displayed in Figure 5.1 to Figure 5.13. The participants who were diagnosed with cancer of the hypopharynx had the lowest three-year survival at 48.1% (95% CI = 40.2% to 55.6%). In contrast, the people who were diagnosed with cancer of the salivary gland had the highest three-year overall at 85.0% (95% CI = 78.2% to 89.9%). As the stage of the cohorts' tumours increased, the three-year overall survival decreased from 89.1% (95% CI = 86.7% to 91.1%) to 69.3% (95% CI = 69.3%) for those diagnosed with stage I and stage IV tumours, respectively. Interestingly, those who had not had their tumours staged had the lowest three-year overall survival at 61.3% (95% CI = 42.0% to 75.9%), which suggests that the people who had not had their tumours staged may have had tumours that were stage IV. The people who were HPV positive had a higher three-year overall survival than the people who were HPV negative which was 88.1% (95% CI = 85.8% to 90.1%) compared with 72.2% (95% CI = 70.2% to 74.0%), respectively.

**Table 5.14 – Three-year survival for all of the tumour and treatment factors**

| Variable | Three-year survival (95% CI) | p-value |
|---|---|---|
| **Anatomical Site** | | <0.001 |
| Oropharynx | 81.7 (79.5, 83.7) | |
| Lip and oral cavity | 71.4 (68.4, 74.3) | |
| Larynx | 79.1 (76.0, 81.9) | |
| Hypopharynx | 48.1 (40.2, 55.6) | |
| Salivary glands | 85.0 (78.2, 89.9) | |
| Other | 67.3 (59.6, 73.7) | |
| **Stage** | | <0.001 |
| I | 89.1 (86.7, 91.1) | |
| II | 78.9 (75.4, 82.0) | |
| III | 75.9 (71.8, 79.5) | |
| IV | 69.3 (67.0, 71.6) | |
| Unknown | 61.3 (42.0, 75.9) | |
| **HPV status** | | <0.001 |
| Negative | 72.2 (70.2, 74.0) | |
| Positive | 88.1 (85.8, 90.1) | |
| Unknown | 73.2 (68.9, 77.0) | |
| **Treatment** | | <0.001 |
| Surgery only | 85.2 (82.5, 87.6) | |
| Chemoradiotherapy only | 77.1 (74.4, 79.5) | |
| Radiotherapy only | 73.2 (69.8, 76.3) | |
| Surgery and chemo/radio | 72.8 (69.7, 75.7) | |
| Chemotherapy only | 13.3 (2.2, 34.6) | |
| No treatment | 13.6 (3.4, 30.9) | |

**Figure 5.10 – Kaplan-Meier plot for overall survival for anatomical site**

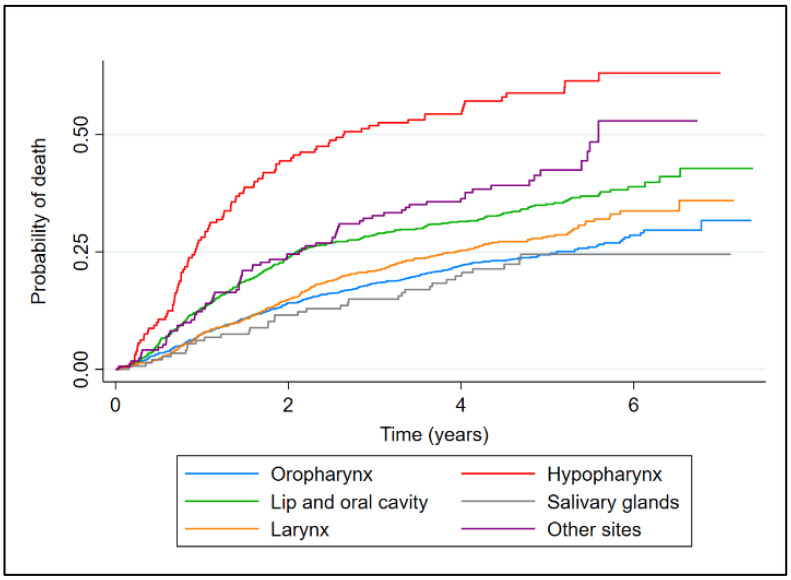



**Figure 5.11 – Kaplan-Meier plot for overall survival for tumour stage**

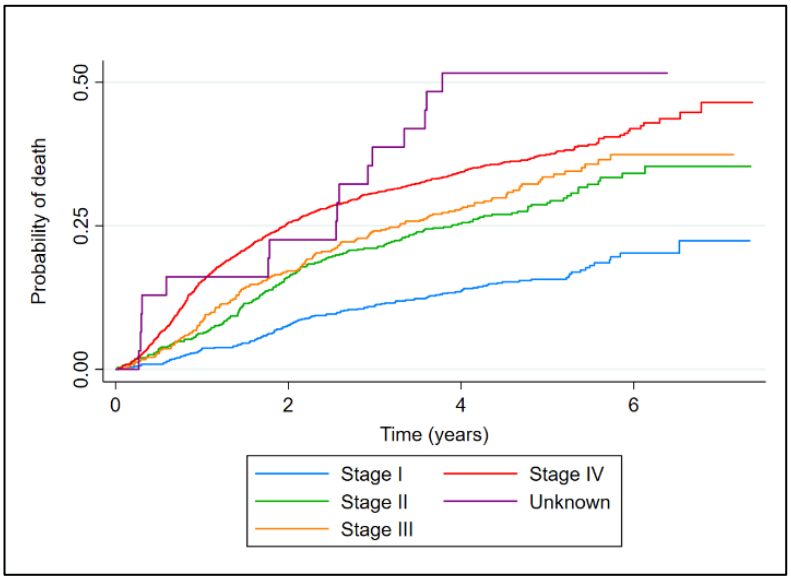



**Figure 5.12 – Kaplan-Meier plot for overall survival for HPV status**

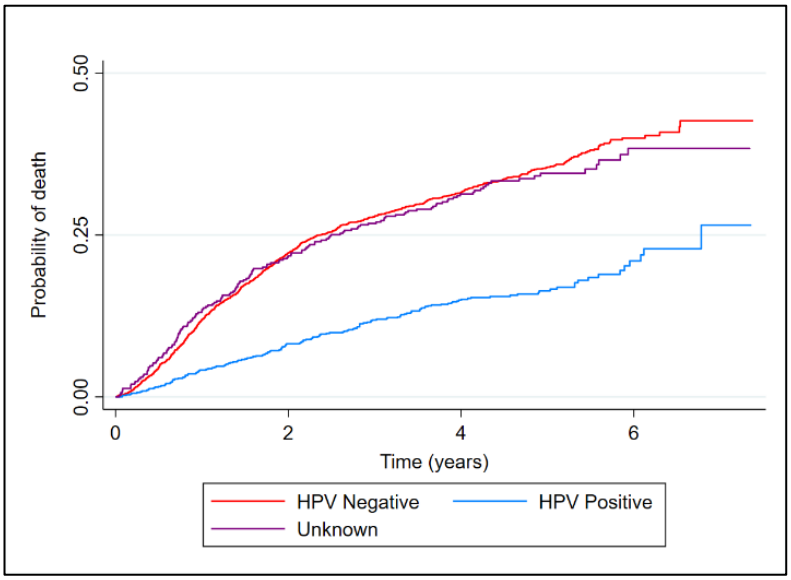
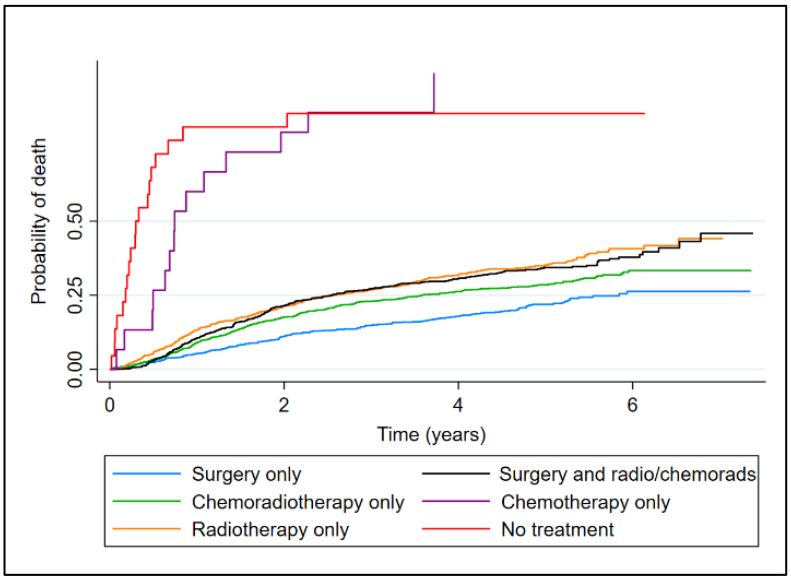


**Figure 5.13 – Kaplan-Meier plot for overall survival for treatment modality**




#### 5.3.5.5 Three-year overall survival by the socioeconomic status factors

The results for three-year overall survival for the tumour and treatment factors are displayed in Table 5.15. The Kaplan-Meier plots for overall survival by the health and behavioural factors are displayed in Figure 5.14 to Figure 5.19. The participants who were from the most deprived IMD Category had the lowest three-year overall survival of 71.2% (95% CI = 67.6% to 74.5%) compared to approximately 77% for all of the other IMD Categories. Those who had obtained an education level of up to secondary school had the lowest three-year overall survival at 74.2% (95% CI = 71.9% to 76.3%), compared with 79.4% (95% CI = 76.5% to 82.0%) for those who had a higher education or had obtained a degree. Likewise, people who had spent fewer years in education also had lower three-year overall survival at 73.2% (95% CI = 70.3% to 75.8%) for those who had spent 10 years or less in education, compared with 78.9% (95% CI = 76.5% to 81.1%) for those who had spent 11 to 13 years in education. Interestingly, the people who had spent 14 years or more in education had a slightly lower three-year overall survival than those who had spent 11 to 13 years in education at 76.3% (95% CI = 73.4% to 79.0%). There was a trend in three-year overall survival across the amount of annual household income the people earned. As the annual household income increased, the patient's three-year overall survival also increased from 70.3% (95% CI = 67.1% to 73.1%) to 83.7% (95% CI = 81.2% to 86.0%) for those who earned £11,999 or less and those who earned £29,000 or more, respectively. The same trend can be observed for the proportion of income the participants' received from benefits. As the proportion of benefits the participants' received reduced, the three-year overall survival increased from 68.4% (95% CI = 64.1% to 72.3%) to 79.9% (95% CI = 78.2% to 81.6%) for those who earned all of their income from benefits and those who earned none of their income from benefits, respectively. There was no clear difference between the people who did and did not have financial concerns

of living with or after cancer with three-year overall survival of 76.5% (95% CI = 73.9% to 78.8%) and 76.7% (95% CI = 74.9% to 78.5%), respectively.

**Table 5.15 – Three-year survival for all of the tumour and treatment factors**

| Variable | Three-year survival (95% CI) | p-value |
|---|---|---|
| **IMD Category** | | 0.002 |
| 1 – Most deprived | 71.2 (67.6, 74.5) | |
| 2 | 77.9 (74.4, 81.0) | |
| 3 | 77.8 (74.6, 80.6) | |
| 4 | 77.4 (74.0, 80.4) | |
| 5 – Least deprived | 77.3 (73.9, 80.3) | |
| Unknown | 77.7 (67.2, 85.1) | |
| **Highest education level** | | <0.001 |
| Up to secondary school | 74.2 (71.9, 76.3) | |
| Further education | 77.8 (74.8, 80.4) | |
| Higher education/degree | 79.4 (76.5, 82.0) | |
| Unknown | 74.5 (68.0, 79.9) | |
| **Time in education** | | <0.001 |
| 10 years or less | 73.2 (70.3, 75.8) | |
| 11 to 13 years | 78.9 (76.5, 81.1) | |
| 14 years or more | 76.3 (73.4, 79.0) | |
| Unknown | 76.6 (71.6, 80.8) | |
| **Household income** | | <0.001 |
| £11,999 or less | 70.3 (67.1, 73.1) | |
| £12,000 to £28,999 | 77.6 (75.0, 79.9) | |
| £29,000 or more | 83.7 (81.2, 86.0) | |
| Unknown | 70.8 (66.7, 74.5) | |
| **Income from benefits** | | <0.001 |
| All | 68.4 (64.1, 72.3) | |
| Some | 71.8 (68.0, 75.2) | |
| None | 79.9 (78.2, 81.6) | |
| Unknown | 72.0 (65.4, 77.5) | |
| **Financial concerns** | | 0.102 |
| Yes | 76.5 (73.9, 78.8) | |
| No | 76.7 (74.9, 78.5) | |
| Unknown | 71.6 (65.0, 77.3) | |

**Figure 5.14 – Kaplan-Meier plot for overall survival for IMD Category**

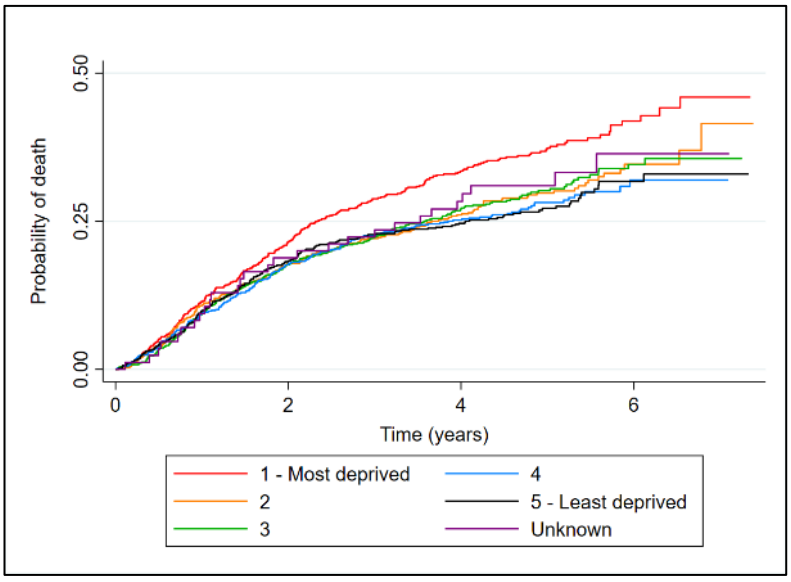


**Figure 5.15 – Kaplan-Meier plot for overall survival for highest education level**

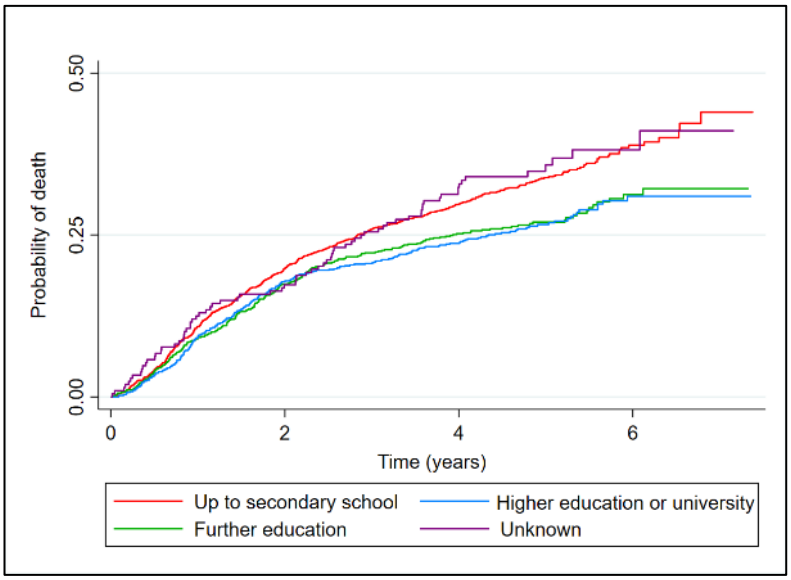



**Figure 5.16 – Kaplan-Meier plot for overall survival for time spent in education**

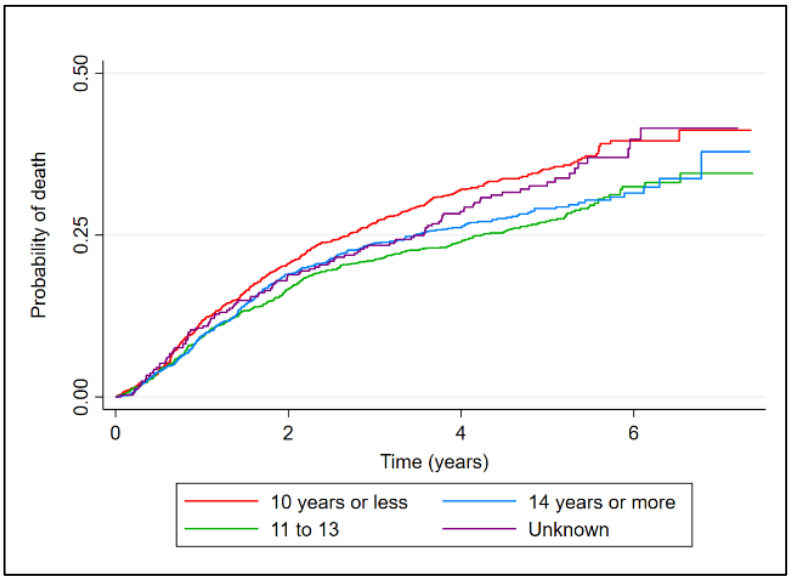



**Figure 5.17 – Kaplan-Meier plot for overall survival for total annual household income**

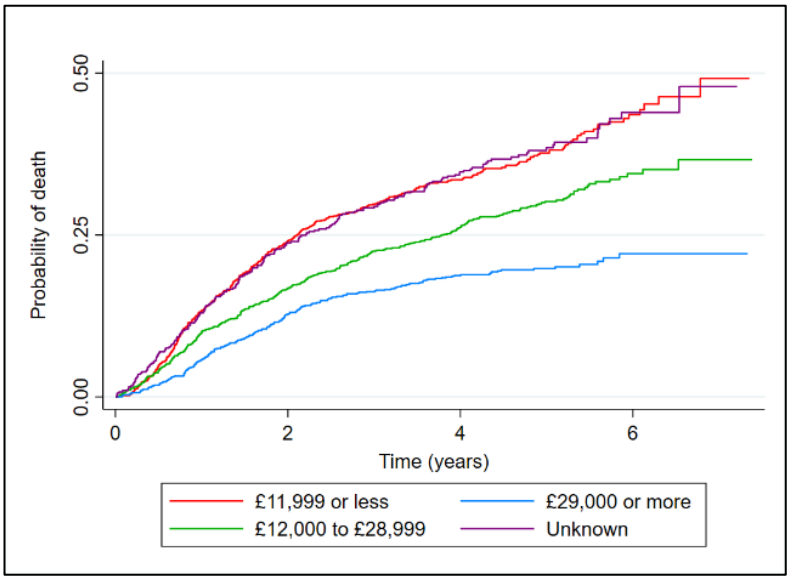


**Figure 5.18 – Kaplan-Meier plot for overall survival for income from benefits**

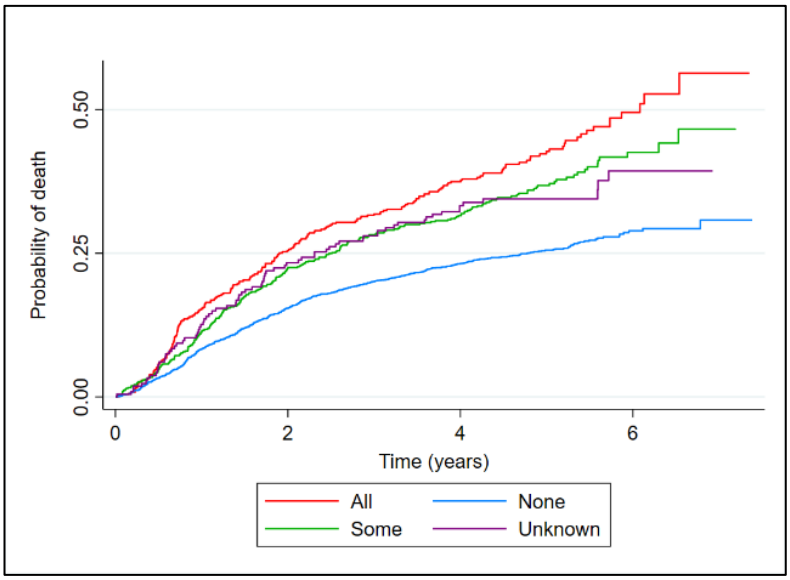
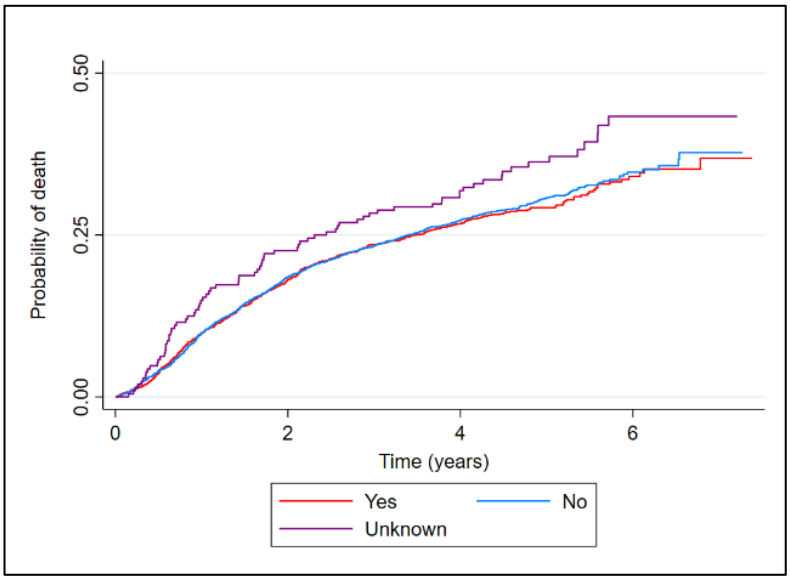



**Figure 5.19 – Kaplan-Meier plot for overall survival for financial concerns**




### 5.3.6 Explanations for inequality in survival

The Cox proportional hazards models that were adjusted for the potential explanatory factors are displayed in Table 5.16 and Table 5.17 prior to multiple imputation, and in Table 5.18 and Table 5.19 following multiple imputation.

#### 5.3.6.1 IMD Category

Following adjustment by age and sex, both prior to and post MI, the participants remained at a higher risk of all-cause mortality if they resided in areas of the most deprived IMD Category (pre-MI HR = 1.50, 95% CI = 1.24 to 1.81; post-MI HR = 1.49, 95% CI = 1.23 to 1.80). Prior to multiple imputation and following adjustment by age and sex with: (a) comorbidity, (b) smoking status, (c) alcohol consumption, or (d) tumour and treatment

factors combined, there was an attenuation in inequality by IMD Category (particularly following the adjustment for smoking status) but inequality by IMD Category remained strong. When the model was adjusted by age, sex and all of the health and behavioural factors combined including comorbidity, smoking status and alcohol consumption, there was no longer inequality in all-cause mortality by IMD Category (most deprived HR = 1.07, 95% CI = 0.88 to 1.31). Following multiple imputation, results were comparable to those of the models prior to multiple imputation for IMD Category.

#### 5.3.6.2 Highest education level attained

Following adjustment by age and sex, both prior to and post multiple imputation, the participants remained at a higher risk of all-cause mortality if they attained an education level of up to secondary school (pre-MI HR = 1.26, 95% CI = 1.08 to 1.47; post-MI HR = 1.26, 95% CI = 1.08 to 1.47). Following adjustment by age and sex with: (a) comorbidity, or (b) alcohol consumption, there was a slight attenuation in inequality by highest education level attained but the inequality remained strong. When the model was adjusted by age, sex and smoking status, the participants who attained an education level up to secondary school were no longer at a higher risk of all-cause mortality (HR = 1.13, 95% CI 0.95 to 1.32) than those who had continued to higher education or degree. Similar results were also observed when the model was adjusted by all of the tumour and treatment factors combined (HR = 1.13, 95% CI 0.97 to 1.33), however there was not one tumour or treatment factor that attenuated the inequality by highest education level attained. Following multiple imputation, the results were comparable to those prior to multiple imputation.

#### 5.3.6.3 Time spent in education

Following age and sex adjustment, there was no longer a difference in all-cause mortality for the participants who had spent less time in full-time education, which would be expected given the higher proportion of older people who had remained in education for less time.

#### 5.3.6.4 Annual household income

Participants were more at risk of all-cause mortality after age and sex adjustment if they earned less than £11,999 per annum (pre-MI HR = 2.00, 95% CI = 1.67 to 2.40; post-MI HR = 1.92, 95% CI = 1.61 to 2.28). Following adjustment by age and sex with: (a) comorbidity, (b) smoking status, (c) alcohol consumption, (d) health and behavioural factors, (e) tumour and treatment factors, or (f) all of the potential explanatory factors,

there was a slight attenuation in inequality by annual household income (particularly by smoking status or all of the health and behavioural factors), however the inequality remained strong. Even after full adjustment, the people who earned less then £11,999 remained 34% (HR = 1.34, 95% CI = 1.01 to 1.63) more at risk of all-cause mortality than those who earned more than £29,000. The results from the imputed models were comparable to those prior to imputation.

#### 5.3.6.5 Income from benefits

Participants were more at risk of all-cause mortality after age and sex adjustment if they earned all of their income from benefits (pre-MI HR = 1.93, 95% CI = 1.64 to 2.26; post-MI HR = 1.91, 95% CI 1.63 to 2.25). Following adjustment by age and sex with:
(a) comorbidity, (b) smoking status, (c) alcohol consumption, (d) health and behavioural factors, (e) tumour and treatment factors, or (f) all of the potential explanatory factors, there was attenuation in inequality by the proportion of income that the participants received from benefits, however inequality remained strong. Even after full adjustment, the participants who earned all of their income from benefits were 35% (HR = 1.35, 95% CI = 1.14 to 1.60) more at risk of all-cause mortality than those who earned none of their income from benefits. Following multiple imputation, results were comparable to those prior to imputation.

#### 5.3.6.6 Financial concerns

Prior to multiple imputation, there was a difference between the participants who had financial concerns of living with or after cancer following age and sex adjustment (HR = 1.19, 95% CI = 1.04 to 1.37). However, following multiple imputation, the difference between the people with and without financial concerns following age and sex adjustment was reversed (HR = 0.83, 95% CI = 0.73 to 0.96). Following adjustment by age and sex with: (a) comorbidity, or (b) alcohol consumption, there was attenuation in the difference by financial concerns, but inequality remained. However, when the model was adjusted by age, sex and smoking status, the participants who had financial concerns were no longer at a higher risk of all-cause mortality (HR = 1.12, 95% CI = 0.97 to 1.28). Similar results were also observed when the model was adjusted by age, sex, and a) health and behavioural factors (HR = 1.07, 95% CI = 0.93 to 1.24), or b) tumour and treatment factors combined (HR = 1.01, 95% CI = 0.88 to 1.17), however there was not one tumour or treatment factor that attenuated the inequality by financial concerns. Following imputation, results were comparable to those prior to imputation.

**Table 5.16 – Cox Proportion Hazards models for each socioeconomic status factors prior to multiple imputation**

| Variable | Age and sex adjusted | | Age, sex, and comorbidity adjusted | | Age, sex, and smoking adjusted | | Age, sex, and alcohol adjusted | |
|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value |
| **IMD Category** | | | | | | | | |
| 1 – Most deprived | 1.50 (1.24, 1.81) | <0.001 | 1.32 (1.09, 1.60) | 0.005 | 1.22 (1.00, 1.48) | 0.046 | 1.40 (1.16, 1.70) | 0.001 |
| 2 | 1.13 (0.92, 1.38) | 0.007 | 1.06 (0.86, 1.30) | 0.596 | 1.00 (0.81, 1.23) | 0.991 | 1.09 (0.89, 1.34) | 0.392 |
| 3 | 1.11 (0.91, 1.35) | 0.129 | 1.05 (0.87, 1.28) | 0.598 | 1.04 (0.85, 1.26) | 0.710 | 1.08 (0.89, 1.32) | 0.431 |
| 4 | 0.98 (0.80, 1.20) | 0.347 | 0.94 (0.77, 1.16) | 0.577 | 0.93 (0.75, 1.14) | 0.464 | 0.95 (0.77, 1.17) | 0.629 |
| 5 – Least deprived | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.18 (0.79, 1.76) | 0.291 | 1.08 (0.73, 1.61) | 0.699 | 1.03 (0.69, 1.54) | 0.874 | 1.09 (0.73, 1.62) | 0.686 |
| **Highest education level** | | | | | | | | |
| Up to secondary school | 1.26 (1.08, 1.47) | 0.003 | 1.20 (1.03, 1.40) | 0.019 | 1.13 (0.96, 1.32) | 0.123 | 1.24 (1.06, 1.45) | 0.005 |
| Further education | 1.07 (0.89, 1.29) | 0.510 | 1.04 (0.86, 1.25) | 0.741 | 1.04 (0.87, 1.25) | 0.680 | 1.07 (0.89, 1.28) | 0.540 |
| Higher education/degree | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.25 (0.96, 1.62) | 0.099 | 1.19 (0.92, 1.55) | 0.182 | 1.14 (0.88, 1.49) | 0.331 | 1.18 (0.90, 1.53) | 0.224 |
| **Time in education** | | | | | | | | |
| 10 years or less | 1.10 (0.94, 1.29) | 0.244 | 1.05 (0.90, 1.24) | 0.519 | 1.06 (0.90, 1.24) | 0.500 | 1.10 (0.94, 1.29) | 0.248 |
| 11 to 13 years | 0.97 (0.82, 1.14) | 0.676 | 0.94 (0.80, 1.11) | 0.489 | 0.97 (0.82, 1.14) | 0.682 | 0.97 (0.83, 1.14) | 0.719 |
| 14 years or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.19 (0.96, 1.49) | 0.116 | 1.18 (0.95, 1.47) | 0.142 | 1.18 (0.94, 1.48) | 0.149 | 1.16 (0.93, 1.45) | 0.181 |
| **Household income** | | | | | | | | |
| £11,999 or less | 2.00 (1.67, 2.40) | <0.001 | 1.76 (1.47, 2.12) | <0.001 | 1.64 (1.36, 1.97) | <0.001 | 1.92 (1.60, 2.31) | <0.001 |
| £12,000 to £28,999 | 1.47 (1.22, 1.76) | <0.001 | 1.39 (1.16, 1.66) | <0.001 | 1.32 (1.10, 1.58) | 0.003 | 1.45 (1.21, 1.74) | <0.001 |
| £29,000 or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.87 (1.52, 2.30) | <0.001 | 1.71 (1.39, 2.10) | <0.001 | 1.64 (1.33, 2.02) | <0.001 | 1.77 (1.43, 2.18) | <0.001 |
| **Income from benefits** | | | | | | | | |
| All | 1.93 (1.64, 2.26) | <0.001 | 1.63 (1.39, 1.92) | <0.001 | 1.61 (1.37, 1.89) | <0.001 | 1.82 (1.55, 2.13) | <0.001 |
| Some | 1.47 (1.26, 1.71) | <0.001 | 1.34 (1.14, 1.57) | <0.001 | 1.39 (1.19, 1.63) | <0.001 | 1.45 (1.24, 1.69) | <0.001 |
| None | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.24 (0.97, 1.58) | 0.088 | 1.13 (0.88, 1.44) | 0.336 | 1.16 (0.91, 1.48) | 0.242 | 1.17 (0.92, 1.51) | 0.194 |
| **Financial concerns** | | | | | | | | |
| Yes | 1.19 (1.04, 1.37) | 0.013 | 1.14 (0.99, 1.31) | 0.062 | 1.12 (0.97, 1.28) | 0.127 | 1.17 (1.02, 1.35) | 0.024 |
| No | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.13 (0.89, 1.44) | 0.301 | 1.10 (0.87, 1.40) | 0.424 | 1.08 (0.85, 1.37) | 0.523 | 1.06 (0.83, 1.35) | 0.626 |

**Table 5.17 – Cox Proportion Hazards models for each socioeconomic status factors prior to multiple imputation**

| Variable | Age, sex, health, and behavioural factors adjusted* | | Age, sex, tumour, and treatment factors adjusted^ | | Fully adjusted+ | |
|---|---|---|---|---|---|---|
| | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value |
| **IMD Category** | | | | | | |
| 1 – Most deprived | 1.07 (0.88, 1.31) | 0.480 | 1.37 (1.13, 1.66) | 0.001 | 1.08 (0.88, 1.31) | 0.473 |
| 2 | 0.94 (0.76, 1.15) | 0.550 | 1.10 (0.89, 1.35) | 0.380 | 0.95 (0.77, 1.16) | 0.597 |
| 3 | 0.98 (0.81, 1.08) | 0.872 | 1.07 (0.88, 1.30) | 0.510 | 0.97 (0.79, 1.18) | 0.744 |
| 4 | 0.88 (0.72, 1.08) | 0.218 | 0.93 (0.76, 1.15) | 0.519 | 0.84 (0.68, 1.03) | 0.101 |
| 5 – Least deprived | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 0.92 (0.62, 1.38) | 0.688 | 0.95 (0.64, 1.43) | 0.817 | 0.72 (0.48, 1.09) | 0.120 |
| **Highest education level** | | | | | | |
| Up to secondary school | 1.09 (0.93, 1.27) | 0.265 | 1.13 (0.97, 1.33) | 0.109 | 1.00 (0.86, 1.18) | 0.882 |
| Further education | 1.02 (0.85, 1.22) | 0.875 | 1.05 (0.88, 1.26) | 0.584 | 1.00 (0.84, 1.21) | 0.893 |
| Higher education/degree | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.07 (0.82, 1.40) | 0.616 | 1.18 (0.91, 1.54) | 0.208 | 1.04 (0.79, 1.36) | 0.788 |
| **Time in education** | | | | | | |
| 10 years or less | 1.03 (0.87, 1.20) | 0.757 | 1.05 (0.89, 1.23) | 0.574 | 0.99 (0.84, 1.17) | 0.895 |
| 11 to 13 years | 0.95 (0.81, 1.12) | 0.528 | 1.02 (0.87, 1.20) | 0.802 | 1.02 (0.86, 1.20) | 0.835 |
| 14 years or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.15 (0.92, 1.43) | 0.236 | 1.21 (0.97, 1.52) | 0.087 | 1.17 (0.93, 1.47) | 0.173 |
| **Household income** | | | | | | |
| £11,999 or less | 1.46 (1.21, 1.76) | <0.001 | 1.67 (1.39, 2.01) | <0.001 | 1.34 (1.01, 1.63) | 0.003 |
| £12,000 to £28,999 | 1.26 (1.05, 1.52) | 0.012 | 1.33 (1.10, 1.59) | 0.002 | 1.17 (0.97, 1.41) | 0.100 |
| £29,000 or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.46 (1.18, 1.80) | 0.001 | 1.48 (1.20, 1.83) | <0.001 | 1.25 (1.00, 1.55) | 0.047 |
| **Income from benefits** | | | | | | |
| All | 1.36 (1.15, 1.60) | <0.001 | 1.69 (1.44, 1.99) | <0.001 | 1.35 (1.14, 1.60) | 0.001 |
| Some | 1.27 (1.08, 1.49) | 0.003 | 1.40 (1.19, 1.63) | <0.001 | 1.27 (1.09, 1.49) | 0.003 |
| None | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.03 (0.81, 1.33) | 0.788 | 1.09 (0.85, 1.40) | 0.483 | 0.96 (0.75, 1.24) | 0.768 |
| **Financial concerns** | | | | | | |
| Yes | 1.07 (0.93, 1.24) | 0.319 | 1.01 (0.88, 1.17) | 0.847 | 0.94 (0.81, 1.08) | 0.371 |
| No | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| Unknown | 1.01 (0.79, 1.29) | 0.936 | 0.96 (0.75, 1.22) | 0.716 | 0.90 (0.71, 1.16) | 0.424 |

**Table 5.18 – Cox Proportion Hazards models for each socioeconomic status factors following multiple imputation**

| Variable | Age and sex adjusted | | Age, sex, and comorbidity adjusted | | Age, sex, and smoking adjusted | | Age, sex, and alcohol adjusted | |
|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value |
| **IMD Category** | | | | | | | | |
| 1 – Most deprived | 1.49 (1.23, 1.80) | <0.001 | 1.32 (1.09, 1.60) | 0.005 | 1.20 (0.99, 1.46) | 0.066 | 1.42 (1.17, 1.72) | <0.001 |
| 2 | 1.13 (0.92, 1.38) | 0.240 | 1.06 (0.87, 1.30) | 0.563 | 0.99 (0.81, 1.22) | 0.938 | 1.10 (0.89, 1.34) | 0.376 |
| 3 | 1.11 (0.92, 1.35) | 0.282 | 1.06 (0.87, 1.29) | 0.554 | 1.03 (0.85, 1.26) | 0.746 | 1.09 (0.90, 1.32) | 0.383 |
| 4 | 1.11 (0.92, 1.35) | 0.816 | 0.94 (0.77, 1.16) | 0.581 | 0.92 (0.75, 1.13) | 0.442 | 0.95 (0.78, 1.17) | 0.654 |
| 5 – Least deprived | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Highest education level** | | | | | | | | |
| Up to secondary school | 1.26 (1.08, 1.47) | 0.003 | 1.21 (1.03, 1.41) | 0.018 | 1.12 (0.96, 1.31) | 0.151 | 1.26 (1.08, 1.47) | 0.004 |
| Further education | 1.07 (0.89, 1.28) | 0.496 | 1.03 (0.86, 1.24) | 0.711 | 1.03 (0.86, 1.24) | 0.712 | 1.06 (0.89, 1.27) | 0.509 |
| Higher education/degree | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Time in education** | | | | | | | | |
| 10 years or less | 1.10 (0.94, 1.30) | 0.229 | 1.06 (0.90, 1.24) | 0.486 | 1.05 (0.90, 1.23) | 0.534 | 1.11 (0.94, 1.30) | 0.216 |
| 11 to 13 years | 0.98 (0.83, 1.15) | 0.766 | 0.96 (0.81, 1.12) | 0.582 | 0.97 (0.83, 1.14) | 0.727 | 0.98 (0.83, 1.16) | 0.834 |
| 14 years or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Household income** | | | | | | | | |
| £11,999 or less | 1.92 (1.61, 2.28) | <0.001 | 1.71 (1.43, 2.04) | <0.001 | 1.57 (1.31, 1.87) | <0.001 | 1.86 (1.56, 2.22) | <0.001 |
| £12,000 to £28,999 | 1.43 (1.20, 1.70) | <0.001 | 1.35 (1.14, 1.61) | 0.001 | 1.29 (1.08, 1.53) | 0.004 | 1.41 (1.19, 1.68) | <0.001 |
| £29,000 or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Income from benefits** | | | | | | | | |
| All | 1.91 (1.63, 2.25) | <0.001 | 1.63 (1.38, 1.93) | <0.001 | 1.60 (1.36, 1.89) | <0.001 | 1.85 (1.57, 1.18) | <0.001 |
| Some | 1.45 (1.25, 1.69) | <0.001 | 1.33 (1.14, 1.55) | <0.001 | 1.37 (1.18, 1.60) | <0.001 | 1.44 (1.24, 1.68) | <0.001 |
| None | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Financial concerns** | | | | | | | | |
| Yes | 0.83 (0.73, 0.96) | 0.011 | 0.87 (0.76, 1.00) | 0.053 | 0.90 (0.78, 1.03) | 0.125 | 0.85 (0.74, 0.98) | 0.021 |
| No | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |

**Table 5.19 – Cox Proportion Hazards models for each socioeconomic status factors following multiple imputation**

| Variable | Age, sex, health, and behavioural factors adjusted* | | Age, sex, tumour, and treatment factors adjusted^ | | Fully adjusted+ | |
|---|---|---|---|---|---|---|
| | HR (95% CI) | p-value | HR (95% CI) | p-value | HR (95% CI) | p-value |
| **IMD Category** | | | | | | |
| 1 – Most deprived | 1.08 (0.89, 1.31) | 0.453 | 1.34 (1.10, 1.62) | 0.003 | 1.06 (0.87, 1.30) | 0.565 |
| 2 | 0.94 (0.76, 1.15) | 0.539 | 1.08 (0.88, 1.33) | 0.472 | 0.93 (0.75, 1.14) | 0.478 |
| 3 | 0.99 (0.81, 1.20) | 0.915 | 1.06 (0.87, 1.30) | 0.550 | 0.97 (0.79, 1.18) | 0.731 |
| 4 | 0.89 (0.72, 1.09) | 0.245 | 0.92 (0.75, 1.13) | 0.452 | 0.84 (0.69, 1.04) | 0.104 |
| 5 – Least deprived | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Highest education level** | | | | | | |
| Up to secondary school | 1.09 (0.93, 1.27) | 0.292 | 1.14 (0.98, 1.34) | 0.082 | 1.02 (0.87, 1.20) | 0.799 |
| Further education | 1.01 (0.84, 1.21) | 0.899 | 1.04 (0.87, 1.25) | 0.658 | 1.00 (0.83, 1.21) | 0.971 |
| Higher education/degree | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Time in education** | | | | | | |
| 10 years or less | 1.02 (0.87, 1.20) | 0.768 | 1.05 (0.89, 1.24) | 0.541 | 0.99 (0.84, 1.17) | 0.951 |
| 11 to 13 years | 0.96 (0.81, 1.13) | 0.594 | 1.02 (0.86, 1.20) | 0.852 | 1.01 (0.86, 1.19) | 0.895 |
| 14 years or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Household income** | | | | | | |
| £11,999 or less | 1.42 (1.18, 1.70) | <0.001 | 1.61 (1.34, 1.94) | <0.001 | 1.32 (1.09, 1.59) | 0.004 |
| £12,000 to £28,999 | 1.23 (1.04, 1.47) | 0.019 | 1.29 (1.08, 1.54) | 0.005 | 1.15 (0.96, 1.37) | 0.123 |
| £29,000 or more | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Income from benefits** | | | | | | |
| All | 1.38 (1.16, 1.64) | <0.001 | 1.67 (1.42, 1.97) | <0.001 | 1.36 (1.14, 1.62) | <0.001 |
| Some | 1.26 (1.08, 1.47) | 0.004 | 1.37 (1.18, 1.61) | <0.001 | 1.25 (1.07, 1.46) | 0.005 |
| None | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |
| **Financial concerns** | | | | | | |
| Yes | 0.93 (0.81, 1.07) | 0.295 | 0.97 (0.84, 1.12) | 0.699 | 1.04 (0.91, 1.20) | 0.541 |
| No | 1.00 (Ref.) | - | 1.00 (Ref.) | - | 1.00 (Ref.) | - |

## 5.4 Discussion

Inequality in survival of people with head and neck cancer was observed via several measurements of socioeconomic status including IMD Category, highest education level, number of years spent in education, annual household income, proportion of income from benefits, and financial concerns of living with or after cancer. The smoking status of the participants had a strong effect on the inequality by IMD Category, however adjustment for age, sex, health, and behavioural factors fully explained the inequality observed by IMD Category. Similar results were observed for highest education attained and financial concerns, however adjustment by smoking status was able to fully explain the inequality by these factors alone, both in the models prior to and following multiple imputation. Inequality by the amount of time the participants spent in education could be fully explained by age, which was to be expected due to the high proportion of people over the age of 65 in this cohort (n = 1,362/39.6%). Inequality by annual household income and the proportion of income from benefits attenuated following the adjustment of all of the potential explanatory factors, however even after full adjustment, inequality remained strong in both models prior to and following multiple imputation.

Previous work investigated inequality in long-term survival as part of the SAHNC – a clinical cohort study of people with head and neck cancer in Scotland diagnosed between 1999 and 2001 (Ingarfield *et al.*, 2018). A gradient in overall survival, disease-specific survival, and net survival was observed after one year, five years, and 12 years. Inequality by all-cause mortality and disease-specific mortality was no longer evident following the adjustment of combined patient, tumour, and treatment factors. The SAHNC study investigated people with head and neck cancer from Scotland who were diagnosed approximately 15 years before the HN5000 cohort, which only included people from England. Survival has differed between both countries for many years (Office for National Statistics, 2019), suggesting that people in England have a longer life expectancy than those in Scotland. In contrast to the HN5000, the SAHNC study investigated survival using the area-based Carstairs 2001 Index (Carstairs and Morris, 1989; McLoone, 2000) which derives deprivation on low social class, lack of car ownership, overcrowding, and male unemployment, and therefore cannot be directly compared to English IMD Categories. In addition, due to the long follow-up period, one limitation of the SAHNC study was that it was recruited ahead of the discovery of the association of HPV positivity and improved prognosis (Kreimer *et al.*, 2005; Ragin and Taioli, 2007; Wang *et al.*, 2015), and as a result, HPV data were not available in the SAHNC study. Moreover, the SAHNC study did not have the advantage of the use of individual measurements of socioeconomic status.

Other UK-based studies have investigated the impact of socioeconomic status on survival of people with head and neck cancer, and suggest that inequality is only apparent for the first 18 months, and can be explained by people from lower socioeconomic status statuses having tumours of higher stage, worse comorbidities, or poorer access to healthcare (Paterson *et al.*, 2002; Andersen *et al.*, 2008; Ellis *et al.*, 2012). In our study, this was not the case, particularly for annual household income and the proportion of income the participants received from benefits. However, it was clear that comorbidity attenuated the inequality by each socioeconomic status factors but did not explain the inequality alone and smoking considerably attenuated inequality more than any other factor for IMD Category and highest education level received. In this study, tumour stage alone did not seem have any influence on survival for any of the socioeconomic status factors.

There are several limitations to this study. Firstly, the proportion of participants across the IMD groups was even, suggesting an under-representation of the people from the most deprived areas in this study. As a result, this study may underestimate the true extent of inequality in survival of people with head and neck cancer. Secondly, the participants were given the option of taking home their baseline questionnaire to complete and return with a pre-paid envelope. As a result, a proportion of 21% of the participants did not return their baseline questionnaires and were therefore excluded from this analysis. We compared the groups of people who did and did not return their questionnaire and discovered that people who did not return their questionnaire were more likely to be from the more deprived IMD Categories (Appendix 5.2). Previous studies have also implied that non-respondents tend to be from backgrounds of lower socioeconomic status and have less time and capacity to participate in research (Fry *et al.*, 2017; James *et al.*, 2018). Thirdly, after excluding a proportion of people who did not return their questionnaire, those with missing data for alcohol consumption and stage were at a higher risk of all-cause mortality compared to the healthier groups of individuals. However, we performed multiple imputation to overcome this issue. Finally, although we linked these data to mortality data, we were unable to obtain information on the cause of the participants' death. Therefore, we were only able to investigate inequality in survival using all-cause mortality. However, due to the short-term follow-up period of this study, it is likely that a high proportion of deaths would be attributed to head and neck cancer, and therefore all-cause and disease-specific mortality results would be unlikely to be substantially different (Ingarfield *et al.*, 2019).

This study has several strengths. Firstly, this was a large, prospective, clinical cohort study which provided a range of measurements of socioeconomic status including area-based and individual measurements. Due to the extent of data collected via medical

records and participant questionnaires, this study allowed investigations into many of the potential explanatory factors of inequality in survival of people with head and neck cancer via a wide range of factors including participant characteristics, demographics, behavioural, health, tumour, and treatment factors.

### 5.4.1 Conclusion

This study discovered that inequality by an area-based measurement of IMD Category could be mostly explained by smoking status, and fully explained by a combination of age, sex, health, and behavioural factors. The same results were observed for the highest education level that was attained by the study population; however, age alone explained the inequality by the number of years spent in education. In this study, we were unable to explain inequality by annual household income or proportion of income of benefits that the participants received. This study adds to the literature by exploring inequality in survival of people with head and neck cancer using both area-based and individual measurements of socioeconomic status, and by investigating the explanations for the inequalities observed. To our knowledge, this is the first study to investigate the inequality in survival of people with head and neck cancer in such depth using both area-based and individual measurements of socioeconomic status and exploring the origins and explanations for the inequalities observed.

# 6 Discussion

## 6.1 Introduction

This chapter begins with a review of the aims and objectives of this thesis, followed by summary of the collective thesis findings from the four studies that were conducted throughout this thesis in relation to the prior knowledge and gaps that were identified in the literature review that was carried out in Chapter 1. This chapter goes on to discuss the thesis strengths and limitations, and finally makes recommendations for policy, practice, and further research on socioeconomic inequalities in head and neck cancer outcomes and survival. Finally, the thesis will end with a conclusion section.

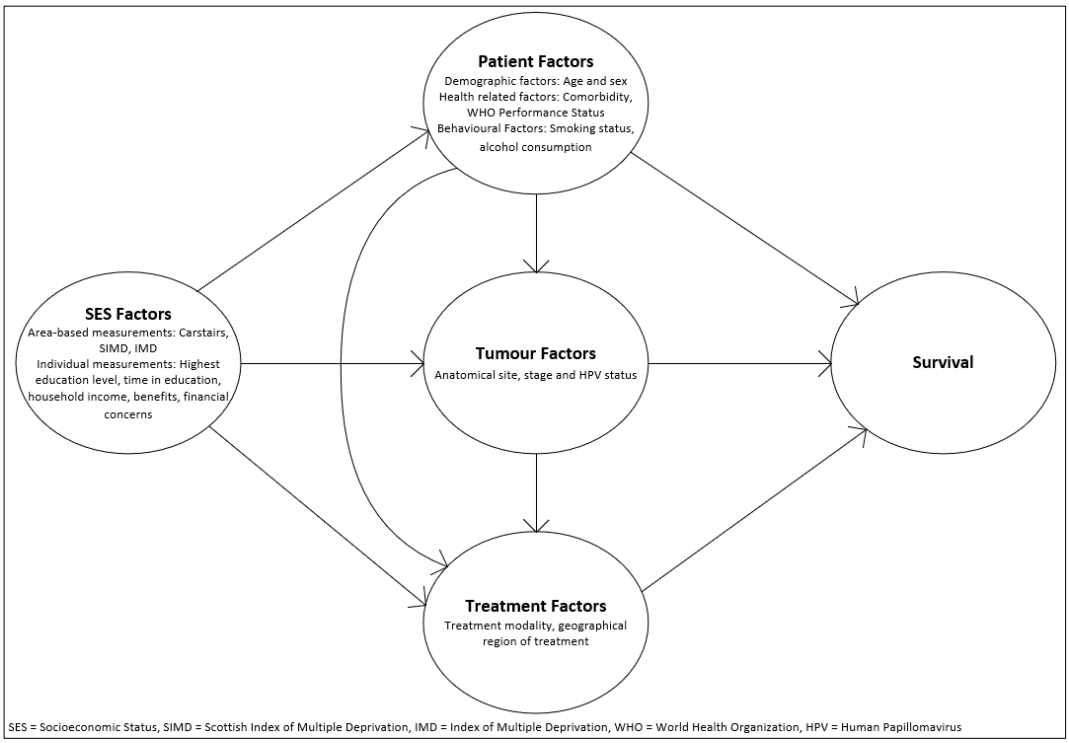
## 6.2 Aims and objectives of the thesis

This thesis aimed to inform patients, clinicians, policy makers, and the public in the UK that are involved with head and neck cancer on the magnitude of socioeconomic inequality observed in survival of people with head and neck cancer and what factors might explain these inequalities. A series of epidemiological studies of multiple existing UK cohort studies explored this topic from different angles. These findings could inform policy and practice in the further development and delivery of head and neck cancer services. This thesis aimed to explore the potential mechanisms and causal relationships between deprivation and survival in people with head and neck cancer, as outlined in Figure 6.1.

Throughout this thesis, the socioeconomic, patient, tumour, and treatment factors were selected and driven by the data availability in each of the studies that were carried out in Chapter 2 to Chapter 5. The socioeconomic factors of interest in Chapter 2, which included data from the Scottish Cancer Registry included Carstairs 1991 categories and SIMD 2004 categories. However, due to limitations around the use and linkage of data from the Scottish Cancer Registry, it was not possible to investigate associations with patient, tumour, and treatment factors with socioeconomic inequality in survival of people with head and neck cancer, and this chapter was limited to a descriptive analyses. Throughout Chapter 3 and Chapter 4, which utilised data from the SAHNC prospective clinical cohort study, the area-based Carstairs 2001 categories were considered as the socioeconomic factor. In addition, multiple patient, tumour, and treatment factors were considered for their association with survival (Chapter 3) and their association with socioeconomic inequality in survival of people with head and neck cancer. The patient

factors in these studies included: age at diagnosis, sex, smoking status, alcohol consumption, and WHO Performance Status. The tumour factors were the anatomical site and stage of the tumour, while the treatment factors that were included were the treatment modality that the patient received and the geographical location within the Scottish health board that the patients received their treatment. Chapter 5 utilised data from the HN5000 cohort study further refined both socioeconomic factors and patient, tumour, and treatment factors into modifiable and non-modifiable explanatory factors. The socioeconomic factors in this study included the area-based English IMD categories, and several individual measurements of socioeconomic status including highest education level attained, number of years spent in full-time education, total annual household income, proportion of income from benefits, and whether the participants had any financial concerns of living with or after cancer. The "patient factors" of interest in this study were refined into demographic data (age and sex), health status data (comorbidity and WHO Performance Status), and behavioural factors data (smoking status and alcohol consumption). The tumour factors included the anatomical site of the tumour, tumour stage, and HPV status, while the treatment factors just included the treatment modality that the patients received for their tumour. Throughout each study, age and sex were considered as confounding factors, while full models looked for the independent risk factors via full adjustment. In addition, these factors were also considered as both modifiable (for example, behavioural factors including smoking status and alcohol consumption) and non-modifiable (for example, tumour and treatment factors).

**Figure 6.1 – Conceptual diagram displaying the causal relationships between deprivation and survival in people with head and neck cancer**



## 6.3 Main findings of the thesis

### 6.3.1 Previous gaps in the literature

Chapter 1 provided a thorough literature review on studies from around the globe that investigated socioeconomic inequality in survival of people with head and neck cancer. These studies showed evidence of socioeconomic inequalities, with lower socioeconomic status and poorer circumstances being associated with worse survival of people with head and neck cancer. However, explanations for this socioeconomic inequality were yet to be thoroughly explored in terms of investigating potential underlying explanatory patient, tumour, and treatment factors. In particular, the underlying determinants of inequality in survival were not grouped as per factors that might be more modifiable (for example, through behaviours such as smoking and alcohol) compared with factors that might be less amenable to control (for example, tumour site, stage, and treatment regimens). In addition, none of the studies from the UK explored socioeconomic inequality in survival of people with head and neck cancer using individual measurements of socioeconomic status such as household income or education level. Additionally, few of the studies that were included in the literature review investigated the long-term impact of inequality in survival of people with head and neck cancer beyond five-years, and few studies examined the trend of inequality in survival of people with head and neck cancer over time. No study formally analysed the extent of absolute and relative inequalities in survival using metrics including RII and SII as per IARC 2019 recommendations (Conway *et al.*, 2019), and there was a lack of clarity and consistency in the survival metric to use throughout the studies.

### 6.3.2 Trends over time in inequality in survival

The aim of Chapter 2 was to describe the trends over calendar time and follow-up time of inequality in survival of people with head and neck cancer in Scotland who were diagnosed between 1986 and 2015 on the Scottish Cancer Registry. Socioeconomic inequality in net survival was measured by utilising the area-based Carstairs 2001 Categories. Inequality was evident for all time periods (after one year, five years, and 10 years) following diagnosis, with survival consistently favouring those who were from the least deprived regions of Scotland. However, the inequalities that were observed for people who were diagnosed between the years of 2011 and 2015 was higher than it was for any of the patients who were diagnosed before this time period and, in addition, socioeconomic inequalities became stronger over the follow-up period for all periods of diagnosis.

Chapter 4 also explored the trends in inequality over follow-up time of people who were recruited to the SAHNC cohort study; a large prospective national clinical cohort study in Scotland between the years of 1999 and 2001. Like the results found in Chapter 2, inequality in disease-specific survival became worse over the follow-up time from one years, five years, and 12 years after diagnosis, but the same trend was not apparent for overall survival and net survival estimates. However, following adjustment for age and sex, this trend for disease-specific survival was no longer apparent. In addition, the results for the net survival analysis demonstrated a gradient across the Carstairs 2001 Categories after one year and five years, but this gradient disappeared by 12 years, suggesting that some of the inequality in long-term survival was partly attributable to background mortality.

### 6.3.3 Determinants of survival of people with head and neck cancer

The primary aim of Chapter 3 was to determine the factors that are independently associated with survival of people with head and neck cancer that were recruited to the SAHNC. Survival was examined at three time points – one year, five years, and 12 years after a diagnosis of head and neck cancer. Prior to adjustment, poor overall survival, disease-specific survival, and net survival were associated with age, poor deprivation status, current or previous smoking status, current or previous alcohol consumption, and worse WHO Performance Status. In addition, poor survival was also more strongly associated with tumours of the hypopharynx, tumours of higher stage, and treatment with chemotherapy. However, in a mutually adjusted forward stepwise Cox proportional hazards model, the patient, tumour, and treatment factors that were associated with one-year, five-year, and 12-year all-cause mortality following the forced inclusion of age at diagnosis, tumour stage, and treatment modality included WHO Performance Status, alcohol consumption, anatomical site, and smoking status. The results for the mutually adjusted models for disease-specific survival differed slightly, in that after one year the factors that had an independent association with disease-specific mortality after the forced inclusion of age at diagnosis, tumour stage, and treatment modality included WHO Performance Status, alcohol consumption, and Scottish Cancer Network. However, by five years and 12 years, the factors that had an independent association with disease-specific mortality after the forced inclusion of age at diagnosis, tumour stage, and treatment modality included WHO Performance Status, alcohol consumption, and anatomical site, which was the same as the results for all-cause mortality. Interestingly, socioeconomic status did not have an independent association with all-cause mortality or disease-specific mortality following mutual adjustment.

### 6.3.4 Explanations for inequality in survival utilising an area-based measurement of socioeconomic status

To add to the research that was carried out in Chapter 3, the aim of Chapter 4 was to explore the underlying causes of inequality in survival for those who were recruited to the SAHNC cohort study. Following multiple individual adjustments of various patient, tumour, and treatment factors, none of the individually adjusted models fully explained socioeconomic inequality in survival. However, when the model was fully adjusted by all of the patient, tumour, and treatment factors combined, the inequality in survival attenuated, suggesting that inequality in survival of people with head and neck cancer is not straightforward, and that many factors play a combined effect in socioeconomic inequality in head and neck cancer survival.

### 6.3.5 Explanations for inequality in survival utilising both an area-based measurement and individual measurements of socioeconomic status

The aim of Chapter 5 was to explore the underlying determinants of inequality in short-term survival of people with head and neck cancer by utilising both an area-based measurement and several individual measurements of socioeconomic status. This study utilised data from the HN5000 cohort study; a prospective clinical cohort study of people diagnosed with head and neck cancer in England between the years of 2011 and 2015. Inequality in survival of people with head and neck cancer was observed via several measurements of socioeconomic status including IMD Category, highest education level attained, number of years spent in education, annual household income, proportion of income from benefits, and financial concerns of living with or after cancer. The smoking status of the participants had a strong effect on inequality by IMD Category, however similarly to the results observed in Chapter 4, adjustment for age, sex, health, and behavioural factors fully explained socioeconomic inequality observed by IMD Category. Adjustment by smoking status was able to fully explain the associations with highest education level the participants attained, and whether they had any financial concerns as a result of living with or after cancer. Survival associations with the amount of time the participants spent in education could be fully explained by age, while the relationship between survival and annual household income and the proportion of income from benefits attenuated following the adjustment of all potential explanatory factors, however even after full adjustment, the inequalities associated with these factors remained strong.

### 6.3.6 Whole thesis findings

As a whole, this thesis demonstrated strong and consistent socioeconomic inequality in survival of people with head and neck cancer. Moreover, these inequalities appeared to become worse over calendar time and also across follow-up period time one year, five years, and ten years after a diagnosis of head and neck cancer (Chapter 2). Chapter 3 found that socioeconomic status was not an independent predictor of survival in a cohort of people with head and neck cancer who were diagnosed in Scotland between the years of 1999 and 2001, while Chapter 4 investigated the underlying factors that may explain the original inequality that was observed in overall survival, disease-specific survival, and net survival estimates. Chapter 4 also highlighted that in models that were adjusted by various patient, tumour, and treatment factors, none of the factors could individually explain the socioeconomic inequality in survival alone, suggesting that socioeconomic inequality in survival of people with head and neck cancer is complex with multiple factors having a combined effect, including background mortality in the long-term follow-up (via net survival estimates). However, the studies that were carried out in Chapter 2 to Chapter 4 only utilised area-based socioeconomic measurements – mainly Carstairs deprivation index categories.

Chapter 5 added to this picture by exploring inequality by using both an area-based (IMD Category) and individual measurements of socioeconomic status including highest education level attained, number of years spent in education, annual household income, proportion of income from benefits, and financial concerns of living with or after cancer in England. Only data from England in the UK HN5000 cohort could be included in this analysis, as it was not possible to pool and standardise the varying measurements of IMD (including SIMD and Welsh IMD) across the UK. This study determined that inequalities were present for all of the measurements of socioeconomic status, however inequality in highest education level, number of years spent in education, and financial concerns of living with or after cancer were explained (fully attenuated) by other factors such as age and smoking status. Inequalities across both annual household income and the proportion of income from benefits partially attenuated following the adjustment of all of the potential explanatory factors, however, even after full adjustment, these inequalities could not be fully explained by a combination of the potential patient, tumour, or treatment factors that were included in this study.

The secondary aim of Chapter 3 was to compare methods of measurements of survival via the use of overall survival, disease-specific survival, and net survival estimates. The substantial differences between these survival metrics demonstrated the overestimation of deaths that are specific to head and neck cancer when using overall survival, and the underestimation of disease-specific mortality when using death certificates when people

have died only from head and neck cancer. These results suggest that people are dying of other causes that are related to their head and neck cancer but that are not as a direct result of their cancer. Therefore, the use of net survival provides a good compromise to traditional methods to estimate the true burden of head and neck cancer in long-term follow-up studies. As a result, throughout Chapter 2 to Chapter 4, net survival estimates have been provided alongside overall survival and disease-specific survival results to compare and contrast the outcomes of people with head and neck cancer. However, in Chapter 5, it was not possible to utilise net survival estimations since lifetables for this time point have not yet been generated.

## 6.4 Comparisons with other studies

### 6.4.1 Trends over calendar time

Of the studies that were included in the literature review that was carried out in Chapter 1, only five of the studies investigated the trends over time in inequality in survival of people with head and neck cancer. One of these studies included patients who were diagnosed with cancer of the larynx on the Scottish Cancer Registry (Shack *et al.*, 2007), three other studies utilised data from cancer registries in England (Paterson *et al.*, 2002; Coleman *et al.*, 2004; Rachet *et al.*, 2008), and one further study utilised data from the British Columbia Cancer Registry (Auluck *et al.*, 2016). No study was found that provided comparisons of inequality in survival of people with head and neck cancer by follow-up period.

Coleman *et al.* (2004) analysed cancer registry data on 2.2 million individuals who had been diagnosed with one of the 20 most common cancers in England and Wales between the years of 1986 and 1999, including 5,666 men with cancer of the larynx. Relative survival up to five-years and a "*deprivation gap*" was presented for each of the cancer sites. Coleman and colleagues discovered that the deprivation gap in relative survival for males with cancer of the larynx was increasing, and in the period of 1996-1999 reached 17% in favour of those from the least deprived areas. A small report by Rachet *et al.* (2008) investigated survival of men with cancer of the larynx in England and Wales. Rachet and colleagues took a deeper look at the 17% deprivation gap of males from the earlier article (Coleman *et al.*, 2004) and reported that this gap had increased by 3.7% every five years, with survival consistently in favour of those from the least deprived areas. In addition, this paper investigated 10-year relative survival and discovered that the gap in 10-year relative survival for men diagnosed in the early 1990s was also wide at 11%, in favour of the people from the least deprived regions.

Shack *et al.* (2007) investigated the socioeconomic inequality in survival of people with cancer in Scotland. This study included a cohort of 357,658 adults with any primary cancer registered on the Scottish Cancer Registry between the years of 1986 and 2000 and followed-up to 2005, including a sub-group of 1,128 men with laryngeal cancer. The authors reported five-year relative survival and the "*deprivation gap*" was presented again. This study demonstrated that the deprivation gap in five-year relative survival was at nearly 11% for men with cancer of the larynx in favour of those from the least deprived areas of Scotland and, in addition, was becoming approximately 3% wider every five years. Paterson *et al.* (2002) investigated trends for 20,131 people who were diagnosed with head and neck cancer from four regional cancer registries in England and Wales between the years of 1981 and 1994. This study examined the effect of deprivation on one-year and five-year relative survival using Carstairs 1991 Categories from several perspectives including age group, sex, and calendar year. Paterson and colleagues investigated the association of deprivation with survival by grouping the data into the years 1981-1985, 1986-1990 and 1991-1994 and found that the effect of deprivation on relative survival was stronger in the period of 1981-1985 and 1991-1994, with survival favouring the people who were from the least deprived areas.

These results coincide with the study that was conducted in Chapter 2 which demonstrated a widening in the inequality in survival of people with head and neck cancer, and this was also evident for those with cancer of the larynx, and for males and females separately. However, in the study conducted in this thesis, the SII and RII were used to quantify inequality as opposed to a "*deprivation gap*", which are recommended measurements for analysing inequality as proposed by IARC (International Agency for Research on Cancer, 2019).

### 6.4.2 Explanations for inequality in survival utilising area-based measurements of socioeconomic status

Only three studies that were included in the literature review extensively explored the underlying determinants of socioeconomic inequality in survival of people with head and neck cancer by utilising area-based measurements of socioeconomic status (Molina *et al.*, 2008; Robertson *et al.*, 2010; Chu *et al.*, 2016). These studies included underlying potential explanatory factors such as various patient, tumour, and treatment factors for their relationship with inequality in survival.

The only study from the UK which investigated the explanations for socioeconomic inequality in survival of people with head and neck cancer was conducted by Robertson *et al.* (2010). This study utilised the SAHNC cohort, which was also used in Chapter 3 and

Chapter 4 of this thesis. In the study by Robertson *et al.* (2010), socioeconomic status was measured using 2001 Deprivation Category (DEPCAT) scores which were categorised into three groups (affluent, intermediate, and deprived) while in the studies carried out in this thesis, Carstairs 1991 Categories were utilised which provided five groups for levels of socioeconomic indication. However, Robertson *et al.* (2010) only investigated all-cause mortality and disease-specific mortality up to five years post-diagnosis, whereas the study conducted in this thesis investigated survival up to 12-years along with a comparison of overall survival and disease-specific survival with net survival estimates. Robertson *et al.* (2010) found that the people who were in the deprived group experienced a 33% (HR = 1.33, 95% CI = 1.06 to 1.68) increased risk of all-cause mortality compared to those from the most affluent group after five years. The similar study in Chapter 3 of this thesis found that those from the most deprived area exhibited a slightly higher excess risk of all-cause mortality of 43% (HR = 1.43, 95% CI = 1.15 to 1.76) in a minimally adjusted model for age and sex, compared to those from the least deprived areas in analyses using Carstairs 1991 Categories after five years. However, this is likely to be related to the differing groups for socioeconomic status that was used in the study conducted in this thesis. In addition, in the study that was carried out in this thesis, inequality in 12-year survival was also investigated. Robertson *et al.* (2010) reported that socioeconomic status was no longer an independent predictor of all-cause or disease-specific mortality following the adjustment for other baseline covariates including WHO Performance Status, tumour stage, age at diagnosis, anatomical site of the tumour, smoking status, and alcohol consumption, which was also reported in this thesis. However, to add to this research, the study carried out in this thesis on the SAHNC delved further into the explanations for the lack of inequality after adjustment in Chapter 4 with the aim to extract further understanding of explanatory factors for socioeconomic inequality in survival. Following multiple individual adjustments of various patient, tumour, and treatment factors, none of the models that adjusted individually by each baseline covariable were able to fully explain the inequality. However, when the models were adjusted by multiple patient, tumour, and treatment factors, the inequalities fully attenuated, which suggests that the socioeconomic inequality in survival of patients with head and neck cancer is multifactorial.

Another similar study that explored the underlying explanations for inequality in survival of people with head and neck cancer outside of the UK was conducted by Chu *et al.* (2016), who explored the prognostic importance of neighbourhood-level socioeconomic status on the overall survival of 2,124 people with newly diagnosed head and neck cancer. The patients were diagnosed at the Toronto's Princess Margaret Cancer Centre between the years of 2003 and 2010. The authors reported that although low socioeconomic status was associated with poorer survival in a univariate model, it was no longer associated with poorer survival following the adjustment for other variables including age, gender, stage,

comorbidity, smoking status, alcohol use, and HPV type 16 status. The authors outlined that those of lower socioeconomic status were more likely to have comorbidities, tumours of higher stage, and were more likely to be smokers and alcohol users. However, Chu *et al.* (2016) had the advantage of including HPV type 16 status as an explanatory factor for inequality which, due to the long-term follow-up of the SAHNC data, was not available for the thesis.

Conversely, the thesis findings differed with a study from the USA that had also thoroughly explored the underlying explanations for inequality in survival of people with head and neck cancer. Molina *et al.* (2008) investigated the association of community poverty level with the survival of 20,915 people diagnosed with head and neck cancer in Florida between the years of 1998 and 2002. The authors investigated five-year overall survival using a variety of demographic, social, and clinical information and recorded socioeconomic status using community poverty levels. The authors discovered that area-based socioeconomic status remained an independent predictor of survival in a stepwise multivariate Cox regression analysis which included participant demographics (age, gender, race, ethnicity, tobacco use and alcohol consumption), comorbidities, clinical characteristics (tumour grade, stage, and location of treatment) and treatment modality.

### 6.4.3 Explanations for inequality in survival utilising individual measurements of socioeconomic status

Only one study that was included in the literature review extensively explored the underlying explanations of socioeconomic inequality in survival of people with head and neck cancer by utilising individual measurements of socioeconomic status, which were similar to the measurements utilised throughout the study undertaken in Chapter 5 of this thesis. The study, conducted by Abrahão *et al.* (2020), investigated the predictors of survival in a cohort of 1,463 people diagnosed with SCC of the head and neck from Argentina, Brazil, Colombia, and Uruguay between the years of 2011 and 2017. Participants for the study were collected from the InterCHANGE study, a multicentre case-control study to investigate the risk factors and outcomes of people with SCC of the head and neck. Patients were followed up to 2018 and the authors reported three-year overall survival outcomes and included the education level of the patients as an exploratory factor. In a univariate Cox proportional hazards model, those who were “illiterate” were more at risk of all-cause mortality compared to those with “superior” education levels. However, in a multivariate model including age, sex, ethnicity, cancer stage, smoking history, alcohol consumption, and anatomical site, education level was no longer a predictor of survival. In the study that was carried out in Chapter 5 of this thesis, education was defined as the number of years spent in education and the highest qualification

attained by the patients. In this study, education was a predictor of three-year survival in a univariate model with survival favouring those with higher levels of education, which was similar to the results observed in the paper by Abrahão *et al.* (2020). However, in the study in this thesis, age alone fully explained the inequality observed for the number of years spent in education, while smoking status was able to fully explain the inequality by highest education attained.

## 6.5 Overall thesis strengths and limitations

The strengths and limitations of each study are outlined in the discussions within each chapter. However, there are several strengths and limitations to this thesis as a whole.

### 6.5.1 Thesis limitations

One limitation of this thesis is the slight variations in the inclusion criteria of head and neck cancer across the three studies that were utilised throughout the analyses in this thesis. There are many different definitions of head and neck cancer, which was discussed in Chapter 1 (Section 1.3.1), and Appendix 6.1 displays the differences in the ICD-10 inclusion criteria across the studies included in this thesis. In the HN5000 study, the lip and the oral cavity were grouped due to low numbers of people with cancer of the lip in this study. While in the Scottish Cancer Registry and SAHNC cohort, these subgroups of the head and neck were analysed separately. In addition, in the HN5000 study, the study team considered tumours of the “minor salivary gland” which were classified as any ICD-10 code with the tumour histology recorded as “salivary gland”. Due to differing clinical input, this was not considered throughout the analyses in the Scottish Cancer Registry or the SAHNC cohort. The final difference related to tumours of the nasopharynx, nasal cavity, and sinuses, which were included in the SAHNC cohort (albeit, a combined grouping) and the HN5000 study. However, these tumours were not requested as part of the Public Benefit and Privacy Panel (PBPP) application form for the Scottish Cancer Registry.

A further limitation of this thesis related to the different groupings of treatment modalities that were considered throughout each chapter, which are highlighted in Appendix 6.2. These differences are largely due to changes over time with guidance on how best to treat head and neck cancers, which had led from a shift away from chemotherapy and towards the use of chemoradiotherapy (NICE, 2017). Some minor differences in the categorisation of treatment modality were also due to low numbers, which needed to therefore be combined with other groups to allow for accurate analyses.

A further limitation of the analyses that were carried out in Chapter 3 and Chapter 4 which utilised the SAHNC cohort study, included the non-proportional hazards that were observed in the long-term follow-up study. Proportional hazards occur when the ratio of the hazards between the groups of the variable that are included in the Cox Proportional Hazards Model are the same over follow-up time. This was not the case for the SAHNC cohort study, and the hazards were displayed over various follow-up times including after one year, five years, and 12 years of a diagnosis of head and neck cancer. The implication of non-proportional hazards may lead to an underestimation or overestimation of the relative risk for covariates over time (Schemper, 1992). An alternative method to using Cox Proportional Hazards Regression in a non-proportional setting could have been to display conditional survival measurements, which present survival outcomes based on the condition that a person has already survived to a certain point (Hieke *et al.*, 2015). This eliminates the issue surrounding non-proportional hazards since the baseline hazard function is not considered (Xu and O'Quigley, 2002).

One limitation to Chapter 5 was also the under-representation of people from the most deprived areas in this study, since it would have been expected to have observed higher numbers of people in the most deprived group (Purkayastha *et al.*, 2016). As a result, this study may underestimate the true extent of inequality in survival of people with head and neck cancer. However, in a paper written by epidemiologists Rothman *et al.* (2013), the authors state that representativeness is not a reasonable aim for scientific studies since a representative sample may not be generalisable to all of the individual subgroups of a population. The authors also concluded that *"…the main road to general statements on nature is through studies that control skilfully for confounding variables and thereby advance our understanding of causal mechanisms. Representative sampling does not take us down that road*". Moreover, this could only therefore be of real concern if there were very small numbers or no cases in a particular group (for example, those from deprived areas), which was not the case in the HN5000 cohort study.

Further limitations of this thesis are the various types of potential biases that can occur in these types of routine national databases and cohort studies (including the SAHNC and the HN5000). Such biases include differential misclassification of outcomes, measurement error in potential exposures, confounders and mediators, ecological fallacy in area-based measurements, immortal time bias in cohort studies, and confounding by indication. Differential misclassification of outcomes is a recognised issue in studies that use routine administrative data and occurs when the health outcome is not equal between people who are exposed or are unexposed (Rothman *et al.*, 2008; Chen *et al.*, 2019). However, Cancer Registry data are population-wide with high quality and completeness and therefore, differential misclassification is unlikely to be an issue in terms of the primary

exposure and outcomes, including cancer diagnosis and survival. Similarly, in the near population-wide coverage of the SAHNC cohort, the issue of SES exposure data would be minimal, however full data capture of patient, tumour, and treatment data may have been impacted differentially across the socioeconomic status groups due to differential treatment uptake which may impact and underestimate the outcome. Ecological fallacy is an information bias when an individuals' socioeconomic status is misclassified based on their area of residence. This may cause bias in studies that include area-based measurements of socioeconomic status since all individuals in one area of residence may not share the same socioeconomic characteristics (Greenland and Morgenstern, 1989; Walter, 1991). Ecological fallacy is well recognised as an issue in this thesis throughout the analyses that included the Scottish Cancer Registry and the SAHNC cohort which both utilised area-based measurements of socioeconomic status. However, the main aim of Chapter 5 which utilised the HN5000 cohort, was to explore both individual and area-based measurements of socioeconomic status, and to compare these outcomes – and multiple individual measures were used. A strong inter-relationship of area and individual socioeconomic measures was observed. Ecological area-based measures can also be considered advantageous since they capture the area and environmental aspects of socioeconomic deprivation, for example, including access to services, healthy food, and cultural aspects. Immortal time bias occurs when the participants included in a study do not experience the outcome of interest when this outcome is measured at a later date in the study (Rothman *et al.*, 2008). Immortal time bias is a bias in which the person-time at risk of an event includes a period of time during which the individual cannot experience the event (Suissa, 2007; Faillie and Suissa, 2015). This typically occurs in pharmacoepidemiology studies when an individual has a delay between their date of diagnosis and the start of their treatment. If the event (for example, death) occurs during this time, the individual is either misclassified to a treated group, or is excluded from the analysis. This typically occurs during the time lapse in between a patient receiving a diagnosis and beginning their allocated treatment regimen. Should a participant die during this time, their treatment allocation would remain as the "planned treatment", although the individual did not receive any treatment before dying, and therefore should be re-allocated as such. Therefore, there was a period of immortal time in these studies when the participants could not experience death. However, the impact of immortal time bias is likely to be small in the Scottish Cancer Registry as the case ascertainment and completeness of these data is high (Public Health Scotland, 2020a). In addition, in the SAHNC and HN5000 cohorts, many of the patients who were either not fit for treatment of curative intent or were given non-curative treatment, were assessed by clinical teams, and were correctly allocated into a no treatment group. Therefore, immortal time bias was unlikely to be an issue in the SAHNC and HN5000 cohorts.

### 6.5.2 Thesis strengths

The studies that were performed as a part of this thesis contribute to the knowledge and understanding of inequality in survival of people with head and neck cancer. Chapter 2 aimed to describe the trends over time in inequality in survival of people diagnosed with head and neck cancer in Scotland by utilising data from the Scottish Cancer Registry. Trends over time were explored for people who were diagnosed between the years of 1986 and 2015. This allowed trends in survival in the short-term, mid-term, and long-term to be investigated over time and by calendar time, which was a strength of this study. However, due to the limitations of cancer registry data (such as lack of staging information and behavioural data), the underlying factors of inequality could not be explored.

The next analyses undertaken in Chapter 3 and Chapter 4 utilised data from the SAHNC, which was a cohort study of people who were diagnosed with head and neck cancer in Scotland between the years of 1999 and 2001. This data provided a snapshot of 77% incident cases of head and neck cancer that were recorded on the Scottish Cancer Registry during the same period. Inequality in survival of people with head and neck cancer was explored in the short-term, mid-term, and long-term in the same way as the methods that were conducted as a part of Chapter 2, and additionally, the underlying factors of inequality could be explored. However, one of the major limitations of this study was the absence of HPV data, which over the last two decades has been associated with the rising incidence of people with head and neck cancer, particularly for those with cancers of the oropharynx, who have a considerably better prognosis. In addition, it was only possible to measure socioeconomic status in the studies in Chapter 2 to Chapter 4 by using the area-based Carstairs and Morris index, which is derived from Census data and considers the proportion of male unemployment, those in social classes IV and V, lack of car ownership, and overcrowding in a dwelling. However, Carstairs and Morris categories may not accurately represent rural and urban populations since it may be essential for these people to own cars in these areas (Valentova, 2011). Moreover, the SAHNC could not be linked to the more updated, small area SIMD index.

This led this thesis into Chapter 5, which explored the underlying causes of inequality in the HN5000 cohort study, by using both an area-based measurement of socioeconomic status and several individual measurements of socioeconomic status. This included the highest education level obtained, number of years spent in education, total annual household income, proportion of income from benefits, and whether the patients had any financial concerns of living with or after their diagnosis of head and neck cancer. In addition, a more thorough exploration of the potential underlying determinants of socioeconomic inequality in survival of people with head and neck cancer was possible, which included data on the HPV status of the patients in the study. However, the main

limitation of this study was the recency of this cohort who were diagnosed between the years of 2011 and 2014, with follow-up to 2018, and therefore it was only possible to investigate inequality in survival in the short-term (three years). In addition, these data could not be linked to cause of death information for disease-specific survival, and lifetables for this time period had not yet been generated at the time of this analysis. Therefore, it was also not possible to explore net survival outcomes for this cohort.

In the literature review that was carried out in Chapter 1, few of the studies that were included explored the underlying causes inequality in survival of people with head and neck cancer, and therefore, this remained poorly understood. Although some of the UK-based studies explored multivariate models which included socioeconomic status as a potential explanatory variable for survival of people with head and neck cancer, this thesis has provided the first UK-based study that explored the underlying causes of socioeconomic inequality in depth with the aim to understand the factors explaining inequality in survival of people with head and neck cancer. In particular, explanations for this inequality were yet to be thoroughly investigated by exploring potential patient, tumour, and treatment factors, including potential underlying determinants which were not grouped as per factors that might be more modifiable (for example, through behaviours such as smoking and alcohol) compared with factors that might be less amenable to control (for example, tumour site, stage, and treatment regimens). In addition, this thesis provides the world's first study that explored socioeconomic inequality in survival of people with head and neck cancer, while also examining the exact underlying factors of inequality in survival using a variety of measurements of inequality including both area-based and individual measurements of socioeconomic status such as annual household income and the proportion of income from benefits (HN5000 study).

A further strength of this thesis is the use of modern net survival to explore survival of people with head and neck cancer. Net survival is defined as the excess mortality between the observed mortality of a group of people under investigation and the expected mortality of a disease-free group in the population with the same demographic characteristics as the study group (Pohar Perme *et al.*, 2012). Net survival is useful when cause of death information is unknown and provides a more accurate representation of the mortality from a disease of interest by disentangling other causes of death. Throughout this thesis, net survival was estimated by utilising the *stns* command in stata, which implements the Pohar-Perme estimator (Pohar Perme *et al.*, 2012) and provides a non-parametric unbiased estimator of net survival (Clerc-Urmes *et al.*, 2014).

## 6.6 Recommendations

This section covers recommendations for practice, policy, and research in turn which are based on the findings from the thesis.

### 6.6.1 Recommendations for practice

#### Improved access to Welfare Benefit Services

The financial burden of cancer on patients is significant – from reducing working hours or stopping work entirely, to paying towards additional costs of utility bills and travel expenses for frequent specialist appointments (Pearce *et al.*, 2001). In addition, this thesis has confirmed that people with lower levels of annual household income and who claim higher levels of benefits are at an increased risk of dying following a diagnosis of head and neck cancer. Therefore, in a cohort of patients who were already more at risk of developing head and neck cancer due to their socioeconomic position, these patients are not only more likely to have the diagnosis of cancer and consequently have to endure the gruelling treatment regimens of living with cancer, this thesis has confirmed that these patients are also at a higher risk of dying following their diagnosis of head and neck cancer. For those who were already more likely to be of more deprived demographics, the financial burden of a diagnosis of head and neck cancer on these patients is therefore substantial.

Macmillan Cancer Support provides thorough information on where financial assistance may be claimed by cancer patients, including those with head and neck cancer, to assist with the additional costs of living with cancer (Macmillan Cancer Support, 2020). This includes detailed information on claiming benefits (such as low-income benefits, disability benefits, and benefits for people of pension age), help with children's costs (such as Disability Living Allowance), help with bills and housing costs (such as Universal Credit and Housing Benefits), and help with health costs (such as financial assistance grants from Macmillan Cancer Support). However, in an earlier systematic review by Adams *et al.* (2006), among those who had been referred to welfare advice services, it was found that there was substantial underclaiming of welfare benefits across all healthcare settings.

More recently welfare benefit services have been embedded into clinical and oncological care settings (The Beatson, 2021), and are available on referral from local authorities or other charitable organisations (Moffatt *et al.*, 2010). Further development, and evaluation where services already exist, of welfare benefit programmes linked specifically to head and neck cancer services needs to be undertaken to encourage, enable, and ensure that

these people are taking up the support that they are entitled to. In particular, these services need to effectively target those who are most likely to benefit from these programmes, such as those who have a lower income or are from more deprived communities.

**Improved assessment of socioeconomic circumstances at the time of diagnosis**

Rogers and colleagues (2014) have produced a Patient Concerns Inventory, developed for head and neck cancer clinics to assist patients in highlighting any concerns they may have, or to indicate whether they wish to see other services within the Multidisciplinary Team (Rogers and Lowe, 2014; Rogers *et al.*, 2016a). They reported that the Patient Concerns Inventory was found to be suitable for use in clinic by both patients and staff, and two thirds of the patients found that the inventory helped them communicate their concerns with their consultant. For the above-mentioned improvements to welfare benefit services to be able to become more effective at targeting the patients who are most at need of these services, the recording of social and economic variables at the time of diagnosis as part of a holistic assessment could be undertaken for all patients with a new diagnosis of head and neck cancer. Further assessments could be incorporated to collect detailed information on patients' financial position before, during, and after a diagnosis of and treatment for head and neck cancer, including information about their annual household income, whether they are claiming any income from benefits, and whether their income has reduced as a result of their diagnosis of cancer. This would not only allow for targeted interventions to ensure those with lower levels of income are able to access and take up the welfare benefits that they are entitled to but would also allow further investigations into these existing inequalities to be undertaken for future comparative research.

**Improved smoking cessation services and alcohol prevention services**

Tobacco use and alcohol consumption to some extent explained the inequalities that were observed in the survival of people with head and neck cancer observed in the thesis. It is currently good practice to refer head and neck cancer patients who are tobacco and alcohol users to smoking or alcohol cessation services. For example, the current Scottish Quality Performance Indicator for head and neck cancer records referral to smoking cessation services (Healthcare Improvement Scotland, 2013). However, it is not possible to routinely determine how many patients take up this service and as a result, a referral is, to some extent, a passive process. Therefore, more engaging or embedded prevention advice services following NICE guidelines within the head and neck cancer team may be more effective, including considering these services as part of the allied health and clinical services for people with head and neck cancer (NICE, 2011a; NICE, 2018). Furthermore,

these prevention services could be extended to include alcohol brief interventions, which have been shown to be effective in primary care settings (O'Donnell *et al.*, 2014).

### 6.6.2 Recommendations for policy

**Primary prevention of tobacco use**

Despite reduced rates of smoking in Scotland and across the UK (Scottish Government, 2020), inequalities in the distribution of smoking remain wide, with higher levels of smoking observed in communities that are of a more deprived classification. Further primary prevention and policy control is therefore warranted. In 2008, the Scottish Government introduced a smoking prevention action plan: *Scotland's Future is Smoke Free.* Despite the ban on smoking in public places which was introduced in Scotland in 2006, and the increase in the age of sale of tobacco products from 16 to 18 in 2007, the Scottish Government remains committed to improving mechanisms that will ultimately discourage children and young adults from taking up smoking. The Scottish Government aimed to target school children by using a holistic approach to health and wellbeing in Scottish schools through the *Health Promoting School and a Curriculum of Excellence* (Scottish Government, 2008c). The plan has been reviewed every five years, and ten years on, *Raising Scotland's tobacco-free generation* (Scottish Government, 2018c) aims for a "*tobacco-free*" generation by 2034 (defined as a rate of smokers of 5% or less). Across the rest of the UK, in 2019 the UK Government announced ambitions for England to be "*smoke-free*" by 2030 (as defined by a smoking rate of 6% or less) with the aim to publish a new *Tobacco Control Plan for England* in July 2021.

Action on Smoking and Health (ASH) (2019) provide the secretariat for the All Party Parliamentary Group (APPG) on Smoking and Health. The aim of the APPG is to "*monitor and discuss the health and social effects of smoking; to review potential changes in existing legislation to reduce levels of smoking; to assess the latest medical techniques to assist in smoking cessation; and to act as a resource for the group's members on all issues relating to smoking and public health*". The No Tobacco unit (TFI) section of the Department of Health and Promotion at the WHO works closely with countries across the globe to plan and implement tobacco control activities (World Health Organization (WHO), 2019) with the aim to reduce the burden of tobacco smoking on health. These actions need to continue to be pushed forward with the aim to improve health, protect future generations, and ultimately, reduce inequality.

**Primary prevention of alcohol consumption**

In 2018, the Scottish Government introduced a minimum price of 50 pence per unit of alcohol with the aim to "*save lives, reduce hospital admissions and, ultimately, have positive impacts across the whole health system in Scotland*" (Scottish Government, 2018a). As a result, this minimum pricing per unit of alcohol aims to ensure that alcohol is sold at sensible prices by leading to drinks with higher alcoholic percentages being sold at higher unit values. Within 20 years, the Scottish Government had modelled that this will lead to 120 fewer alcohol-related deaths per year and 2,000 fewer alcohol-related hospital admissions per year (Angus *et al.*, 2016; Scottish Government, 2018a). Additionally, the *Alcohol Framework 2018: Preventing Harm from Improving Scotland's Health* (Scottish Government, 2018b) aims to evaluate the impact of the introduction of the minimum unit pricing.

**Socioeconomic reform**

The Scottish Government has long aimed to improve life expectancy at birth in the most deprived regions of Scotland from the *Achieving Our Potential: A Framework to tackle poverty and income inequality in Scotland* (Scottish Government, 2008a). The *Equally Well* report of the ministerial Task Force on health inequalities in Scotland was launched in 2008 with the aim of tackling the significant health inequalities in Scotland (Scottish Government, 2008b). The Task Force aims to understand the underlying causes of health inequalities in Scotland to be able to take action to make Scotland "Smarter, Wealthier and Fairer, Greener, Safer and Stronger and, ultimately, Healthier". *Health Inequalities Policy Review for the Scottish Ministerial Task Force on Health Inequalities* (Beeston *et al.*, 2014) was set up to describe the underlying factors that drive inequalities in health in Scotland and "*commends the policy principle of proportionate universalism (the whole population having access as of right to benefits and opportunities, but greater investment for those in more disadvantaged circumstances) and notes that policies to reduce inequalities in health need to extend beyond health care to cover numerous other sectors such as environmental regulation, and education, housing, employment, welfare and transport needs*". The report highlights that downstream interventions to tackle inequality which rely on individual engagement are likely to be ineffective compared to more upstream interventions by improving environments and life circumstances of people from more deprived areas.

The Institute of Health Equity aims to highlight the social determinants of health and improve health equity by considering four areas including "*influencing global, national and local policies; advising on and learning from practice; building the evidence base; and capacity building*" (Institute of Health Equity, 2021). *The Marmot Review: Fair Society,*

*Healthy Lives* reported that people in England could have lived between 1.3 and 2.5 million additional years of life had premature deaths due to health inequalities not existed (Marmot *et al.*, 2010). The report outlined that six key objectives needed to be tackled to reduce health inequalities which included: "*give every child the best start in life; enable all children, young people and adults to maximise their capabilities to have control over their lives; create fair employment and good work for all; ensure healthy standard of living for all; create and develop healthy and sustainable places and communities; strengthen the role and impact of ill health prevention*" (Marmot *et al.*, 2010).

**Improved surveillance for head and neck cancer diagnoses**

The Scottish Cancer Registry is collected by the Information Service Division of the NHS Scotland (now Public Health Scotland), with the aim to "*collect, validate, analyse and store accurate, timely and comprehensive data on cancer"* (ISD Scotland, 2010b). The database holds information such as personal and demographic data, and details on the tumour diagnosis, including the anatomical site of the tumour and its histology. However, detailed information on the person's tumour, including vital information on the stage of their tumour, is not collected for those with head and neck cancer malignancies. Staging information is currently collected for people with cancers of the breast, colorectum, or cervix, however due to the complex nature of cancers of the head and neck, which often present at various stages, depending on the anatomical subsite of the head and neck that the primary tumour is found, this information would be invaluable to future research involving head and neck cancer. In addition, due to the association of HPV and head and neck cancer, it would be important to consider this alongside all new diagnoses, particularly for those with cancer of the oropharynx.

**Assessing the impact of COVID-19 on cancer outcomes and inequality in survival**

The recommended referral time for a cancer screening examination in the UK is two weeks (NICE, 2021). However, in June 2020 following the peak of the COVID-19 pandemic, more than 2.4 million people in the UK were awaiting vital cancer screening, tests, or treatment for their cancer due to the disruption that COVID-19 has caused on cancer services in the UK (Cancer Research UK, 2020). This included approximately 2.1 million people awaiting cancer screening tests, nearly 300,000 people waiting for an urgent referral to a cancer team, and more than 21,000 people awaiting treatment for their cancer (Cancer Research UK, 2020). In October 2020, there were more than nine times the usual amount of people waiting six weeks or more for endoscopy test, and 11 times more people waiting six weeks or more for radiology tests (such as MRI and CT scans) for cancer diagnostics (NHS England, 2021). Prompt screening and early diagnosis of cancer leads to improved treatment outcomes and therefore, improved survival. Data on the

impact of the COVID-19 pandemic on cancer diagnostics, treatment, and prognosis are yet to be available, including survival and inequality in survival of people with head and neck cancer, but there are likely to be significant impacts. It is imperative that the impact of COVID-19 on survival outcomes of cancer diagnoses is thoroughly monitored and evaluated immediately following the COVID-19 pandemic, including comparisons of inequality in survival of people with cancer. However, the recovery of services needs to be prioritised, including re-establishing the primary care and secondary care interfaces.

### 6.6.3 Recommendations for further research

#### Further evaluation of welfare benefit programmes

Further evaluation of welfare benefit programmes that are presently linked to head and neck cancer services need to be undertaken to explore whether the patients are encouraged, and are able, to take up the support that they are entitled to. In particular, research needs to be undertaken to ensure that those who are most likely to benefit from these programmes, such as those who have a lower income or are from more deprived communities, are having these discussions with healthcare professionals, including the best means to approach people of these demographics.

#### Quality Performance Indicators

The intentions with the Scottish Cancer Registry study were to link the data to the new Quality Performance Indicators which provide detailed information in several prognostic indicators of head and neck cancer. This linkage would have allowed the opportunity to explore underlying drivers of socioeconomic inequality in survival of people with head and neck cancer in Scotland in recent years. In addition, the linkage would have allowed for pilot studies to establish a framework for future evaluations into the impact of the introduction of the QPIs on inequality in survival of people with head and neck cancer. However, limitations and delays around the access of the Quality Performance Indicators meant that only the East of Scotland data were available at the time of these analyses, and so this analysis was not possible within the scope of the thesis – although this work is still a recommended next step for research in this area.

#### SMR00 and SMR01 data linkage

Further analyses with the Scottish Cancer Registry could investigate linkage to SMR00 and SMR01 databases, which include detailed information on inpatient and outpatient treatment. This could allow further analyses on diagnoses and hospital admissions for other conditions to infer alcohol-related comorbidities and smoking-related comorbidities.

These data could be extracted to investigate the effects of specific comorbidities on inequality in survival of people with head and neck cancer.

**Further research with the HN5000 cohort**

The HN5000 cohort study provided valuable knowledge on several measurements of individual and area-based socioeconomic status. However, since the study was so recent, this meant that only short-term follow-up was provided. Therefore, future research into socioeconomic inequality in survival could be performed to explore the effects of inequality at five years and longer when the database has matured. In addition, further outcomes could be explored with the HN5000 cohort that related to inequalities in survival and quality of life.

**The HEAD and neck cancer in South America and Europe (HEADSpAcE) study**

The HEADSpAcE study is a project that is funded by the European Union Horizon 2020 programme that brings together a consortium of 15 institutions in the study of head and neck cancer from January 2019 (International Agency for Research on Cancer, 2021). The HEADSpAcE study will aim to determine the reasons for the late stage at diagnosis of people with head and neck cancer, and in particular aims to determine the most appropriate method of diagnosing HPV-positive head and neck cancer. In addition, the study aims to provide genomic evidence of predictors of outcomes of people with head and neck cancer, with the aim to improve care and reduce treatment-related morbidity. The HEADSpAcE study will provide a unique opportunity to explore the underlying causes of inequality in survival of people with head and neck cancer across the globe, including considering various genomic factors. Importantly, a planned workstream will focus on inequalities in late stage of diagnosis, and health care system factors associated with late-stage diagnosis. However, this study is going to be fundamentally impacted by the COVID-19 pandemic.

**Between- and within-country comparisons of lower income regions across the globe**

Despite the burden of both incidence and mortality of head and neck cancers being greatest in lower income countries, particularly in South East Asia (Ferlay *et al.*, 2020), there is a lack of research on head and neck cancer survival or outcomes from this part of the world. Inequalities between countries exist and are well recognised (International Agency for Research on Cancer, 2019), and further research needs to be undertaken to investigate inequalities in survival in these regions of the globe, and between countries across the world.

## 6.7 Conclusions

This thesis has examined socioeconomic inequality in survival of people with head and neck cancer. First, a thorough literature review was conducted to frame the rationale for the thesis, which included studies that investigated inequality in survival of people with head and neck cancer in the UK, Europe, the Americas, and other parts of the globe. Collectively, it was evident that inequality in survival for people with head and neck cancer existed. However, few studies explored the potential underlying explanatory factors for inequality in survival of people with head and neck cancer, namely, as per factors that might be more modifiable (for example, through behaviours such as smoking and alcohol) compared with factors that might be less amenable to control (for example, tumour site, stage, and treatment regimens). No study previously aimed to pinpoint the exact potential underlying causes of inequality in survival of people with head and neck cancer, and no study in the UK explored socioeconomic inequality in survival by utilising individual measurements of socioeconomic status or by using the IARC recommended measurements for inequality such as the SII or the RII.

The thesis studied socioeconomic inequality in survival of people with head and neck cancer in the UK using data from three sources – the Scottish Cancer Registry, the SAHNC cohort study, and the HN5000 cohort study of people in England. As a whole, this thesis reported that inequality in survival of people with head and neck cancer is a persistent problem, a problem which seems to be getting worse – despite general improvements in head and neck cancer survival. Moreover, the main premise of this thesis was to explore explanatory factors of socioeconomic inequality in survival of people with head and neck cancer. Although socioeconomic inequality in survival utilising an area-based measurement of socioeconomic status was explained by various underlying factors, inequality by annual household income and the proportion of income from benefits only attenuated following the adjustment of all potential explanatory factors for patients in England. However, even after full adjustment, inequality in survival by annual household income and the proportion of income from benefits could not be explained by any of the potential underlying factors that were included in this study. Therefore, further investigations considering individual measurements of patients' income following a diagnosis of cancer should be conducted.

In addition, a number of recommendations were drawn including in relation to developing and evaluating welfare benefit services and preventative services within multidisciplinary teams; further upstream action on smoking, alcohol, and underlying socioeconomic policies; and in a number of directions for future research that are worth considering.

This thesis has provided a comprehensive examination of socioeconomic inequalities in survival of people with head and neck cancer – a relatively underexplored field. The research involved in-depth analyses of multiple datasets and from a number of perspectives. It has shown that inequalites in survival are a substantial and growing problem, and has endeavored to explore the explanatory factors. This work provides a platfrom through which policy and practice development, along with evaluation and research, can be based to reduce inequalities in survival and improve outcomes for people who are diagnosed with head and neck cancer.

# Appendices

**Appendix 1.1 – Ethical approval letter for this PhD from the University of Glasgow College of Medicine, Veterinary and Life Science Research Ethics Committee**

University of Glasgow

**01/08/2016**

**MVLS College Ethics Committee**

***Project Title: Inequalities in head and neck cancer survival***
***Project No: 200150181***

Dear Professor Conway

The College Ethics Committee has reviewed your application and has agreed that there is no objection on ethical grounds to the proposed study. It is happy therefore to approve the project subject to the following conditions.

- Project end date: End June 2018
- The data should be held securely for a period of ten years after the completion of the research project, or for longer if specified by the research funder or sponsor, in accordance with the University's Code of Good Practice in Research: (http://www.gla.ac.uk/media/media_227599_en.pdf)
- The research should be carried out only on the sites, and/or with the groups defined in the application.
- Any proposed changes in the protocol should be submitted for reassessment, except when it is necessary to change the protocol to eliminate hazard to the subjects or where the change involves only the administrative aspects of the project. The Ethics Committee should be informed of any such changes.
- You should submit a short end of study report to the Ethics Committee within 3 months of completion.

Yours sincerely,

**Appendix 1.2 – Anatomical subsites of the head and neck based on ICD-10 Version 2010**

| Main site<br>Subsite | ICD-10<br>Code |
|---|---|
| **Malignant neoplasms of lip** | **C00** |
| External upper lip | C00.0 |
| External lower lip | C00.1 |
| External lip, unspecified | C00.2 |
| Upper lip, inner aspect | C00.3 |
| Lower lip, inner aspect | C00.4 |
| Lip, unspecified, inner aspect | C00.5 |
| Commissure of lip | C00.6 |
| Overlapping lesion of lip | C00.8 |
| Lip, unspecified | C00.9 |
| **Malignant neoplasm of base of tongue** | **C01** |
| **Malignant neoplasm of other and unspecified part of tongue** | **C02** |
| Dorsal surface of tongue | C02.2 |
| Border of tongue | C02.1 |
| Ventral surface of tongue | C02.2 |
| Anterior two-thirds of tongue, part unspecified | C02.3 |
| Lingual tonsil | C02.4 |
| Overlapping lesion of tongue | C02.8 |
| Tongue, unspecified | C02.9 |
| **Malignant neoplasm of gum** | **C03** |
| Upper gum | C03.0 |
| Lower gum | C03.1 |
| Gum, unspecified | C03.9 |
| **Malignant neoplasm of floor of mouth** | **C04** |
| Anterior floor of mouth | C04.0 |
| Lateral floor of mouth | C04.1 |
| Overlapping lesion of floor of mouth | C04.8 |
| Floor of mouth, unspecified | C04.9 |
| **Malignant neoplasm of palate** | **C05** |
| Hard palate | C05.0 |
| Soft palate | C05.1 |
| Uvula | C05.2 |
| Overlapping lesion of palate | C05.8 |
| Palate, unspecified | C05.9 |
| **Malignant neoplasm of other and unspecified parts of mouth** | **C06** |
| Cheek mucosa | C06.0 |
| Vestibule of mouth | C06.1 |
| Retromolar area | C06.2 |
| Overlapping lesion of other and unspecified parts of mouth | C06.8 |
| Mouth, unspecified | C06.9 |
| **Malignant neoplasm of parotid gland** | **C07** |
| **Malignant neoplasm of other and unspecified major salivary glands** | **C08** |
| Submandibular gland | C08.0 |
| Sublingual gland | C08.1 |
| Overlapping lesion of major salivary glands | C08.8 |
| Major salivary glands, unspecified | C08.9 |
| **Malignant neoplasm of tonsil** | **C09** |
| Tonsillar fossa | C09.0 |
| Tonsilla pillar (anterior)(posterior) | C09.1 |
| Overlapping lesion of tonsil | C09.8 |
| Tonsil, unspecified | C09.9 |
| **Malignant neoplasm of oropharynx** | **C10** |
| Vallecula | C10.0 |
| Anterior surface of epiglottis | C10.1 |
| Lateral wall of oropharynx | C10.2 |
| Posterior wall of oropharynx | C10.3 |
| Branchial cleft | C10.4 |
| Overlapping lesion of oropharynx | C10.8 |
| Oropharynx, unspecified | C10.9 |
| **Malignant neoplasm of nasopharynx** | **C11** |
| Superior wall of nasopharynx | C11.0 |
| Posterior wall of nasopharynx | C11.1 |
| Lateral wall of nasopharynx | C11.2 |
| Anterior wall of nasopharynx | C11.3 |
| Overlapping lesion of nasopharynx | C11.8 |
| Nasopharynx, unspecified | C11.9 |

**Appendix 1.1 continued**

| | |
|---|---|
| **Malignant neoplasm of piriform sinus** | **C12** |
| **Malignant neoplasm of hypopharynx** | **C13** |
| Postcricoid region | C13.0 |
| Aryepiglottic fold, hypopharyngeal aspect | C13.1 |
| Posterior wall of hypopharynx | C13.2 |
| Overlapping lesion of hypopharynx | C13.8 |
| Hypopharynx, unspecified | C13.9 |
| **Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx** | **C14** |
| Pharynx, unspecified | C14.0 |
| Waldeyer ring | C14.2 |
| Overlapping lesion of lip, oral cavity, and pharynx | C14.9 |
| **Malignant neoplasm of nasal cavity and middle ear** | **C30** |
| Nasal cavity | C30.0 |
| Middle ear | C30.1 |
| **Malignant neoplasm of accessory sinuses** | **C31** |
| Maxillary sinus | C31.0 |
| Ethmoidal sinus | C31.1 |
| Frontal sinus | C31.2 |
| Sphenoidal sinus | C31.3 |
| Overlapping lesion of accessory sinus | C31.8 |
| Accessory sinus, unspecified | C31.9 |
| **Malignant neoplasm of larynx** | **C32** |
| Glottis | C32.0 |
| Supraglottis | C32.1 |
| Subglottis | C32.2 |
| Laryngeal cartilage | C32.3 |
| Overlapping lesion of larynx | C32.8 |
| Larynx, unspecified | C32.9 |
| **Malignant neoplasm of other and ill-defined sites** | **C76** |
| Head, face and neck | C76.0 |

**Appendix 1.3 – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| Author | Country | Data origin | Sample size | Site included | Time period | Survival measurement | SES measurement | Key findings |
|---|---|---|---|---|---|---|---|---|
| Edwards and Jones (1999) | England, UK | Registry data | 25,903 | All head and neck cancer | 1984-1993 | Crude and cause-specific | Carstairs 1991 Category | Deprivation had an independent effect on survival. |
| Coleman *et al.* (2001) | England and Wales, UK | Registry data | 8,671 | Larynx (males and females) | 1971-1990 | Relative survival | Carstairs 1991 Category | A gap of 9.3% in relative survival between those from the least and most deprived areas, in favour of the patients from the least deprived area. |
| Paterson *et al.* (2002) | England and Wales, UK | Registry data | 20,131 | All head and neck cancer | 1981-1994 | Relative survival | Carstairs 1991 Category | Survival was substantially worse for those from the most deprived areas, but not for the patients who were below 39 years. |
| Coleman *et al.* (2004) | England and Wales, UK | Registry data | 5,666 | Larynx (males) | 1986-1999 | Relative survival | Carstairs 1995 Category and IMD/WIMD Category | Deprivation gap of 17% in favour of the least deprived, which was the highest of all cancers included in the study. |
| Shack *et al.* (2007) | Scotland, UK | Registry data | 1,128 | Larynx (males) | 1986-2000 | Relative survival | Carstairs 1995 Category and SIMD Categories | Deprivation gap was 11% and became wider by approximately 3% every five years. |
| Warnakulasuriya *et al.* (2007) | England, UK | Registry data | 5,319 | Oral cavity | 1986-2002 | Unspecified survival | IMD Category | Difference in survival, favouring the less deprived group. However, socioeconomic inequality attenuated following adjustment for stage and treatment. |
| Rachet *et al.* (2008) | England and Wales, UK | Registry data | 5,666 | Larynx (males) | 1986-1999 | Relative survival | Carstairs 1995 Category and IMD/WIMD Category | Deeper look into earlier study which reported a deprivation gap of 17%. This study reported that this gap increased by 3.7% every five years. The gap in 10-year survival was also reported at 11%. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Anandan *et al.* (2008) | Scotland, UK | Registry data | 556 | Nasopharynx | 1975-2001 | Relative survival | Carstairs 1991 Category | Difference between those from the least deprived and most deprived areas, with survival in favour of those who were least deprived. |
| Robertson *et al.* (2010) | Scotland, UK | SAHNC | 1,901 | All head and neck cancer | 1999-2001 | Overall and disease-specific survival | Deprivation Category (DEPCAT) | The patients from the most deprived area experienced a 33% increased risk of all-cause mortality. However, following adjustment for WHO Performance Status, stage, age, anatomical site, smoking status and alcohol consumption, SES was no longer an independent predictor of survival. |
| Ellis *et al.* (2012) | England and Wales, UK | Registry data | 29,420 | Larynx (males and females) | 1991-2006 | Relative survival | IMD/WIMD Categories | No difference in survival between the least deprived and most deprived females. However, difference was much clearer for males with a deprivation gap of 7% and 13% after one and five years, respectively. |
| Rylands *et al.* (2016) | England, UK | Hospital records | 523 | Oral cavity | 2008-2012 | Overall survival | IMD Category | No gradient in survival across IMD quintiles. |
| Rosso *et al.* (1996) | Italy, Europe | Registry data | 568 | All head and neck cancer | 1985-1987 | Case fatality ratio | Education | No trend by education was apparent. |
| Boffetta *et al.* (1997) | Italy, Europe | Unclear | 355 | Larynx | 1979-1982 | Overall survival | Education and occupation | A statistically insignificant association between education level and survival following adjustment for anatomical site, stage, and smoking. |
| de Graeff *et al.* (2001) | The Netherlands, Europe | Unclear | 208 | All head and neck cancer | 1994-1996 | Overall survival | Income and occupation | A statistically insignificant association between family income and occupational with survival. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Andersen *et al.* (2008) | Denmark, Europe | Registry data | 4,857 | All head and neck cancer | 1994-2003 | Relative survival | Education, income, work market, social class, housing tenure, dwelling size, district type | Improved survival observed for most patients who had higher levels of education, higher levels of income, were homeowners and lived-in larger dwelling sizes. |
| Dalton *et al.* (2019) | Denmark, Europe | Registry data | 3,928 | All head and neck cancer | 1987-2013 | Relative survival | Household income the year prior to diagnosis | Improvement in survival more prominent in those who had higher income levels, particularly for those with cancer of the head and neck. Inequality in survival of people with head and cancer had increased over time. |
| Konski *et al.* (2003) | USA | RCT | 1,073 | All head and neck cancer - advanced stage | 1991-1997 | Overall survival | Neighbourhood-level: education status | Improved survival for those who had graduated from high school or had a general education diploma. |
| Chen and Halpern (2007) | USA | National Cancer Database | 7,019 | Larynx - advanced stage | 1995-1998 | All-cause mortality Cox models | Neighbourhood-level: percentage of high school graduates and median household income | No difference observed between those who resided in areas of lower or higher education or income level. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Molina *et al.* (2008) | Florida, USA | Florida Cancer Data System | 20,915 | All head and neck cancer | 1998-2002 | Overall survival | Neighbourhood-level: poverty | Area-based socioeconomic status was an independent predictor of survival following adjustment for participant demographics (age, gender, race, ethnicity, tobacco use and alcohol consumption), comorbidities, clinical characteristics (tumour grade, stage, and location of treatment) and treatment modality. |
| Chu *et al.* (2011) | California, USA | Registry data | 53,544 | All head and neck cancer | 1988-2007 | Median survival | Neighbourhood-level combined measurement of SES | Those who were of lower socioeconomic status were more at risk of cancer-specific deaths, and those with cancer of the oropharynx had the greatest difference in survival between the lowest and highest socioeconomic groups. This association continued to be significant after the adjustment for additional baseline covariates including stage, age, and year of diagnosis. |
| Reitzel *et al.* (2012) | Texas, USA | Hospital records | 1,151 | All head and neck cancer | 1996-2009 | Overall, disease-specific, and disease-free | Neighbourhood-level combined measurement of SES | For those with oropharyngeal cancer, a high level of neighbourhood deprivation was associated with poor overall survival even following the adjustment of additional covariates such as age, sex, stage, smoking status, and annual household income. |
| Guo *et al.* (2015) | Florida, USA | Florida Cancer Data System | 25,157 | All head and neck cancer | 1996-2010 | All-cause and disease-specific mortality | Neighbourhood-level: poverty | Following adjustment for demographic and clinical information, socioeconomic inequality remained between those who resided in the poorer areas of Florida, who had a substantially higher risk of all-cause and disease-specific mortality. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Megwalu (2017) | USA | SEER Database | 18,791 | Oropharynx | 2004-2012 | Overall and disease-specific survival | Neighbourhood-level: various measurements | Worse five-year overall and disease-specific survival was observed for people residing in areas with lower rates of high school completion, bachelor's degree completion, percentage of families living below the poverty line, high unemployment rates, low percentage of individuals working in white-collar professions and low socioeconomic indices. Multivariate analysis was performed which confirmed that this observation remained for people from low socioeconomic neighbourhoods following adjustment for age, sex, race, marital status, year of diagnosis, cancer site, stage, and treatment. |
| Xu *et al.* (2017) | USA | SEER Database | 37,995 | All head and neck cancer - non-metastatic | 2007-2012 | Overall and disease-specific survival | Neighbourhood-level: various measurements | Those who resided in areas of lower median income had a lower overall survival and disease-specific survival in multivariate analyses following the adjustment for age, sex, race, marital status, insurance status, cancer subsite, stage, and treatment. |
| Shin *et al.* (2017) | USA | National Cancer Database | 35,559 | Pharynx | 2004-2013 | All-cause mortality Cox models | Neighbourhood-level: median household income and high school diploma | Clear trend in survival across median household income groups – those who resided in areas of lower median household income had a lower overall survival than those who live in areas of higher median household incomes. The same trend was also apparent for those who resided in areas with a lower proportion high school diploma attainment. Following the adjustment for insurance status, race, comorbidity, cancer site and stage, the socioeconomic inequality no longer remained for either median household income or the proportion of people who attained a high school diploma. |

**Appendix 1.3 continued – Summary of all of the all studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Gaubatz *et al.* (2019) | USA | National Cancer Database | 260,035 | All head and neck cancer | 2004-2014 | All-cause mortality Cox models | Neighbourhood-level: median household income | The participants who resided in areas with lower median household income had poorer 90-day survival following adjustment for comorbidity, stage, tumour site, HPV status, facility type, waiting times for treatment and treatment type. |
| Mackillop *et al.* (1997) | Ontario, Canada | Registry data | 15,731 | All head and neck cancer | 1982-1991 | Overall survival | Median household income | Strong associations between income and overall survival for people with head and neck cancer, favouring those with higher levels of income. In addition, those who earned lower income also experienced higher rates of death. |
| Groome *et al.* (2006) | Ontario, Canada | Registry data | 1,156 | Larynx | 1982-1995 | Disease-specific survival | Average income areas | The authors reported cause-specific survival and discovered that the individuals with cancer of the glottis who resided in areas of lower income had substantially worse survival than those who were from areas of higher income. However, this difference was not clear for those with cancer of the supraglottic. |
| Booth *et al.* (2010) | Ontario, Canada | Registry data | 854 | Larynx | 2003-2007 | Overall survival and disease-specific survival | Median household income | Small difference across the median income groups for overall survival and disease-specific survival for those who were recorded in the Ontario Cancer Registry. Results for the individuals who were diagnosed in Regional Cancer Centres did not demonstrate substantial differences in overall and disease-specific survival across the median household income groups. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| McDonald *et al.* (2014) | Canada | Registry data | 30,228 | All head and neck cancer | 1992-2005 | Overall survival | Average household income | Lower income was strongly associated with worse survival outcomes for all those with head and neck cancer. Gap in socioeconomic inequality increased over time. |
| Auluck *et al.* (2016) | British Columbia, Canada | Registry data | 6,378 | Oral cavity and oropharynx | 1981-2009 | Disease-specific survival | Residential neighbourhood deprivation (VANDIX) | Significantly better disease-specific survival for men with cancer of the oropharynx who resided in affluent areas. |
| Chu *et al.* (2016) | Toronto, Canada | Hospital records | 2,124 | All head and neck cancer | 2003-2010 | Overall survival | Neighbourhood-level SES | Although low socioeconomic status was associated with poorer survival in a univariate model, it was no longer associated with poorer survival following the adjustment for other variables including age, gender, stage, comorbidity, smoking status, alcohol use and HPV type 16 status. |
| Lopez *et al.* (2011) | Brazil, South America | Hospital records | 455 | Oral cavity, oropharynx, larynx, and hypopharynx | 1998-2002 | All-cause mortality Cox models | Education | For people with cancer of the oral cavity, oropharynx, and hypopharynx the risk of death from head and neck cancer increased as the number of years the participant spent in education increased. However, the results were contrasting for those with cancer of the larynx since these people had a lower risk of disease-specific mortality as the number of years in education increased. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Abrahao *et al.* (2020) | Argentina, Brazil, Columbia, and Uruguay | InterCHANGE study | 1,463 | Larynx, hypopharynx, oral cavity, and oropharynx | 2011-2017 | All-cause mortality | Education | In a univariate Cox proportional hazards model, those who were "illiterate" were 44% more at risk of all-cause mortality compared to those with "superior" education levels (HR = 1.44, 95% CI = 0.63 to 3.32). However, in a multivariate model including age, sex, rate, cancer stage, smoking history, alcohol consumption and anatomical site, education level was no longer a predictor of survival. |
| Wong *et al.* (2006) | Taiwan | Hospital records | 1,010 | Oral cavity | 1995-2002 | Overall survival | Education level | No observed difference in survival between those who had varying levels of education. |
| Lee *et al.* (2012) | Taiwan | NHIRB | 3,607 | Oral cavity | 2005-2008 | Cumulative survival | Individual-level defined by the labour enrolee category as part of an insurance fee submission, and neighbourhood-level SES from the Taiwan census | Differences between the socioeconomically advantaged and disadvantaged groups, with survival favouring the advantaged groups. In addition, people of lower socioeconomic position remained at a higher risk of all-cause mortality following adjustment for age, gender, comorbidity, urbanisation, area of residence, treatment modality, hospital characteristics and year of diagnosis. |
| Chang *et al.* (2013) | Taiwan | NHIRB | 4,691 | Nasopharynx | 2002-2006 | Overall survival | Individual-level defined by the labour enrolee category as part of an insurance fee submission, and neighbourhood-level SES from the Taiwan census | Socioeconomic status remained a significant predictor of survival when adjusting by factors including age, gender, comorbidity, urbanisation, area of residence, treatment, and hospital characteristics. |

**Appendix 1.3 continued – Summary of all of the studies from the literature review on socioeconomic inequality in survival of people with head and neck cancer**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Chien *et al.* (2018) | Taiwan | NHIRB | 5,307 | Oral cavity, oropharynx, and larynx | 1992-2011 | Net survival | Income | The authors investigated five-year net survival proportions and reported that socioeconomic inequality existed for people with cancer of the larynx, oral cavity, and oropharynx. |
| Lai *et al.* (2018) | Taiwan | NHIRB | 40,985 | All head and neck cancer | 2000-2013 | Overall survival | Income | The authors reported that low income or living in residential areas of lower socioeconomic status had a detrimental effect on survival, regardless of the location in Taiwan that the person lived. |
| Yu *et al.* (2008) | Australia | Registry data | 6,331 | All head and neck cancer | 1992-2000 | Relative survival | Summary of education and occupational levels derived from the 1996 Census | The authors confirmed socioeconomic inequality in five-year relative survival for both men and women from an area-based measurement of socioeconomic status. |

**Appendix 2.1 – First letter of approval from the Public Benefit and Privacy Panel for Health and Social Care**

**Public Benefit and Privacy Panel for Health and Social Care**
nss.PBPP@nhs.net
www.informationgovernance.scot.nhs.uk

Miss Kate Ingarfiled
University of Glasgow Dental School
Community Oral Health
378 Sauchiehall Street
Glasgow
G2 3JZ

Date: 10th August 2016
Your Ref:
Our Ref: 1516-0611

Dear Miss Ingarfield

**Re: Application 1516-0611/Ingarfield: Inequalities in the survival of head and neck cancer patients**

Thank you for your application for consideration by the Public Benefit and Privacy Panel for Health and Social Care. Your application has undergone proportionate governance review and has been approved.

This approval is given to process data as specified in the approved application form, and is limited to this. Approval is valid for the period specified in your application. You are required to notify the Panel Manager of any proposed change to any aspect of your proposal, including purpose or method of processing, data or data variables being processed, study cohorts, individuals accessing and processing data, timescales, technology/infrastructure, or any other relevant change.

I would take this opportunity to remind you of the declaration you have made in your application form committing you to undertakings in respect of information governance, confidentiality and data protection. In particular you should be aware that once personal data (irrespective of de-identification or other controls applied) has been extracted from NHSS Board(s) and transferred to you, that you will then become the Data Controller as defined by the Data Protection Act (1998).

Please note that summary information about your application and its approval, including the title and nature of your proposal, will be published on the panel website (www.informationgovernance.scot.nhs.uk).

I hope that your proposal progresses well,

Yours Sincerely

Ashley Gray
Panel Manager
NHS Scotland Public Benefit and Privacy Panel for Health and Social Care
Email: nss.PBPP@nhs.net

**Appendix 2.2 – Second letter of approval from the Public Benefit and Privacy Panel for Health and Social Care**

**Public Benefit and Privacy Panel for Health and Social Care**
nss.PBPP@nhs.net
www.informationgovernance.scot.nhs.uk

Miss Kate Ingarfiled
University of Glasgow Dental School
Community Oral Health
378 Sauchiehall Street
Glasgow
G2 3JZ

Date: 28th November 2017
Your Ref:
Our Ref: 1516-0611

Dear Miss Ingarfield

**Re: Application 1516-0611/Ingarfield: Inequalities in the survival of head and neck cancer patients**
**Version: V2**

Further to your approval issued by the Public Benefit and Privacy Panel for Health and Social Care on 10th August 2016 I am writing to confirm that we accept the amendment(s) to the proposal notified on 27th November 2017. The changes accepted are as follows:

- Extension of project duration; 30th April 2020
- Inclusion of Head & Neck Cancer Data from 1st April 2016 – 31st March 2017

Please note that any conditions attached to your original approval remain in place and you should continue to comply with those conditions outlined in the approval letter.

This approval is given to process data as specified in the approved application form, and is limited to this. Approval is valid for the period specified in your application. You are required to notify the Panel Manager of any proposed change to any aspect of your proposal, including purpose or method of processing, data or data variables being processed, study cohorts, individuals accessing and processing data, timescales, technology/infrastructure, or any other relevant change.

I would take this opportunity to remind you of the declaration you have made in your application form committing you to undertakings in respect of information governance, confidentiality and data protection. In particular you should be aware that once personal data (irrespective of de-identification or other controls applied) has been extracted from NHSS Board(s) and transferred to you, that you will then become the Data Controller as defined by the Data Protection Act (1998).

Yours Sincerely

Ashley Gray
Panel Manager
NHS Scotland Public Benefit and Privacy Panel for Health and Social Care
Email: nss.PBPP@nhs.net

**Appendix 2.3 – Baseline characteristics and proportion of deaths for males**

| Variable | Frequency (Column %) | Died by 30th September 2017 (Row %) |
|---|---|---|
| **Total** | 17,508 (100.0%) | 13,040 (74.5%) |
| **Age at incidence** | | |
| Less than 45 | 903 (5.2%) | 395 (43.7%) |
| 45 to 54 | 3,212 (18.3%) | 1,992 (62.0%) |
| 55 to 64 | 5,694 (32.5%) | 4,126 (72.5%) |
| 65 to 74 | 5,008 (28.6%) | 4,081 (81.5%) |
| 75 and over | 2,691 (15.4%) | 2,446 (90.9%) |
| **ICD group** | | |
| Oral cavity | 5,162 (29.5%) | 3,849 (74.6%) |
| Larynx | 6,133 (35.0%) | 4,632 (75.5%) |
| Oropharynx | 2,437 (13.9%) | 1,569 (64.4%) |
| Hypopharynx | 1,190 (6.8%) | 1,084 (91.1%) |
| Lip | 1,009 (5.8%) | 695 (68.9%) |
| Salivary gland | 603 (3.4%) | 409 (67.8%) |
| Other | 974 (5.6%) | 802 (82.3%) |
| **Pathology** | | |
| SCC | 15,448 (88.2%) | 11,570 (74.9%) |
| Non-SCC | 2,060 (11.8%) | 1,470 (71.4%) |
| **Treatment** | | |
| Surgery only | 2,823 (16.1%) | 1,507 (53.4%) |
| Radiotherapy only | 2,346 (13.4%) | 1,608 (68.5%) |
| Surgery and radiotherapy | 1,904 (10.9%) | 1,362 (71.5%) |
| Chemoradiotherapy | 1,873 (10.7%) | 1,125 (60.1%) |
| Surgery and chemoradiotherapy | 1,147 (6.6%) | 647 (56.4%) |
| Chemotherapy +/- surgery | 403 (2.3%) | 323 (80.1%) |
| No treatment | 1,211 (6.9%) | 1,130 (93.3%) |
| Unknown | 5,801 (33.1%) | 5,338 (92.0%) |
| **Year group** | | |
| 1986-1990 | 2,280 (13.0%) | 2,154 (94.5%) |
| 1991-1995 | 2,694 (15.4%) | 2,468 (91.6%) |
| 1996-2000 | 2,925 (16.7%) | 2,516 (86.0%) |
| 2001-2005 | 2,962 (16.9%) | 2,270 (76.6%) |
| 2006-2010 | 3,202 (18.3%) | 2,056 (64.2%) |
| 2011-2015 | 3,445 (19.7%) | 1,576 (45.7%) |
| **Network of residence** | | |
| West of Scotland (WoSCAN) | 9,095 (51.9%) | 7,016 (77.1%) |
| East of Scotland (SCAN) | 4,311 (24.6%) | 3,055 (70.9%) |
| North of Scotland (NOSCAN) | 4,102 (23.4%) | 2,969 (72.4%) |
| **Carstairs 1991 Category** | | |
| 1 – Least deprived | 2,506 (14.3%) | 1,686 (67.3%) |
| 2 | 3,109 (17.8%) | 2,201 (70.8%) |
| 3 | 3,403 (19.4%) | 2,527 (74.3%) |
| 4 | 3,720 (21.2%) | 2,801 (75.3%) |
| 5 – Most deprived | 4,770 (27.2%) | 3,825 (80.2%) |

**Appendix 2.4 – Baseline characteristics and proportion of deaths for females**

| Variable | Frequency (Column %) | Died by 30th September 2017 (Row %) |
|---|---|---|
| **Total** | 7,270 (100.0%) | 5,282 (72.7%) |
| **Age at incidence** | | |
| Less than 45 | 479 (6.6%) | 146 (30.5%) |
| 45 to 54 | 1,026 (14.1%) | 561 (54.7%) |
| 55 to 64 | 1,907 (26.2%) | 1,292 (67.8%) |
| 65 to 74 | 1,980 (27.2%) | 1,582 (79.9%) |
| 75 and over | 1,878 (25.8%) | 1,701 (90.6%) |
| **ICD group** | | |
| Oral cavity | 3,027 (41.6%) | 2,179 (72.0%) |
| Larynx | 1,573 (21.6%) | 1,222 (77.7%) |
| Oropharynx | 942 (13.0%) | 635 (67.4%) |
| Hypopharynx | 396 (5.4%) | 363 (91.7%) |
| Lip | 370 (5.1%) | 253 (68.4%) |
| Salivary gland | 572 (7.9%) | 311 (54.4%) |
| Other | 390 (5.4%) | 319 (81.8%) |
| **Pathology** | | |
| SCC | 5,955 (81.9%) | 4,473 (75.1%) |
| Non-SCC | 1,315 (18.1%) | 809 (61.5%) |
| **Treatment** | | |
| Surgery only | 1,561 (21.5%) | 771 (49.4%) |
| Radiotherapy only | 750 (10.3%) | 553 (73.7%) |
| Surgery and radiotherapy | 858 (11.8%) | 555 (64.7%) |
| Chemoradiotherapy | 539 (7.4%) | 305 (56.6%) |
| Surgery and chemoradiotherapy | 355 (4.9%) | 185 (52.1%) |
| Chemotherapy +/- surgery | 149 (2.0%) | 116 (77.9%) |
| No treatment | 617 (8.5%) | 597 (96.8%) |
| Unknown | 2,441 (33.6%) | 2,200 (90.1%) |
| **Year group** | | |
| 1986-1990 | 977 (13.4%) | 879 (90.0%) |
| 1991-1995 | 1,066 (14.7%) | 978 (91.7%) |
| 1996-2000 | 1,226 (16.9%) | 1,035 (84.4%) |
| 2001-2005 | 1,264 (17.4%) | 942 (74.5%) |
| 2006-2010 | 1,317 (18.1%) | 819 (62.2%) |
| 2011-2015 | 1,420 (19.5%) | 629 (44.3%) |
| **Network of residence** | | |
| West of Scotland (WoSCAN) | 3,755 (51.7%) | 2,818 (75.0%) |
| East of Scotland (SCAN) | 1,843 (25.4%) | 1,307 (70.9%) |
| North of Scotland (NOSCAN) | 1,672 (23.0%) | 1,157 (69.2%) |
| **Carstairs 1991 Category** | | |
| 1 – Least deprived | 1,117 (15.4%) | 722 (64.6%) |
| 2 | 1,378 (19.0%) | 979 (71.0%) |
| 3 | 1,415 (19.5%) | 1,023 (72.3%) |
| 4 | 1,536 (21.1%) | 1,149 (74.8%) |
| 5 – Most deprived | 1,824 (25.1%) | 1,409 (77.2%) |

**Appendix 2.5 – Baseline characteristics and proportion of deaths for people with cancer of the oral cavity**

| Variable | Frequency (Column %) | Died by 30th September 2017 (Row %) |
|---|---|---|
| **Total** | 8,189 (100.0%) | 6,028 (73.6%) |
| **Age at incidence** | | |
| Less than 45 | 508 (6.2%) | 220 (43.3%) |
| 45 to 54 | 1,481 (18.1%) | 930 (62.8%) |
| 55 to 64 | 2,438 (29.8%) | 1,717 (70.4%) |
| 65 to 74 | 2,191 (26.8%) | 1,738 (79.3%) |
| 75 and over | 1,571 (19.2%) | 1,423 (90.6%) |
| **Sex** | | |
| Male | 5,162 (63.0%) | 3,849 (74.6%) |
| Female | 3,027 (37.0%) | 2,179 (72.0%) |
| **Pathology** | | |
| SCC | 7,397 (90.3%) | 5,498 (74.3%) |
| Non-SCC | 792 (9.7%) | 530 (66.9%) |
| **Treatment** | | |
| Surgery only | 2,327 (28.4%) | 1,182 (50.8%) |
| Radiotherapy only | 424 (5.2%) | 373 (88.0%) |
| Surgery and radiotherapy | 1,014 (12.4%) | 758 (74.8%) |
| Chemoradiotherapy | 579 (7.1%) | 315 (54.4%) |
| Surgery and chemoradiotherapy | 524 (6.4%) | 321 (61.3%) |
| Chemotherapy +/- surgery | 161 (2.0%) | 127 (78.9%) |
| No treatment | 638 (7.8%) | 613 (96.1%) |
| Unknown | 2,522 (30.8%) | 2,339 (92.7%) |
| **Year group** | | |
| 1986-1990 | 954 (11.6%) | 906 (95.0%) |
| 1991-1995 | 1,177 (14.4%) | 1,092 (92.8%) |
| 1996-2000 | 1,319 (16.1%) | 1,151 (87.3%) |
| 2001-2005 | 1,460 (17.8%) | 1,110 (76.0%) |
| 2006-2010 | 1,597 (19.5%) | 1,016 (63.6%) |
| 2011-2015 | 1,682 (20.5%) | 753 (44.8%) |
| **Network of residence** | | |
| West of Scotland (WoSCAN) | 4,208 (51.4%) | 3,197 (76.0%) |
| East of Scotland (SCAN) | 2,060 (25.2%) | 1,465 (71.1%) |
| North of Scotland (NOSCAN) | 1,921 (23.5%) | 1,366 (71.1%) |
| **Carstairs 1991 Category** | | |
| 1 – Least deprived | 1,278 (15.6%) | 840 (65.7%) |
| 2 | 1,520 (18.6%) | 1,061 (69.8%) |
| 3 | 1,575 (19.2%) | 1,150 (73.0%) |
| 4 | 1,714 (20.9%) | 1,301 (75.9%) |
| 5 – Most deprived | 2,102 (25.7%) | 1,676 (79.7%) |

**Appendix 2.6 – Baseline characteristics and proportion of deaths for people with cancer of the oropharynx**

| Variable | Frequency (Column %) | Died by 30th September 2017 (Row %) |
|---|---|---|
| **Total** | 3,379 (100.0%) | 2,204 (65.2%) |
| **Age at incidence** | | |
| Less than 45 | 209 (6.2%) | 79 (37.8%) |
| 45 to 54 | 860 (25.5%) | 427 (49.7%) |
| 55 to 64 | 1,202 (35.6%) | 783 (65.1%) |
| 65 to 74 | 779 (23.1%) | 616 (79.1%) |
| 75 and over | 329 (9.7%) | 299 (90.9%) |
| **Sex** | | |
| Male | 2,437 (72.1%) | 1,569 (64.4%) |
| Female | 942 (27.9%) | 635 (67.4%) |
| **Pathology** | | |
| SCC | 3,010 (89.1%) | 2,005 (66.6%) |
| Non-SCC | 369 (10.9%) | 199 (53.9%) |
| **Treatment** | | |
| Surgery only | 319 (9.4%) | 173 (54.2%) |
| Radiotherapy only | 373 (11.0%) | 277 (74.3%) |
| Surgery and radiotherapy | 384 (11.4%) | 232 (60.4%) |
| Chemoradiotherapy | 694 (20.5%) | 338 (48.7%) |
| Surgery and chemoradiotherapy | 512 (15.2%) | 166 (32.4%) |
| Chemotherapy +/- surgery | 124 (3.7%) | 90 (72.6%) |
| No treatment | 253 (7.5%) | 249 (98.4%) |
| Unknown | 720 (21.3%) | 679 (94.3%) |
| **Year group** | | |
| 1986-1990 | 272 (8.0%) | 258 (94.9%) |
| 1991-1995 | 332 (9.8%) | 316 (95.2%) |
| 1996-2000 | 468 (13.9%) | 396 (84.6%) |
| 2001-2005 | 541 (16.0%) | 396 (73.2%) |
| 2006-2010 | 751 (22.2%) | 446 (59.4%) |
| 2011-2015 | 1,015 (30.0%) | 392 (38.6%) |
| **Network of residence** | | |
| West of Scotland (WoSCAN) | 1,686 (49.9%) | 1,163 (69.0%) |
| East of Scotland (SCAN) | 855 (25.3%) | 529 (61.9%) |
| North of Scotland (NOSCAN) | 838 (24.8%) | 512 (61.1%) |
| **Carstairs 1991 Category** | | |
| 1 – Least deprived | 511 (15.1%) | 289 (56.6%) |
| 2 | 647 (19.1%) | 390 (60.3%) |
| 3 | 645 (19.1%) | 414 (64.2%) |
| 4 | 703 (20.8%) | 473 (67.3%) |
| 5 – Most deprived | 873 (25.8%) | 638 (73.1%) |

**Appendix 2.7 – Baseline characteristics and proportion of deaths for people with cancer of the larynx**

| Variable | Frequency (Column %) | Died by 30th September 2017 (Row %) |
|---|---|---|
| **Total** | 7,706 (100.0%) | 5,854 (76.0%) |
| **Age at incidence** | | |
| Less than 45 | 210 (2.7%) | 96 (45.7%) |
| 45 to 54 | 1,123 (14.6%) | 704 (62.7%) |
| 55 to 64 | 2,513 (32.6%) | 1,817 (72.3%) |
| 65 to 74 | 2,513 (32.6%) | 2,027 (80.7%) |
| 75 and over | 1,347 (17.5%) | 1,210 (89.8%) |
| **Sex** | | |
| Male | 6,133 (79.6%) | 4,632 (75.5%) |
| Female | 1,573 (20.4%) | 1,222 (77.7%) |
| **Pathology** | | |
| SCC | 7,076 (91.8%) | 5,305 (75.0%) |
| Non-SCC | 630 (8.2%) | 549 (87.1%) |
| **Treatment** | | |
| Surgery only | 671 (8.7%) | 376 (56.0%) |
| Radiotherapy only | 1,914 (24.8%) | 1,169 (61.1%) |
| Surgery and radiotherapy | 844 (11.0%) | 583 (69.1%) |
| Chemoradiotherapy | 507 (6.6%) | 331 (65.3%) |
| Surgery and chemoradiotherapy | 242 (3.1%) | 179 (74.0%) |
| Chemotherapy +/- surgery | 104 (1.3%) | 86 (82.7%) |
| No treatment | 493 (6.4%) | 435 (88.2%) |
| Unknown | 2,931 (38.0%) | 2,695 (91.9%) |
| **Year group** | | |
| 1986-1990 | 1,131 (14.7%) | 1,075 (95.0%) |
| 1991-1995 | 1,345 (17.5%) | 1,230 (91.4%) |
| 1996-2000 | 1,392 (18.1%) | 1,189 (85.4%) |
| 2001-2005 | 1,320 (17.1%) | 1,009 (76.4%) |
| 2006-2010 | 1,303 (16.9%) | 812 (62.3%) |
| 2011-2015 | 1,215 (15.8%) | 539 (44.4%) |
| **Network of residence** | | |
| West of Scotland (WoSCAN) | 4,227 (54.9%) | 3,296 (78.0%) |
| East of Scotland (SCAN) | 1,932 (25.1%) | 1,397 (72.3%) |
| North of Scotland (NOSCAN) | 1,547 (20.1%) | 1,161 (75.0%) |
| **Carstairs 1991 Category** | | |
| 1 – Least deprived | 938 (12.2%) | 668 (71.2%) |
| 2 | 1,245 (16.2%) | 938 (75.3%) |
| 3 | 1,513 (19.6%) | 1,135 (75.0%) |
| 4 | 1,699 (22.0%) | 1,275 (75.0%) |
| 5 – Most deprived | 2,311 (30.0%) | 1,838 (79.5%) |

**Appendix 2.8 – Cross-tabulation of Carstairs 1991 Category with baseline characteristics for males**

| Variable | Carstairs 1991 Category (row %) | | | | | Chi-sq. p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Age at incidence** | | | | | | <0.001 |
| Less than 45 | 142 (5.7%) | 167 (5.4%) | 174 (5.1%) | 188 (5.1%) | 232 (4.9%) | |
| 45 to 54 | 417 (16.6%) | 530 (17.0%) | 595 (17.5%) | 694 (18.7%) | 976 (20.5%) | |
| 55 to 64 | 721 (28.8%) | 983 (31.6%) | 1,124 (33.0%) | 1,256 (33.8%) | 1,610 (33.8%) | |
| 65 to 74 | 715 (28.5%) | 899 (28.9%) | 957 (28.1%) | 1,087 (29.2%) | 1,350 (28.3%) | |
| 75 and over | 511 (20.4%) | 530 (17.0%) | 553 (16.3%) | 495 (13.3%) | 602 (12.6%) | |
| **ICD group** | | | | | | <0.001 |
| Oral cavity | 760 (30.3%) | 885 (28.5%) | 973 (28.6%) | 1,086 (29.2%) | 1,458 (30.6%) | |
| Larynx | 789 (31.5%) | 1021 (32.8%) | 1219 (35.8%) | 1,329 (35.7%) | 1,775 (37.2%) | |
| Oropharynx | 363 (14.5%) | 456 (14.7%) | 457 (13.4%) | 531 (14.3%) | 630 (13.2%) | |
| Hypopharynx | 151 (6.0%) | 202 (6.5%) | 212 (6.2%) | 290 (7.8%) | 335 (7.0%) | |
| Lip | 181 (7.2%) | 251 (8.1%) | 239 (7.0%) | 185 (5.0%) | 153 (3.2%) | |
| Salivary gland | 138 (5.5%) | 128 (4.1%) | 119 (3.5%) | 109 (2.9%) | 109 (2.3%) | |
| Other | 124 (4.9%) | 166 (5.3%) | 184 (5.4%) | 190 (5.1%) | 310 (6.5%) | |
| **Pathology** | | | | | | <0.001 |
| SCC | 2,134 (85.2%) | 2,714 (87.3%) | 2,997 (88.1%) | 3,337 (89.7%) | 4,266 (89.4%) | |
| Non-SCC | 372 (14.8%) | 395 (12.7%) | 406 (11.9%) | 383 (10.3%) | 504 (10.6%) | |
| **Treatment** | | | | | | <0.001 |
| Surgery only | 441 (17.6%) | 580 (18.7%) | 573 (16.8%) | 576 (15.5%) | 653 (13.7%) | |
| Radiotherapy only | 381 (15.2%) | 376 (12.1%) | 459 (13.5%) | 500 (13.4%) | 630 (13.2%) | |
| Surgery and radiotherapy | 299 (11.9%) | 386 (12.4%) | 380 (11.2%) | 385 (10.3%) | 454 (9.5%) | |
| Chemoradiotherapy | 232 (9.3%) | 327 (10.5%) | 352 (10.3%) | 433 (11.6%) | 529 (11.1%) | |
| Surgery and chemoradiotherapy | 198 (7.9%) | 238 (7.7%) | 214 (6.3%) | 237 (6.4%) | 260 (5.5%) | |
| Chemotherapy +/- surgery | 52 (2.1%) | 52 (1.7%) | 93 (2.7%) | 82 (2.2%) | 124 (2.6%) | |
| No treatment | 142 (5.7%) | 172 (5.5%) | 224 (6.6%) | 253 (6.8%) | 420 (8.8%) | |
| Unknown | 761 (30.4%) | 978 (31.5%) | 1,108 (32.6%) | 1,254 (33.7%) | 1,700 (35.6%) | |
| **Network** | | | | | | <0.001 |
| West of Scotland (WoSCAN) | 845 (33.7%) | 963 (31.0%) | 1,360 (40.0%) | 1,926 (51.8%) | 4,001 (83.9%) | |
| East of Scotland (SCAN) | 703 (28.1%) | 1,001 (32.2%) | 1,080 (31.7%) | 1,204 (32.4%) | 323 (6.8%) | |
| North of Scotland (NOSCAN) | 958 (38.2%) | 1145 (36.8%) | 963 (28.3%) | 590 (15.9%) | 446 (9.4%) | |

**Appendix 2.9 – Cross-tabulation of Carstairs 1991 Category with baseline characteristics for females**

| Variable | Carstairs 1991 Category (row %) | | | | | Chi-sq. p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Age at incidence** | | | | | | <0.001 |
| Less than 45 | 90 (8.1%) | 91 (6.6%) | 91 (6.4%) | 97 (6.3%) | 110 (6.0%) | |
| 45 to 54 | 148 (13.2%) | 175 (12.7%) | 198 (14.0%) | 202 (13.2%) | 303 (16.6%) | |
| 55 to 64 | 256 (22.9%) | 335 (24.3%) | 356 (25.2%) | 437 (28.5%) | 523 (28.7%) | |
| 65 to 74 | 306 (27.4%) | 379 (27.5%) | 378 (26.7%) | 409 (26.6%) | 508 (27.9%) | |
| 75 and over | 317 (28.4%) | 398 (28.9%) | 392 (27.7%) | 391 (25.5%) | 380 (20.8%) | |
| **ICD group** | | | | | | <0.001 |
| Oral cavity | 518 (46.4%) | 635 (46.1%) | 602 (42.5%) | 628 (40.9%) | 644 (35.3%) | |
| Larynx | 149 (13.3%) | 224 (16.3%) | 294 (20.8%) | 370 (24.1%) | 536 (29.4%) | |
| Oropharynx | 148 (13.2%) | 191 (13.9%) | 188 (13.3%) | 172 (11.2%) | 243 (13.3%) | |
| Hypopharynx | 49 (4.4%) | 72 (5.2%) | 62 (4.4%) | 89 (5.8%) | 124 (6.8%) | |
| Lip | 77 (6.9%) | 73 (5.3%) | 84 (5.9%) | 77 (5.0%) | 59 (3.2%) | |
| Salivary gland | 126 (11.3%) | 118 (8.6%) | 122 (8.6%) | 100 (6.5%) | 106 (5.8%) | |
| Other | 50 (4.5%) | 65 (4.7%) | 63 (4.5%) | 100 (6.5%) | 112 (6.1%) | |
| **Pathology** | | | | | | <0.001 |
| SCC | 853 (76.4%) | 1,112 (80.7%) | 1,138 (80.4%) | 1,282 (83.5%) | 1,570 (86.1%) | |
| Non-SCC | 264 (23.6%) | 266 (19.3%) | 277 (19.6%) | 254 (16.5%) | 254 (13.9%) | |
| **Treatment** | | | | | | <0.001 |
| Surgery only | 291 (26.1%) | 293 (21.3%) | 333 (23.5%) | 338 (22.0%) | 306 (16.8%) | |
| Radiotherapy only | 86 (7.7%) | 136 (9.9%) | 146 (10.3%) | 172 (11.2%) | 210 (11.5%) | |
| Surgery and radiotherapy | 142 (12.7%) | 181 (13.1%) | 174 (12.3%) | 152 (9.9%) | 209 (11.5%) | |
| Chemoradiotherapy | 63 (5.6%) | 106 (7.7%) | 103 (7.3%) | 119 (7.7%) | 148 (8.1%) | |
| Surgery and chemoradiotherapy | 64 (5.7%) | 72 (5.2%) | 76 (5.4%) | 68 (4.4%) | 75 (4.1%) | |
| Chemotherapy +/- surgery | 14 (1.3%) | 26 (1.9%) | 26 (1.8%) | 32 (2.1%) | 51 (2.8%) | |
| No treatment | 91 (8.1%) | 116 (8.4%) | 125 (8.8%) | 127 (8.3%) | 158 (8.7%) | |
| Unknown | 366 (32.8%) | 448 (32.5%) | 432 (30.5%) | 528 (34.4%) | 667 (36.6%) | |
| **Network** | | | | | | <0.001 |
| West of Scotland (WoSCAN) | 377 (33.8%) | 431 (31.3%) | 570 (40.3%) | 811 (52.8%) | 1,566 (85.9%) | |
| East of Scotland (SCAN) | 305 (27.3%) | 488 (35.4%) | 451 (31.9%) | 482 (31.4%) | 117 (6.4%) | |
| North of Scotland (NOSCAN) | 435 (38.9%) | 459 (33.3%) | 394 (27.8%) | 243 (15.8%) | 141 (7.7%) | |

**Appendix 2.10 – Cross-tabulation of Carstairs 1991 Category with baseline characteristics for people with cancer of the oral cavity**

| Variable | Carstairs 1991 Category (row %) | | | | | Chi-sq. p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Age at incidence** | | | | | | <0.001 |
| Less than 45 | 77 (6.0%) | 99 (6.5%) | 107 (6.8%) | 109 (6.4%) | 116 (5.5%) | |
| 45 to 54 | 218 (17.1%) | 235 (15.5%) | 293 (18.6%) | 293 (17.1%) | 442 (21.0%) | |
| 55 to 64 | 362 (28.3%) | 435 (28.6%) | 446 (28.3%) | 535 (31.2%) | 660 (31.4%) | |
| 65 to 74 | 330 (25.8%) | 426 (28.0%) | 417 (26.5%) | 451 (26.3%) | 567 (27.0%) | |
| 75 and over | 291 (22.8%) | 325 (21.4%) | 312 (19.8%) | 326 (19.0%) | 317 (15.1%) | |
| **Sex** | | | | | | <0.001 |
| Male | 760 (59.5%) | 885 (58.2%) | 973 (61.8%) | 1,086 (63.4%) | 1,458 (69.4%) | |
| Female | 518 (40.5%) | 635 (41.8%) | 602 (38.2%) | 628 (36.6%) | 644 (30.6%) | |
| **Pathology** | | | | | | <0.001 |
| SCC | 1,136 (88.9%) | 1,360 (89.5%) | 1,402 (89.0%) | 1,545 (90.1%) | 1,954 (93.0%) | |
| Non-SCC | 142 (11.1%) | 160 (10.5%) | 173 (11.0%) | 169 (9.9%) | 148 (7.0%) | |
| **Treatment** | | | | | | <0.001 |
| Surgery only | 413 (32.3%) | 439 (28.9%) | 463 (29.4%) | 495 (28.9%) | 517 (24.6%) | |
| Radiotherapy only | 64 (5.0%) | 76 (5.0%) | 75 (4.8%) | 87 (5.1%) | 122 (5.8%) | |
| Surgery and radiotherapy | 155 (12.1%) | 204 (13.4%) | 208 (13.2%) | 202 (11.8%) | 245 (11.7%) | |
| Chemoradiotherapy | 78 (6.1%) | 106 (7.0%) | 114 (7.2%) | 127 (7.4%) | 154 (7.3%) | |
| Surgery and chemoradiotherapy | 101 (7.9%) | 100 (6.6%) | 102 (6.5%) | 107 (6.2%) | 114 (5.4%) | |
| Chemotherapy +/- surgery | 18 (1.4%) | 23 (1.5%) | 35 (2.2%) | 37 (2.2%) | 48 (2.3%) | |
| No treatment | 92 (7.2%) | 105 (6.9%) | 121 (7.7%) | 126 (7.4%) | 194 (9.2%) | |
| Unknown | 357 (27.9%) | 467 (30.7%) | 457 (29.0%) | 533 (31.1%) | 708 (33.7%) | |
| **Network** | | | | | | <0.001 |
| West of Scotland (WoSCAN) | 435 (34.0%) | 468 (30.8%) | 626 (39.7%) | 899 (52.5%) | 1,780 (84.7%) | |
| East of Scotland (SCAN) | 375 (29.3%) | 495 (32.6%) | 516 (32.8%) | 539 (31.4%) | 135 (6.4%) | |
| North of Scotland (NOSCAN) | 468 (36.6%) | 557 (36.6%) | 433 (27.5%) | 276 (16.1%) | 187 (8.9%) | |

**Appendix 2.11 – Cross-tabulation of Carstairs 1991 Category with baseline characteristics for people with cancer of the oropharynx**

| Variable | Carstairs 1991 Category (row %) | | | | | Chi-sq. p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Age at incidence** | | | | | | 0.45 |
| Less than 45 | 37 (7.2%) | 43 (6.6%) | 40 (6.2%) | 36 (5.1%) | 53 (6.1%) | |
| 45 to 54 | 121 (23.7%) | 167 (25.8%) | 170 (26.4%) | 161 (22.9%) | 241 (27.6%) | |
| 55 to 64 | 170 (33.3%) | 228 (35.2%) | 231 (35.8%) | 270 (38.4%) | 303 (34.7%) | |
| 65 to 74 | 125 (24.5%) | 141 (21.8%) | 137 (21.2%) | 172 (24.5%) | 204 (23.4%) | |
| 75 and over | 58 (11.4%) | 68 (10.5%) | 67 (10.4%) | 64 (9.1%) | 72 (8.2%) | |
| **Sex** | | | | | | 0.22 |
| Male | 363 (71.0%) | 456 (70.5%) | 457 (70.9%) | 531 (75.5%) | 630 (72.2%) | |
| Female | 148 (29.0%) | 191 (29.5%) | 188 (29.1%) | 172 (24.5%) | 243 (27.8%) | |
| **Pathology** | | | | | | <0.001 |
| SCC | 425 (83.2%) | 579 (89.5%) | 575 (89.1%) | 641 (91.2%) | 790 (90.5%) | |
| Non-SCC | 86 (16.8%) | 68 (10.5%) | 70 (10.9%) | 62 (8.8%) | 83 (9.5%) | |
| **Treatment** | | | | | | <0.001 |
| Surgery only | 42 (8.2%) | 66 (10.2%) | 63 (9.8%) | 63 (9.0%) | 85 (9.7%) | |
| Radiotherapy only | 54 (10.6%) | 60 (9.3%) | 72 (11.2%) | 85 (12.1%) | 102 (11.7%) | |
| Surgery and radiotherapy | 82 (16.0%) | 80 (12.4%) | 72 (11.2%) | 66 (9.4%) | 84 (9.6%) | |
| Chemoradiotherapy | 96 (18.8%) | 135 (20.9%) | 132 (20.5%) | 152 (21.6%) | 179 (20.5%) | |
| Surgery and chemoradiotherapy | 95 (18.6%) | 119 (18.4%) | 106 (16.4%) | 103 (14.7%) | 89 (10.2%) | |
| Chemotherapy +/- surgery | 14 (2.7%) | 20 (3.1%) | 27 (4.2%) | 24 (3.4%) | 39 (4.5%) | |
| No treatment | 32 (6.3%) | 39 (6.0%) | 43 (6.7%) | 46 (6.5%) | 93 (10.7%) | |
| Unknown | 96 (18.8%) | 128 (19.8%) | 130 (20.2%) | 164 (23.3%) | 202 (23.1%) | |
| **Network** | | | | | | <0.001 |
| West of Scotland (WoSCAN) | 153 (29.9%) | 190 (29.4%) | 258 (40.0%) | 342 (48.6%) | 743 (85.1%) | |
| East of Scotland (SCAN) | 130 (25.4%) | 213 (32.9%) | 214 (33.2%) | 237 (33.7%) | 61 (7.0%) | |
| North of Scotland (NOSCAN) | 228 (44.6%) | 244 (37.7%) | 173 (26.8%) | 124 (17.6%) | 69 (7.9%) | |

**Appendix 2.12 – Cross-tabulation of Carstairs 1991 Category with baseline characteristics for people with cancer of the larynx**

| Variable | Carstairs 1991 Category (row %) | | | | | Chi-sq. p-value |
|---|---|---|---|---|---|---|
| | 1 – Least deprived | 2 | 3 | 4 | 5 – Most deprived | |
| **Age at incidence** | | | | | | <0.001 |
| Less than 45 | 21 (2.2%) | 26 (2.1%) | 41 (2.7%) | 46 (2.7%) | 76 (3.3%) | |
| 45 to 54 | 106 (11.3%) | 173 (13.9%) | 202 (13.4%) | 259 (15.2%) | 383 (16.6%) | |
| 55 to 64 | 251 (26.8%) | 381 (30.6%) | 505 (33.4%) | 583 (34.3%) | 793 (34.3%) | |
| 65 to 74 | 334 (35.6%) | 412 (33.1%) | 495 (32.7%) | 544 (32.0%) | 728 (31.5%) | |
| 75 and over | 226 (24.1%) | 253 (20.3%) | 270 (17.8%) | 267 (15.7%) | 331 (14.3%) | |
| **Sex** | | | | | | <0.001 |
| Male | 789 (84.1%) | 1,021 (82.0%) | 1,219 (80.6%) | 1,329 (78.2%) | 1,775 (76.8%) | |
| Female | 149 (15.9%) | 224 (18.0%) | 294 (19.4%) | 370 (21.8%) | 536 (23.2%) | |
| **Pathology** | | | | | | 0.90 |
| SCC | 862 (91.9%) | 1,146 (92.0%) | 1,391 (91.9%) | 1,566 (92.2%) | 2,111 (91.3%) | |
| Non-SCC | 76 (8.1%) | 99 (8.0%) | 122 (8.1%) | 133 (7.8%) | 200 (8.7%) | |
| **Treatment** | | | | | | <0.001 |
| Surgery only | 66 (7.0%) | 117 (9.4%) | 147 (9.7%) | 156 (9.2%) | 185 (8.0%) | |
| Radiotherapy only | 281 (30.0%) | 317 (25.5%) | 387 (25.6%) | 426 (25.1%) | 503 (21.8%) | |
| Surgery and radiotherapy | 112 (11.9%) | 152 (12.2%) | 172 (11.4%) | 184 (10.8%) | 224 (9.7%) | |
| Chemoradiotherapy | 44 (4.7%) | 78 (6.3%) | 100 (6.6%) | 121 (7.1%) | 164 (7.1%) | |
| Surgery and chemoradiotherapy | 27 (2.9%) | 39 (3.1%) | 48 (3.2%) | 47 (2.8%) | 81 (3.5%) | |
| Chemotherapy +/- surgery | 10 (1.1%) | 13 (1.0%) | 20 (1.3%) | 22 (1.3%) | 39 (1.7%) | |
| No treatment | 55 (5.9%) | 60 (4.8%) | 98 (6.5%) | 112 (6.6%) | 168 (7.3%) | |
| Unknown | 343 (36.6%) | 469 (37.7%) | 541 (35.8%) | 631 (37.1%) | 947 (41.0%) | |
| **Network** | | | | | | <0.001 |
| West of Scotland (WoSCAN) | 341 (36.4%) | 428 (34.4%) | 635 (42.0%) | 875 (51.5%) | 1,948 (84.3%) | |
| East of Scotland (SCAN) | 274 (29.2%) | 430 (34.5%) | 499 (33.0%) | 575 (33.8%) | 154 (6.7%) | |
| North of Scotland (NOSCAN) | 323 (34.4%) | 387 (31.1%) | 379 (25.0%) | 249 (14.7%) | 209 (9.0%) | |

**Appendix 2.13 – Overall survival by each baseline characteristic**

| Variable | One-year overall survival (95% CI) | Five-year overall survival (95% CI) | 10-year overall survival (95% CI) |
|---|---|---|---|
| **Total** | 75.1 (74.6, 75.7) | 47.0 (46.4, 47.6) | 32.1 (31.4, 32.7) |
| **Age at incidence** | | | |
| Less than 45 | 89.6 (87.8, 91.1) | 73.0 (70.6, 75.3) | 65.8 (63.1, 68.4) |
| 45 to 54 | 84.0 (82.8, 85.0) | 59.7 (58.2, 61.2) | 47.9 (46.3, 49.5) |
| 55 to 64 | 79.5 (78.6, 80.4) | 51.3 (50.1, 52.4) | 36.1 (34.9, 37.3) |
| 65 to 74 | 72.8 (71.7, 73.8) | 42.6 (41.4, 43.8) | 25.0 (23.9, 26.2) |
| 75 and over | 59.0 (57.5, 60.4) | 27.0 (25.7, 28.3) | 11.6 (10.6, 12.6) |
| **Sex** | | | |
| Male | 75.7 (75.0, 76.3) | 46.2 (45.5, 47.0) | 31.3 (30.6, 32.1) |
| Female | 73.8 (72.8, 74.8) | 48.8 (47.6, 50.0) | 33.8 (32.6, 35.0) |
| **ICD group** | | | |
| Oral cavity | 73.3 (72.4, 74.3) | 45.1 (44.0, 46.2) | 30.8 (29.7, 31.9) |
| Larynx | 80.8 (79.9, 81.6) | 52.1 (51.0, 53.2) | 34.4 (33.3, 35.5) |
| Oropharynx | 74.3 (72.7, 75.7) | 48.0 (46.3, 49.7) | 34.3 (32.4, 36.1) |
| Hypopharynx | 53.3 (50.8, 55.7) | 19.6 (17.7, 21.7) | 10.7 (9.1, 12.4) |
| Lip | 92.9 (91.4, 94.1) | 69.1 (66.5, 71.5) | 48.1 (45.3, 50.8) |
| Salivary gland | 82.0 (79.7, 84.1) | 55.5 (52.6, 58.4) | 45.3 (42.3, 48.3) |
| Other | 58.0 (55.3, 60.6) | 29.1 (26.7, 31.6) | 19.6 (17.4, 21.9) |
| **Treatment** | | | |
| Surgery only | 88.9 (87.9, 89.8) | 66.4 (64.9, 67.8) | 48.8 (47.1, 50.5) |
| Radiotherapy only | 79.2 (77.8, 80.6) | 49.7 (47.9, 51.5) | 32.7 (30.9, 34.6) |
| Surgery and radiotherapy | 85.0 (83.6, 86.3) | 51.3 (49.4, 53.2) | 33.8 (31.9, 35.8) |
| Chemoradiotherapy | 81.7 (80.1, 83.2) | 49.7 (47.6, 51.7) | 33.7 (31.3, 36.1) |
| Surgery and chemoradiotherapy | 87.3 (85.5, 88.9) | 54.5 (51.8, 57.0) | 40.8 (37.9, 43.7) |
| Chemotherapy +/- surgery | 56.9 (52.6, 60.9) | 30.9 (27, 34.8) | 21.1 (17.6, 24.8) |
| No treatment | 17.3 (15.6, 19.1) | 7.9 (6.7, 9.2) | 5.3 (4.3, 6.5) |
| Unknown | 72.9 (71.9, 73.9) | 42.1 (41.0, 43.1) | 27.7 (26.7, 28.6) |
| **Network of residence** | | | |
| West of Scotland (WoSCAN) | 73.3 (72.5, 74.0) | 44.5 (43.7, 45.4) | 29.2 (28.4, 30.1) |
| East of Scotland (SCAN) | 77.6 (76.5, 78.6) | 50.5 (49.3, 51.8) | 36.1 (34.8, 37.4) |
| North of Scotland (NOSCAN) | 76.7 (75.6, 77.8) | 48.7 (47.4, 50.0) | 34.3 (33.0, 35.6) |
| **Year group** | | | |
| 1986-1990 | 74.9 (73.4, 76.3) | 44.2 (42.4, 45.8) | 29.2 (27.6, 30.7) |
| 1991-1995 | 72.1 (70.6, 73.5) | 40.8 (39.2, 42.4) | 27.0 (25.6, 28.4) |
| 1996-2000 | 74.5 (73.1, 75.8) | 45.9 (44.4, 47.4) | 30.7 (29.3, 32.1) |
| 2001-2005 | 75.7 (74.4, 77.0) | 47.7 (46.2, 49.2) | 33.7 (32.3, 35.1) |
| 2006-2010 | 75.9 (74.7, 77.2) | 49.8 (48.4, 51.3) | 34.9 (33.4, 36.4) |
| 2011-2015 | 77.0 (75.8, 78.2) | 52.0 (50.5, 53.6) | N/A |
| **Carstairs Category** | | | |
| 1 – Least deprived | 78.6 (77.2, 79.9) | 53.1 (51.4, 54.7) | 38.4 (36.7, 40.1) |
| 2 | 77.2 (75.9, 78.4) | 49.9 (48.4, 51.4) | 35.5 (34.0, 37.1) |
| 3 | 77.4 (76.2, 78.5) | 48.0 (46.5, 49.4) | 32.6 (31.1, 34.0) |
| 4 | 74.0 (72.8, 75.2) | 46.8 (45.4, 48.1) | 32.1 (30.7, 33.4) |
| 5 – Most deprived | 71.1 (70.0, 72.2) | 41.1 (39.9, 42.4) | 26.0 (24.9, 27.1) |
| *SII (95% CI)* | *9.0 (4.4, 13.6)* | *14.0 (8.2, 19.9)* | *14.6 (8.1, 21.0)* |
| *RII (95% CI)* | *0.12 (0.06, 0.18)* | *0.30 (0.17, 0.42)* | *0.45 (0.25, 0.65)* |

**Appendix 2.14 – Disease-specific survival by each baseline characteristic**

| Variable | One-year disease-specific survival (95% CI) | Five-year disease-specific survival (95% CI) | 10-year disease-specific survival (95% CI) |
|---|---|---|---|
| **Total** | 80.2 (79.7, 80.7) | 61.8 (61.1, 62.4) | 56.0 (55.3, 56.7) |
| **Age at incidence** | | | |
| Less than 45 | 91.4 (89.8, 92.7) | 78.3 (75.9, 80.4) | 73.8 (71.3, 76.2) |
| 45 to 54 | 86.5 (85.4, 87.5) | 68.7 (67.3, 70.2) | 63.4 (61.8, 65.0) |
| 55 to 64 | 83.5 (82.7, 84.4) | 64.1 (62.9, 65.2) | 58.1 (56.8, 59.3) |
| 65 to 74 | 78.5 (77.5, 79.5) | 59.4 (58.2, 60.6) | 52.7 (51.3, 54.1) |
| 75 and over | 67.3 (65.8, 68.7) | 48.9 (47.3, 50.5) | 43.0 (41.2, 44.8) |
| **Sex** | | | |
| Male | 80.7 (80.1, 81.3) | 61.4 (60.6, 62.2) | 55.5 (54.7, 56.4) |
| Female | 78.9 (77.9, 79.9) | 62.6 (61.5, 63.8) | 57.1 (55.8, 58.3) |
| **ICD group** | | | |
| Oral cavity | 78.2 (77.3, 79.1) | 59.0 (57.8, 60.1) | 52.6 (51.4, 53.9) |
| Larynx | 85.6 (84.8, 86.4) | 68.6 (67.5, 69.7) | 62.2 (61.0, 63.4) |
| Oropharynx | 78.3 (76.9, 79.7) | 59.6 (57.8, 61.3) | 53.9 (51.9, 55.8) |
| Hypopharynx | 59.3 (56.8, 61.8) | 30.2 (27.7, 32.7) | 24.9 (22.3, 27.6) |
| Lip | 98.3 (97.4, 98.9) | 94.3 (92.9, 95.5) | 93.0 (91.3, 94.4) |
| Salivary gland | 87.4 (85.3, 89.2) | 70.4 (67.5, 73.0) | 66.3 (63.2, 69.2) |
| Other | 64.5 (61.8, 67.1) | 38.9 (36.1, 41.7) | 32.3 (29.4, 35.2) |
| **Treatment** | | | |
| Surgery only | 92.4 (91.6, 93.1) | 82.9 (81.7, 84.1) | 78.2 (76.7, 79.6) |
| Radiotherapy only | 83.4 (82.1, 84.7) | 66.7 (64.9, 68.4) | 61.5 (59.4, 63.4) |
| Surgery and radiotherapy | 88.2 (87.0, 89.4) | 64.2 (62.3, 66.1) | 56.6 (54.4, 58.7) |
| Chemoradiotherapy | 84.2 (82.7, 85.6) | 62.2 (60.1, 64.2) | 55.9 (53.3, 58.3) |
| Surgery and chemoradiotherapy | 89.1 (87.4, 90.6) | 65.0 (62.4, 67.4) | 60.9 (58.0, 63.6) |
| Chemotherapy +/- surgery | 63.5 (59.2, 67.5) | 42.4 (38.0, 46.8) | 36.2 (31.7, 40.8) |
| No treatment | 24.4 (22.2, 26.6) | 15.0 (13.1, 17.0) | 13.8 (12.0, 15.8) |
| Unknown | 79.0 (78.1, 79.9) | 57.4 (56.3, 58.5) | 50.9 (49.7, 52.1) |
| **Network of residence** | | | |
| West of Scotland (WoSCAN) | 78.6 (77.9, 79.3) | 59.7 (58.8, 60.6) | 52.9 (51.9, 53.9) |
| East of Scotland (SCAN) | 82.1 (81.1, 83.0) | 64.3 (63.0, 65.5) | 60.0 (58.6, 61.3) |
| North of Scotland (NOSCAN) | 81.7 (80.6, 82.7) | 63.7 (62.4, 65.0) | 58.5 (57.1, 60.0) |
| **Year group** | | | |
| 1986-1990 | 81.2 (79.8, 82.5) | 61.0 (59.2, 62.8) | 55.4 (53.5, 57.3) |
| 1991-1995 | 78.3 (76.9, 79.6) | 55.3 (53.6, 57.0) | 48.2 (46.5, 50.0) |
| 1996-2000 | 78.5 (77.2, 79.7) | 57.0 (55.5, 58.6) | 50.6 (48.9, 52.2) |
| 2001-2005 | 79.3 (78.1, 80.6) | 62.0 (60.4, 63.5) | 57.1 (55.5, 58.7) |
| 2006-2010 | 81.3 (80.1, 82.5) | 65.6 (64.1, 67.0) | 61.0 (59.4, 62.6) |
| 2011-2015 | 82.0 (80.9, 83.1) | 68.5 (67.1, 69.9) | N/A |
| **Carstairs Category** | | | |
| 1 – Least deprived | 83.7 (82.5, 84.9) | 67.2 (65.5, 68.8) | 62.3 (60.5, 64.1) |
| 2 | 81.9 (80.7, 83.0) | 64.5 (63.0, 65.9) | 59.4 (57.7, 61.0) |
| 3 | 81.9 (80.7, 82.9) | 62.9 (61.4, 64.3) | 57.4 (55.8, 58.9) |
| 4 | 79.2 (78.0, 80.3) | 61.2 (59.7, 62.5) | 55.1 (53.6, 56.6) |
| 5 – Most deprived | 76.6 (75.5, 77.6) | 56.6 (55.3, 57.9) | 49.8 (48.4, 51.2) |
| *SII (95% CI)* | *8.8 (5.1, 12.6)* | *12.6 (8.6, 16.6)* | *19.1 (9.6, 28.5)* |
| *RII (95% CI)* | *0.11 (0.06, 0.16)* | *0.20 (0.14, 0.27)* | *0.33 (0.17, 0.50)* |

**Appendix 2.15 – Overall survival by Carstairs 1991 Category per year group of diagnosis for the whole cohort**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 77.4 (73.3, 80.9) | 73.0 (68.9, 76.7) | 80.1 (76.7, 83.0) | 80.9 (77.6, 83.8) | 78.0 (74.6, 81.0) | 81.2 (78.3, 83.8) |
| 2 | 75.9 (72.1, 79.2) | 74.7 (71.3, 77.9) | 78.7 (75.5, 81.6) | 75.8 (72.7, 78.6) | 76.5 (73.5, 79.3) | 80.5 (77.9, 82.9) |
| 3 | 78.4 (75.0, 81.5) | 75.9 (72.6, 78.9) | 76.8 (73.8, 79.6) | 77.4 (74.3, 80.1) | 78.1 (75.3, 80.7) | 78.3 (75.5, 80.8) |
| 4 | 71.5 (68.0, 74.7) | 71.6 (68.4, 74.5) | 71.7 (68.6, 74.5) | 76.0 (73.1, 78.6) | 76.7 (73.9, 79.2) | 76.0 (73.2, 78.6) |
| 5 – Most deprived | 73.5 (70.5, 76.2) | 67.9 (65.0, 70.6) | 69.8 (67.0, 72.4) | 71.8 (69.0, 74.3) | 72.9 (70.2, 75.3) | 71.8 (69.1, 74.2) |
| *SII (95% CI)* | *6.1 (-6.1, 18.2)* | *8.6 (-3.0, 20.2)* | *14.1 (9.1, 19.1)* | *9.0 (-0.2, 18.1)* | *5.7 (-2.2, 13.6)* | *12.2 (7.5, 16.9)* |
| *RII (95% CI)* | *0.08 (-0.08, 0.24)* | *0.12 (-0.04, 0.28)* | *0.19 (0.12, 0.26)* | *0.12 (0.00, 0.24)* | *0.08 (-0.03, 0.18)* | *0.16 (0.10, 0.22)* |
| **Five-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 46.3 (41.7, 50.8) | 43.1 (38.7, 47.3) | 51.4 (47.4, 55.3) | 57.0 (53.0, 60.9) | 56.0 (52.1, 59.7) | 62.4 (58.6, 66.0) |
| 2 | 45.4 (41.2, 49.5) | 42.9 (39.1, 46.6) | 51.4 (47.6, 55.0) | 47.6 (44.1, 51) | 52.7 (49.2, 56.0) | 57.5 (53.9, 60.9) |
| 3 | 46.7 (42.7, 50.6) | 43.4 (39.8, 47.1) | 47.2 (43.7, 50.5) | 48.7 (45.2, 52.1) | 50.2 (46.9, 53.4) | 52.3 (48.8, 55.8) |
| 4 | 44.4 (40.7, 48.1) | 42.5 (39.1, 45.9) | 45.6 (42.3, 48.9) | 48.4 (45.1, 51.6) | 50.7 (47.5, 53.8) | 48.4 (44.9, 51.9) |
| 5 – Most deprived | 40.5 (37.3, 43.7) | 35.4 (32.5, 38.3) | 39.2 (36.3, 42.0) | 41.8 (38.9, 44.7) | 44.2 (41.3, 47.0) | 47.1 (43.9, 50.2) |
| *SII (95% CI)* | *7.5 (-0.3, 15.4)* | *9.9 (-2.8, 22.6)* | *16.2 (8.9, 23.6)* | *14.1 (-1.5, 29.8)* | *13.0 (4.3, 21.7)* | *19.2 (10.5, 27.9)* |
| *RII (95% CI)* | *0.17 (0.00, 0.35)* | *0.24 (-0.07, 0.55)* | *0.35 (0.19, 0.52)* | *0.30 (-0.03, 0.62)* | *0.26 (0.09, 0.43)* | *0.36 (0.20, 0.53)* |
| **10-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 34.6 (30.2, 38.9) | 29.4 (25.4, 33.4) | 34.9 (31.2, 38.6) | 43.3 (39.3, 47.2) | 41.2 (37.1, 45.3) | N/A |
| 2 | 30.3 (26.5, 34.1) | 29.6 (26.2, 33.1) | 36.9 (33.3, 40.5) | 34.9 (31.6, 38.2) | 38.7 (35.0, 42.3) | N/A |
| 3 | 30.8 (27.2, 34.5) | 27.8 (24.5, 31.1) | 31.4 (28.3, 34.6) | 34.7 (31.5, 38.0) | 35.0 (31.6, 38.3) | N/A |
| 4 | 28.2 (24.9, 31.6) | 29.0 (26.0, 32.2) | 30.9 (27.9, 34.0) | 34.4 (31.3, 37.4) | 35.9 (32.7, 39.2) | N/A |
| 5 – Most deprived | 25.6 (22.8, 28.4) | 22.1 (19.6, 24.6) | 24.1 (21.6, 26.6) | 26.8 (24.2, 29.4) | 29.2 (26.4, 32.1) | N/A |
| *SII (95% CI)* | *10.1 (4.5, 15.6)* | *9.2 (-2.2, 20.5)* | *15.1 (4.3, 26.0)* | *16.4 (2.3, 30.5)* | *13.7 (4.7, 22.7)* | *N/A* |
| *RII (95% CI)* | *0.34 (0.15, 0.53)* | *0.34 (-0.08, 0.76)* | *0.49 (0.14, 0.85)* | *0.48 (0.07, 0.90)* | *0.39 (0.13, 0.64)* | *N/A* |

**Appendix 2.16 – Overall survival by Carstairs 1991 Category per year group of diagnosis for males**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 78.3 (73.3, 82.5) | 73.8 (68.8, 78.1) | 82.4 (78.5, 85.6) | 80.4 (76.2, 84.0) | 81.1 (77.2, 84.4) | 80.0 (76.4, 83.1) |
| 2 | 77.2 (72.6, 81.1) | 77.5 (73.4, 81.0) | 80.6 (76.7, 83.9) | 75.0 (71.2, 78.3) | 77.5 (73.8, 80.7) | 83.5 (80.5, 86.2) |
| 3 | 79.1 (75.0, 82.7) | 78.9 (75.1, 82.2) | 76.7 (73.1, 79.9) | 77.7 (74.0, 81.0) | 78.8 (75.4, 81.8) | 78.3 (75.0, 81.2) |
| 4 | 70.9 (66.7, 74.8) | 72.7 (69.0, 76.1) | 72.2 (68.5, 75.6) | 75.3 (71.8, 78.4) | 77.4 (74.1, 80.3) | 75.8 (72.5, 78.8) |
| 5 – Most deprived | 74.1 (70.6, 77.2) | 68.4 (65.0, 71.6) | 70.0 (66.8, 73.1) | 71.2 (67.9, 74.2) | 72.4 (69.3, 75.3) | 71.9 (68.7, 74.8) |
| *SII (95% CI)* | *7.0 (-7.8, 21.9)* | *10.8 (-6.0, 27.6)* | *16.7 (12.0, 21.2)* | *9.1 (-1.3, 19.5)* | *9.3 (0.5, 18.1)* | *13.1 (2.8, 23.5)* |
| *RII (95% CI)* | *0.09 (-0.10, 0.29)* | *0.15 (0.08, 0.37)* | *0.22 (0.16, 0.28)* | *0.12 (-0.02, 0.26)* | *0.12 (0.01, 0.24)* | *0.17 (0.04, 0.30)* |
| **Five-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 46.0 (40.3, 51.4) | 42.9 (37.7, 48.1) | 51.4 (46.6, 55.9) | 56.3 (51.3, 61.0) | 57.2 (52.6, 61.6) | 63.0 (58.6, 67.2) |
| 2 | 44.6 (39.6, 49.5) | 43.3 (38.7, 47.8) | 52.3 (47.7, 56.7) | 46.6 (42.4, 50.6) | 52.6 (48.5, 56.7) | 58.5 (54.3, 62.5) |
| 3 | 44.8 (40.0, 49.4) | 43.9 (39.6, 48.1) | 45.8 (41.7, 49.7) | 49.0 (44.7, 53.1) | 50.5 (46.6, 54.4) | 52.0 (47.8, 56.0) |
| 4 | 41.6 (37.2, 46.0) | 41.9 (37.9, 45.9) | 43.0 (39.0, 46.9) | 47.1 (43.2, 50.9) | 50.9 (47.1, 54.6) | 46.2 (42.0, 50.4) |
| 5 – Most deprived | 39.6 (35.9, 43.3) | 34.3 (31.0, 37.7) | 39.5 (36.1, 42.8) | 39.8 (36.4, 43.2) | 42.4 (39.0, 45.7) | 45.7 (41.8, 49.4) |
| *SII (95% CI)* | *8.4 (4.5, 12.4)* | *11.9 (-2.1, 25.8)* | *16.9 (9.2, 24.5)* | *15.9 (-0.5, 32.3)* | *16.2 (4.5, 27.9)* | *22.0 (9.2, 34.8)* |
| *RII (95% CI)* | *0.20 (0.11, 0.29)* | *0.29 (0.05, 0.64)* | *0.37 (0.20, 0.54)* | *0.34 (-0.01, 0.69)* | *0.33 (0.09, 0.56)* | *0.42 (0.18, 0.67)* |
| **10-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 32.4 (27.2, 37.6) | 30.0 (25.2, 34.8) | 33.7 (29.3, 38.1) | 42.2 (37.3, 47.0) | 40.4 (35.5, 45.2) | N/A |
| 2 | 28.6 (24.2, 33.2) | 30.1 (26.0, 34.3) | 36.9 (32.6, 41.3) | 34.9 (31.0, 38.8) | 38.7 (34.3, 43.0) | N/A |
| 3 | 28.5 (24.4, 32.9) | 28.8 (25.0, 32.8) | 29.5 (25.9, 33.1) | 34.7 (30.8, 38.7) | 35.7 (31.7, 39.7) | N/A |
| 4 | 25.8 (22.0, 29.7) | 29.6 (26.0, 33.3) | 30.1 (26.5, 33.8) | 34.4 (30.8, 38.1) | 36.7 (32.9, 40.6) | N/A |
| 5 – Most deprived | 23.8 (20.7, 27.1) | 20.3 (17.5, 23.2) | 24.2 (21.3, 27.2) | 25.8 (22.8, 28.9) | 27.6 (24.4, 30.9) | N/A |
| *SII (95% CI)* | *9.8 (5.3, 14.3)* | *12.3 (-3.1, 27.9)* | *13.9 (1.3, 26.5)* | *16.8 (2.8, 30.8)* | *15.0 (2.1, 28.0)* | *N/A* |
| *RII (95% CI)* | *0.36 (0.20, 0.53)* | *0.46 (0.12, 1.04)* | *0.46 (0.04, 0.88)* | *0.50 (0.08, 0.93)* | *0.43 (0.06, 0.80)* | *N/A* |

**Appendix 2.17 – Overall survival by Carstairs 1991 Category per year group of diagnosis for females**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 75.5 (67.8, 81.6) | 71.3 (63.6, 77.7) | 74.4 (67.4, 80.2) | 82.0 (75.9, 86.7) | 70.6 (63.7, 76.5) | 84.3 (78.9, 88.4) |
| 2 | 73.0 (65.7, 79.0) | 68.6 (61.8, 74.4) | 74.7 (68.3, 79.9) | 77.9 (72.0, 82.7) | 74.4 (68.5, 79.4) | 73.9 (68.5, 78.5) |
| 3 | 76.9 (70.1, 82.3) | 67.7 (60.6, 73.8) | 77.2 (71.2, 82.2) | 76.7 (71.1, 81.4) | 76.6 (71.2, 81.2) | 78.2 (72.8, 82.7) |
| 4 | 72.8 (66.2, 78.4) | 68.6 (62.1, 74.1) | 70.4 (64.6, 75.5) | 77.6 (72.0, 82.1) | 75.1 (69.6, 79.7) | 76.5 (71.1, 81.0) |
| 5 – Most deprived | 71.9 (65.9, 77.0) | 66.5 (60.7, 71.7) | 69.2 (63.9, 73.9) | 73.3 (67.9, 77.9) | 74.1 (68.9, 78.6) | 71.5 (66.4, 76.0) |
| *SII (95% CI)* | *4.1 (-5.6, 13.8)* | *4.6 (-0.6, 9.7)* | *8.5 (-3.9, 20.8)* | *8.6 (0.6, 16.6)* | *-2.6 (-13.4, 8.1)* | *10.9 (-7.8, 29.6)* |
| *RII (95% CI)* | *0.06 (0.08, 0.19)* | *0.07 (-0.01, 0.14)* | *0.12 (-0.05, 0.29)* | *0.11 (0.01, 0.22)* | *-0.04 (-0.18, 0.11)* | *0.14 (-0.10, 0.39)* |
| **Five-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 47.0 (38.9, 54.7) | 43.3 (35.5, 50.9) | 51.7 (44.1, 58.7) | 58.5 (51.3, 65.0) | 53.1 (45.8, 59.8) | 61.0 (53.7, 67.6) |
| 2 | 47.1 (39.6, 54.3) | 42.0 (35.3, 48.6) | 49.3 (42.5, 55.8) | 50.2 (43.7, 56.4) | 52.8 (46.4, 58.8) | 55.0 (48.3, 61.2) |
| 3 | 51.1 (43.7, 58.0) | 42.2 (35.1, 49.0) | 50.9 (44.2, 57.2) | 48.1 (41.9, 54.0) | 49.3 (43.3, 55.0) | 53.3 (46.5, 59.5) |
| 4 | 51.0 (44.0, 57.6) | 44.1 (37.6, 50.4) | 51.5 (45.4, 57.2) | 51.7 (45.5, 57.6) | 50.2 (44.2, 55.9) | 53.6 (47.1, 59.6) |
| 5 – Most deprived | 43.0 (36.9, 48.9) | 38.4 (32.7, 44.1) | 38.4 (33.2, 43.6) | 47.2 (41.5, 52.7) | 49.2 (43.6, 54.6) | 50.4 (44.6, 56.0) |
| *SII (95% CI)* | *4.2 (-15.4, 23.7)* | *4.7 (-6.1, 15.6)* | *14.9 (-8.9, 38.7)* | *9.4 (-7.8, 26.8)* | *4.9 (-0.9, 10.7)* | *10.8 (1.5, 20.1)* |
| *RII (95% CI)* | *0.09 (-0.32, 0.50)* | *0.11 (-0.15, 0.37)* | *0.31 (-0.19, 0.81)* | *0.19 (-0.15, 0.53)* | *0.10 (-0.02, 0.21)* | *0.20 (0.03, 0.37)* |
| **10-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 73.0 (68.9, 76.7) | 77.4 (73.3, 80.9) | 73.0 (68.9, 76.7) | 77.4 (73.3, 80.9) | 73.0 (68.9, 76.7) | N/A |
| 2 | 33.9 (27.0, 41.0) | 28.5 (22.5, 34.8) | 36.9 (30.5, 43.3) | 34.9 (28.9, 41.0) | 38.7 (32.1, 45.3) | N/A |
| 3 | 36.0 (29.2, 42.9) | 25.0 (19.1, 31.3) | 36.6 (30.3, 42.9) | 34.7 (29.0, 40.5) | 33.2 (26.9, 39.6) | N/A |
| 4 | 34.0 (27.6, 40.5) | 27.5 (21.9, 33.4) | 32.8 (27.4, 38.4) | 34.2 (28.5, 40.0) | 34.1 (28.1, 40.1) | N/A |
| 5 – Most deprived | 30.1 (24.6, 35.8) | 27.0 (22.0, 32.3) | 23.8 (19.3, 28.5) | 29.4 (24.3, 34.6) | 33.5 (27.7, 39.4) | N/A |
| *SII (95% CI)* | *9.2 (0.0, 18.5)* | *1.2 (-5.9, 8.4)* | *18.2 (4.2, 32.2)* | *15.4 (-0.8, 31.6)* | *10.5 (-2.6, 23.5)* | *N/A* |
| *RII (95% CI)* | *0.27 (0.0, 0.54)* | *0.05 (-0.22, 0.31)* | *0.56 (0.13, 0.99)* | *0.44 (-0.02, 0.90)* | *0.29 (-0.07, 0.65)* | *N/A* |

**Appendix 2.18 – Overall survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the oral cavity**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 72.8 (64.1, 79.7) | 72.1 (64.7, 78.2) | 73.5 (66.9, 79.0) | 83.3 (77.7, 87.6) | 76.8 (70.9, 81.7) | 81.8 (77.0, 85.6) |
| 2 | 72.1 (64.6, 78.3) | 70.2 (63.9, 75.5) | 77.1 (71.0, 82.1) | 70.8 (64.8, 76.0) | 71.3 (65.8, 76.1) | 81.6 (77.0, 85.3) |
| 3 | 69.3 (61.9, 75.5) | 72.2 (65.6, 77.8) | 74.3 (68.5, 79.2) | 75.4 (70.0, 80.0) | 79.5 (74.7, 83.5) | 76.1 (71.0, 80.5) |
| 4 | 63.5 (56.4, 69.7) | 68.4 (62.2, 73.8) | 67.3 (61.2, 72.6) | 74.9 (69.9, 79.3) | 74.6 (69.6, 78.9) | 76.5 (71.6, 80.7) |
| 5 – Most deprived | 70.6 (64.9, 75.5) | 65.5 (59.9, 70.5) | 69.8 (64.9, 74.2) | 71.3 (66.4, 75.7) | 72.5 (67.8, 76.6) | 70.6 (65.7, 74.9) |
| *SII (95% CI)* | *4.1 (-15.7, 23.9)* | *8.2 (0.1, 16.2)* | *8.7 (-6.6, 24.0)* | *8.8 (-12.7, 30.2)* | *3.1 (-15.3, 21.4)* | *14.2 (5.2, 23.1)* |
| *RII (95% CI)* | *0.06 (-0.23, 0.34)* | *0.12 (0.00, 0.23)* | *0.12 (-0.09, 0.33)* | *0.12 (-0.17, 0.40)* | *0.04 (-0.20, 0.29)* | *0.18 (0.07, 0.30)* |
| **Five-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 35.2 (26.9, 43.5) | 39.0 (31.7, 46.2) | 46.1 (39.1, 52.7) | 58.6 (51.8, 64.7) | 55.3 (48.7, 61.3) | 63.0 (56.8, 68.5) |
| 2 | 37.0 (29.7, 44.3) | 41.2 (34.9, 47.3) | 46.6 (40.0, 53.0) | 44.4 (38.2, 50.3) | 50.9 (45.0, 56.4) | 61.1 (55.3, 66.5) |
| 3 | 40.2 (33.0, 47.3) | 39.7 (33.1, 46.3) | 44.4 (38.2, 50.3) | 48.8 (42.9, 54.4) | 54.1 (48.6, 59.3) | 52.7 (46.5, 58.5) |
| 4 | 39.5 (32.7, 46.2) | 38.9 (32.8, 44.9) | 40.8 (34.8, 46.7) | 43.7 (38.3, 49.0) | 47.0 (41.6, 52.3) | 48.3 (42.2, 54.2) |
| 5 – Most deprived | 36.9 (31.3, 42.5) | 33.5 (28.3, 38.8) | 39.4 (34.4, 44.4) | 39.1 (34.1, 44.1) | 42.9 (38.0, 47.8) | 44.2 (38.4, 49.9) |
| *SII (95% CI)* | *-1.1 (-12.1, 9.9)* | *8.2 (-2.7, 19.2)* | *10.1 (4.9, 15.3)* | *18.9 (-2.9, 40.5)* | *14.9 (1.7. 28.1)* | *25.4 (17.3, 33.6)* |
| *RII (95% CI)* | *-0.03 (-0.32, 0.26)* | *0.22 (-0.07, 0.50)* | *0.23 (0.11, 0.36)* | *0.41 (-0.06, 0.88)* | *0.30 (0.03, 0.57)* | *0.48 (0.32, 0.63)* |
| **10-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 26.4 (19.0, 34.3) | 27.3 (20.9, 34.1) | 31.4 (25.1, 37.8) | 47.7 (41.0, 54.1) | 37.0 (30.0, 44.0) | N/A |
| 2 | 22.4 (16.4, 29.0) | 27.7 (22.2, 33.5) | 30.5 (24.6, 36.6) | 35.0 (29.2, 40.8) | 38.5 (32.6, 44.5) | N/A |
| 3 | 24.6 (18.5, 31.1) | 23.0 (17.5, 28.9) | 33.9 (28.1, 39.7) | 35.1 (29.6, 40.6) | 35.6 (29.9, 41.3) | N/A |
| 4 | 24.5 (18.8, 30.6) | 26.3 (21.0, 31.9) | 25.0 (19.9, 30.4) | 29.7 (24.8, 34.7) | 32.8 (27.5, 38.1) | N/A |
| 5 – Most deprived | 22.7 (18.0, 27.7) | 21.6 (17.2, 26.3) | 23.9 (19.7, 28.4) | 24.8 (20.5, 29.3) | 33.3 (28.5, 38.3) | N/A |
| *SII (95% CI)* | *2.4 (-5.1, 10.0)* | *7.0 (-3.3, 17.3)* | *11.4 (-4.1, 27.0)* | *24.4 (7.9, 40.8)* | *6.6 (-0.3, 13.6)* | *N/A* |
| *RII (95% CI)* | *0.10 (-0.21, 0.42)* | *0.28 (-0.13, 0.69)* | *0.40 (-0.15, 0.95)* | *0.73 (0.24, 1.23)* | *0.19 (0.01, 0.39)* | *N/A* |

**Appendix 2.19 – Overall survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the oropharynx**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 70.6 (52.2, 83.0) | 57.8 (42.1, 70.6) | 85.9 (75.4, 92.2) | 80.7 (70.8, 87.5) | 75.9 (67.0, 82.7) | 83.6 (76.9, 88.6) |
| 2 | 68.6 (54.0, 79.5) | 74.1 (60.8, 83.5) | 69.9 (58.8, 78.5) | 76.9 (67.7, 83.7) | 83.0 (75.7, 88.3) | 82.6 (76.8, 87.1) |
| 3 | 77.8 (62.6, 87.4) | 56.7 (43.2, 68.1) | 76.8 (67.0, 84.1) | 79.5 (70.7, 85.8) | 81.3 (73.9, 86.7) | 78.4 (71.9, 83.6) |
| 4 | 54.3 (42.0, 65.1) | 59.2 (46.8, 69.5) | 70.7 (60.2, 78.8) | 73.4 (64.0, 80.7) | 78.9 (71.9, 84.4) | 79.5 (73.0, 84.6) |
| 5 – Most deprived | 66.2 (54.2, 75.7) | 63.3 (52.9, 71.9) | 65.9 (57.0, 73.4) | 66.1 (57.2, 73.6) | 69.9 (62.7, 75.9) | 72.8 (67.0, 77.8) |
| *SII (95% CI)* | *11.1 (-35.9, 58.1)* | *2.1 (-36.3, 40.6)* | *19.0 (-7.0, 45.0)* | *17.1 (1.3, 32.8)* | *10.9 (-13.5, 35.3)* | *13.3 (4.1, 22.4)* |
| *RII (95% CI)* | *0.17 (-0.54, 0.88)* | *0.03 (0.58, 0.65)* | *0.26 (-0.10, 0.62)* | *0.23 (0.02, 0.44)* | *0.14 (-0.17, 0.46)* | *0.17 (0.05, 0.28)* |
| **Five-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 32.4 (17.6, 48.0) | 31.1 (18.4, 44.7) | 50.7 (38.6, 61.6) | 54.5 (43.6, 64.2) | 52.6 (43.1, 61.2) | 69.3 (60.8, 76.3) |
| 2 | 35.3 (22.6, 48.2) | 39.7 (27.2, 51.9) | 34.9 (24.9, 45.1) | 50.0 (40.3, 59.0) | 64.5 (56.0, 71.8) | 60.8 (52.6, 68.1) |
| 3 | 31.1 (18.4, 44.7) | 18.3 (9.8, 29.0) | 50.5 (40.1, 60.0) | 46.4 (37.0, 55.3) | 54.2 (45.7, 61.9) | 60.6 (52.7, 67.6) |
| 4 | 30.0 (19.8, 40.9) | 31.0 (20.7, 41.8) | 40.2 (30.2, 50.0) | 53.2 (43.4, 62.0) | 52.4 (44.5, 59.7) | 57.9 (49.7, 65.3) |
| 5 – Most deprived | 31.1 (21.0, 41.7) | 30.6 (21.8, 39.8) | 32.6 (24.7, 40.7) | 43.3 (34.6, 51.7) | 45.2 (37.9, 52.1) | 54.0 (47.4, 60.1) |
| *SII (95% CI)* | *4.0 (-5.3, 13.3)* | *3.0 (-38.7, 44.8)* | *17.0 (-21.9, 55.8)* | *9.6 (-11.2, 30.4)* | *16.0 (-12.6, 44.7)* | *16.2 (5.2, 27.3)* |
| *RII (95% CI)* | *0.13 (-0.17, 0.42)* | *0.10 (-1.28, 1.49)* | *0.42 (-0.54, 1.37)* | *0.20 (-0.23, 0.62)* | *0.30 (-0.24, 0.84)* | *0.27 (0.09, 0.46)* |
| **10-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 26.5 (13.2, 41.8) | 26.7 (14.9, 40.0) | 38.0 (26.9, 49.1) | 42.0 (31.7, 52.1) | 48.1 (38.7, 56.8) | N/A |
| 2 | 27.5 (16.1, 40.0) | 24.1 (14.1, 35.7) | 26.5 (17.6, 36.3) | 38.0 (28.9, 47.0) | 50.9 (41.7, 59.4) | N/A |
| 3 | 22.2 (11.5, 35.1) | 10 (4.1, 19.1) | 34.7 (25.4, 44.3) | 36.6 (27.8, 45.5) | 42.5 (34.2, 50.5) | N/A |
| 4 | 18.6 (10.5, 28.4) | 22.5 (13.7, 32.8) | 28.3 (19.5, 37.7) | 39.4 (30.3, 48.5) | 41.4 (33.7, 49.0) | N/A |
| 5 – Most deprived | 13.5 (6.9, 22.3) | 11.2 (6.0, 18.4) | 20.9 (14.4, 28.3) | 26.0 (18.7, 33.8) | 28.7 (21.9, 35.8) | N/A |
| *SII (95% CI)* | *18.5 (11.5, 25.5)* | *16.1 (-17.0, 49.2)* | *17.3 (-7.2, 41.8)* | *16.1 (-6.1, 38.3)* | *26.0 (5.9, 46.1)* | *N/A* |
| *RII (95% CI)* | *0.90 (0.56, 1.25)* | *0.91 (-0.96, 2.77)* | *0.60 (-0.25, 1.46)* | *0.45 (-0.17, 1.07)* | *0.63 (0.14, 1.12)* | *N/A* |

**Appendix 2.20 – Overall survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the larynx**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 80.1 (72.6, 85.8) | 79.7 (72.5, 85.3) | 84.0 (77.8, 88.6) | 79.9 (72.6, 85.4) | 85.0 (78.5, 89.7) | 83.1 (76.0, 88.3) |
| 2 | 84.4 (78.3, 89.0) | 83.2 (77.5, 87.5) | 84.8 (79.2, 89.0) | 81.6 (76.0, 86.0) | 80.5 (74.4, 85.2) | 82.4 (76.1, 87.1) |
| 3 | 85.8 (80.2, 89.9) | 83.5 (78.4, 87.5) | 83.5 (78.5, 87.3) | 79.7 (74.1, 84.2) | 82.6 (77.5, 86.7) | 84.0 (79.0, 88.0) |
| 4 | 80.0 (74.2, 84.6) | 82.6 (77.8, 86.5) | 79.1 (74.3, 83.1) | 82.5 (77.5, 86.4) | 82.6 (77.7, 86.5) | 77.6 (72.0, 82.1) |
| 5 – Most deprived | 80.2 (75.7, 83.9) | 77.5 (73.1, 81.2) | 78.1 (73.7, 81.8) | 79.8 (75.6, 83.5) | 77.0 (72.4, 80.9) | 76.6 (71.9, 80.7) |
| *SII (95% CI)* | *4.1 (-9.9, 18.0)* | *5.6 (-7.4, 18.7)* | *9.3 (3.0, 15.7)* | *0.6 (-7.0, 8.1)* | *7.6 (-3.9, 19.1)* | *9.8 (-0.2, 20.0)* |
| *RII (95% CI)* | *0.05 (-0.12, 0.22)* | *0.07 (-0.09, 0.23)* | *0.11 (0.04, 0.19)* | *0.01 (-0.09, 0.10)* | *0.09 (-0.05, 0.24)* | *0.12 (0.00, 0.25)* |
| **Five-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 48.9 (40.5, 56.9) | 49.7 (41.5, 57.3) | 58.6 (51.0, 65.3) | 56.5 (48.3, 63.9) | 66.9 (59.0, 73.6) | 64.2 (55.3, 71.7) |
| 2 | 55.0 (47.4, 61.9) | 48.2 (41.4, 54.6) | 61.6 (54.7, 67.8) | 51.7 (45.1, 57.9) | 53.3 (46.4, 59.8) | 56.7 (48.4, 64.2) |
| 3 | 52.0 (44.9, 58.6) | 54.6 (48.4, 60.4) | 54.0 (47.9, 59.6) | 53.7 (47.2, 59.7) | 51.3 (45.1, 57.1) | 52.0 (44.9, 58.7) |
| 4 | 52.2 (45.5, 58.4) | 54.5 (48.7, 60.0) | 51.8 (46.3, 57.1) | 56.8 (50.9, 62.4) | 58.0 (52.2, 63.4) | 48.8 (41.7, 55.5) |
| 5 – Most deprived | 47.7 (42.6, 52.7) | 45.3 (40.5, 50.1) | 46.3 (41.4, 51.2) | 47.4 (42.4, 52.2) | 48.9 (43.8, 53.9) | 49.3 (43.1, 55.2) |
| *SII (95% CI)* | *5.6 (-8.5, 19.7)* | *5.3 (-18.8, 29.5)* | *18.1 (7.5, 28.7)* | *8.1 (-11.3, 27.6)* | *13.0 (-15.9, 41.8)* | *15.4 (-1.4, 32.2)* |
| *RII (95% CI)* | *0.11 (-0.17, 0.39)* | *0.11 (-0.38, 0.59)* | *0.34 (0.14, 0.54)* | *0.15 (0.22, 0.53)* | *0.24 (-0.29, 0.77)* | *0.29 (-0.03, 0.61)* |
| **10-year overall survival (95% CI)** | | | | | | |
| 1 – Least deprived | 33.3 (25.7, 41.1) | 32.7 (25.4, 40.1) | 35.4 (28.5, 42.3) | 35.1 (27.6, 42.6) | 49.7 (41.3, 57.6) | N/A |
| 2 | 34.4 (27.6, 41.4) | 33.6 (27.5, 39.9) | 44.5 (37.8, 51.1) | 35.9 (29.8, 42.0) | 35.5 (28.5, 42.6) | N/A |
| 3 | 31.4 (25.1, 37.8) | 38.1 (32.2, 43.9) | 32.4 (27.0, 37.9) | 37.8 (31.8, 43.8) | 35.3 (29.0, 41.6) | N/A |
| 4 | 31.3 (25.4, 37.3) | 37.5 (32.0, 42.9) | 37.6 (32.4, 42.8) | 42.1 (36.3, 47.8) | 38.7 (32.5, 44.8) | N/A |
| 5 – Most deprived | 30.3 (25.7, 35.0) | 28.7 (24.4, 33.1) | 28.5 (24.1, 33.0) | 28.7 (24.3, 33.2) | 27.8 (22.9, 32.9) | N/A |
| *SII (95% CI)* | *4.7 (0.3, 9.1)* | *6.5 (-15.6, 28.6)* | *12.5 (-13.9, 38.8)* | *8.0 (-20.6, 36.7)* | *18.6 (-7.9, 45.2)* | *N/A* |
| *RII (95% CI)* | *0.15 (0.01, 0.29)* | *0.19 (-0.46, 0.85)* | *0.36 (-0.40, 1.12)* | *0.23 (-0.59, 1.04)* | *0.52 (-0.22, 1.26)* | *N/A* |

**Appendix 2.21 – Disease-specific survival by Carstairs 1991 Category per year group of diagnosis for the whole cohort**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 84.3 (80.5, 87.4) | 79.3 (75.4, 82.6) | 83.3 (80.1, 86.0) | 84.8 (81.6, 87.4) | 84.2 (81.1, 86.8) | 85.7 (82.9, 88.0) |
| 2 | 82.4 (78.9, 85.4) | 80.2 (76.9, 83.1) | 82.4 (79.3, 85.1) | 78.9 (75.9, 81.6) | 82.3 (79.4, 84.7) | 84.7 (82.2, 86.8) |
| 3 | 84.3 (81.1, 87.0) | 80.5 (77.3, 83.3) | 80.6 (77.7, 83.2) | 80.6 (77.6, 83.2) | 82.9 (80.3, 85.2) | 82.7 (80.1, 85.0) |
| 4 | 78.1 (74.7, 81.0) | 78.1 (75.0, 80.8) | 75.9 (72.9, 78.7) | 79.5 (76.7, 82.1) | 81.5 (78.8, 83.8) | 81.4 (78.8, 83.8) |
| 5 – Most deprived | 79.2 (76.4, 81.7) | 75.3 (72.5, 77.9) | 74.2 (71.5, 76.7) | 75.8 (73.1, 78.3) | 78.0 (75.4, 80.3) | 77.5 (74.9, 79.8) |
| *SII (95% CI)* | *7.2 (-3.0, 17.5)* | *6.3 (-0.6, 13.1)* | *12.7 (7.8, 17.6)* | *8.4 (-1.5, 18.2)* | *7.0 (1.4, 12.7)* | *10.3 (6.4, 14.2)* |
| *RII (95% CI)* | *0.09 (-0.03, 0.21)* | *0.08 (-0.01, 0.17)* | *0.16 (0.10, 0.22)* | *0.11 (-0.02, 0.23)* | *0.09 (0.02, 0.16)* | *0.13 (0.08, 0.17)* |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 63.0 (58.1, 67.5) | 59.3 (54.6, 63.7) | 62.4 (58.3, 66.2) | 70.2 (66.2, 73.8) | 70.7 (66.9, 74.2) | 73.9 (70.3, 77.1) |
| 2 | 63.1 (58.6, 67.2) | 56.6 (52.5, 60.5) | 62.4 (58.5, 66.0) | 62.8 (59.2, 66.1) | 68.2 (64.7, 71.4) | 71.2 (67.9, 74.2) |
| 3 | 64.8 (60.7, 68.7) | 55.7 (51.7, 59.4) | 58.6 (55.0, 62.0) | 62.4 (58.8, 65.8) | 66.6 (63.2, 69.7) | 69.1 (65.7, 72.2) |
| 4 | 59.9 (56.0, 63.7) | 55.5 (51.8, 59.0) | 56.1 (52.6, 59.4) | 63.2 (59.8, 66.3) | 65.2 (62.0, 68.3) | 66.7 (63.3, 69.8) |
| 5 – Most deprived | 56.8 (53.3, 60.2) | 52.0 (48.7, 55.2) | 50.6 (47.5, 53.6) | 56.1 (53.0, 59.1) | 60.6 (57.6, 63.5) | 63.9 (60.7, 66.8) |
| *SII (95% CI)* | *9.3 (-1.0, 19.5)* | *8.0 (3.3, 12.6)* | *16.0 (10.1, 21.9)* | *13.6 (-0.1, 27.3)* | *11.9 (7.5, 16.3)* | *12.3 (11.3, 13.3)* |
| *RII (95% CI)* | *0.15 (-0.02, 0.32)* | *0.14 (0.06, 0.23)* | *0.28 (0.18, 0.38)* | *0.22 (-0.02, 0.44)* | *0.18 (0.11, 0.25)* | *0.18 (0.16, 0.19)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 59.5 (54.4, 64.2) | 52.0 (47.0, 56.8) | 57.4 (53.1, 61.3) | 66.0 (61.9, 69.9) | 66.4 (62.3, 70.2) | N/A |
| 2 | 58.1 (53.4, 62.5) | 50.4 (46.2, 54.5) | 56.2 (52.2, 60.0) | 58.7 (54.9, 62.2) | 64.5 (60.7, 67.9) | N/A |
| 3 | 58.4 (54.0, 62.6) | 49.6 (45.5, 53.5) | 53.0 (49.3, 56.6) | 57.7 (53.9, 61.2) | 61.6 (57.9, 65.1) | N/A |
| 4 | 54.4 (50.2, 58.4) | 48.7 (44.9, 52.4) | 49.5 (45.9, 53.0) | 56.9 (53.4, 60.3) | 60.5 (57.0, 63.9) | N/A |
| 5 – Most deprived | 50.5 (46.8, 54.0) | 43.6 (40.1, 47.0) | 42.5 (39.3, 45.6) | 51.2 (48.0, 54.4) | 55.6 (52.4, 58.8) | N/A |
| *SII (95% CI)* | *12.0 (5.3, 18.6)* | *10.1 (3.7, 16.6)* | *19.6 (12.8, 26.3)* | *15.2 (4.6, 25.7)* | *13.1 (8.7, 17.4)* | *N/A* |
| *RII (95% CI)* | *0.22 (0.10, 0.34)* | *0.21 (0.08, 0.34)* | *0.39 (0.25, 0.52)* | *0.25 (0.08, 0.45)* | *0.21 (0.14, 0.29)* | *N/A* |

**Appendix 2.22 – Disease-specific survival by Carstairs 1991 Category per year group of diagnosis for males**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 85.7 (81.1, 89.2) | 80.1 (75.4, 84.1) | 85.9 (82.2, 88.8) | 85.0 (81.1, 88.2) | 86.9 (83.3, 89.7) | 85.1 (81.7, 87.8) |
| 2 | 83.6 (79.4, 87.1) | 83.4 (79.6, 86.6) | 84.3 (80.7, 87.3) | 78.0 (74.3, 81.2) | 83.2 (79.8, 86.1) | 87.1 (84.2, 89.4) |
| 3 | 83.5 (79.6, 86.7) | 83.0 (79.4, 86.0) | 80.4 (77.0, 83.4) | 81.1 (77.5, 84.2) | 83.8 (80.7, 86.5) | 82.5 (79.3, 85.2) |
| 4 | 77.0 (72.9, 80.6) | 79.3 (75.7, 82.4) | 76.7 (73.1, 79.9) | 79.4 (76.0, 82.3) | 82.7 (79.6, 85.3) | 81.2 (78.1, 84.0) |
| 5 – Most deprived | 78.5 (75.2, 81.5) | 75.9 (72.6, 78.8) | 74.1 (70.9, 77.1) | 75.6 (72.4, 78.5) | 77.1 (74.1, 79.8) | 78.2 (75.3, 80.9) |
| *SII (95% CI)* | *10.0 (-0.7, 20.6)* | *8.4 (-2.9, 19.7)* | *15.6 (12.2, 19.1)* | *8.3 (-4.1, 20.6)* | *10.6 (1.8, 19.4)* | *10.4 (2.7, 18.2)* |
| *RII (95% CI)* | *0.12 (-0.01, 0.25)* | *0.11 (-0.04, 0.25)* | *0.20 (0.15, 0.24)* | *0.10 (-0.05, 0.26)* | *0.13 (0.02, 0.24)* | *0.13 (0.03, 0.22)* |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 64.9 (58.9, 70.3) | 61.7 (56.0, 66.9) | 63.1 (58.3, 67.6) | 69.5 (64.5, 73.9) | 72.4 (67.9, 76.4) | 74.9 (70.7, 78.6) |
| 2 | 64.4 (59.0, 69.3) | 58.5 (53.5, 63.1) | 64.3 (59.6, 68.5) | 62.1 (57.8, 66.1) | 69.9 (65.8, 73.7) | 71.3 (67.3, 75.0) |
| 3 | 63.6 (58.5, 68.1) | 55.9 (51.3, 60.3) | 56.8 (52.5, 60.8) | 62.2 (57.8, 66.2) | 66.7 (62.7, 70.4) | 70.1 (66.2, 73.7) |
| 4 | 58.4 (53.6, 62.9) | 55.0 (50.6, 59.1) | 54.1 (49.8, 58.1) | 61.7 (57.7, 65.5) | 65.0 (61.2, 68.6) | 65.1 (61.0, 68.9) |
| 5 – Most deprived | 56.9 (52.8, 60.8) | 50.3 (46.4, 54.1) | 50.3 (46.6, 53.8) | 54.0 (50.3, 57.6) | 58.3 (54.7, 61.7) | 63.3 (59.5, 66.9) |
| *SII (95% CI)* | *11.6 (5.2, 18.0)* | *13.2 (8.6, 17.8)* | *18.2 (9.2, 27.2)* | *15.6 (2.4, 28.9)* | *17.2 (11.2, 23.2)* | *14.6 (9.7, 19.6)* |
| *RII (95% CI)* | *0.19 (0.08, 0.30)* | *0.24 (0.16, 0.32)* | *0.32 (0.16, 0.48)* | *0.26 (0.04, 0.48)* | *0.26 (0.17, 0.35)* | *0.21 (0.14, 0.29)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 61.4 (55.1, 67.1) | 53.9 (47.8, 59.6) | 57.9 (52.9, 62.7) | 65.7 (60.5, 70.4) | 67.1 (62.0, 71.6) | N/A |
| 2 | 58.0 (52.2, 63.4) | 52.4 (47.2, 57.3) | 58.0 (53.1, 62.6) | 58.2 (53.8, 62.4) | 67.9 (63.6, 71.8) | N/A |
| 3 | 56.7 (51.3, 61.7) | 50.1 (45.4, 54.7) | 49.9 (45.5, 54.1) | 57.0 (52.4, 61.3) | 62.5 (58.2, 66.6) | N/A |
| 4 | 53.3 (48.3, 58.1) | 47.8 (43.3, 52.1) | 48.2 (43.9, 52.4) | 56.1 (51.9, 60.2) | 61.8 (57.8, 65.6) | N/A |
| 5 – Most deprived | 48.8 (44.4, 53.0) | 41.3 (37.2, 45.3) | 41.5 (37.8, 45.2) | 49.4 (45.5, 53.1) | 53.8 (50.0, 57.4) | N/A |
| *SII (95% CI)* | *15.5 (12.3, 18.7)* | *16.1 (9.8, 22.4)* | *22.0 (12.8, 31.2)* | *16.9 (5.9, 28.0)* | *17.7 (6.8, 28.6)* | *N/A* |
| *RII (95% CI)* | *0.28 (0.23, 0.34)* | *0.34 (0.20, 0.47)* | *0.44 (0.26, 0.63)* | *0.30 (0.10, 0.50)* | *0.29 (0.11, 0.46)* | *N/A* |

**Appendix 2.23 – Disease-specific survival by Carstairs 1991 Category per year group of diagnosis for females**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 81.4 (74.0, 86.8) | 77.4 (69.8, 83.3) | 77.0 (70.1, 82.5) | 84.3 (78.5, 88.7) | 77.8 (71.0, 83.1) | 87.1 (81.9, 90.8) |
| 2 | 79.6 (72.7, 85.0) | 73.0 (66.3, 78.6) | 78.3 (72.1, 83.3) | 81.0 (75.4, 85.5) | 80.1 (74.5, 84.6) | 79.4 (74.2, 83.6) |
| 3 | 86.3 (80.3, 90.6) | 73.5 (66.4, 79.3) | 81.1 (75.3, 85.7) | 79.5 (74.0, 83.9) | 80.7 (75.5, 85.0) | 83.3 (78.3, 87.3) |
| 4 | 80.6 (74.3, 85.5) | 74.8 (68.6, 80.0) | 74.2 (68.5, 79.0) | 79.9 (74.5, 84.3) | 78.5 (73.2, 82.9) | 81.9 (76.9, 86.0) |
| 5 – Most deprived | 81.0 (75.4, 85.4) | 73.8 (68.1, 78.7) | 74.3 (69.1, 78.8) | 76.4 (71.2, 80.9) | 80.3 (75.4, 84.4) | 75.5 (70.5, 79.8) |
| *SII (95% CI)* | *0.5 (-14.3, 15.4)* | *1.9 (-6.5, 10.4)* | *5.8 (-7.6, 19.3)* | *8.3 (2.4, 14.2)* | *-1.3 (-7.9, 5.3)* | *10.3 (-6.2, 26.9)* |
| *RII (95% CI)* | *0.01 (-0.18, 0.19)* | *0.03 (-0.09, 0.14)* | *0.08 (-0.10, 0.25)* | *0.10 (0.03, 0.18)* | *-0.02, (-0.10, 0.07)* | *0.13 (-0.08, 0.33)* |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 59.5 (50.7, 67.2) | 54.4 (45.7, 62.2) | 60.6 (52.9, 67.5) | 71.6 (64.6, 77.4) | 66.7 (59.3, 73.1) | 71.6 (64.5, 77.5) |
| 2 | 60.0 (52.0, 67.2) | 52.4 (45.0, 59.2) | 58.3 (51.2, 64.7) | 64.3 (57.6, 70.2) | 64.3 (57.7, 70.1) | 70.9 (65.2, 75.9) |
| 3 | 67.9 (60.1, 74.5) | 55.0 (47.2, 62.2) | 63.6 (56.7, 69.8) | 62.9 (56.5, 68.6) | 66.2 (60.0, 71.7) | 66.8 (60.1, 72.7) |
| 4 | 63.5 (56.2, 70.0) | 56.8 (49.8, 63.2) | 60.4 (54.1, 66.0) | 66.6 (60.4, 72.1) | 65.8 (59.7, 71.2) | 70.4 (64.3, 75.7) |
| 5 – Most deprived | 56.9 (50.1, 63.2) | 56.6 (50.2, 62.5) | 51.4 (45.6, 56.9) | 61.5 (55.5, 66.9) | 67.1 (61.3, 72.2) | 64.9 (59.2, 69.9) |
| *SII (95% CI)* | *3.4 (-21.2, 28.0)* | *-4.7 (-11.0, 1.7)* | *10.6 (-10.6, 31.9)* | *8.2 (-7.8, 24.2)* | *-1.6 (-7.1, 3.9)* | *7.3 (-3.6, 18.3)* |
| *RII (95% CI)* | *0.06 (-0.34, 0.46)* | *-0.08 (-0.20, 0.03)* | *0.18 (-0.18, 0.55)* | *0.13 (-0.12, 0.37)* | *-0.02 (-0.11, 0.06)* | *0.11 (-0.05, 0.27)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 55.9 (47.0, 63.9) | 48.2 (39.4, 56.4) | 55.9 (48.0, 63.1) | 66.8 (59.5, 73.2) | 64.7 (57.1, 71.3) | N/A |
| 2 | 57.8 (49.6, 65.1) | 46.0 (38.5, 53.2) | 52.3 (45.1, 59.1) | 59.6 (52.5, 66.0) | 57.2 (49.9, 63.8) | N/A |
| 3 | 62.5 (54.3, 69.6) | 48.1 (40, 55.6) | 61.3 (54.2, 67.6) | 59.1 (52.4, 65.1) | 59.2 (52.0, 65.8) | N/A |
| 4 | 57.0 (49.3, 64.1) | 51.0 (43.8, 57.8) | 52.2 (45.8, 58.3) | 58.8 (52.0, 64.9) | 57.3 (50.1, 63.9) | N/A |
| 5 – Most deprived | 54.6 (47.6, 61) | 50.0 (43.3, 56.2) | 45.1 (39.2, 50.9) | 56.0 (49.7, 61.8) | 60.8 (54.3, 66.7) | N/A |
| *SII (95% CI)* | *3.4 (13.3, 20.0)* | *-4.6 (-12.3, 3.2)* | *13.5 (-12.7, 39.7)* | *10.4 (-0.7, 21.5)* | *2.1 (-13.9, 18.2)* | *N/A* |
| *RII (95% CI)* | *0.06 (-0.23, 0.35)* | *-0.09 (-0.25, 0.07)* | *0.26 (-0.24, 0.76)* | *0.17 (-0.01, 0.36)* | *0.04 (-0.23, 0.31)* | *N/A* |

**Appendix 2.24 – Disease-specific survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the oral cavity**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 80.6 (72.3, 86.7) | 78.9 (71.8, 84.5) | 76.4 (69.9, 81.7) | 85.8 (80.4, 89.8) | 82.4 (76.8, 86.8) | 87.1 (82.8, 90.4) |
| 2 | 79.9 (72.7, 85.4) | 76.3 (70.2, 81.2) | 81.6 (75.8, 86.2) | 74.5 (68.6, 79.4) | 78.6 (73.4, 83.0) | 84.5 (80.2, 88.0) |
| 3 | 76.4 (69.2, 82.1) | 77.1 (70.7, 82.3) | 77.0 (71.3, 81.7) | 77.3 (72.0, 81.8) | 83.1 (78.5, 86.8) | 81.2 (76.3, 85.2) |
| 4 | 72.2 (65.1, 78.0) | 76.2 (70.2, 81.1) | 71.8 (65.7, 76.9) | 77.6 (72.6, 81.8) | 79.6 (74.8, 83.6) | 80.8 (76.1, 84.7) |
| 5 – Most deprived | 77.5 (72.0, 82.0) | 71.6 (66.1, 76.4) | 75.1 (70.2, 79.3) | 75.6 (70.7, 79.7) | 75.2 (70.5, 79.2) | 75.3 (70.5, 79.4) |
| *SII (95% CI)* | 4.9 (-11.5, 21.2) | 7.9 (0.2, 15.6) | 6.0 (-10.4, 22.4) | 7.2 (-12.2, 26.6) | 7.4 (6.2, 20.9) | 14.0 (8.1, 19.8) |
| *RII (95% CI)* | 0.06 (-0.15, 0.28) | 0.10 (0.00, 0.21) | 0.08 (-0.14, 0.29) | 0.09 (-0.15, 0.34) | 0.09 (-0.08, 0.26) | 0.17 (0.10, 0.24) |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 53.2 (43.1, 62.4) | 51.6 (43.2, 59.3) | 59.1 (51.7, 65.7) | 71.2 (64.6, 76.8) | 67.9 (61.3, 73.6) | 75.3 (69.4, 80.1) |
| 2 | 53.9 (45.4, 61.7) | 52.7 (45.8, 59.1) | 59.1 (52.0, 65.5) | 61.0 (54.5, 66.8) | 64.4 (58.3, 69.8) | 72.0 (66.4, 76.8) |
| 3 | 55.0 (47.0, 62.4) | 49.2 (41.8, 56.1) | 55.2 (48.7, 61.2) | 60.0 (53.9, 65.5) | 68.0 (62.5, 72.9) | 64.9 (58.6, 70.4) |
| 4 | 56.5 (48.8, 63.5) | 50.8 (44.0, 57.3) | 51.8 (45.3, 58.0) | 59.1 (53.3, 64.5) | 60.4 (54.8, 65.6) | 65.6 (59.7, 70.9) |
| 5 – Most deprived | 51.8 (45.3, 57.9) | 47.5 (41.5, 53.4) | 51.3 (45.8, 56.5) | 53.8 (48.2, 59.0) | 57.0 (51.8, 61.9) | 58.6 (52.5, 64.3) |
| *SII (95% CI)* | *1.8 (-9.0, 12.6)* | *5.7 (-1.4, 12.7)* | *11.4 (4.8, 17.9)* | *17.3 (2.4, 32.2)* | *13.6 (-0.5, 27.7)* | *20.2 (10.5, 29.9)* |
| *RII (95% CI)* | *0.03 (-0.17, 0.23)* | *0.11 (-0.03, 0.25)* | *0.21 (0.09, 0.33)* | *0.29 (0.04, 0.54)* | *0.22 (-0.01, 0.44)* | *0.30 (0.16, 0.45)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 49.1 (38.8, 58.7) | 45.8 (37.4, 53.8) | 53.0 (45.4, 60.0) | 67.2 (60.2, 73.2) | 62.3 (55.0, 68.7) | N/A |
| 2 | 48.3 (39.3, 56.7) | 46.3 (39.3, 53.1) | 50.2 (42.9, 57.1) | 56.3 (49.5, 62.5) | 60.5 (53.9, 66.4) | N/A |
| 3 | 47.1 (38.7, 55.0) | 39.5 (32.1, 46.7) | 52.6 (46.0, 58.7) | 55.5 (49.3, 61.3) | 61.4 (54.9, 67.2) | N/A |
| 4 | 49.1 (41.0, 56.6) | 44.9 (38.0, 51.6) | 43.1 (36.4, 49.5) | 52.2 (46.1, 57.9) | 53.9 (47.5, 59.8) | N/A |
| 5 – Most deprived | 45.1 (38.4, 51.6) | 40.3 (34.1, 46.4) | 43.3 (37.6, 48.8) | 47.5 (41.7, 53.1) | 51.7 (46.1, 56.9) | N/A |
| *SII (95% CI)* | *4.3 (-3.0, 11.6)* | *6.5 (-7.9, 20.8)* | *13.7 (-0.8, 28.1)* | *20.6 (6.3, 34.9)* | *14.5 (3.8, 25.1)* | *N/A* |
| *RII (95% CI)* | *0.09 (-0.06, 0.24)* | *0.15 (-0.18, 0.48)* | *0.29 (-0.02, 0.59)* | *0.38 (0.12, 0.64)* | *0.25 (0.07, 0.44)* | *N/A* |

**Appendix 2.25 – Disease-specific survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the oropharynx**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 83.2 (64.1, 92.6) | 64.9 (48.7, 77.2) | 88.6 (78.5, 94.1) | 84.8 (75.3, 90.9) | 81.9 (73.4, 87.9) | 85.9 (79.4, 90.5) |
| 2 | 71.9 (57.3, 82.3) | 79.9 (66.6, 88.3) | 70.7 (59.6, 79.3) | 79.4 (70.4, 85.9) | 85.5 (78.5, 90.4) | 84.8 (79.2, 89.0) |
| 3 | 79.8 (64.7, 88.9) | 60.3 (46.6, 71.6) | 79.6 (69.9, 86.5) | 82.0 (73.5, 88.0) | 84.5 (77.4, 89.5) | 82.2 (75.9, 87.0) |
| 4 | 60.6 (47.7, 71.3) | 66.8 (54.0, 76.7) | 73.4 (63.0, 81.3) | 76.5 (67.2, 83.5) | 82.6 (75.8, 87.6) | 82.8 (76.6, 87.5) |
| 5 – Most deprived | 68.8 (56.8, 78.0) | 70.4 (60.1, 78.6) | 69.9 (61.0, 77.1) | 71.8 (62.8, 79.0) | 76.9 (69.9, 82.4) | 77.4 (71.7, 82.1) |
| *SII (95% CI)* | *17.1 (-22.6, 56.9)* | *0.4 (-40.0, 40.8)* | *16.3 (-14.0, 46.7)* | *14.5 (2.5, 26.6)* | *8.1 (-6.1, 22.3)* | *10.2 (3.1, 17.4)* |
| *RII (95% CI)* | *0.24 (-0.32, 0.80)* | *0.01 (-0.59, 0.59)* | *0.22 (-0.19, 0.62)* | *0.19 (0.03, 0.34)* | *0.10 (-0.07, 0.27)* | *0.12 (0.04, 0.21)* |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 54.0 (33.8, 70.5) | 49.1 (33.0, 63.3) | 57.6 (44.7, 68.5) | 67.6 (56.3, 76.5) | 64.7 (54.8, 72.9) | 76.1 (67.9, 82.5) |
| 2 | 51.1 (35.8, 64.6) | 44.5 (31.0, 57.1) | 42.8 (31.7, 53.3) | 62.6 (52.3, 71.3) | 73.7 (65.4, 80.3) | 71.3 (63.8, 77.5) |
| 3 | 46.0 (30.0, 60.5) | 23.6 (13.2, 35.8) | 61.0 (50.0, 70.3) | 59.9 (49.9, 68.5) | 67.7 (59.1, 74.9) | 69.1 (61.6, 75.4) |
| 4 | 37.4 (25.5, 49.2) | 43.2 (30.7, 55.2) | 51.9 (40.8, 61.8) | 62.7 (52.7, 71.2) | 65.0 (56.9, 71.9) | 67.9 (60.0, 74.7) |
| 5 – Most deprived | 36.3 (25.1, 47.6) | 47.2 (36.1, 57.5) | 41.5 (32.5, 50.2) | 54.1 (44.6, 62.6) | 59.0 (51.0, 66.1) | 64.9 (58.5, 70.6) |
| *SII (95% CI)* | *23.8 (10.7, 36.9)* | *-4.5 (-61.4, 52.3)* | *14.2 (-30.3, 58.7)* | *13.4 (-1.2, 28.0)* | *12.4 (-10.0, 34.7)* | *12.7 (7.2, 18.2)* |
| *RII (95% CI)* | *0.55 (0.25, 0.86)* | *-0.11 (-1.47, 1.25)* | *0.28 (-0.60, 1.17)* | *0.22 (-0.02, 0.46)* | *0.19 (-0.15, 0.53)* | *0.18 (0.10, 0.26)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 54.0 (33.8, 70.5) | 42.1 (26.1, 57.3) | 51.0 (38.1, 62.4) | 62.7 (50.9, 72.4) | 63.6 (53.6, 71.9) | N/A |
| 2 | 51.1 (35.8, 64.6) | 35.7 (22.9, 48.7) | 39.7 (28.8, 50.4) | 58.9 (48.4, 68) | 68.9 (59.6, 76.5) | N/A |
| 3 | 35.6 (20.3, 51.2) | 17.2 (8.3, 28.8) | 56.6 (45.3, 66.4) | 55.0 (44.7, 64.1) | 62.6 (53.3, 70.5) | N/A |
| 4 | 33.2 (21.6, 45.3) | 39.2 (26.8, 51.3) | 46.1 (35.0, 56.5) | 59.4 (49.2, 68.2) | 61.2 (52.7, 68.6) | N/A |
| 5 – Most deprived | 24.3 (14.6, 35.5) | 28.0 (17.2, 39.8) | 33.7 (24.9, 42.6) | 51.4 (41.7, 60.3) | 54.0 (45.7, 61.5) | N/A |
| *SII (95% CI)* | *37.8 (20.0, 55.6)* | *9.7 (-42.5, 62.0)* | *17.9 (-26.8, 62.6)* | *11.0 (-4.3, 26.3)* | *15.1 (-1.8, 32.0)* | *N/A* |
| *RII (95% CI)* | *1.02 (0.54, 1.50)* | *0.31 (-1.34, 1.95)* | *0.40 (-0.60, 1.41)* | *0.19 (-0.08, 0.46)* | *0.25 (-0.03, 0.52)* | *N/A* |

**Appendix 2.26 – Disease-specific survival by Carstairs 1991 Category per year group of diagnosis for people with cancer of the larynx**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 86.7 (79.7, 91.4) | 83.9 (77.0, 88.9) | 87.6 (81.8, 91.7) | 84.7 (77.9, 89.6) | 91.0 (85.2, 94.6) | 90.8 (84.7, 94.6) |
| 2 | 90.8 (85.4, 94.3) | 87.0 (81.7, 90.8) | 86.6 (81.2, 90.6) | 83.9 (78.5, 88.1) | 85.9 (80.4, 90.0) | 87.9 (82.2, 91.9) |
| 3 | 90.9 (85.9, 94.1) | 86.7 (81.9, 90.3) | 86.2 (81.5, 89.7) | 83.4 (78.0, 87.5) | 86.9 (82.2, 90.5) | 89.3 (84.8, 92.5) |
| 4 | 85.0 (79.6, 89.1) | 85.8 (81.2, 89.3) | 83.6 (79.1, 87.2) | 85.7 (81.0, 89.3) | 88.0 (83.6, 91.3) | 85.1 (80.1, 88.9) |
| 5 – Most deprived | 84.7 (80.6, 88.1) | 85.3 (81.4, 88.5) | 80.8 (76.5, 84.4) | 82.2 (78.0, 85.6) | 83.7 (79.5, 87.2) | 84.1 (79.7, 87.6) |
| *SII (95% CI)* | *6.7 (-6.4, 19.9)* | *0.5 (-5.6, 6.6)* | *8.9 (5.8, 12.1)* | *2.2 (-5.2, 9.6)* | *6.0 (-4.3, 16.3)* | *8.1 (1.6, 14.7)* |
| *RII (95% CI)* | *0.08 (-0.07, 0.23)* | *0.01 (-0.07, 0.08)* | *0.11 (0.07, 0.14)* | *0.03 (0.06, 0.12)* | *0.07 (-0.05, 0.19)* | *0.09 (-0.02, 0.17)* |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 66.4 (57.4, 73.9) | 68.2 (59.8, 75.3) | 68.5 (60.9, 74.9) | 69.4 (61.0, 76.3) | 84.8 (78.0, 89.6) | 83.7 (76.3, 89.0) |
| 2 | 70.5 (62.8, 76.9) | 65.8 (58.6, 72.0) | 69.6 (62.8, 75.5) | 67.1 (60.5, 72.8) | 75.2 (68.4, 80.7) | 78.7 (71.8, 84.1) |
| 3 | 73.3 (66.2, 79.2) | 65.4 (59.0, 71.0) | 62.4 (56.2, 67.9) | 68.0 (61.5, 73.6) | 70.8 (64.6, 76.2) | 81.9 (76.1, 86.4) |
| 4 | 66.5 (59.7, 72.5) | 66.8 (60.9, 72.0) | 62.9 (57.2, 68.0) | 71.9 (66.0, 76.8) | 74.4 (68.8, 79.3) | 75.6 (69.3, 80.7) |
| 5 – Most deprived | 66.5 (61.2, 71.3) | 62.7 (57.4, 67.5) | 58.2 (53.0, 63.0) | 63.3 (58.2, 68.0) | 68.9 (63.6, 73.6) | 75.0 (69.7, 79.5) |
| *SII (95% CI)* | *4.2 (-11.9, 20.4)* | *5.4 (-2.1, 12.8)* | *13.7 (3.7, 23.6)* | *5.6 (-12.3, 23.5)* | *13.6 (-6.3, 33.4)* | *10.1 (-1.4, 21.5)* |
| *RII (95% CI)* | *0.06 (-0.17, 0.30)* | *0.08 (-0.03, 0.20)* | *0.22 (0.06, 0.37)* | *0.08 (-0.18, 0.35)* | *0.18 (-0.09, 0.45)* | *0.13 (-0.02, 0.28)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 61.5 (51.8, 69.7) | 61.1 (51.9, 69.0) | 61.3 (53.3, 68.4) | 64.4 (55.5, 71.9) | 82.6 (75.2, 88.0) | N/A |
| 2 | 63.7 (55.3, 70.9) | 57.1 (49.5, 64.0) | 62.7 (55.4, 69.0) | 64.3 (57.4, 70.4) | 71.6 (64.1, 77.9) | N/A |
| 3 | 66.8 (58.9, 73.5) | 59.3 (52.7, 65.4) | 53.0 (46.5, 59.0) | 63.8 (57.0, 69.8) | 66.4 (59.6, 72.3) | N/A |
| 4 | 61.2 (53.9, 67.7) | 57.3 (51.0, 63.1) | 57.3 (51.5, 62.8) | 65.9 (59.7, 71.5) | 70.8 (64.7, 76.0) | N/A |
| 5 – Most deprived | 59.9 (54.1, 65.2) | 53.5 (47.8, 58.8) | 48.4 (42.9, 53.6) | 57.4 (51.8, 62.5) | 64.3 (58.6, 69.5) | N/A |
| *SII (95% CI)* | *5.1 (-8.2, 18.4)* | *8.0 (-0.3, 16.3)* | *16.0 (-2.6, 34.7)* | *8.7 (-6.8, 24.2)* | *15.6 (-7.6, 38.7)* | *N/A* |
| *RII (95% CI)* | *0.08 (-0.13, 0.30)* | *0.14 (0.0, 0.29)* | *0.29 (-0.05, 0.63)* | *0.14 (-0.11, 0.39)* | *0.22 (-0.11, 0.56)* | *N/A* |

**Appendix 2.27 – Net survival by the nearest Carstairs Category per year group of diagnosis for the whole cohort**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 82.8 (78.2, 87.5) | 77.5 (72.7, 82.3) | 84.7 (81.1, 88.4) | 81.9 (77.9, 85.9) | 82.7 (79.0, 86.4) | 81.6 (78.2, 85.0) |
| 2 | 80.7 (76.4, 85.0) | 80.7 (76.8, 84.7) | 83.2 (79.5, 86.9) | 76.9 (73.3, 80.6) | 79.3 (75.8, 82.9) | 85.2 (82.3, 88.1) |
| 3 | 82.0 (78.0, 86.0) | 82.5 (78.8, 86.1) | 79.9 (76.4, 83.4) | 80.5 (76.9, 84.1) | 81.0 (77.7, 84.2) | 79.7 (76.5, 82.9) |
| 4 | 74.8 (70.6, 78.9) | 75.8 (72.1, 79.6) | 74.7 (71.1, 78.4) | 77.7 (74.3, 81.1) | 79.3 (76.1, 82.5) | 77.4 (74.1, 80.6) |
| 5 – Most deprived | 78.3 (74.9, 81.8) | 72.1 (68.7, 75.5) | 72.6 (69.3, 75.9) | 74.6 (71.3, 77.8) | 74.6 (71.5, 77.7) | 73.9 (70.9, 77.0) |
| *SII (95% CI)* | *6.6 (-7.3, 20.5)* | *10.7 (-5.8, 27.1)* | *16.5 (11.4, 21.6)* | *6.9 (-3.8, 17.7)* | *8.7 (-0.2, 17.6)* | *12.5 (1.1, 23.9)* |
| *RII (95% CI)* | *0.08 (-0.09, 0.26)* | *0.14 (-0.08, 0.35)* | *0.21 (0.15, 0.28)* | *0.09 (-0.05, 0.23)* | *0.11 (0.0, 0.22)* | *0.16 (0.01, 0.30)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 55.5 (48.4, 62.6) | 54.7 (47.8, 61.6) | 59.8 (54.1, 65.5) | 60.9 (55.5, 66.3) | 63.0 (57.9, 68.2) | 67.7 (62.8, 72.7) |
| 2 | 54.4 (47.7, 61.1) | 52.2 (46.5, 58.0) | 60.9 (55.5, 66.3) | 53.0 (48.2, 57.8) | 58.0 (53.1, 62.9) | 63.8 (59.1, 68.4) |
| 3 | 54.5 (48.4, 60.5) | 53.1 (47.6, 58.5) | 56.0 (51.0, 60.9) | 56.7 (51.6, 61.8) | 57.7 (53.2, 62.3) | 57.3 (52.6, 62.0) |
| 4 | 52.7 (47.0, 58.3) | 50.5 (45.6, 55.5) | 50.5 (45.7, 55.2) | 53.3 (48.8, 57.9) | 57.5 (53.2, 61.8) | 50.6 (45.7, 55.5) |
| 5 – Most deprived | 49.0 (44.1, 53.8) | 42.5 (38.2, 46.9) | 47.7 (43.5, 51.8) | 48.1 (43.9, 52.3) | 48.5 (44.7, 52.4) | 50.7 (46.2, 55.2) |
| *SII (95% CI)* | *8.4 (2.1, 13.6)* | *15.0 (2.5, 27.5)* | *17.9 (9.6, 26.2)* | *12.5 (-1.8, 26.8)* | *15.6 (2.1, 29.2)* | *22.9 (10.3, 35.5)* |
| *RII (95% CI)* | *0.16 (0.06, 0.26)* | *0.30 (0.05, 0.56)* | *0.33 (0.18, 0.49)* | *0.23 (-0.03, 0.50)* | *0.28 (0.04, 0.52)* | *0.40 (0.18, 0.62)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 47.9 (38.7, 57.1) | 38.2 (27.9, 48.5) | 47.7 (40.4, 55.0) | 50.8 (44.7, 56.8) | 47.7 (39.3, 56.1) | N/A |
| 2 | 40.8 (33.1, 48.5) | 47.3 (39.5, 55.2) | 50.3 (43.1, 57.6) | 47.4 (41.3, 53.6) | 48.9 (42.4, 55.4) | N/A |
| 3 | 41.7 (33.6, 49.7) | 40.6 (34.1, 47.1) | 43.0 (35.7, 50.4) | 47.6 (41.1, 54.2) | 44.6 (35.2, 54.0) | N/A |
| 4 | 44.5 (37.0, 51.9) | 45.3 (39.1, 51.5) | 43.1 (37.4, 48.8) | 46.4 (41.2, 51.6) | 49.2 (43.6, 54.9) | N/A |
| 5 – Most deprived | 37.8 (31.9, 43.7) | 32.6 (27.7, 37.5) | 34.2 (29.5, 39.0) | 38.3 (33.3, 43.2) | 37.6 (32.9, 42.3) | N/A |
| *SII (95% CI)* | *8.4 (-7.4, 24.2)* | *11.4 (-18.7, 41.4)* | *18.8 (4.3, 33.3)* | *14.2 (2.0, 26.3)* | *12.0 (-9.3, 33.3)* | *N/A* |
| *RII (95% CI)* | *0.20 (-0.18, 0.58)* | *0.28 (-0.46, 1.03)* | *0.44 (0.10, 0.78)* | *0.31 (0.04, 0.58)* | *0.27 (-0.21, 0.74)* | *N/A* |

**Appendix 2.28 – Overall survival by the nearest Carstairs Category per year group of diagnosis for the whole cohort**

| | Year group of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 77.4 (73.3, 80.9) | 73.0 (68.9, 76.7) | 82.0 (78.6, 84.9) | 81.1 (77.7, 84.1) | 79.5 (76.0, 82.5) | 82.4 (79.5, 84.9) |
| 2 | 75.9 (72.1, 79.2) | 74.7 (71.3, 77.9) | 77.9 (74.6, 80.9) | 75.5 (72.2, 78.5) | 74.1 (70.9, 77.0) | 80.4 (77.6, 82.9) |
| 3 | 78.4 (75.0, 81.5) | 75.9 (72.6, 78.9) | 76.0 (72.9, 78.9) | 77.5 (74.5, 80.2) | 79.2 (76.4, 81.7) | 77.7 (74.9, 80.3) |
| 4 | 71.5 (68.0, 74.7) | 71.6 (68.4, 74.5) | 72.0 (69.0, 74.8) | 76.3 (73.4, 79.0) | 75.1 (72.1, 77.7) | 75.0 (72.1, 77.6) |
| 5 – Most deprived | 73.5 (70.5, 76.2) | 67.9 (65.0, 70.6) | 70.0 (67.3, 72.5) | 71.6 (69.0, 74.1) | 73.7 (71.2, 76.1) | 72.6 (70.1, 74.9) |
| *SII (95% CI)* | *6.1 (-6.1, 18.2)* | *8.6 (-3.0, 20.2)* | *14.7 (9.8, 19.5)* | *9.1 (-1.5, 19.7)* | *5.3 (-7.5, 18.0)* | *12.6 (11.4, 13.7)* |
| *RII (95% CI)* | *0.08 (-0.08, 0.24)* | *0.12 (-0.04, 0.28)* | *0.20 (0.13, 0.26)* | *0.12 (-0.02, 0.26)* | *0.07 (-0.10, 0.24)* | *0.16 (0.15, 0.18)* |
| **Five-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 46.3 (41.7, 50.8) | 43.1 (38.7, 47.3) | 53.7 (49.5, 57.7) | 55.8 (51.7, 59.7) | 58.0 (53.9, 61.8) | 60.7 (56.8, 64.3) |
| 2 | 45.4 (41.2, 49.5) | 42.9 (39.1, 46.6) | 49.3 (45.5, 53.0) | 48.2 (44.5, 51.7) | 49.2 (45.7, 52.7) | 59.9 (56.2, 63.4) |
| 3 | 46.7 (42.7, 50.6) | 43.4 (39.8, 47.1) | 47.2 (43.7, 50.6) | 49.5 (46.0, 52.9) | 52.0 (48.7, 55.1) | 51.8 (48.3, 55.3) |
| 4 | 44.4 (40.7, 48.1) | 42.5 (39.1, 45.9) | 45.7 (42.4, 48.9) | 48.2 (44.9, 51.4) | 47.2 (44.0, 50.4) | 46.0 (42.4, 49.5) |
| 5 – Most deprived | 40.5 (37.3, 43.7) | 35.4 (32.5, 38.3) | 39.8 (37.1, 42.5) | 41.8 (39.0, 44.6) | 46.7 (44.0, 49.5) | 46.3 (43.2, 49.2) |
| *SII (95% CI)* | *7.5 (-0.3, 15.4)* | *9.9 (-2.8, 22.6)* | *16.1 (10.1, 22.1)* | *13.8 (0.9, 26.7)* | *11.0 (-3.3, 25.4)* | *21.0 (7.1, 34.9)* |
| *RII (95% CI)* | *0.17 (0.00, 0.35)* | *0.24 (-0.07, 0.55)* | *0.35 (0.21, 0.48)* | *0.29 (0.02, 0.56)* | *0.22 (-0.07, 0.51)* | *0.40 (0.14, 0.67)* |
| **10-year net survival (95% CI)** | | | | | | |
| 1 – Least deprived | 34.6 (30.2, 38.9) | 29.4 (25.4, 33.4) | 36.6 (32.6, 40.5) | 40.7 (36.7, 44.7) | 42.3 (38.0, 46.6) | N/A |
| 2 | 30.3 (26.5, 34.1) | 29.6 (26.2, 33.1) | 34.3 (30.7, 37.9) | 35.8 (32.4, 39.3) | 38.1 (34.5, 41.7) | N/A |
| 3 | 30.8 (27.2, 34.5) | 27.8 (24.5, 31.1) | 32.3 (29.0, 35.6) | 35.6 (32.3, 38.9) | 36.3 (33.0, 39.6) | N/A |
| 4 | 28.2 (24.9, 31.6) | 29.0 (26.0, 32.2) | 30.6 (27.7, 33.7) | 34.7 (31.6, 37.8) | 31.4 (28.1, 34.7) | N/A |
| 5 – Most deprived | 25.6 (22.8, 28.4) | 22.1 (19.6, 24.6) | 25.0 (22.7, 27.5) | 27.0 (24.5, 29.6) | 31.0 (28.3, 33.8) | N/A |
| *SII (95% CI)* | *10.1 (4.5, 15.6)* | *9.2 (-2.2, 20.5)* | *14.2 (9.1, 19.4)* | *14.8 (3.5, 26.1)* | *13.9 (6.3, 21.4)* | *N/A* |
| *RII (95% CI)* | *0.34 (0.15, 0.53)* | *0.34 (-0.08, 0.76)* | *0.46 (0.30, 0.63)* | *0.44 (0.10, 0.77)* | *0.40 (0.18, 0.61)* | *N/A* |

**Appendix 2.29 – Disease-specific survival by the nearest Carstairs Category per year group of diagnosis for the whole cohort**

| | Year of diagnosis | | | | | |
|---|---|---|---|---|---|---|
| **Carstairs 1991 Category** | **1986-1990** | **1991-1995** | **1996-2000** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 85.7 (81.1, 89.2) | 80.1 (75.4, 84.1) | 85.9 (82.2, 88.8) | 85.0 (81.1, 88.2) | 86.9 (83.3, 89.7) | 85.1 (81.7, 87.8) |
| 2 | 83.6 (79.4, 87.1) | 83.4 (79.6, 86.6) | 84.3 (80.7, 87.3) | 78.0 (74.3, 81.2) | 83.2 (79.8, 86.1) | 87.1 (84.2, 89.4) |
| 3 | 83.5 (79.6, 86.7) | 83.0 (79.4, 86.0) | 80.4 (77.0, 83.4) | 81.1 (77.5, 84.2) | 83.8 (80.7, 86.5) | 82.5 (79.3, 85.2) |
| 4 | 77.0 (72.9, 80.6) | 79.3 (75.7, 82.4) | 76.7 (73.1, 79.9) | 79.4 (76.0, 82.3) | 82.7 (79.6, 85.3) | 81.2 (78.1, 84.0) |
| 5 – Most deprived | 78.5 (75.2, 81.5) | 75.9 (72.6, 78.8) | 74.1 (70.9, 77.1) | 75.6 (72.4, 78.5) | 77.1 (74.1, 79.8) | 78.2 (75.3, 80.9) |
| *SII (95% CI)* | *10.0 (-0.7, 20.6)* | *8.4 (-2.9, 19.7)* | *15.6 (12.2, 19.1)* | *8.3 (-4.1, 20.6)* | *10.6 (1.8, 19.4)* | *10.4 (2.7, 18.2)* |
| *RII (95% CI)* | *0.12 (-0.01, 0.25)* | *0.11 (-0.04, 0.25)* | *0.20 (0.15, 0.24)* | *0.10 (-0.05, 0.26)* | *0.13 (0.02, 0.24)* | *0.13 (0.03, 0.22)* |
| **Five-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 64.9 (58.9, 70.3) | 61.7 (56.0, 66.9) | 63.1 (58.3, 67.6) | 69.5 (64.5, 73.9) | 72.4 (67.9, 76.4) | 74.9 (70.7, 78.6) |
| 2 | 64.4 (59.0, 69.3) | 58.5 (53.5, 63.1) | 64.3 (59.6, 68.5) | 62.1 (57.8, 66.1) | 69.9 (65.8, 73.7) | 71.3 (67.3, 75.0) |
| 3 | 63.6 (58.5, 68.1) | 55.9 (51.3, 60.3) | 56.8 (52.5, 60.8) | 62.2 (57.8, 66.2) | 66.7 (62.7, 70.4) | 70.1 (66.2, 73.7) |
| 4 | 58.4 (53.6, 62.9) | 55.0 (50.6, 59.1) | 54.1 (49.8, 58.1) | 61.7 (57.7, 65.5) | 65.0 (61.2, 68.6) | 65.1 (61.0, 68.9) |
| 5 – Most deprived | 56.9 (52.8, 60.8) | 50.3 (46.4, 54.1) | 50.3 (46.6, 53.8) | 54.0 (50.3, 57.6) | 58.3 (54.7, 61.7) | 63.3 (59.5, 66.9) |
| *SII (95% CI)* | *11.6 (5.2, 18.0)* | *13.2 (8.6, 17.8)* | *18.2 (9.2, 27.2)* | *15.6 (2.4, 28.9)* | *17.2 (11.2, 23.2)* | *14.6 (9.7, 19.6)* |
| *RII (95% CI)* | *0.19 (0.08, 0.30)* | *0.24 (0.16, 0.32)* | *0.32 (0.16, 0.48)* | *0.26 (0.04, 0.48)* | *0.26 (0.17, 0.35)* | *0.21 (0.14, 0.29)* |
| **10-year disease-specific survival (95% CI)** | | | | | | |
| 1 – Least deprived | 61.4 (55.1, 67.1) | 53.9 (47.8, 59.6) | 57.9 (52.9, 62.7) | 65.7 (60.5, 70.4) | 67.1 (62.0, 71.6) | N/A |
| 2 | 58.0 (52.2, 63.4) | 52.4 (47.2, 57.3) | 58.0 (53.1, 62.6) | 58.2 (53.8, 62.4) | 67.9 (63.6, 71.8) | N/A |
| 3 | 56.7 (51.3, 61.7) | 50.1 (45.4, 54.7) | 49.9 (45.5, 54.1) | 57.0 (52.4, 61.3) | 62.5 (58.2, 66.6) | N/A |
| 4 | 53.3 (48.3, 58.1) | 47.8 (43.3, 52.1) | 48.2 (43.9, 52.4) | 56.1 (51.9, 60.2) | 61.8 (57.8, 65.6) | N/A |
| 5 – Most deprived | 48.8 (44.4, 53.0) | 41.3 (37.2, 45.3) | 41.5 (37.8, 45.2) | 49.4 (45.5, 53.1) | 53.8 (50.0, 57.4) | N/A |
| *SII (95% CI)* | *15.5 (12.3, 18.7)* | *16.1 (9.8, 22.4)* | *22.0 (12.8, 31.2)* | *16.9 (5.9, 28.0)* | *17.7 (6.8, 28.6)* | *N/A* |
| *RII (95% CI)* | *0.28 (0.23, 0.34)* | *0.34 (0.20, 0.47)* | *0.44 (0.26, 0.63)* | *0.30 (0.10, 0.50)* | *0.29 (0.11, 0.46)* | *N/A* |

**Appendix 2.30 – Net survival by the SIMD 2004 Category per year group of diagnosis for the whole cohort**

| | Year group of diagnosis | | |
|---|---|---|---|
| **Carstairs 1991 Category** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | |
| 1 – Least deprived | 84.5 (79.2, 89.9) | 71.4 (64.9, 77.9) | 85.5 (80.6, 90.4) |
| 2 | 79.7 (74.2, 85.1) | 76.3 (70.8, 81.8) | 75.7 (70.6, 80.9) |
| 3 | 79.6 (74.4, 84.9) | 78.5 (73.4, 83.6) | 79.6 (74.5, 84.6) |
| 4 | 79.4 (74.2, 84.5) | 76.9 (71.7, 82.1) | 78.7 (73.6, 83.7) |
| 5 – Most deprived | 75.5 (70.4, 80.7) | 75.4 (70.4, 80.4) | 72.5 (67.6, 77.5) |
| *SII (95% CI)* | *8.9 (1.1, 16.7)* | *-2.8 (-16.0, 10.4)* | *11.1 (-7.5, 29.7)* |
| *RII (95% CI)* | *0.11 (0.01, 0.21)* | *-0.04 (-0.21, 0.14)* | *0.14 (-0.10, 0.38)* |
| **Five-year net survival (95% CI)** | | | |
| 1 – Least deprived | 64.2 (56.5, 72.0) | 56.1 (48.4, 63.7) | 65.1 (56.7, 73.4) |
| 2 | 56.8 (49.2, 64.3) | 58.0 (50.8, 64.2) | 60.6 (53.2, 68.0) |
| 3 | 55.1 (47.9, 62.3) | 54.5 (47.7, 61.2) | 56.8 (48.9, 64.6) |
| 4 | 57.8 (50.7, 64.8) | 56.8 (50.1, 63.5) | 57.4 (49.8, 65.0) |
| 5 – Most deprived | 53.1 (46.6, 59.7) | 54.8 (48.5, 61.0) | 54.2 (47.5, 61.0) |
| *SII (95% CI)* | *9.8 (-4.9, 24.5)* | *2.1 (-5.5, 9.7)* | *12.1 (4.1, 20.1)* |
| *RII (95% CI)* | *0.17 (-0.09, 0.43)* | *0.04 (-0.10, 0.17)* | *0.21 (0.07, 0.34)* |
| **10-year net survival (95% CI)** | | | |
| 1 – Least deprived | 53.2 (44.0, 62.4) | 49.4 (40.3, 58.5) | N/A |
| 2 | 45.7 (36.9, 54.6) | 49.5 (40.2, 58.8) | N/A |
| 3 | 49.8 (40.3, 59.2) | 41.3 (32.9, 49.8) | N/A |
| 4 | 41.1 (33.1, 49.1) | 49.7 (40.1, 59.3) | N/A |
| 5 – Most deprived | 37.1 (30.0, 44.2) | 42.6 (34.6, 50.6) | N/A |
| *SII (95% CI)* | *18.5 (2.3, 34.7)* | *6.4 (-15.2, 28.1)* | *N/A* |
| *RII (95% CI)* | *0.41 (0.05, 0.78)* | *0.14 (-0.33, 0.61)* | *N/A* |

**Appendix 2.31 – Overall survival by the SIMD 2004 Category per year group of diagnosis for the whole cohort**

| | Year group of diagnosis | | |
|---|---|---|---|
| **Carstairs 1991 Category** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | |
| 1 – Least deprived | 84.5 (81.0, 87.5) | 80.0 (76.3, 83.1) | 84.8 (81.7, 87.3) |
| 2 | 79.6 (76.4, 82.5) | 79.5 (76.4, 82.3) | 80.0 (77.2, 82.6) |
| 3 | 74.8 (71.6, 77.7) | 76.3 (73.3, 79.0) | 79.9 (77.2, 82.3) |
| 4 | 74.6 (71.8, 77.2) | 76.3 (73.5, 78.7) | 73.7 (71.0, 76.2) |
| 5 – Most deprived | 71.8 (69.3, 74.2) | 71.8 (69.3, 74.1) | 71.7 (69.2, 74.0) |
| *SII (95% CI)* | *14.1 (4.8, 23.5)* | *10.2 (4.5, 15.9)* | *16.2 (8.6, 23.7)* |
| *RII (95% CI)* | *0.19 (0.06, 0.31)* | *0.13 (0.06, 0.21)* | *0.21 (0.11, 0.31)* |
| | *9.0 (-0.2, 18.1)* | *5.7 (-2.2, 13.6)* | *12.2 (7.5, 16.9)* |
| | *0.12 (0.00, 0.24)* | *0.08 (-0.03, 0.18)* | *0.16 (0.10, 0.22)* |
| **Five-year net survival (95% CI)** | | | |
| 1 – Least deprived | 58.4 (53.8, 62.6) | 61.6 (57.4, 65.5) | 63.4 (59.2, 67.4) |
| 2 | 54.5 (50.7, 58.1) | 55.8 (52.1, 59.4) | 59.6 (55.9, 63.1) |
| 3 | 47.9 (44.4, 51.3) | 49.1 (45.7, 52.4) | 52.9 (49.3, 56.4) |
| 4 | 46.1 (43.0, 49.2) | 50.5 (47.4, 53.5) | 47.7 (44.3, 51.0) |
| 5 – Most deprived | 41.1 (38.4, 43.8) | 41.7 (39.0, 44.3) | 44.1 (41.0, 47.1) |
| *SII (95% CI)* | *21.1 (14.3, 27.8)* | *22.1 (8.5, 35.6)* | *25.1 (19.3, 30.9)* |
| *RII (95% CI)* | *0.43 (0.29, 0.57)* | *0.44 (0.17, 0.71)* | *0.48 (0.37, 0.59)* |
| | *14.1 (-1.5, 29.8)* | *13.0 (4.3, 21.7)* | *19.2 (10.5, 27.9)* |
| | *0.30 (-0.03, 0.62)* | *0.26 (0.09, 0.43)* | *0.36 (0.20, 0.53)* |
| **10-year net survival (95% CI)** | | | |
| 1 – Least deprived | 44.9 (40.5, 49.3) | 47.4 (42.9, 51.8) | N/A |
| 2 | 40.8 (37.1, 44.5) | 41.4 (37.4, 45.3) | N/A |
| 3 | 33.6 (30.3, 36.9) | 35.0 (31.6, 38.5) | N/A |
| 4 | 33.1 (30.2, 36.0) | 35.3 (32.1, 38.4) | N/A |
| 5 – Most deprived | 26.3 (23.9, 28.7) | 26.0 (23.4, 28.5) | N/A |
| *SII (95% CI)* | *22.2 (13.4, 31.0)* | *24.1 (11.9, 36.4)* | *N/A* |
| *RII (95% CI)* | *0.64 (0.39, 0.90)* | *0.68 (0.33, 1.02)* | *N/A* |
| | *16.4 (2.3, 30.5)* | *13.7 (4.7, 22.7)* | |
| | *0.48 (0.07, 0.90)* | *0.39 (0.13, 0.64)* | |

**Appendix 2.32 – Disease-specific survival by the SIMD 2004 Category per year group of diagnosis for the whole cohort**

| | Year group of diagnosis | | |
|---|---|---|---|
| **Carstairs 1991 Category** | **2001-2005** | **2006-2010** | **2011-2015** |
| **One-year net survival (95% CI)** | | | |
| 1 – Least deprived | 84.3 (78.5, 88.7) | 77.8 (71.0, 83.1) | 87.1 (81.9, 90.8) |
| 2 | 81.0 (75.4, 85.5) | 80.1 (74.5, 84.6) | 79.4 (74.2, 83.6) |
| 3 | 79.5 (74.0, 83.9) | 80.7 (75.5, 85.0) | 83.3 (78.3, 87.3) |
| 4 | 79.9 (74.5, 84.3) | 78.5 (73.2, 82.9) | 81.9 (76.9, 86.0) |
| 5 – Most deprived | 76.4 (71.2, 80.9) | 80.3 (75.4, 84.4) | 75.5 (70.5, 79.8) |
| *SII (95% CI)* | *8.3 (2.4, 14.2)* | *-1.3 (-7.9, 5.3)* | *10.3 (-6.2, 26.9)* |
| *RII (95% CI)* | *0.10 (0.03, 0.18)* | *-0.02, (-0.10, 0.07)* | *0.13 (-0.08, 0.33)* |
| **Five-year net survival (95% CI)** | | | |
| 1 – Least deprived | 71.6 (64.6, 77.4) | 66.7 (59.3, 73.1) | 71.6 (64.5, 77.5) |
| 2 | 64.3 (57.6, 70.2) | 64.3 (57.7, 70.1) | 70.9 (65.2, 75.9) |
| 3 | 62.9 (56.5, 68.6) | 66.2 (60.0, 71.7) | 66.8 (60.1, 72.7) |
| 4 | 66.6 (60.4, 72.1) | 65.8 (59.7, 71.2) | 70.4 (64.3, 75.7) |
| 5 – Most deprived | 61.5 (55.5, 66.9) | 67.1 (61.3, 72.2) | 64.9 (59.2, 69.9) |
| *SII (95% CI)* | *8.2 (-7.8, 24.2)* | *-1.6 (-7.1, 3.9)* | *7.3 (-3.6, 18.3)* |
| *RII (95% CI)* | *0.13 (-0.12, 0.37)* | *-0.02 (-0.11, 0.06)* | *0.11 (-0.05, 0.27)* |
| **10-year net survival (95% CI)** | | | |
| 1 – Least deprived | 66.8 (59.5, 73.2) | 64.7 (57.1, 71.3) | N/A |
| 2 | 59.6 (52.5, 66.0) | 57.2 (49.9, 63.8) | N/A |
| 3 | 59.1 (52.4, 65.1) | 59.2 (52.0, 65.8) | N/A |
| 4 | 58.8 (52.0, 64.9) | 57.3 (50.1, 63.9) | N/A |
| 5 – Most deprived | 56.0 (49.7, 61.8) | 60.8 (54.3, 66.7) | N/A |
| *SII (95% CI)* | *10.4 (-0.7, 21.5)* | *2.1 (-13.9, 18.2)* | *N/A* |
| *RII (95% CI)* | *0.17 (-0.01, 0.36)* | *0.04 (-0.23, 0.31)* | *N/A* |

**Appendix 3.1 – Privacy Advisory Committee approval for the Scottish Audit of Head and Neck Cancer study**

**From:** Nogueira Rita (NATIONAL SERVICES SCOTLAND)
**Sent:** 08 April 2013 14:17
**To:** Savage Shirley-Anne (NHS FIFE)
**Subject:** XRB13078 - Head and Neck Cancer Audit - 10 Year Survival

Dear Dr Savage,

We have been advised by the Privacy Advisory Committee that your application PAC 49/12 has been approved. I have been allocated as your Research Co-ordinator as per the new service provided by ISD as part of SHIP.

I am sending you details of this new service below. Please note that as your PAC application has been approved under the old system, the part regarding the National Safe Haven and the researcher training does not apply to you. However, I am sending you the information for future reference.

It would be useful if you could contact me to discuss delivery timescales and costs associated with the linkage that you requested. My number is 0131 275 7933.

**Overview**
ISD is one of the partner organisations in the ScottisH Informatics Programme (SHIP), a Scotland-wide research platform for the collation, management, dissemination and analysis of anonymised Electronic Patient Records (EPRs). ISD's record linkage team is supporting the achievement of one of core programme of SHIP - to provision datasets for research.
**ISD Service**
In January 2013, ISD started offering researchers a new, state-of-the-art technical environment (managed by the ATOS Origin Alliance) for linkage, analysis (if required) and output. Known as the National Safe Haven, it provides a high powered computing service, secure analytic environment, secure file transfer protocol, and provision of a range of analytic software (SPSS, STATA, SAS and R). This has improved security and enhanced anonymisation of data before, during and after the linkage process.
**How it works**
To deliver this service, ISD separated the current functions of the record linkage team into two services, an indexing service and a research co-ordination service (including analytical services).
Each request is managed throughout its duration by a member of ISD staff who acts as a Research Coordinator (RC). They support each application through the linkage, analysis and release process. This works in the following way:

- The indexing team receives patient identifiers from the Data Provider/s.
- The team indexes and attaches an ISD generated number unique to that study.
- They return the file and the Data Provider then sends in the remaining content / attribute data file, with the unique study number, to the National Safe Haven.
- An automated linkage agent joins all the study files together.
- The linked dataset will then be stored in a secure area where it can be accessed, remotely or by coming into the Safe Haven at our Edinburgh office in South Gyle Crescent.
- Final outputs will then be disclosure controlled by the RC before releasing to you.

**Researcher Training**
Researchers using these services must demonstrate that they have undertaken an approved researcher training course prior to accessing the linked dataset for analysis. Approved courses include the SHIP Information Governance Training Course and the Administrative Data Liaison Service Safe Researcher.

**Privacy Advisory Committee - Governance**
Our Privacy Advisory Committee (PAC) has reviewed and revised the PAC application form in light of these changes. The new form is currently being piloted and if you have not yet submitted your application we would be grateful if you would use the new form when you apply for permission. Contact the PAC administrator at nss.pac@nhs.net for a copy of the form. There is no administrative charge for applying to PAC.

**Appendix 3.1 continued – Privacy Advisory Committee approval for the Scottish Audit of Head and Neck Cancer study**

**More Information**
Our web pages have been updated and now include a Q&A to help explain the new process. If you would like to discuss any aspects of this new service or would like to discuss your project in more detail, please do not hesitate to call me directly on 0131 275 7933 for further advice. If I am not available and you need an urgent response you can phone the central number on 0131 275 7333 and one of my colleagues can assist you.

Best regards,

Rita

Rita Sa Nogueira

*Senior Information Analyst*
*eDRIS Team*
*Area 159A*
*Gyle Square*
*1 South Gyle Crescent*
*Edinburgh*
*EH12 9EB*

*Tel: 0131 275 7933*
*Email: Rita.Nogueira@nhs.net*

*Website: www.isdscotland.org*

**Appendix 5.1 – Approval for an honorary contract to complete the Head and Neck 5000 analysis at the University of Bristol**

University of BRISTOL

**Mr James Tubman**
*School Manager*
***School of Oral and Dental Sciences***

**Bristol Dental School**
Chapter House Building
Lower Maudlin Street
Bristol BS1 2LY
T +44 (0)117 34 29635
James.tubman@bristol.ac.uk

**11 July 2017**

Ref: JT/khb/HonStat/Let

68 Meadow Lane,
Westbury,
Wiltshire
BA13 3AL

Dear Kate,

**Re: Honorary status: Research Associate**

I am pleased to confirm the award of honorary status in relation to your association with the University of Bristol ("The University").

The purpose of awarding you honorary status is for access to online systems for Head and Neck 5000. Your University sponsor is **Mrs Vanessa Marshall** and you are based in **BRC / School of Oral and Dental Sciences.**

You do not currently have an employer and your honorary status is based on this understanding of your employment status. You must inform us if there are any changes to your employment status in this regard.

In consideration of the award of honorary status you agree to the following;

1. **Start date**
   The award of honorary status takes effect on **10 July 2017** and will end on **9 July 2018** but can be withdrawn at any time (for whatever reason) by the University. If you wish to end this honorary arrangement you should write to your University sponsor.

2. **E-mail**
   If you do not already have one you will be assigned a University of Bristol email address. To gain access to this or to University websites you will need to obtain your username and temporary password. Please check that your name has appeared on the University contact directory then go to the Computer Centre in Tyndall Avenue. You will need to take some photographic identification, and this letter with you. If you are unable to go in person, please telephone the IT helpdesk direct on 0117 9287870 (internal x87870) or email them (service-desk@bristol.ac.uk) for advice.

3. **Identity Card**
   To obtain a University of Bristol identity card please follow the instructions on this webpage: http://www.bristol.ac.uk/cardservices/other-cardholders.

4. **Confidential Information**

4.1 For the purposes of this clause 4 "Confidential Information" means trade secrets or information of a confidential nature which is important to and belongs or relates to the University or its business which you may have received or obtained as a result of or in any way in connection with your

association with the University and includes but is not limited to information relating to employees, students of the University, clients or customers or potential clients or customers, suppliers, agents or distributors of the University, commercial, financial or marketing information, customer lists, technical information, inventions, formulae, ideas, processes, projects, research, production information, business confidences and know-how comprising trade secrets and any information the release of which would damage the University's commercial interests, endanger staff or students together with any information that is legally privileged. It also means any information which you are told is confidential, any information that is treated as confidential and any information in respect of which the University has a duty of confidentiality to a third party including patients.

4.2 You should assume that any information you receive whilst you undertake the Purpose, whilst on University premises or elsewhere is Confidential Information.

4.3 Access to the University's information and information systems and networks will be granted to an honorary member of staff in accordance with the University's Information Security policy (link to http://www.bristol.ac.uk/infosec/policies/).

4.4 You shall not (except in the proper performance of your duties in association with the University) during your association with the University or at any time without limit after the termination of the association or status:

(a) divulge or communicate to any persons;
(b) use for your own purposes or for the purposes of any person other than the University; or
(c) through any failure to exercise due care and diligence cause any unauthorised disclosure of any Confidential Information relating to the University provided that these restrictions shall cease to apply to any information which shall become available to the public generally otherwise than through your unauthorised disclosure.

4.5 Nothing in this Agreement shall preclude you from making a protected disclosure Under the Employment Rights Act 1996.

**5. Delivery upon Termination**

5.1 Upon the termination of your honorary status (howsoever caused) or upon demand you shall:

(a) Deliver up to the University (or a designated representative) all and any property belonging to the University or relating to its business in your power, possession or control including but not limited to, all materials falling within the scope of clause 4.
(b) Inform the University of all passwords used by you in relation to any computers belonging to the University; and
(c) Irretrievably delete any information relating to the business of the University (and all matters derived from them) that is stored on any computer or storage media or otherwise in any electronic form and which is in your possession, custody or control.

**6. Data Protection**

6.1 You consent to the University (or any agent thereof) processing personal data relating to you in the course of this agreement for the purposes of the administration and management of the University and its employees and to ensure compliance with any applicable laws, regulations and procedures. You consent to the University making such data available to persons other than the University where the University considers this is necessary or otherwise to be in the interests of the University including, without limitation, to any person providing products and/or services to the University, any regulatory authority, any potential purchaser of the University or its business or otherwise as required by law and to the University (or any agents thereof) transferring such data outside the European Union.

6.2 You agree to abide at all times with any policy or procedure in relation to data protection issued by the University from time to time and the provisions of the Data Protection Act 1998 in relation to any processing by you of the personal data of others whilst associated with the University.

**7. Intellectual Property Rights**

7.1 The Intellectual Property Rights ("IPR") in all works created by you pursuant to your association with the University shall be vested in the University.

7.2 To the extent that such IPR in works created by you pursuant to your association with the University, do not automatically vest in the University, you hereby assign and agree to assign by way of present, and where possible, future assignment, all such IPR. You will execute and give such assurance as the University may require to secure the vesting in the University of all such IPR.

7.3 You waive any moral rights in all works created by you in association with the University to which you are now or may at any future time be entitled under Chapter IV of the Copyright Designs and Patents Act 1988 or any similar provisions of law in any jurisdiction.

7.4 Where the Purpose requires you to use third party IPR (for example IPR which belongs to your Employer) you undertake to ensure that an appropriate licence agreement exists between the University and the owner (or third party which controls) the IPR before you use it or allow it to be disclosed to the University employees, students or contractors.

7.5 For the purposes of this clause 7 "Intellectual Property Rights" ("IPR") means patents, rights to any invention, idea, discovery, development, improvement or innovation, whether or not patentable or capable of registration, and whether or not recorded in any medium, copyright and related rights, trademarks, trade names and domain names, rights in get-up, goodwill and the right to sue for passing off, unfair competition rights, rights in designs, rights in computer software, database rights, topography rights, rights to use and preserve the confidentiality of information (including know-how and trade secrets) and any other intellectual property rights, in each case whether registered or unregistered and including all applications (or rights to apply) for and be granted, renewals or extensions of, and rights to claim priority from, such rights and all similar or equivalent rights or forms of protection which subsist or will subsist now or in the future in any part of the world.

**8. Rules and Procedures**

We expect you to perform your honorary role to the best of your ability and to follow the University's procedures and standards including the Equality and Diversity Policy Computer use and comply with our Anti-bribery Policy and procedures.

All policies can be found on the intranet site under Human Resources. It is your responsibility to ensure that you read and understand them.

**9. Visibility on Explore Bristol Research**

By default, the majority of honorary staff with an academic appointment will appear publicly on Explore Bristol Research: http://research-information.bristol.ac.uk

Explore Bristol Research is a searchable and browsable view of research related information drawing directly from records maintained in Pure. Details that will appear on Explore Bristol Research are:

- title and name
- email address
- University postal address

Honorary staff may also chose to upload a photo of themselves, a statement about their research and information about any research activities they have undertaken.

**Appendix 5.1 continued – Approval for an honorary contract to complete the Head and Neck 5000 analysis at the University of Bristol**

Should any honorary staff wish to opt-out of appearing on Explore Bristol Research they may do so at any time by contacting pure-support@bristol.ac.uk.

Further information about Pure is available at http://www.bristol.ac.uk/pure

If you need any guidance you should contact your University Sponsor in the first instance who will assist you.

The award of honorary status is not intended to establish, and shall not be construed by either you or the University in the future as having established an employment or other working relationship between us.

We look forward to welcoming you to the University and wish you a happy and fulfilling association with us.

Yours sincerely

_____
**James Tubman**
**School Manager**
.....
On behalf of the University of Bristol

I understand and accept the contents of this letter

signed [name]

11th July 2017 date

**Appendix 5.2 – Comparison between responders and non-responders for the HN5000 study**

| Variable | Returned questionnaire | Did not return questionnaire | p-value |
|---|---|---|---|
| **Total** | 3,440 | 1,154 | |
| **Age group** | | | 0.840 |
| Less than 44 | 210 (6.1%) | 70 (6.1%) | |
| 45 to 54 | 676 (19.7%) | 224 (19.4%) | |
| 55 to 64 | 1,192 (34.7%) | 384 (33.3%) | |
| 65 to 74 | 940 (27.3%) | 322 (27.9%) | |
| 75 and over | 422 (12.3%) | 154 (13.3%) | |
| **Sex** | | | 0.006 |
| Male | 2,526 (73.4%) | 894 (77.5%) | |
| Female | 914 (26.6%) | 260 (22.5%) | |
| **Comorbidity** | | | <0.001 |
| No comorbidity | 1,484 (44.1%) | 407 (36.0%) | |
| Mild comorbidity | 1,149 (34.1%) | 400 (35.4%) | |
| Moderate/severe comorbidity | 732 (21.8%) | 324 (28.6%) | |
| **Anatomical Site** | | | 0.580 |
| Oropharynx | 1,334 (38.8%) | 445 (38.6%) | |
| Lip and oral cavity | 900 (26.2%) | 289 (25.0%) | |
| Larynx | 728 (21.2%) | 254 (22.0%) | |
| Hypopharynx | 160 (4.7%) | 64 (5.5%) | |
| Salivary glands | 147 (4.3%) | 40 (3.5%) | |
| Other | 171 (5.0%) | 62 (5.4%) | |
| **Stage** | | | 0.030 |
| I | 788 (23.1%) | 219 (19.1%) | |
| II | 593 (17.4%) | 216 (18.8%) | |
| III | 473 (13.9%) | 156 (13.6%) | |
| IV | 1,555 (45.6%) | 557 (48.5%) | |
| **HPV status** | | | 0.011 |
| Negative | 2,114 (70.9%) | 681 (75.2%) | |
| Positive | 867 (29.1%) | 224 (24.8%) | |
| **Treatment** | | | <0.001 |
| Surgery only | 765 (22.2%) | 222 (19.2%) | |
| Chemoradiotherapy only | 1,064 (30.9%) | 346 (30.0%) | |
| Radiotherapy only | 702 (20.4%) | 256 (22.2%) | |
| Surgery and chemo/radio | 872 (25.3%) | 291 (25.2%) | |
| Chemotherapy only | 15 (0.4%) | 13 (1.1%) | |
| No treatment | 22 (0.6%) | 26 (2.3%) | |
| **IMD Category** | | | <0.001 |
| 1 – Most deprived | 674 (20.1%) | 300 (26.5%) | |
| 2 | 616 (18.4%) | 258 (22.8%) | |
| 3 | 746 (22.2%) | 230 (20.3%) | |
| 4 | 664 (19.8%) | 169 (14.9%) | |
| 5 – Least deprived | 655 (19.5%) | 175 (15.5%) | |

**Appendix 6.1 – ICD codes inclusion criteria for each study**

| f | Scottish Audit of Head and Neck Cancer | Head and Neck 5000 |
|---|---|---|
| Lip (C00) | Lip (C00) | lip (C00) and oral cavity (C02-C04, C05.0, C06) |
| oral cavity (C02-C04, C05.0, C06) | oral cavity (C02-C04, C05.0, C06) | *Grouped above* |
| oropharynx (C01, C05.1, C05.2, C09, C10) | oropharynx (C01, C05.1, C05.2, C09, C10) | oropharynx (C01, C05.1, C05.2, C09, C10) |
| hypopharynx (C12, C13) | hypopharynx (C12, C13) | hypopharynx (C12, C13) |
| larynx (C32, C10.1) | larynx (C32, C10.1) | larynx (C32, C10.1) |
| salivary glands (C07, C08) | salivary glands (C07, C08) | major salivary glands (C07, C08) |
| *Not considered* | *Not considered* | minor salivary glands (any ICD-10 code with histology recorded as “salivary gland”) |
| *Not included* | nasopharynx, nasal cavity, and sinuses (C11, C30.0, C31) | nasopharynx (C11) |
| *Not included* | *Grouped above* | Nasal cavity (C30.0) |
| *Not included* | *Grouped above* | Sinuses (C31) |
| other sites of the head and neck (C14.0, C30.1, C41.1, C69.5) | other ill-defined areas of the head and neck (C14, C30.1, C41, C44, C76, C77) | other sites of the head and neck (C14.0, C30.1, C41.1, C69.5) |

**Appendix 6.2 – Treatment groupings for each study**

| Scottish Cancer Registry | Scottish Audit of Head and Neck Cancer | Head and Neck 5000 |
|---|---|---|
| Surgery only | Surgery only | Surgery only |
| Radiotherapy only | Radiotherapy only | Radiotherapy only |
| Surgery and radiotherapy | Surgery and radiotherapy | *Combined below* |
| *Separated below* | *Combined below* | Surgery combined with chemotherapy, chemoradiotherapy or radiotherapy |
| *Separated below* | Chemotherapy only, chemotherapy combined with surgery, chemotherapy combined with radiotherapy, and chemotherapy combined with both surgery and radiotherapy | *Separated* |
| Chemoradiotherapy only | *Combined above* | Chemoradiotherapy only |
| Surgery and chemoradiotherapy | *Combined above* | *Combined above* |
| Chemotherapy with or without surgery | *Combined above* | *Combined above* |
| *Combined above* | *Combined above* | Chemotherapy only |
| No treatment | No treatment | No treatment |

## Appendix 6.3 – Approval for request to change to part time studies, December 2016

Thesis submission dates

Reply | Reply All | Forward | ...

Fri 02/12/2016 16:09

AH **Audrey Hillis**
To Kate Ingarfield

You forwarded this message on 24/05/2017 13:07.

Admission letter.pdf
64 KB

Action Items | Get more add-ins

Dear Kate

In your recent application to the Higher Degrees Committee you stated:

*"From 1st November 2016, I will be working 50% hours on my PhD (of which I currently have 20 months remaining) - this would then mean that I require 40 months to complete my PhD (excluding the final 6 months that must be taken full time). This takes my new end date to 29th February 2020 with the extra 6 months full time working to 31st August 2020"*

The Committee approves your request to change to part time for the remainder of your studies.

2014/15 - full time
2015/16 - full time
2016/17 - part time from 01/11/2016
2017/18 - part time 01/10/2017 - 30/09/2018
(include 3 months suspension)
30/12/2018
Plus one year of thesis pending registration = 30/12/2019 for thesis submission (amended to first day of term after Christmas holidays - early January 2020 (not 29 February 2020). I'm not clear what you mean about the "the final 6 months must be full time" - at the end of your studies you will be a thesis pending student which is neither full time or part time.

The Committee has agreed to grant you a 4 month suspension of studies (which can be backdated) to a time when you were unable to devote as much time due to your work. If you provide me with a stop date and a start date dd/mm/yyyyy, I will add this to your MyCampus record and this time period will be added back onto your record, giving an additional 4 months. This takes your submission date to early May 2020. Extensions are not granted to students during their supervised registration period.

Kind regards

Audrey

Ms Audrey Hillis
MVLS Graduate School Administrative Assistant
R362 Wolfson Link Building
University of Glasgow
Glasgow, G12 8QQ
Scotland
UK

## Appendix 6.4 – Approval for request to suspend studies, October 2018

Suspension of studies - Kate Ingarfield

Reply | Reply All | Forward | ...

Thu 18/10/2018 15:10

AH **Audrey Hillis**
To Kate Ingarfield
Cc Alex McMahon; David Conway; J Alastair Gracie; Janette McBride

You forwarded this message on 19/10/2018 11:47.

Dear Kate

The Higher Degrees Committee has approved your request for a suspension of studies from 07/09/2018 - 07/01/2019 on health grounds. You were originally due to submit your thesis by 27/04/2020 and this has now been revised to 27/08/2020. Please notify me of any change to your expected return date.

Kind regards

Audrey

Ms Audrey Hillis
MVLS Graduate School Administrative Assistant
R111 West Medical Building
University of Glasgow
Glasgow, G12 8QQ
Scotland
UK
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Email: Audrey.Hillis@glasgow.ac.uk
URL https://www.gla.ac.uk/mvls-pgrden

## Appendix 6.5 – Approval for request to suspend studies, June 2020

Extension request for thesis submission

Reply | Reply All | Forward | ...

Tue 16/06/2020 10:51

AH Audrey Hillis
To Kate Ingarfield (PGR)
Cc Alex McMahon; David Conway; Gordon Ramage; Carly Thomson

You forwarded this message on 16/06/2020 13:08.

Dear Kate

The Chair of the Higher Degrees Committee has considered your request for a thesis extension until 23/10/2020 on health grounds and has noted that the medical certificate which you provided is limited to a 2 week period (1-14 June 2020) and your GP confirms on it that he does not require a follow up appointment. In light of this, it has been agreed that you may have an extension but it will be limited to 30/09/2020. Please arrange to submit your thesis to the Graduate School office for examination no later than **30/09/2020**.

Kind regards

Audrey Hillis
For MVLS Graduate School office

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