An Investigation into Patient & Professional Delays in the Diagnosis of Head & Neck Cancer.

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Abstract

Background: Head and neck cancer is a significant cause of morbidity and mortality worldwide and in Australia. Early diagnosis of this group of diseases has been shown to improve both survival and decrease morbidity. Unfortunately, a significant number of patients still present at a late stage of disease. The purpose of this study was to identify factors which may be associated with diagnostic delay in head and neck cancers.

Methods: a retrospective chart review of patients who had been referred to the Multidisciplinary Head & Neck Clinic at the Newcastle Mater Misericordiae Hospital in 2004 was performed. Patients with the following disease classifications were included in the study; ID9 codes 140 -149 and 173. Forty five patients were included in the study. Patient delay and professional delay were calculated from the data. In addition referral delay (the time from the date of the referral letter to being assessed in the clinic), the biopsy delay (the period from presentation to the initial clinician to the date of biopsy) and the delay to assessment at the Head & Neck Clinic (the period from initial consultation to being seen in the clinic) were determined. Non-parametric statistical tests were used to detect an association between these five types of diagnostic delay and the following potential predictor variables; age, gender, ECOG score, presence of chronic disease(s), marital status, occupation, family history of cancer, previous diagnosis of cancer, stage of tumour at diagnosis and smoking history.

Results: Disease stage at diagnosis was not associated with any of the five types of diagnostic delay examined. None of the other variables examined reached statistical significance.

Conclusions: No association between 10 predictor variables and diagnostic delay in head and neck cancer were demonstrated.

Statement

The work in this thesis is original and was completed by the author as a postgraduate student of the Faculty of Medicine, University of Sydney. The work was supervised by Dr. Jane Young and Professor James May of The University of Sydney..

I certify that the presented thesis has not been submitted wholly or in part for any other degree.

Any help or sources used in this work and preparation of the thesis have been acknowledged.

Signed

Peter Aquilina, April 2007.

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List of Abbreviations

ASR	Age Standardised Rates
ICD	International Classification of Diseases
TNM	Tumour Node Metastases
AJCC	American Joint Committee on Cancer
UICC	International Union Against Cancer
HCP	Health Care Professional
ECOG	Eastern Cooperative Oncology Group

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Introduction & Literature Review

Malignant disease of the head and neck region is a significant cause of morbidity and mortality both in Australia and throughout the world.[1, 2] During 2002, globally there were 274,000 new cases of oral cancer alone.[3] This figure does not include the extra-oral cancers which also comprise head and neck cancers. In New South Wales in 2002, there were 785 new cases of head and neck cancer (575 male, 210 female) representing 3.5% and 1.5% of new cancers in males and females respectively.[2] This corresponds to a crude incidence rate of 17.4 per 100,000 for men and 6.3 per 100,000 in women.[2] Head and neck cancer incidence in NSW ranked seventh for males and 16th for females, and the mortality rates were 7.7 and 2.9 in males and females respectively. [2] It has been estimated that globally in 1990 there were 66,000 and 34,100 deaths due to oral cancer in men and women respectively.[4] The combined figures for Australia and New Zealand for the same year were 300 and 100 deaths in males and females respectively.[4]

The burden of head and neck malignancies varies geographically and accounts for a significant impact in many areas of the world. Melanesia has the highest incidence with an incidence in 2002 of 31.5 per 100,000 in men and 21.2 per 100,000 in women.[3] The age standardized rates (ASR) per 100,000 for mortality in 1990 of some cancers affecting the head and neck region reflect this high disease burden. In Melanesia the ASR for mortality per 100,000 for mouth cancer (ICD140-145) was 22.8 for men and 14.2 for women.[4] The ASR for mortality per 100,000 for combined mouth and pharynx (ICD 140-149) was 23.9 for men and 14.8 for women.[4] This compares to the ASR for mortality per 100,000 in Australia & New Zealand which are 2.3 & 1.0 for mouth cancer in men and women respectively, and 4.4 and 1.4 for combined mouth and pharynx in men and women respectively.[4] In comparison, the ASR for mortality per 100,000 for cervical cancer incidence and mortality in Australia in 2002 was 7.4 and 2.0 respectively.[3] The incidence of head and neck malignancy in Australia in men in 2002 was 10.2 per 100,000.[3] This rate is high due

to the inclusion of large numbers of squamous cell carcinomas of the lip secondary to solar irradiation.

In common with other malignant neoplasms, cancers of the head and neck are most commonly staged using the TNM (Tumour, Node, Metastases) system of the American Joint Committee on Cancer (AJCC) [5] and of the International Union Against Cancer (UICC). The TNM system is an anatomically based classification system [6,7,8] that categorizes malignant neoplasms according to the anatomical extent of their spread. The underlying assumption of this system, as applied to any particular malignancy, is that the staging of a cancer, which is derived from the various combinations of the TNM classification, has a direct application to clinical treatment planning, prognosis and research.

For the purposes of the TNM system, cancers are defined according to the anatomical area in which they arise, and different rules may pertain depending on the region in which the cancer has arisen. For example, a given tumour size in different anatomical areas may give rise to a different T stage.

Within the TNM system, T refers to tumour size as measured by the maximal surface diameter of the tumour[6,7,8], N refers to the presence or absence of spread to regional draining lymph nodes and M refers to the presence or absence of distant metastases. The T stage can be Tx, T0, Tis, T1, T2, T3 or T4.[7,8] There are various subcategories on N stage, depending on the particular cancer in question.[6] For head and neck cancers, the M status is either Mx (distant metastases cannot be assessed) M0 (no distant metastasis detected) or M1 (distant metastases present). Table 1 illustrates the assignment of a T stage to cancers of the lip and oral cavity, and Table 2 provides details of the assignment of an N stage to head and neck tumours.

Once a T score, N score and M score have been assigned to a cancer, the three categories are then condensed to a stage, either I, II, II or IV. Table 3 summarises the staging of head and neck cancers. Many articles further classify stage I and II tumours as being early, and stage II and IV tumours as being late or advanced.[9,10]

Table 1. T stages for carcinomas of the lip & oral cavity (adapted from Broumand et al [8])

T Classification	Description
TX	TX
T0	No evidence of primary tumour
Tis Carcinoma in situ	Tumour hasn't penetrated the basement membrane
T1	Tumour 2 cm or less in greatest dimension
T2	Tumour more than 2 cm but not more than 4 cm In greatest dimension
T3	Tumour more than 4 cm in greatest dimension
T4a Lip	Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face
T4a Oral cavity	Tumour invades through cortical bone, into the deep extrinsic muscles of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, or skin of face
T4b Oral Cavity	Tumour involves masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

Table 2. N staging for all head and neck cancers except for nasopharynx and thyroid cancers.
(adapted from Patel et al [7])

N Classification	Description
Nx	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis.
N1	Metastasis in a single ipsilateral lymph node, 3cm or less in greatest dimension.
N2	Metastasis in a single ipsilateral lymph node, more than 3 cm but less than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral contralateral lymph nodes, none more than 6 cm in greatest dimension.
N2a	Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension.
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

Table 3: Stage grouping for all head and neck cancers except for the nasopharynx and thyroid. (Adapted from Patel et al [7])

Stage Group	T Stage	N Stage	M Stage
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
IVB	T4b	Any N	M0
	Any T	N3	M0
IVC	Any T	Any N	M1

It is generally accepted that early diagnosis and treatment of head and neck cancers is desirable.[11,12,13,14,15,16] Oral cancer has an overall five year survival rate of 50%.[4] This rate is significantly improved to 90% if the tumour is less than 2cm when referred for definitive treatment.[12] Cancers in the head and neck region which are treated at an early stage result in lower morbidity[17] and also have a shorter duration of treatment.[18]

Previous papers have looked at the issue of delay in the diagnosis of head and neck cancer.[11, 18-29] Diagnostic delay can be divided into patient delay and professional delay. Patient delay is defined as the time from the patient first being aware of a

symptom or sign, to their first consultation with a health professional. Professional delay is defined as the time period from first consultation to a definitive diagnosis being made or referral to a specialist. Previous studies have had conflicting conclusions with some finding no relation between diagnostic delay and tumour stage[18,19,23,24,25,26] whilst others have found a correlation.[18,20] Many of these studies have significant design faults and do not provide high level evidence. For example, many are retrospective studies and often the data required has not been recorded.

The finding of many of these studies that there is no relation between diagnostic delay and stage of disease in head and neck cancers is somewhat counterintuitive. It is logical to assume that there would be a simple relation between delay in diagnosis and stage at presentation for head and neck cancers. In other cancer types, there is evidence to support a relation between delay in diagnosis and disease stage. For example, in patients presenting with breast cancer, a strong correlation between patient delay and stage at diagnosis has been demonstrated.[30,31] However, as is the case for head and neck cancers, there also is disagreement in the literature as to whether a relation exists between delay in diagnosis and stage of breast cancer at diagnosis with some authors denying such a relationship exists.[32]

Investigations have been directed towards understanding both patient related factors and health care professional related factors influencing patient delay.[9,10,11,18-27,29] Most studies have found patient delay to be more significant than professional delay.[11,14,15,25]

Kowalski et al[18] examined factors relating to the lateness of diagnosis of oropharyngeal cancer. A prospective study of 336 consecutive patients presenting in Brazil from February 1986 to December 1988 were analysed. This study defined excessive patient delay as being present if the patient delay exceeded the median site specific value for patient delay within that cohort of patients. Professional delay was defined as any time period greater than a month between first consulting a health care professional and being seen at the head and neck cancer unit. The following variables were examined to see if there was a relation to patient or professional delay; income level, educational level, stage of disease and sex. Unifactorial analysis found no association between duration of symptoms, professional or patient delay, educational

or income levels and the risk of advanced disease (stage III or IV). Male gender was found to be related to the incidence of advanced tumours in this study.

The paper by Kowalski et al[18] may not necessarily be applicable to countries such as Australia. The population it studied was largely from a socio-economically depressed area of Brazil where economic, societal, cultural and aspects of the health system are likely different from those in developed nations. Some criticism can also be made regarding their definition of what constituted unacceptable patient delay. By defining this parameter as being any period in excess of the median value for a particular cohort, they may derive a bench mark that could be either excessive or insufficient. For example, if the cohort under consideration comprised of patients with very long time periods between symptom onset and presentation, then the median value will also be large. A study incorporating this figure as the cut-off for acceptable delay, may miss a potential statistical correlation because a large number of patients will be classified as not having delay, even if their delay was excessive compared to other populations.

Gorsky et al[9] analysed data for 543 patients with oral or oropharyngeal cancers. The data was obtained from a government cancer registry. Patients were excluded if the data base did not include all the variables under investigation. The data were analysed using univariate statistical methods. No significant relation between delay and stage was shown and no difference was found between the types of referrer (doctor versus dentist). These results may be criticized on the basis of the statistical analysis used and for the exclusion of patients with some data missing which may introduce a selection bias.

Professional delay was specifically examined by Allison et al.[24] One hundred and eighty eight patients with cancer of the oral cavity, oropharynx, hypopharynx and larynx who were referred to a head and neck clinic in Montreal, Canada were enrolled in the study. A structured interview with each patient was conducted to elicit study data. The data obtained was analysed using multiple logistic regression analysis to calculate the odds ratio for professional delay longer than one month versus professional delay less than one month for the study variables. No analysis of the relation of delay to stage was undertaken. This study found that the presence of

comorbid diseases increased the odds for professional delay of greater than one month, whilst older age, higher educational status an oral cancer reduced the odds. No relation between professional delay and gender, cohabitation or type of referrer was found.

Schentler [22] compared professional delay in the diagnosis of oral cancer between medical practitioners and dentists. Data was obtained by analyzing the referral letters of patients diagnosed with an intra-oral tumour and who were referred to one of three oral & maxillofacial surgery departments in three district hospitals in the United Kingdom. Patients were excluded if the referral letters were deemed to not include sufficient information. The remainder of the patient file was apparently not examined. The criteria used to define professional delay were that delay in referral was considered to be present if referral from the primary health care professional did not occur within two days of initial presentation. No statistical tests measuring the significance of relations between variables was undertaken, however this study claimed that general medical practitioners were better at referring cases of oral cancer earlier than their dental colleagues. Unfortunately this study is weak in terms of its statistical analysis as well as its recruitment of patients.

Amir et al [15] studied diagnostic delay in a United Kingdom population. One hundred and eighty eight subjects with head and neck cancer referred to a Head and Neck Clinic at a UK hospital were interviewed. Data was analysed using descriptive and non-parametric statistics. No significant association between diagnostic delay and gender, age or tumour size was found.

In a retrospective study, Hollows et al[11] examined the records of 100 consecutive patients presenting to a department of oral and maxillofacial surgery in a district general hospital in the United Kingdom. Data was analysed utilizing unifactorial techniques. No correlation between patient delay, T stage, alcohol or cigarette use was found.

Scott and colleagues studied 245 patients who presented with oral squamous cell carcinoma to a head and neck cancer unit in London, UK.[25] This study excluded patients with a previous diagnosis of cancer anywhere. A standardized structured

interview was completed in order to identify factors which may influence the time taken to achieve a diagnostic outcome. When the data was analysed using multivariate analysis, no statistically significant association between diagnostic delay and tumour stage could be shown. Factors predictive of advanced stage disease were being of non-white racial background. Being female or married was predictive of presenting with early stage disease. The type of referrer (doctor, dentist, specialist) was not significantly related to duration of delay.

McGurk et al [26] examined two cohorts of patients with squamous cell cancer of the mouth or throat. The first cohort was obtained from patients treated at a district general hospital in the United Kingdom between 1961 and 1986. The second cohort was obtained prospectively from patients with head and neck cancer presenting to a "cancer care centre" from 1992 till 1999. They defined delay as being any period greater than three months from the onset of symptoms. Univariate statistical analysis was performed. This study found no correlation between delay and stage of disease or survival. Being of non-white ethnic background or having high grade histology did predict advanced disease.

Kerdpon et al [33] studied factors relating to the delay in diagnosis of oral squamous cell carcinoma in a population from southern Thailand. One hundred and sixty one patients who presented to the Head and Neck Clinic, the Radiotherapy Clinic or the Dental Clinic were interviewed using a structured interview questionnaire. The resulting data was analysed using both univariate and multivariate analyses. None of the following variables were found to be significantly related to either professional or patient delay; sex, age, marital status, tumour size, lymph node metastasis, occupation, or referrer type (doctor or dentist). Only the use of traditional herbal treatments was associated with a significant relation to delay. The authors of this study note that some social, cultural and economic factors peculiar to this area of Thailand may influence the results of this study.

Professional and patient delays in the diagnosis of oral cancer were investigated in a Japanese population by Onizawa et al.[29] This study categorized the process of diagnosis of oral cancer into four stages; step one was the time from first awareness of symptoms by a patient to presentation to a health care professional, step two was

the time from the date of the first consultation to the receipt by the patient of a referral letter, step three was the period from the receipt of the letter by the patient till the first consultation at the tertiary treatment facility and step four was the period from visiting the referral centre till a diagnosis was made. This reflects a referral pattern not commonly encountered within the Australian context in that referral letters are usually sent directly to the head and neck unit rather than relying on the patient to make an appointment after receiving a referral letter. Data was derived from a retrospective chart review which yielded 152 subjects. Exclusion criteria included patients whose referral letters had incomplete information. The subjects were then divided into a delay group and a non delay group on the basis of the median value for each of the four steps in the diagnostic process as proposed by these authors. The authors classified steps one and three as being dependent on patient actions, and steps two and four as being dependent on professional factors. Multivariate analysis showed that dentists were more likely to delay referral than general medical practitioners. No relation between delay and gender, past history of cancer, age, smoking, alcohol use or incidence of daily medication use was demonstrated. There was no relation between patient delay and T or N stage. This paper used the same definition of unacceptable delay as used by Kowalski et al.[18] However unlike Kowalski et al [18] who only used the median value of delay as the marker for unacceptable delay in patient delay whilst using the figure of 1 month for professional delay, Onizawa et al [29] use the median value for both patient and professional delay. The criticisms made previously of this also apply here.

Pitipaht et al [34] analysed factors influencing delay in diagnosis of oral and oropharyngeal cancers in a Greek population. A structured interview of 105 consecutive patients referred to one of three teaching hospitals in Athens was undertaken. Patients with a prior history of oral carcinoma were excluded. The data was analysed using multivariate techniques. This study did not analyse professional delays, and it defined a delay in diagnosis as being present if more than 21 days elapsed from the patient becoming aware of symptoms and presenting to a HCP. This study did show a significant relation between delay in diagnosis and stage IV tumours. Patients who were unmarried and who were ex-smokers were also significantly associated with a delay in diagnosis. This study found no relation between gender, age, educational level or alcohol use.

Jovanovic et al [23] analysed 50 consecutive Dutch patients with oral squamous cell cancer who presented to a department of oral and maxillofacial surgery in the Netherlands. This study looked at patient delay, professional delay and total delay. Patient delay was defined as the period of time between a patient first noticing a symptom till their presentation to a HCP. Professional delay, which was termed "doctor delay" in this study, was defined as the time period between the first consultation with a HCP and the final diagnosis. The data was analysed using unifactorial techniques. No relation between gender, tumour size or site of tumour and delay was found. No difference in professional delay between doctors and dentists was found.

There are two papers from Australia which are relevant to this topic.[21,22] Both have design flaws and are retrospective and descriptive studies rather than studies analysing the outcomes of delay in referral and diagnosis.

Dimitroulis et al [21] analysed 51 consecutive patients presenting to the Royal Melbourne Dental Hospital and who were eventually diagnosed with oral squamous cell carcinoma of the mouth. Only descriptive statistics were provided and no attempt was made to investigate statistically significant correlations between delay in diagnosis and other factors. This paper claims that dentists referred significantly more patients with oral squamous cell carcinoma than general medical practitioners and that patients referred by general medical practitioners had higher stage tumours than those referred by dentists. No attempt to justify these claims statistically was made. This study is really only useful for obtaining descriptive statistics. Besides the significant statistical weaknesses as mentioned previously, this study has a significant selection bias built into its recruitment of patients. The institution in which the study was performed is not a tertiary head and neck referral service. It is a dental hospital which sees eligible patients referred by dentists and general medical practitioners as well as seeing eligible self referred patients. Only patients eligible for public dental treatment, such as those with pensions and health care cards are able to be seen in public dental health institutions in Australia. This introduces several selection biases; the patients are more likely to be from lower socioeconomic backgrounds and they are more likely to be referred by dental practitioners than medical practitioners to a dental hospital. Very little useful information applicable to

the Australian situation can be derived from this paper.

The paper by Chandu & Smith [22] excludes patients who didn't undergo surgical treatment and also those patients who were subsequently treated by other units. This significantly detracts from the utility of this paper as it introduces significant biases. It is also evident that the patients comprising this data set were drawn from a very skewed referral base in that the referrals to the authors department were principally from a dental hospital or from private dental practitioners.

As can be seen from the previous discussion, there is a considerable body of literature pertaining to delays in the diagnosis of head and neck cancers as well as other malignancies such as breast cancer. The literature applicable to the Australian setting is limited and little is known about delays in the diagnosis of head and neck cancer, or reasons for these, in Australia. Therefore, this preliminary retrospective study was undertaken to describe patient and professional delays for a cohort of patients attending the Multidisciplinary Head and Neck Clinic at the Newcastle Mater Misericordiae Hospital, New South Wales. This study will inform the design of a more detailed, prospective study that will further investigate predictors of professional and patient delay in the diagnosis of head and neck cancers.

Aims

The overall objective of this project is to investigate the incidence of diagnostic delay in the diagnosis of head & neck cancer. Specific aims are:

a. To describe patient and professional delay in the diagnosis of head and neck cancer.

b. To investigate associations between these delays and various factors related to the referral pathway and patient characteristics.

Variables, such as the type of referrer (dentist versus doctor, specialist versus non-specialist), and patient factors, such as pre-existing medical conditions and ECOG Performance Status (Eastern Cooperative Oncology Group)[35], marital status, employment status, private health insurance status, the existence of a previous malignancy and gender will be analysed to determine the presence of any

relationship. The relation of diagnostic delay to stage of cancer at diagnosis will also be examined.

Hypotheses

The working hypotheses for this study are as follows:

1. Professional delay will be less for specialist medical practitioners than general practitioners or dentists
2. Professional delay will be less for general practitioners than dentists
3. Patient delay will be less in patients with a previous history of cancer elsewhere
4. Patient delay will be less in patients with a family history of cancer
5. Patient delay will be less in patients who are married/de facto
6. Patient delay will be less in patients with private health insurance
7. Patient delay will be greater in patients who are unemployed
8. Patient delay will be greater in patients with higher ECOG scores
9. Patient delay will be greater in patients with chronic medical conditions
10. Patient delay will be greater in smokers
11. There will be no relation between delay (professional or patient) and stage of tumour at diagnosis
12. Patient delay will be greater for males than females.

Professional delay will be shorter for specialist medical practitioners compared to general practitioners or dentists

The basis for this hypothesis is the assumption that specialists in medical fields associated with head and neck malignancies (i.e. ear, nose & throat surgeons, maxillofacial surgeons, dermatologists, plastic surgeons and general/head & neck surgeons) will be better trained and have more experience in diagnosing and managing head and neck malignancies when compared to general practitioners or dentists.

Professional delay will be less for general practitioners than dentists

The basis for this hypothesis are the assumptions that

a. Dental practitioners may treat the presentation of oral malignancy initially with local "surgical" or "mechanical" measures, such as denture adjustment or smoothing of a sharp tooth cusp that may be traumatizing local tissues, rather than immediately referring off to a specialist. Most oral lesions seen by dentists are not malignant and are often due to local mechanical irritation. General practitioners do not have the opportunity to readily treat oral lesions and would therefore be expected to refer more readily, and
b. Dental practitioners are less likely to encounter life threatening diseases in their day to day practice compared to general practitioners. General practitioners may therefore be more aware of the possibility of malignant disease processes in general and thus refer more readily.

Patient delay will be less in patients with a previous history of cancer elsewhere **and**
Patient delay will be less in patients with a family history of cancer

Both these hypothesis are predicated on the assumption that patients who have been exposed to malignant disease will have a greater awareness of the possibility of neoplastic conditions and thus present more rapidly to a HCP and possibly raise the issue of a possible diagnosis of cancer with the HCP.

Patient delay will be less in patients who are married/de facto

The rationale for this hypothesis is that patients in a stable and supportive environment may be encouraged by their partners to seek medical attention in a more timely fashion than patients who are single.

Patient delay will be less in patients with private health insurance **and**
Patient delay will be greater in patients who are unemployed

Both these hypotheses are based on the conjecture that there is a link between socioeconomic status and health outcomes. This study assumes that private health insurance status and employment status are markers of socioeconomic status. The hypotheses postulate that lower socioeconomic status is associated with longer delays in diagnosis.

Patient delay will be greater in patients with higher ECOG scores **and**
Patient delay will be greater in patients with chronic medical conditions

Both ECOG score and the presence of chronic medical conditions are assumed in this study to be markers of the global health of the patients in this data set. The hypotheses assume that patients with significant comorbidities will experience longer diagnostic delays because the primary HCP will be preoccupied with their other medical conditions and may assign a low priority to what may appear to be a relatively innocuous sign or symptom, which is in reality the sentinel event warning of a head and neck malignancy.

Patient delay will be greater in smokers
The assumption underlying this hypothesis is that smokers will in general be less well than non-smokers and may ignore early warning signs of malignancy. Some signs and symptoms of head and neck cancer, such as a hoarse voice, may be attributed by smokers to being “normal” effects of smoking.

There will be no relation between delay (professional or patient) and stage of tumour at diagnosis
As stated in the introduction, there are multiple papers which have failed to show an association between diagnostic delay and stage of tumour at diagnosis.
Patient delay will be greater for males than females

The supposition of this theory is that women are more health conscious than men and are more likely to seek medical attention, thus resulting in shorter delays.

Methods

Sample selection

A retrospective chart analysis of patients who had presented with head and neck cancers at the Newcastle Mater Misericordiae Hospital Multidisciplinary Head and Neck Clinic during 2004 was undertaken. Patients were eligible for inclusion in the sample if they had first presented to the clinic during 2004 and their subsequent diagnosis was classified as a malignancy of the head or neck according to the International Classification for Diseases (ICD9) (codes 140-149 and 173).[36] Patients who were found to have malignant melanoma and lymphoma were excluded from the analysis as these types of cancer are clinically distinct from other malignancies of the head and neck. Patients who presented to the clinic but who did not have a malignant lesion were excluded.

Data abstraction

A standard data recording sheet was developed (Appendix A). Data items included demographic characteristics of patients, whether or not they had a regular general practitioner (GP) or dentist, the presence of other concurrent medical conditions and regular medications, personal or family history of cancer, smoking and alcohol history. ECOG (Eastern Co-operative Oncology Group) performance status[35] was used as a marker for health status in general. Table 4 outlines ECOG performance status scores.

In addition, five significant dates were identified for each patient with regards to their diagnostic journey:

1. The date the patient first noticed symptoms or signs
2. The date the patient first presented to a health care professional
3. The date the patient was referred to the head and neck clinic
4. The date the patient first attended the head and neck clinic
5. The date a biopsy was taken.

Table 4: ECOG Performance Status

Grade	ECOG
0	Fully active & able to carry out all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature such as light house work
2	Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited self care. Confined to bed or chair for more than 50% of waking hours
4	Completely disabled. Cannot carry out any self care. Totally confined to bed or chair.
5	Dead

For some records, an exact date for onset of symptoms was not recorded in the medical record. This may have occurred, for example, if patients could not remember an exact date of noticing a symptom when asked about this at initial presentation to the clinic. In these cases, the nearest month was recorded and the date the patient first noticed symptoms was taken to be the first day of that month. The five remaining dates were able to be derived exactly from the patient records.

Data were abstracted by one researcher (the candidate) and entered into a database (Microsoft Excel). Statistical analysis was carried out using statistical software (*The SAS System for Windows Version 9.1*. Cary, NC: SAS Institute Inc, 2005)

Classification of diagnostic delay

The delay experienced by a patient from noticing a symptom to receiving a diagnosis of head and neck cancer was divided into three components;

1. patient delay
2. professional delay
3. total delay

Patient delay was defined as the time period from a patient first becoming aware of symptoms till their first presentation to a health care professional (HCP).

Professional delay was further subdivided into the following categories;

1. Clinic assessment delay - time period from first presentation to a HCP to first assessment at the head and neck clinic (in days).
2. Referral delay - time period from date of referral to the head and neck clinic, as indicated by the date of the referral letter, to first assessment at the Head & Neck Clinic clinic (in days).
3. Biopsy delay - time period from first presentation to a HCP to first biopsy of the lesion as recorded by the date on the pathology report form (in days).
4. Total professional delay – time from initial presentation to a HCP to date of referral letter to the Head & Neck Clinic (in days).

Total delay was defined as the time period from the patient first being aware of a symptom to the confirmation of a biopsy-proven diagnosis of head and neck cancer.

Statistical analyses

Descriptive statistics were generated, including proportions for categorical variables and mean, standard deviation, median and interquartile range for continuous variables.

The following five continuous outcome measures were assessed:

1. Patient delay
2. Clinic assessment delay (total professional delay)
3. Referral delay
4. Biopsy delay
5. Total delay

For each of these outcomes, Wilcoxon rank sum tests were used to investigate univariate relations between the following categorical variables:

1. Sex (male/female)
2. Marital status (Married/De facto or single)
3. Family history of cancer (yes/no)
4. Patient ECOG status (0,1,2,3,4,5)
5. Patient occupation
    a. employed
    b. unemployed
    c. retired
    d. home duties
6. Previous history of cancer (yes/no)
7. Referrer type (doctor / dentist / specialist)
8. Patient age
9. Stage of cancer at diagnosis
10. Smoking History
    a. Current smoker
    b. Ex-smoker
    c. Never smoked.

The following variables were not dichotomous; ECOG status, Stage of cancer, occupation, referrer type and smoking history. In order to facilitate statistical analysis, these variables were dichotomised in the following manner. The ECOG status was condensed into group 1 (ECOG = 0) and group 2 (ECOG = groups 1,2,3 or 4). Cancer stage was dichotomised into early (stage I and II) and late (stage III and IV) groups. Referrer type was dichotomised into group 1 (general dentist or medical practitioner) and group 2 (specialist). Smoking history was dichotomised into patients who were current smokers or who had ever smoked, and patients who had never smoked.

The correlation between each outcome and age also was assessed and a Pearson correlation co-efficient was calculated.

Ethics approval

This study was submitted to the Human Research Ethics Committee of Hunter New England Area Health Service but the candidate was advised that formal ethics approval was not necessary as the project was considered to be ‘quality assurance’ (see Appendix B).

Results

The demographics of the cohort studied are shown in table 5.

Table 5: Summary of the Cohorts.

		Number	Percentage
Gender	Male	33	73
	Female	12	27
Marital Status	Married/De Facto	31	69
	Single	14	31
Occupation	Retired	29	64
	Unemployed	6	13
	Employed	8	18
	Home Duties	2	4
Medical Insurance	Insured	9	20
	Un-insured	36	80
Regular GP or Dentist	Regular GP	36	80
	Regular Dentist	5	11
Chronic Medical Condition		28	62
ECOG Score	0	28	62
	1	10	22
	2	3	7
	3	3	7
	4	1	2
Exposure to Cancer	Family History of Cancer	3	7
	Previous Diagnosis of Cancer	23	51
HCP referring	GP	20	44
	Dentist	8	18
	Specialist	17	38
Smoking History	Current Smoker	20	44
	Ex-Smoker	8	18
	Never Smoked	17	38
Stage at Diagnosis	Stage I	8	18.2
	Stage II	5	11.4
	Stage III	12	27.3
	Stage IV	19	43.2
	Early Stage (I/II)	13	29.5
	Late Stage (III/IV)	31	70.5

There was no difference in the mean age of men or women in the study ($t=0.53$, $df=43$, $p=0.6$).

Table 6 summarises the ages of the patients in the study according to gender.

Table 6: Breakdown of patient age according to gender.

Gender	Percentage	Mean Age (years)	Median Age (years)	Standard Deviation of the Mean	Age Range (years)
Male & Female	100	65.4	66.0	13.7	25 – 91
Male	73.3	66.0	66.0	12.6	43 – 90
Female	26.7	63.6	66.5	16.8	25 - 91

Table 7 summarises the sites affected by cancer in this study.

Table 7: Sites of cancer occurrence.

Site	Number	Percentage
Skin (not lip)	15	33
Lip	2	4.4
Floor of Mouth	4	9.1
Larynx/Vocal Cords	5	11.4
Nasopharyngeal	1	2.27
Parotid	4	9.1
Tongue	5	11.4
Sinuses	2	4.4

Table 8 summarises the delay in diagnosis according to the five categories of delay used in this study and defined previously.

Table 8: Summary of delays in diagnosis.

	Mean (days)	Median (days)	Standard Deviation of the Mean	Range (days)
Patient Delay	106	32	262	0 - 1736
Total Professional Delay	83	39	117	3 – 668
Referral Delay	15	10	13	0 - 51
Delay to Biopsy	62	21	114	0-629
Total Delay	167	75	297	0 - 1913

Each of the five types of delay investigated in this study where analysed using the Mann-Whitney U test for non-parametric data to determine if a relation existed between each form of delay and the following variables; gender, marital status, ECOG group (group 1 = ECOG 0, group 2 = ECOG 1,2,3 or 4), the presence of a chronic medical condition, the employment status, the presence or absence of health insurance, the presence of a family history of cancer, the presence of a regular

dentist, the presence of a regular general practitioner, a previous diagnosis of cancer, smoking history, and type of referrer.

No relation could be demonstrated between any of the variables examined and the five types of delay. Tables 9 - 13 summarise the associations between predictor variables and the five types of delay analysed.

Some variables, such as the level of alcohol consumption, were not able to be incorporated into the study as they were not consistently reported in the patient notes. Other variables not included for this reason included the presence or absence of a regular dental practitioner and educational level achieved.

Table 9: Associations between potential predictor variables and patient delay.

	Variable	Median (days)	P value
Gender	Male	31	0.6
	Female	33	
ECOG Group	ECOG 0	32.5	0.9
	ECOG 1 – 4	32.0	
Smoking History	Smoker/Ex-Smoker	36.0	0.4
	Never Smoked	54.1	
Marital Status	Married/De-facto	40.0	0.6
	Single	27.0	
Employment status	Employed	45.5	0.6
	Unemployed	32.0	
Health Insurance	Insured	40.0	0.7
	Un-insured	31.5	
Chronic Medical Condition	Yes	31.0	0.2
	No	60.0	
Family History of Cancer	Yes	32.0	0.4
	No	35.5	
Previous diagnosis of cancer	Yes	31.0	0.5
	No	46.0	
Referrer	General Practitoner (doctor or dentist)	31.5	0.98
	Specialist	53.0	
Stage at Diagnosis (early stage I & II Late stage II & IV)	Early	60.0	0.3
	Late	31.0	

Table 10: Associations between predictor variables and total professional delay. (time from initial presentation to being seen in the clinic)).

	Variable	Median (days)	P value
Gender	Male	43.0	0.8
	Female	39.0	
ECOG Group	ECOG 0	34.0	0.6
	ECOG 1 – 4	52.0	
Smoking History	Smoker/Ex-Smoker	39.0	0.6
	Never Smoked	43.0	
Marital Status	Married/De-facto	39.0	0.6
	Single	52.0	
Employment status	Employed	35.5	0.7
	Unemployed	43.0	
Health Insurance	Insured	26.0	0.4
	Uninsured	41.0	
Chronic Medical Condition	Yes	55.0	0.09
	No	33.0	
Family History of Cancer	Yes	39.0	0.8
	No	41.0	
Previous diagnosis of cancer	Yes	38.0	0.9
	No	43.0	
Referrer	General Practitioner (doctor or dentist)	39.0	0.4
	Specialist	43.0	
Stage at Diagnosis (early stage I & II Late stage II & IV)	Early	29.0	0.1
	Late	49.0	

Table 11: Associations between predictor variables and referral delay.

	Variable	Median (days)	P value
Gender	Male	12.0	0.5
	Female	6.5	
ECOG Group	ECOG 0	12.5	0.2
	ECOG 1 – 4	7.0	
Smoking History	Smoker/Ex-Smoker	8.0	0.4
	Never Smoked	18.0	
Marital Status	Married/De-facto	13.0	0.3
	Single	6.5	
Employment status	Employed	6.5	0.3
	Unemployed	11.0	
Health Insurance	Insured	12.0	0.9
	Un-insured	8.0	
Chronic Medical Condition	Yes	10.0	0.7
	No	10.0	
Family History of Cancer	Yes	14.0	0.4
	No	9.5	
Previous diagnosis of cancer	Yes	16	0.1
	No	7.0	
Referrer	General Practitioner (doctor or dentist)	9.5	0.9
	Specialist	13.0	
Stage at Diagnosis (early stage I & II Late stage II & IV)	Early	12.0	0.50
	Late	7.0	

Table 12: Associations between predictor variables and delay to biopsy.

	Variable	Median (days)	P value
Gender	Male	18.0	0.6
	Female	24.0	
ECOG Group	ECOG 0	15.5	0.5
	ECOG 1 – 4	26.0	
Smoking History	Smoker/Ex-Smoker	19.5	0.9
	Never Smoked	22.0	
Marital Status	Married/De-facto	21.0	0.8
	Single	20.0	
Employment status	Employed	12.5	0.8
	Unemployed	22.0	
Health Insurance	Insured	14.0	0.6
	Un-insured	21.5	
Chronic Medical Condition	Yes	25.5	0.2
	No	14.0	
Family History of Cancer	Yes	26.0	0.9
	No	19.5	
Previous diagnosis of cancer	Yes	18.0	0.4
	No	24.5	
Referrer	General Practitioner (doctor or dentist)	21.5	0.1
	Specialist	7.0	
Stage at Diagnosis (early stage I & II Late stage II & IV)	Early	11.0	0.06
	Late	32.0	

Table 13: Associations between predictor variables and total delay.

	Variable	Median	P value
Gender	Male	74.0	0.4
	Female	99.0	
ECOG Group	ECOG 0	95.0	0.6
	ECOG 1 – 4	72.0	
Smoking History	Smoker/Ex-Smoker	82.5	0.9
	Never Smoked	75.0	
Marital Status	Married/De-facto	75.0	0.5
	Single	98.0	
Employment status	Employed	99.0	0.7
	Unemployed	75.0	
Health Insurance	Insured	74.0	0.6
	Un-insured	86.0	
Chronic Medical Condition	Yes	73.5	0.6
	No	107.0	
Family History of Cancer	Yes	58.0	0.2
	No	86.0	
Previous diagnosis of cancer	Yes	75.0	0.6
	No	86.0	
Referrer	General Practitioner (doctor or dentist)	78.0	0.4
	Specialist	61.0	
Stage at Diagnosis (early stage I & II Late stage II & IV)	Early	74.0	0.6
	Late	81.0	

Table 14 summarises each of the five types of delay studied according to the stage of the cancer at diagnosis.

Table14: Duration of delay according to stage and delay type.

Stage	Delay Type	Mean Delay (days)	Median Delay (days)	Range (days)	Standard Deviation of the Mean
I	Patient delay	47.1	30.5	4 – 121	40.8
	Delay to clinic appointment	46.6	27.5	7 – 152	45.6
	Referral delay	15.0	14.0	1 – 33	11.8
	Biopsy delay	14.1	12.5	0 – 31	10.3
	Total delay	61.3	55.0	9 – 121	36.3
II	Patient delay	170.2	168.0	32 – 347	129.6
	Delay to clinic appointment	38.6	32.0	14 – 89	29.9
	Referral delay	18.6	10.0	7 – 37	14.7
	Biopsy delay	16.0	7.0	0 – 43	18.1
	Total delay	186.2	168.0	58 – 351	116.7
III	Patient delay	68.5	32.5	0 – 243	76.2
	Delay to clinic appointment	117.9	36.5	3 – 668	191.6
	Referral delay	13.7	9.0	1 – 34	12.0
	Biopsy delay	94.4	6.5	0 – 629	190.7
	Total delay	163.0	80.0	0 – 660	199.4
IV	Patient delay	142.5	31.0	1 – 1736	392.7
	Delay to clinic appointment	90.7	65.0	12 – 380	88.1
	Referral delay	15.4	7.0	0 – 51	15.5
	Biopsy delay	74.8	42.0	0 – 327	82.3
	Total delay	217.3	81.0	3 - 1913	423.1

Discussion

The demographics of this cohort of patients are broadly in keeping with those reported in previous studies. There was a predominance of men in the sample. This is in agreement with other studies and with the epidemiology of this group of cancers.[2,3,4,9] The median duration of patient delay has been reported to vary from 2 weeks to 4 months.[11,21,23] this compares with the median delay for patient delay in this study of 32 days. Professional delay has been stated to be in the order of 11 to 18 days.[19,21,23,33]. The median professional delay in this study is longer than this (32 days). This may reflect the particular geographic referral area for the Head & Neck Unit in Newcastle that this cohort was drawn from. This unit has a very large referral footprint which encompasses a large part of rural and remote New South Wales. It may be that distance from a major centre impedes early referral, especially if patients are resistant to travelling long distances from home. The biopsy delay is another measure of professional delay and the median value for this study was 21 days which compares more favourably to other reported values in the literature. Once the decision to refer was made, the median time till the patient was assessed in the Head & Neck Clinic was 10 days. This would comply with the "two week rule" introduced in the UK National Health Service as the benchmark for seeing referrals of patients with suspected head and neck cancer.[14,37]

The findings of this study that there was no significant association between the five types of delay analysed (patient, professional, referral, biopsy and total delay) and the variables examined, agrees with the conclusions of previous investigators.[9,11,15,18,24,25,26,33]

No significant associations which would support the 12 hypothesis of this study were found. This is not surprising given the small number of patients in this study and the consequent lack of statistical power. This issue is being addressed by a prospective study which is currently being conducted. Nonetheless, some trends are apparent in the data. These will be discussed with regards to each of the potential predictor variables analysed. Tables 15 through 25 are adapted from tables 8 through 13 and show in one place trends in the data for each potential predictor variable with respect to each of the five delay types analysed. As none of the results reached significance,

the p values have been omitted from these tables for clarity. The corresponding significance values can be found in tables 9 through 13.

Gender

Table 15: Summary of delay types according to gender (median in days).

	Patient delay	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Male	31.0	43.0	74.0	18.0	12.0
Female	33.0	39.0	99.0	24.0	6.5

There was no significant association between gender and any of the five categories of delay examined. This is in accord with other studies.[15,23,24,29,33,34]A possible emerging trend to a longer referral delay is seen with the median delay for males being almost double that of females (12.0 days and 6.5 days respectively). Conversely, there is also a possible trend towards greater total delay in women compared to men.

Previous studies have shown that there is a gender difference when stage of tumour at diagnosis is examined.[18,25] Kowalski et al[18] found males were more likely to present with advanced tumours and Scott et al[25] showed early stage tumours were more likely to be found in women. Neal and Allgar [38] interestingly found that females had longer referral delay for colorectal cancer and Non Hodgkins Lymphoma. This is in contrast to the accepted wisdom which is that when gender differences are detected, females generally have shorter delays than males. The authors of this study were unclear as to the aetiology of this finding. There is evidence that women have a greater somatic awareness and present more often to medical practitioners than do men[39], and this may account for the findings in other studies that being female is associated with smaller tumours and shorter delay. The possibility of a trend to longer total delay in females is in conflict with the findings of repeated studies that gender is not related to diagnostic delay in head and neck cancers is intriguing and warrants further investigation. This is being addressed by the prospective trial currently in progress.

I postulated that being female would be associated with a shorter duration of delay. This hypothesis is not supported by the data.

ECOG group

Table 16: Summary of delay types according to ECOG group (median in days).

ECOG Group	Patient delay	Total Professional Delay	Total delay	Biopsy delay	Referral delay
ECOG 0	32.5	34.0	95.0	15.5	12.5
ECOG 1 - 4	32.0	52.0	72.0	26.0	7.0

There was no significant association between ECOG group and any of the five categories of delay examined. The was a possible tendency for the median delay to be larger for ECOG group 1 (ECOG score = 0) with regards to total delay and referral delay, and for the median delay to be longer for ECOG group 2 (ECOG scores 1,2,3 or 4) for professional delay and biopsy delay.

Only one other study looking specifically at performance status and delay was found [25], however other markers which measure similar factors such as the presence of comorbidity [24] and the use of medications [29] have been reported. Scott et al[25] found no association between performance status, the presence of cardiovascular disease or respiratory disease and diagnostic delay. Allison et al [24] found that the presence of comorbidity increased the likelihood for professional delay greater than one month. They also found that higher education level and the presence of oral cancer decreased the odds ratio for professional delay greater than one month. In contrast, Onizawa et al [29] found no association between the use of medications (a marker for the presence of other diseases) and delay in diagnosis of oral cancer.

It may be postulated that the presence of co-morbid disease may either encourage earlier presentation or equally it may delay presentation. Patients with a number of chronic illnesses may present with what appears to the primary care physician to be a minor oral symptom that is consequently placed on the "back burner" whilst seemingly more pressing issues are addressed. Alternatively, as patients with chronic illness would be expected to consult their primary physician more often than healthy people, it could be argued that they may present earlier as they have a greater opportunity to inform a HCP of their signs or symptoms.

The tendency towards a lesser professional delay and biopsy delay in patients with ECOG score 0, would give support to the theory that patients with more co-morbidities, as measured by their ECOG score, may have their symptoms of head and neck malignancy masked by their other diseases. In other words, their primary care clinicians may give a higher priority to the management of their other diseases and thus delay addressing definitively their signs and symptoms of head and neck cancer.

Once the decision to refer a patient to the Head & Neck Clinic was made, there was a tendency for patients with higher ECOG scores to have a smaller referral delay (time from the date of referral to the date of being seen in the clinic). This may reflect the referring practitioner lobbying the referral co-ordinator at the clinic to prioritise these patients as having greater urgency. This is an area which should be examined further as it potentially raises issues of resource allocation and triaging of referrals to the clinic.

It is of interest that in this study the median patient delay for ECOG scores 0 and ECOG scores 1, 2, 3 or 4 were essentially the same. This may indicate that patients in this cohort give equal weight to signs and symptoms of head and neck cancer regardless of their medical condition. This is an area that needs further investigation. If this supposition is borne out by the prospective study currently underway, steps to alert primary care physicians and dentists to this potential pitfall could be undertaken.

Chronic Medical Conditions

Table 17: Summary of delay types according to the presence of chronic medical conditions (median in days).

Chronic Medical Condition	**Patient delay**	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Yes	31.0	55.0	73.5	25.5	10.0
No	60.0	33.0	107.0	14.0	10.0

There was no association found between delay in diagnosis and the presence of chronic medical conditions. The discussion contained in the ECOG section also is

pertinent to this marker of patient health status. As with the ECOG variable, there was a possible tendency to increased professional delay and biopsy delay in patients with a chronic medical condition. It is a reasonable assumption that many of the patients with a chronic medical condition would also be accounted for within ECOG group 2 (ie ECOG scores 1, 2, 3 or 4) and for this reason it is perhaps understandable why the same possible trends in the data are seen. The discussion as to possible reasons for this are the same as those stated previously when analysing the ECOG data.

Family History of Cancer

Table 18: Summary of delay types according to the presence of a family history of cancer (median in days).

Family History	**Patient delay**	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Yes	32.0	39.0	58.0	26.0	14.0
No	35.5	41.0	86.0	19.5	9.5

No association between diagnostic delay and the presence or absence of a family history of cancer was demonstrated.

To my knowledge, the relation of a family history of cancer, or being exposed to the experience of family members with malignant disease, has not been previously investigated. This is an area which is currently being examined by the author and others in a prospective study.

The data suggests a possible trend towards longer total delay in patients denying a family history of neoplasia. This could suggest that being aware of the possibility of malignant disease secondary to seeing family members with it, may encourage patients to attend earlier.

Previous Diagnosis of Cancer

Table 19: Summary of delay types and previous diagnosis of cancer (median in days).

Previous cancer?	Patient delay	Professional Delay	Total delay	Biopsy delay	Referral delay
Yes	31.0	38.0	75.0	18.0	16.0
No	46.0	43.0	86.0	24.5	7.0

No association between a previous diagnosis of cancer and delay could be found. This is in agreement with Onizawa et al[29]. there may be a slight tendency for increased referral delay in patients previously diagnosed with cancer. This need further investigation.

This is finding does not support my hypothesis that a history of cancer elsewhere would be associated reduced diagnostic delay because patients would be more aware of the possibility of malignant disease and thus present earlier. This will be an important aspect of further study. If we can demonstrate factors inhibiting early presentation and diagnosis of head and neck cancer in this group of patients, strategies may be able to be formulated to overcome these barriers.

Smoking History

Table 20: summary of delay types according to smoking history. (Median delay in days.)

	Patient delay	Professional Delay	Total delay	Biopsy delay	Referral delay
Smoker/Ex-Smoker	36.0	39.0	82.5	19.5	8.0
Never Smoked	54.1	43.0	75	22.0	18.0

There was no association found between smoking history and the five types of delay examined. These results concur with those reported previously.[11,29,34]

The tendency was for the delay to be less in patients with a smoking history; this tendency was slightly reversed with respect to total delay and was most marked for referral delay. This may reflect a higher index of suspicion being held by clinicians for the possibility of head and neck cancers in patients who have a positive smoking history. This possibility is supported by the observation that referral delay is more than double in the non-smoking group, suggesting that the referrers may have indicated greater urgency was indicated when referring this group of patients.

Marital Status

Table 21: Summary of delay types according to marital status. (Median delay in days).

	Patient delay	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Married/De-facto	40.0	39.0	75.0	21.0	13.0
single	27.0	52.0	98.0	20.0	6.5

No association between marital status and the five types of delay analysed was found. This is at variance with the conclusions of some previous studies examining diagnostic delay in head and neck cancer [34] as well as findings in other cancer types.[38] Other studies however concur with this finding.[24,29,33]

It is difficult to suggest a trend in the figures for this variable. It will be the subject of further investigation in the prospective study currently underway.

Employment Status

Table 22: Summary of delay types according to employment status. (Median delay in days.)

	Patient delay	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Employed	45.5	35.5	99.0	12.5	6.5
Unemployed	32.0	43.0	75.0	22.0	11.0

There was no relation between employment status and diagnostic delay demonstrated. This was also found in previous studies.[29]

Socioeconomic factors have been suggested as being predictive or responsible for increased risk of oral cnacer[40] and other cancers.[38] Employment status can be considered a marker of social and economic status and it is surprising that there is not more evidence in the literature to support this proposed link. The rationale for this theory is that patients from socially or economically deprived backgrounds are more likely to have difficulties in accessing health care than patients from more privileged backgrounds. This is a complex area of public health and other factors such as lower educational level, the ability to navigate a sometimes complex public health and physical access to health care facilities and professionals are also intricately intertwined with this and other socioeconomic factors.

Interestingly, there is a trend towards decreased delay in unemployed patients for total delay and possible patient delay in this study. The other measures of diagnostic delay show the opposite trend. This will be a focus of the prospective study currently underway.

Health Insurance

Table 23: summary of delay types according to health insurance status. (Median delay in days.)

	Patient delay	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Insured	40.0	26.0	74.0	14.0	12.0
Un-insured	31.5	41.0	86.0	21.5	8.0

No significant association between the health insurance status and diagnostic delay was demonstrated.

Health insurance, like employment status, can be a marker for socioeconomic background. No studies relevant to head and neck cancers and looking at health insurance status were able to be located during the literature search for this project.

However it is likely that the same comments made with regards to employment status and diagnostic delay above, also pertain to health insurance status.

In this study there was a trend towards increased professional delay, total delay and biopsy delay amongst uninsured patients. This may be accounted for by the possible existence of barriers to accessing health care by un-insured patients. This possibility is an area that will be further investigated in future studies.

Type of Referrer

Table 24: Summary of delay types according to referrer type. (Median delay in days.)

	Patient delay	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Dentist/GP	31.5	39.0	78.0	21.5	9.5
Specialist	53.0	43.0	61.0	7.0	13.0

No association between delay and type of referrer was demonstrated. This does not support my hypothesis that there would be shorter delay associated with patients referred by medical practitioners.

The literature is divided on this question. Some studies have reported no effect on diagnostic delay by the type of referrer [9, 23,24,25,32,41] whilst others report the opposite. [27, 29] where differences between doctors and dentists are shown, the differences tend to show that medical practitioners refer earlier than dental practitioners. Some authors have attempted to account for this discrepancy by claiming that dentists tend to treat patients presenting with oral ulceration by mechanical means such as denture adjustment and that dentists have a low index of suspicion for malignant disease[29]. Many of the presenting signs and symptoms of oral cancer such as oral ulceration, ill fitting dentures, loosening of teeth, tooth or jaw pain are common presentations to dentists and are usually accounted for by local dental causes.[41] It is perhaps understandable why there may be increased referral delay from dentists when this is considered.

Stage of Tumour at Diagnosis

Table 25: Summary of delay types according to stage of tumour at diagnosis. (Median delay in days.)

	Patient delay	**Professional Delay**	**Total delay**	**Biopsy delay**	**Referral delay**
Early Stage	60.0	29.0	74.0	11.0	12.0
Late Stage	31.0	49.0	81.0	32.0	7.0

No association was shown to exist between stage of tumour at diagnosis and length of diagnostic delay. This supports my hypothesis that there would be no relation between delay and stage and has been reported in other studies. [18,19,23,24,25,26]

There is a possible tendency for a shorter patient delay and shorter referral delay to be associated with late stage tumours in this study. Longer professional delay , total delay and biopsy delay may be showing a tendency to be associated with late stage tumours at diagnosis. This will be the subject of further analysis in the prospective study currently in progress.

The finding in many studies that length of delay in diagnosis is not related to stage of tumour at diagnosis has been the subject of much conjecture. Two main theories have been suggested to account for it[25]; the tumour aggressiveness hypothesis and the silent tumour hypothesis.

The tumour aggressiveness hypothesis explains the lack of relationship by suggesting that different tumours have different levels of aggressiveness. Rapidly growing, aggressive tumours would be expected to present with late stage disease and a short period of delay. Conversely, relatively indolent tumours may be present for many years and present as early stage disease despite a long period of delay.

The silent tumour hypothesis accepts that disease stage will be to some extent determined by diagnostic delay, however, it suggests that some tumours remain relatively asymptomatic whilst others become asymptomatic early on in the history of the disease. Whether tumours are symptomatic or not is determined more by patient factors than by the biology of the tumour. It also assumes that the kinetics of

tumour growth are similar on a population basis. Thus some patients may ignore malignant disease for a long period of time allowing them to present with advanced disease whilst other patients will notice signs very rapidly and present with early stage disease.

Weaknesses of This Study

The principle weaknesses of this study are

1. lack of statistical power
2. study design - retrospective chart review.

The small numbers in this study preclude the unmasking of potential predictors of diagnostic delay. Whilst certain trends in the data may be noted, it is not possible to comment any further with any scientific rigour. No statistically significant findings were made. Conversely, the lack of statistical power also means that true associations between predictor variables and diagnostic delay are unable to be demonstrated.

The study design also has inherent limitations. It is a retrospective chart review and relies on the accuracy of the medical record to extract data. In many cases the data may not be accurately recorded and assumptions necessarily are made. For example, often patients could not recall an exact onset of symptoms and an estimate of the date of onset (as described in the methods section) needed to be made.

Conclusions

No association between the potential predictor variables examined and five types of diagnostic delay were demonstrated. Of the 12 hypotheses proposed, only one was supported by this studies statistical analysis. The hypothesis supported was that there would be no association between diagnostic delay and stage of tumour at diagnosis.

Whilst this study has insufficient statistical power to show any actual relations which may be present, it did suggest some interesting trends which are being further investigated by a larger, prospective study which is currently in progress.

References

1. Tracey E A, Supramaniam R. Cancer in New South Wales: incidence and mortality 2000 featuring projections to 2010 for selected sites. Sydney: Cancer Council NSW, 2002

2. The Cancer Council of New South Wales. Cancer in NSW 2002 – Head and Neck Cancer. www.nswcc.org.au/editorial.asp?pageid=288. Accessed 1st July 2007.

3. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics 2002. CA Cancer J Clin 2005;55:74-108

4. Pisani P, Parkin DM, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. Int J Cancer 1999; 83:18-29.

5. Greene FL, Page DL, Fleming ID, et al: ‘‘AJCC cancer staging manual.’’ 6th ed. New York: Springer-Verlag; 2002.

6. Sobin LH. TNM; Principles, history and relation to other prognostic factors. Cancer 2001;97:1589-1592

7. Patel SG, Shah JP. TNM staging of cancers of the head and neck: Striving for uniformity amongst diversity. CA Cancer J Clin 2005;55(4):242-258

8. Broumand V, Lozano TE, Gomez J. Evaluation and staging of oral cancer. Oral Maxillofacial Surg Clin N Am 2006;18:435-444.

9. Gorsky M, Dayan D. Referral delay in diagnosis of oro/oro-pharyngeal cancer in Israel. Eur J Cancer B Oral Oncol 1995;31B(3):166-168.

10. Mashberg A, Samit AM: Early diagnosis of asymptomatic oral and oropharyngeal squamous cancers. CA Cancer J Clin 45:328, 1995

11. Hollows P, McAndrew PG, Perini MG. Delays in the referral and treatment of oral squamous cell carcinoma. British Dent Journal 2000;188:262-265.

12. Janot F, Klijanienko J, Russo A et al. Prognostic value of clinicopathological parameters in head and neck squamous cell carcinoma: a prospective analysis. Br J Cancer 1996;73:531-8

13. Shah JP, Lydiatt W. Treatment of cancer of the head and neck. CA Cancer J Clin 1995;45:352-368.

14. Shah HV, Williams RW, Irvine GH. Fast track referrals for oral lesions: A prospective study. Br J Oral Maxillofacial Surg 2006; 44:207-208.

15. Amir Z, Kwan SYL, Landes D, Feber T, Williams SA. Diagnostic delays in head and neck cancers. Eur J Cancer Care. 1999; 8:193-203.

16. Silverman S. Early diagnosis of oral cancer. Cancer 1988; 62:1796-1799.

17. Dolan RW, Vaughan CW, Fuleihan N. Symptoms in early head and neck cancer: an inadequate indicator. otolaryngol Head Neck Surg 1998;119(5)463-7.

18. Kowalski LP, Franco EL, Torloni H. Lateness of diagnosis of oral and oropharyngeal carcinoma: factors related to the tumour, the patient and health professionals. Eur J Cancer B Oral Oncol 1994; 30B(3):167-73.

19. Wildt J, Bunngaard T, Bentzen SM: Delay in the diagnosis of oral squamous cell carcinoma. Clin Otolaryngol 20:21 1995.

20. Holmes JD, Dierks EJ, Homer LD et al. Is detection of oral and oropharyngeal cancer by a dental health care provider associated with a lower stage at diagnosis? J Oral Maxfac Surg 2003; 61: 285-291.

21. Dimitroulis G, Reade P, Wiesenfeld D. Referral patterns of patients with oral squamous cell carcinoma, Australia. Oral Oncol, Eur J Cancer 1992; 28B(1)23-27.

22. Chandu A, Smith ACH. Patterns of referral of patients undergoing surgical management for oral cancer. Australian Dental Journal 2002;47: (4) 309 – 313.

23. Jovanovic A, Kostense PJ, Schulten EA et al. Delay in diagnosis of oral squamous cell carcinoma; a report from the Netherlands. Oral Oncol, Eur J Cancer 1992; 28B(1)37-38.

24. Allison P, Franco E, Black M, Reine J. The role of professional diagnostic delays in the prognosis of upper aerodigestive tract carcinoma. Oral Oncol 1998;34(2):147-53.

25. Scott SE, Grunfeld EA, McGurk M. The idiosyncratic relationship between diagnostic delay and stage of oral squamous cell carcinoma. Oral Oncol 2005; 41: 396-403.

26. McGurk M, Chan C, Jones J, et al. Delay in diagnosis and its effect on outcome in head and neck cancer. Br J Oral Maxillofacial Surg 2005; 43: 281-284.

27. Schnetler JF. Oral cancer diagnosis and delays in referral British Journal of Oral Maxillofacial Surgery 1992;30:210-213.

28. O'Sullivan EM. Some insights into the potential for earlier detection of oral cancer: a population based study. Oral Oncol 2001;37:S53.

29. Onizawa K, Nishihara K, Yamagata K et al. Factors associated with diagnostic delay of oral squamous cell carcinoma. Oral Oncol. 2003;39(8):781-8.

30. Arndt V, Sturmer T, Stegmaier C, Ziegler H, Dhom G, Brenner H. Patient delay and stage of diagnosis among breast cancer patients in Germany- a population based study. Brit J Cancer 2002;86:1034-1040.

31. Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. Lancet 1999; 353:1119-1126.

32. Sainsbury R, Johnston C, Haward B. Effect on survival of delays in referral of patients with breast cancer symptoms: a retrospective analysis. Lancet 1999; 353: 1132-1135.

33. Kerdpon D, Sriplung H. Factors related to delay in diagnosis of oral squamous cell carcinoma in southern Thailand. Oral Oncology 2001;31:127-131.

34. Pitiphat W, Diehl SR, Laskaris G, Cartsos V, Douglas CW, Zavras AI. Factors associated with delay in the diagnosis of oral cancer. J Dent Res 2002;81(3):192-197.

35. http://www.ecog.org/general/perf_stat.html accessed 1st April 2007.

36. http://icd9cm.chrisendres.com/index.php?action=child&recordid=1012 accessed 1st April 2007.

37. Bradley PJ. Editorial. Head and neck cancer, England, UK – action is getting faster, have you noticed? Br J Oral Maxfac 2005; 43: 481 - 483.

38. Neal RD, Allgar VL. Sociodemographic factors and delays in the diagnosis of six cancers: analysis of data from the 'National Survey of NHS Patients: Cancer'. B J Cancer 2005; 92:1971 – 1975.

39. Cecile MT, Van Wijk G, Kolk AM. Sex differences in physical symptoms: the contribution of symptom perception theory. Soc Sci Med 1997;45:231–46.

40. Conway DI, Brewster DH, McKinney PA, Stark J et al. Widening socio-economic inequalities in oral cancer incidence in Scotland, 1976 – 2002. B J Cancer 2007; 96: 818 – 820.

41. Guggenheimer J, Verbin RS, Johnson JT et al. Factors delaying the diagnosis of oral and oropharyngeal carcinomas. Cancer 1989; 64:932 – 935.

Appendix A: Data Collection Sheet

ID code	
Post Code	
Age (years)	
Sex (M/F)	
Marital status/De Facto (Y/N)	
Chronic medical condition (Y/N)	
Medications	
Medical conditions	
Employment status 1. retired 2. employed 3. unemployed 4. home duties?	
Private health insurance? (Y/N)	
Regular GP? (Y/N)	
Regular dental check ups? (Y/N)	
Family member/close friend with cancer or mouth cancer (Y/N)	
Previous Diagnosis of Cancer Elsewhere Y/N	
Date first noticed symptoms (best estimate) (A?)	
Initial presentation to (tick one) 1. GP 2. Dentist 3. Specialist 4. Other (describe)	
Date of initial presentation (B)	
Date referred to H&N clinic (C)	
Date first attended H&N clinic (D)	
Date of biopsy (E)	
Patient Delay (B-A)	
Professional Delay (C-B)	
ECOG Score	
Smoking History 1. Current smoker 2. Ex-smoker 3. Never smoked	
Number smoked per day	
Number of years smoking	
Chewing tobacco or other? Other risk factors for oral cancer Alcohol?	
Diagnosis	
TNM	
Site 1. oral tongue 2. floor of mouth 3. buccal mucosa 4. alveolus (maxilla) 5. alveolus (mandible) 6. soft palate 7. hard palate 8. tonsil 9. nasopharynx 10. oropharynx 11. larynx 12. maxillary sinus 13. lip 14. skin	

Appendix B: Ethics approval

Hi Peter

Definitely an audit and so doesn't need ethics approval

How is the other study going

Nicole

Regards

Nicole

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