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**Opportunities for achieving early diagnosis of
oral cancer within the medical profession in Australia**

Dr John Douglas Webster

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ABSTRACT

Most oral cancers lack early symptoms that would prompt a patient to seek diagnosis; hence at presentation more than 60% of patients are diagnosed with stage III or IV advanced disease. Survival rates and morbidity are dramatically improved if the disease is treated at an early stage, preferably asymptomatic in stage one. Therefore, early detection of oral cancer and oral potentially malignant lesions in the asymptomatic phase via an oral cancer screening examination is important.

The core objective of this thesis is to determine whether asymptomatic diagnosis of oral cancer at an early stage of disease is achievable in Australia. We achieve this by evaluating the awareness of, and attitudes toward, oral cancer and opportunistic screening held by recently-diagnosed oral cancer patients, experienced general medical practitioners, and recently-graduated medical students.

Two studies are detailed herein. The first involved recruitment of a cohort of 103 Australian patients diagnosed with pathologically verified oral cancer (excluding lip) through the Royal Brisbane and Women's Hospital (RBWH) Head and Neck Clinic to complete a 36-part questionnaire to address the above aims. The second study involved a questionnaire that was mailed to 553 General Medical Practitioners (GMPs) randomly selected from a database developed from GMPs working in locations expected to refer suspected oral cancer patients to the RBWH Head and Neck Clinic. A similar questionnaire was designed to collect data from a sample of 151 Graduated Medical Students (GMSs) commencing work as intern medical officers at the RBWH and the Princess Alexandra Hospital (PAH) in Brisbane, Australia.

From these studies we found that participants with oral cancer had poor awareness of oral cancer and poor knowledge of risk factors prior to diagnosis. Nearly all were over 40 years of age and most consumed tobacco or alcohol or both, suggesting a target population for opportunistic screening in the primary healthcare setting. Patient, professional, and total diagnostic

delay were better than in many other countries. In the asymptomatic phase before diagnosis, participants with oral cancer were more likely to visit a GMP over a General Dental Practitioner (GDP), and likely to do so multiple times each year, identifying significant opportunities for GMPs to perform opportunistic oral cancer screening.

We also found that Australian GMPs and GMSs have an inadequate level of knowledge of oral cancer, OPMLs, risk factors, and inadequate skill in performing opportunistic oral cancer screening examinations. At the present level of knowledge and confidence, it would be unlikely for a GMP to conduct a thorough visual and tactile oral cancer screening examination even if a high-risk individual presented to his or her clinic. Only 7% of participants with oral cancer were diagnosed in the asymptomatic phase, and all were diagnosed by health practitioners with a dental qualification.

We conclude that asymptomatic diagnosis of oral cancer at an early stage of disease is achievable in the primary medical healthcare setting in Australia via opportunistic oral cancer screening. Initiating a consultation with a GMP or GDP for an oral cancer screening examination would require a patient to have an improved awareness of oral cancer and knowledge of his or her personal risk factors for developing it. To increase opportunistic oral cancer screening activity from Australian GMPs, interventions need to ensure that GMPs and GMSs reach competence in risk factors for oral cancer, identifying high-risk populations, diagnostic confidence, and skill in performing the nine-step visual and tactile opportunistic oral cancer screening examination.

DECLARATION BY AUTHOR

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

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No publications.

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Contributions by others to the thesis

Professor Camile S Farah – significant contribution to the questionnaire design, provision of printing and mailing materials, mailing costs, and critically revising drafts, manuscripts, and the final thesis submission.

Dr Marie AT Matias – significant contribution of critically revising drafts, manuscripts, and final thesis submission.

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None.

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List of Abbreviations

ACOMS	Asian Congress Oral and Maxillofacial Surgeons
AIHW	Australian Institute of Health and Welfare
ANZHNCS	Australian and New Zealand Head and Neck Cancer Society
CME	Continued Medical Education
GDP	General Dental Practitioner
GMP	General Medical Practitioner
GMS	Graduated Medical Student
HNC	Head and Neck Cancer
HPV	Human papilloma virus
LESIONS	Lesion Evaluation, Screening and Identification of Oral Neoplasia Study
NICDR	National Institute of Dental and Craniofacial Research
OC	Oral cancer
OED	Oral epithelial dysplasia
OPML	Oral potentially malignant lesion
OSCC	Oral squamous cell carcinoma
PAH	Princess Alexandra Hospital
RACGP	Royal Australian College of General Practitioners
RBWH	Royal Brisbane and Women's Hospital
RCT	Randomised controlled trial
UK	United Kingdom
USA	United States of America
UV	Ultraviolet
UQCCR	University of Queensland Centre for Clinical Research
WHO	World Health Organisation

CHAPTER ONE: INTRODUCTION

Oral cancer (OC) refers to all aggressive neoplasms that affect the external lip, oral cavity, and oropharynx; however, the predominant type is oral squamous cell carcinoma (OSCC) and can affect all tissues of epithelial origin.^{1, 2} Worldwide, oral cancer has one of the highest mortality rates among all malignancies.³ It is recognized as the sixth most common cancer, and 270,000 new cases are expected each year.^{1, 3, 4} There is significant disparity in geographical incidence across the world, suggesting geographical differences in risk factors, most of which have been identified in other epidemiological studies.⁵⁻⁷ In South Asia and the Indian Subcontinent oral cancer accounts for almost one third of all malignancies, in contrast to the Western world, where it is comparatively uncommon and accounts for only 2-5% of all malignancies.^{5, 8} India, Sri Lanka, and Pakistan have the highest levels of the disease, and it is the most common cancer for men in these countries and accounts for up to 30% of all new cases of cancer compared, to just 3% in the United Kingdom (UK) and 6% in France.⁹ The prevalence of oral cancers is high in countries of South Asia and the Indian Subcontinent, where distinct cultural practices, such as betel nut chewing, and varying patterns of tobacco and alcohol use are important risk factors that predispose people to cancer of the oral cavity.¹⁰

To add an Australian context, between 1992 and 2008, 60826 cases of lip, oral cavity, and oropharyngeal cancer were diagnosed and registered on the Australian Cancer Database with the Australian Institute of Health and Welfare (AIHW).¹¹ These cases represented 2.9% of the total cancer burden in Australia and caused 1.6% of all cancer deaths, which is very similar to the UK population.^{9, 11} The incidence rate of all sites was between 10 and 14 per 100,000 population for both sexes combined.¹¹ Males accounted for 71% of all cases diagnosed compared to 29% for females.¹¹ Over the 27-year period of Australian data analysed by Farah et al. (2014), there was no significant change in incidence, and overall mortality associated with oral cancers remained stable despite advances in imaging and treatment modalities, however cancers of the tongue and oropharynx showed an increasing trend over time.¹¹

Overall, the five-year survival rate for oral cancer is approximately 50% for all anatomical sites and stages.¹¹ The most important prognostic marker for oral cancer remains tumour stage at diagnosis.^{6, 12} Unfortunately, most oral cancers lack early symptoms, and hence

more than 60% of patients present with advanced disease, either stage III or IV oral cancer.^{13, 14} The reported five-year survival rate of stage III or IV oral cancer ranges between 15% and 55%.¹⁵⁻¹⁸ In contrast, oral cancers diagnosed at a smaller size and without lymph node involvement in stage I or II report a five-year survival rate ranging between 66% and 85%.^{11, 15, 19} A recent analysis of 22,204 pathologically verified oral cancers followed up over ten years concluded that early diagnosis and intervention before stage II can significantly improve life expectancy and decrease expected years of life lost to oral cancer.¹⁸ This is ideally when the patient is likely asymptomatic with a tumour less than 2cm in diameter and with less than 4mm of invasion.^{18, 20} Therefore, early detection of malignant lesions and oral potentially malignant lesions (OPMLs) is an important goal for reducing morbidity and mortality.^{14, 15, 21, 22}

The Cochrane collaboration and other expert consortia agree that whilst population-based annual or semi-annual screening for oral cancer is not cost-effective, targeting high-risk populations to be opportunistically screened using a visual and tactile examination should be encouraged in the primary care setting.²³⁻²⁶ Opportunistic oral cancer screening by general medical practitioners (GMPs) and general dental practitioners (GDPs) should remain an integral part of the routine daily work of these groups, and particular attention should be paid to high-risk individuals.²⁷ In Australia the most significant risk factors for the development of oral cancer are likely to be increased age and tobacco and alcohol consumption.^{28, 29} Prevention and early-stage diagnosis may be important for oral cancers because these known risk factors enable identification of high-risk populations, and identifying oral cancers and oral potentially malignant lesions (OPMLs) is relatively easy via a simple visual and tactile oral cancer screening examination.

Recent research suggests that GDPs in Australia are actively screening the oral mucosa for most patients as part of their routine daily work, but falls short of determining whether the GDPs perform all nine steps of the visual and tactile oral cancer screening examination suggested by the World Health Organisation (WHO) and National Institute of Dental and Craniofacial Research (NIDCR).^{27, 30, 31} There have been no investigations into the awareness of, knowledge of, and attitudes toward opportunistic oral cancer screening in the Australian GMP population. Similarly, there is no study that investigates these same attributes in graduated medical students (GMSs) as they exit medical school and enter the workforce. Chapter 4 of this thesis establishes these two Australian datasets via a survey of GMS and practicing GMPs in Brisbane. Chapter 3 investigates a cohort of Australian

patients with pathologically confirmed oral cancer attending the Head and Neck Clinic at the RBWH in Brisbane. These patients are studied regarding patient awareness, knowledge of risk factors, actual risk factors, patient delay, professional delay, diagnostic delay, and access to health practitioners in the Australian health system in the asymptomatic phase. Prior research has focused on review of patient and professional delay, but importantly this research precedes the patient delay phase and focuses on the asymptomatic phase wherein the oral cancer may be present and detected at an earlier stage of disease.³² A key aim is to identify missed opportunities for early diagnosis of malignant lesions or OPMLs by investigating patient interactions with GMPs and GDPs in the asymptomatic phase.

The purpose of these research endeavours is to establish three Australian datasets that will provide valuable insights and lead to development of public health messages and policy, development of educational and training interventions at the undergraduate and postgraduate level, and ultimately to increased rates of visual and tactile opportunistic oral cancer screening in the primary medical healthcare setting. Asymptomatic diagnosis of oral cancer in the early stages of the disease should be achievable in Australia and is key to reducing mortality and morbidity caused by oral cancer.

CHAPTER TWO: LITERATURE REVIEW

2.1 Oral Potentially Malignant Lesions and Oral Epithelial Dysplasia

Globally, over 90% of oral cancers are OSCC, a malignancy that has a high tendency to metastasize to regional lymph nodes and occurs most often in individuals over 40 years of age.^{1, 4} Tumour stage at diagnosis remains the most important prognostic marker for oral cancer.^{19, 33} Therefore, there is a need for early diagnosis of oral cancer, ideally at the premalignant or potentially malignant stage, in order to reduce morbidity and mortality.^{14, 15, 21, 25, 34} Oral potentially malignant lesions (OPMLs) is the collective term for the wide range of clinical presentations of oral lesions that may harbour oral epithelial dysplasia (OED). Clinically, OPMLs can appear as leukoplakia, erythroplakia, or erythro-leukoplakia (speckled erythroplakia).²² Although various other factors, such as smoking history, patient age and gender, and lesion size and location may contribute to the suspicion of malignant potential, the clinical appearance is often the primary driving factor toward the decision to biopsy or offer intervention.³⁵ Leukoplakias, the most common OPMLs, show a low rate of malignant progression (4-18%) irrespective of the histopathologic diagnosis of mild, moderate, or severe dysplasia.³⁶ In contrast, erythroplakias and erythro-leukoplakias have been shown to have a much higher risk of malignant transformation (14-50%).³⁷ We can confidently state that lesions exhibiting redness or a non-homogenous texture are strongly associated with OED and should be considered for biopsy at presentation.³⁸⁻⁴⁰ Homogenous lesions that presented on the tongue or floor of the mouth are also significantly more likely to be dysplastic, and more so if tobacco consumption is part of the presentation.^{41, 42} Unfortunately, these clinical features at presentation may estimate the rate of OED in OPMLs but there is no way of differentiating OPMLs into dysplastic and non-dysplastic on clinical findings alone, because OED can manifest clinically in any number of presentations.⁴²⁻⁴⁴

OED is the histopathologic diagnosis that describes this precancerous stage, and it is characterized by a range of cellular and morphologic tissue changes which are similar to those of SCC but are restricted to epithelial cells and remain non-invasive.¹ The most recently accepted histological classification developed by the WHO divides OED into mild, moderate, and severe dysplasia (otherwise known as carcinoma *in situ*).¹ However, unlike the stepwise progression in severity of cervical pre-cancerous lesions, there is no step-wise pattern of progression in oral cancer.

A recent retrospective study of 368 patients showed that for all oral sites and all WHO dysplasia grades, the annual malignant transformation rate was 1% and the annual progression to higher grade of dysplasia was 3%.⁴¹ In a comparable population the annual malignant transformation rate was 1.8% and 5.6% for moderate and severe dysplasia, respectively, indicating that histological grading was a risk factor for transformation to malignancy.⁴⁵ In contrast, other studies showed no association between transformation rates and grading of dysplasia.^{44, 46} The use of histopathology for the diagnosis and categorization of OED has long been considered imprecise, with poor inter- and intra-observer agreement and low levels of reproducibility.^{47, 48} Therefore, the usefulness of grading OED has been contested in the literature, and there is currently no consensus regarding risk of malignant transformation based on histopathologic grading of the OED.⁴⁹

The most current systematic review of the literature regarding treatment and follow-up of oral dysplasia suggests that removing dysplasia reduces but does not eliminate the risk of OSCC formation.⁵⁰ However, given the lack of consistent correlation of OED histopathologic grading with transformation to malignancy, it appears only prudent to perform a more definitive treatment of OPMLs exhibiting any grade of dysplasia, rather than to limit treatment to severe cases.⁴¹ This is an unfortunate outcome of the poor predictive value of the WHO OED grading classification, which cannot be used reliably as a guide for treatment decision-making.⁴¹ Although complete excision of OED may be considered by some as overtreatment, in contrast, the ongoing surveillance of retained OED even with regular review is increasing risk of harm to the patient by malignant transformation over time and should be regarded as an ineffective treatment option.^{42, 44, 46,}

⁵¹ In summary, definitive treatment of all OED is recommended.

2.2 Risk Factors for Oral Cancer

Oral cancer is a multifactorial disease and the pathogenesis is equally complex. Oral cavity carcinomas are predominantly caused by chemical carcinogens, although evidence implicating infectious factors (e.g. human papilloma viruses) and physical stimuli (e.g. recurrent trauma or chronic inflammation) in some carcinomas continues to grow.^{52, 53} The most prominent modifiable risk factors are lifestyle factors, including tobacco and tobacco products, alcohol, betel quid chewing, and poor diet, while the non-modifiable risk factors are increasing age (>40 years) and sex (male > female).^{15, 21, 54}

2.2.1 Tobacco

A considerable body of evidence supports a strong association between oral cancer and tobacco use.⁵ The use of smokeless tobacco has been shown to increase the risk of developing oral cancer by up to four times, but smoking tobacco is far worse.⁵ Smoking tobacco increases the risk of developing oral cancer from three to seventeen times that of a non-smoker.^{21, 55-58} The data also suggest that a lifetime dosage relationship exists. Smokers of greater than thirty pack-years show an odds ratio of 2.9 (1.8 ~ 4.5 95% CI) compared to those with greater than forty pack-years with an odds ratio of 8.46 (6.22 ~ 11.50 95%CI) and those with a greater than sixty pack-year history an odds ratio of 10.1 (6.1 ~ 16.7 95%CI).⁵⁶⁻⁵⁸ In addition, approximately 80% of oral cancer patients are smokers and thus are a target population for screening activities.^{59, 60}

2.2.2 Alcohol

Alcohol consumption is often cited as a known risk factor for oral cancer.⁶¹⁻⁶³ In epidemiological studies controlled for smoking, a moderate to heavy alcohol consumption has been shown to increase the risk of developing oral cancer from three to nine times that of abstainers.^{59, 60, 64, 65} Whilst the definition of moderate to heavy alcohol consumption varies from study to study, the conclusion of the majority of the literature is that higher lifetime alcohol consumption is correlated with increased risk of oral cancer. There is also significant evidence to suggest a synergistic effect between alcohol and tobacco consumption in the development of oral cancer.^{58, 59}

2.2.3 Areca Nut Consumption

The areca nut is carcinogenic to humans and has been declared as such by the International Agency for Research on Cancer.⁶⁶⁻⁷¹ It is often consumed during betel quid

chewing and is more commonly referred to as betel nut chewing, which is a misnomer given the nut component of the betel quid is the nut of the areca palm. Betel quid is prepared by adding different ingredients such as betel fruit, betel leaf, lime juice, tobacco, and other flavours to the betel nut according to local traditions that vary across Asia and the subcontinent.⁷²⁻⁷⁴ Whilst areca nut consumption and betel quid chewing is not prominent in the Australian population, it is practised by 600 million people worldwide, and is the fourth most commonly used drug in the world, after alcohol, tobacco, and caffeine.⁶⁶ Gene expression is distorted by hypermethylation with alkaloids from the betel nut, which may block tumour suppressor genes such as p14, p15, p16, and p53.⁷⁵⁻⁷⁷ People who chew areca nut, but do not smoke or consume alcohol, have an odds ratio of 10.97 (3.22 ~ 37.34 95%CI) for developing oral cancer.^{58, 78} There is also significant epidemiological evidence of a synergistic effect between tobacco, alcohol, and areca nut consumption in the development of oral cancer.^{63, 79, 80}

2.2.4 Human Papilloma Virus (HPV)

The evidence for the role of HPV as an aetiologic agent in oral cancer has grown rapidly. Two recent meta-analyses found HPV to be an independent risk factor for oral cancer, but predominantly in the anatomical subset of oropharyngeal cancers.^{81, 82} HPV infections in the progression of head and neck cancer (HNC) have been consistently noted in 25% of cases.^{81, 83, 84} Over 100 different types of HPV exist; however, fewer than twenty are thought to have oncogenic potential.⁸⁵ HPV-16 is the most common genotype found in oral cavity and oropharyngeal cancer.⁸⁶ The E6 and E7 proteins produced by HPV-infected cells are thought to dysregulate the function of two oncosuppressors, p53 and pRb, resulting in uncontrolled DNA replication and impairment of apoptosis.⁸⁷ The combined effects of these leads to an increased tendency toward carcinogenic change. Studies suggest that HPV is a sexually transmitted infection.⁸⁸ Rates of survival and local recurrence are much better in HPV-positive oral cancer.^{89, 90} Individuals who also smoke are at high risk of developing HPV-16 positive HNC, and the prevalence of HPV-related HNC is increasing; this trend may be attributable to changes in sexual behaviours, particularly oral sex.^{57, 91, 92}

2.2.5 Poor Diet and Nutritional Deficiencies

Poor diet, or a diet lacking fresh fruit and vegetables, has emerged as a significant risk factor for HNC, independent of tobacco, alcohol, betel nut consumption, and HPV.^{93, 94} As

with other carcinomas outside the oral cavity, a diet high in consumption of fruits and vegetables appears protective against oral cancer when epidemiologic studies are controlled for tobacco and alcohol use.⁹⁵ Further investigation into this phenomenon has shown that β -carotene and vitamin A supplementation resulted in substantial regression of some OPMLs.^{96, 97} Increased consumption of green leafy vegetables and non-starchy tubers such as carrots reduces the risk of oropharyngeal cancer.⁹⁸ Iron deficiency anaemia in animal and human studies of the oral epithelium is often atrophic, in addition to showing rapid epithelial turnover.^{99, 100} One hypothesis for this as a risk factor for oral cancer is that iron deficiency may increase one's susceptibility to chemical carcinogens from the thin, atrophic, more permeable epithelium, and also from the high number of vulnerable dividing cells due to increased turnover.¹⁰⁰ The effect of individual food components and trace elements on carcinogenesis remains unclear.¹⁰¹

2.2.6 Ultraviolet (UV) Radiation

UV irradiation is the main cause of lip cancer, which is responsible for 30% of all OSCC.¹⁰² A high incidence of lip cancer has been reported among Caucasians and is approximately three times higher in males than females, which may be due to more outdoor occupations, UV exposure, and tobacco exposure amongst men.^{103, 104}

2.2.7 Age

There is no doubt that increasing age is a significant risk factor for developing oral cancer. In Europe, 98% of all head and neck cancer patients were more than 40 years old.¹⁰⁵ Similarly, in Australia it is rare to diagnose oral cancer (excluding lip) under the age of 40 years.¹⁰⁶

2.2.8 Sex

Overall, incidence and mortality rates are higher for males than females worldwide. In Australia over the 27-year period between 1982 and 2008, 71% of cases were diagnosed in males and 29% in females.¹¹ This may relate to higher lifetime consumption of alcohol and tobacco. The incidence trend among females is beginning to increase at higher rates than in the past, and again it is theorized that females collectively may be consuming larger amounts of alcohol and tobacco than before.¹⁰⁷

2.2.9 Socio-economic Status

Oral cancer is seen more often in people from lower socio-economic groups and those living in deprived areas.⁵⁴ Individuals with lower occupational status or social class, lower education level, or lower incomes, and those in manual labour roles, have a greater risk of developing oral cancer independent of lifestyle habits such as tobacco and alcohol consumption.^{108, 109} Hypothesized explanations for these socio-economic factors are plentiful and include limited access to healthcare and health information, exposure to harmful physical environments or agents, and stresses caused by job insecurity or unemployment.¹⁰⁹

2.2.10 Controversial Risk Factors with Limited Evidence

2.2.10.1 Oral Hygiene and Chronic Inflammation

Although poor oral hygiene and poor dentition (faulty restorations, sharp teeth, and ill-fitting dentures) have been implicated in a few epidemiological studies, it is not clear whether confounding by tobacco and alcohol have been addressed in these studies.^{54, 110, 111} Periodontal disease has been correlated with increased risk of oral cancer.¹¹² It is argued that chronic infection from periodontal disease results in low-grade inflammation and oxidative stress, which may contribute to carcinogenesis.¹¹² A recent case-control study from Japan found that frequent tooth brushing could reduce the risk of cancer of the upper aerodigestive tract, especially in the high-risk group of heavy tobacco and alcohol consumers.¹¹³ Several oral bacteria also metabolise alcohol to acetaldehyde, a known carcinogen.¹¹⁴ *Candida albicans* can also efficiently convert alcohol to the carcinogenic acetaldehyde, similarly to several bacteria in the oral flora.^{62, 114} Fungal infections, most commonly secondary to *Candida albicans*, may invade the oral epithelium and be involved in producing dysplastic change.^{62, 114} Evidence suggests that in addition to the inflammatory response, nitrosamines produced by the fungus may activate proto-oncogenes.¹¹⁴

2.2.10.2 Ethnicity

There is much discussion regarding the susceptibility to oral cancer based on ethnicity and race, as oral cancer incidence rates vary considerably across different groups in the world.⁴ For example, one study of African-American males showed a 15% higher incidence than in white American males.¹¹⁵ Another highlighted that south Asians have a far higher incidence than most other groups in the world.⁴ Nutritional differences, smoking patterns, differences in amounts smoked or alcohol consumed, and the two-way and

three-way interaction of betel quid chewing with smoking and alcohol, rather than genetic factors, may play a role in these observed variations in populations and high incidence in some ethnic and racial groups.⁵⁴

2.2.10.3 Heredity and Familial Risk

Recently, genetic factors such as p53 mutations, aberrant expression of epidermal growth factor receptor (EGFR) and/or ligands for it, and promoter methylation of human MutL homolog1 (hMLH1) have all been correlated with oral cancers.¹¹⁶⁻¹¹⁸ Although oral cancer is in part a genetic disease caused by environmental exposure to carcinogens, there are no associations with hereditary cancer syndromes to suggest heredity.⁵⁴ The relative risk of oral cavity cancer was between 1.2% and 3.8% for those who had a family history of HNC when compared with those with no such family history.¹¹⁹ Knowledge of heredity and genetic factors is increasing, but at present it does little to assist the general medical practitioner (GMP) or general dental practitioner (GDP) in performing a risk assessment, as the evidence for familial aggregation is limited.⁵⁴

2.2.10.4 Other Risk Factors

This literature review does not allow discussion of all risk factors, but it is important to mention some others from the literature. High levels of heavy metals, such as nickel (Ni), chromium (Cr), and arsenic (As), have been correlated with increased risk for oral cancer development.¹²⁰ Immunosuppression is certainly reported to increase lip cancer following kidney transplantation and is significantly related to use of azathioprine and cyclosporine.^{121, 122} Other controversial debated risk factors with limited evidence include diabetic immunosuppression, HIV infection and resultant immunosuppression, cannabis smoking, Khat (qat) chewing, alcohol containing mouthwash, indoor air pollution, and nicotine replacement products.⁵⁴

2.2.11 Oral Cancer Risk Factors in the Australian Population

In Australia the most significant risk factors in the development of oral cancer are increased age, tobacco use, and alcohol consumption.^{28, 29} Prevalence data on tobacco smoking in Australia shows that the daily smoking rate has fallen from 20% in 2001 to 17% in 2007 and again to 15% in 2010.^{123, 124} In contrast, our indigenous Australians had a smoking prevalence of 50% in 2007.¹²⁵ In 2010, 46% of people aged 12 years and over drank alcohol at least weekly.¹²⁴ It is also widely known that Australia's consumption of alcohol per capita is high by world standards, at approximately 10L/year of pure alcohol

among individuals over the age of 15 compared to very high at approximately 15L/year for indigenous Australians.¹²⁶ As a nation Australia is at increased risk for developing OC based on this level of alcohol consumption.

Whilst it is rare to diagnose oral cancer (excluding lip) under the age of 40 years in Australia, the number of oral cancer cases is increasing in females under 45 years of age with no history of no alcohol or tobacco use, and ongoing research has implicated, though not proven, the role of HPV in such cases.^{2, 15, 54, 106} The incidence of male and female HPV-related cancers has drastically increased annually in Australia, predominantly in the oropharyngeal location.⁹¹ As a result, the current National HPV Vaccination Programme has included both males and females aged 12 to 13 years since 2013 and may have an effect on the future incidence of these HPV-related cancers.¹²⁷

Practising GMPs and GDPs in Australia should be aware of the modifiable and non-modifiable risk factors discussed above. In the developed world the most significant risk factors in the development of oral cancer are increased age, tobacco use, and alcohol consumption.^{28, 29} A recent large international pooled study estimated the population attributable risks for tobacco and alcohol use to be 64% (95%CI:45-75%), showing that these two risk factors alone are responsible for a large number of cases.²⁸ In summation, reasonable populations to place in the higher-risk category for developing oral cancer in Australia are those over 40 years of age and those who regularly consume of tobacco and/or alcohol.

2.3 Timing of Diagnosis and Prognostic Implications

2.3.1 Prognostic Markers

Current markers that have been allocated independent prognostic value include age, gender, immunological status, nutritional status, size and location of tumour, stage of disease, nodal status, oncogene expression, proliferation markers, and DNA content. Of these, tumour stage at diagnosis remains the most important prognostic marker for OSCC.^{6, 12} As stated in the Introduction, most oral cancers lack early symptoms and hence more than 60% of patients present in stage III or IV.^{13, 14, 16, 17} The reported five-year survival rate of stage III or IV oral cancer ranges between 15% and 55%.¹⁵⁻¹⁸ Survival rates improve significantly if the disease is treated at an early stage; hence, early detection of malignant lesions and OPMLs is important for reducing morbidity and mortality.^{14, 15, 21, 22}

2.3.2 Early Stage Diagnosis

Early detection of disease is a confusing term that can imply either a small tumour at diagnosis or a short time interval since development of the oral cancer, which introduces the concept of diagnostic delay.²³ An early stage at diagnosis is the aim of early detection strategies. To achieve an early stage at diagnosis the tumour should be small, less than 2cm in diameter, and less than 4mm in invasion depth, and is usually asymptomatic.²⁰ A difficulty with small-size tumour diagnosis is that by the time the cancer reaches a measurable size, it is possible that lymphatic or metastatic spread has already taken place.²³ A rational conclusion is that clinicians must be vigilant when monitoring OPMLs for malignant changes and opportunistic in their screening of higher-risk asymptomatic patients such as tobacco and alcohol consumers over 40 years of age.

For this to be achievable in the Australian population, both GMPs and GDPs must be knowledgeable regarding oral pathologies and competent to perform oral cancer screening examinations. In addition, patients must be aware of oral cancer and their individual risk factors for developing it before increased rates of early diagnosis are likely to be seen in Australia.

2.3.3 Diagnostic Delay

In addition to the challenge of finding and diagnosing these lesions at early stage of disease, it is also important to note that a significant body of literature suggests that diagnostic delay is also a determinant factor in oral cancer survival.^{25, 128, 129} Diagnostic delay generally refers to the time that elapses from the time the patient first becomes aware of symptoms until a definitive diagnosis is made following specialist review. This is commonly divided into patient and professional delay. Patient delay refers to the time that elapses from when symptoms begin until the patient first meets with a professional for a consultation regarding diagnosis.¹³⁰ Professional delay is the time that elapses from this initial consultation, often in the primary care setting, until a definitive diagnosis is made, often after referral to a specialist setting. In Australia this often involves biopsy, awaiting results, and referral to a specialised head and neck cancer clinic. The total diagnostic delay from the literature review averages 3 to 6 months and is roughly evenly distributed between patient and professional delay.²³ Whilst there is no Australian dataset on diagnostic delay, it is anticipated from anecdotal experience that the total delay is similar in

the Australian population, and this is investigated in our research.

Causes of patient delay are related to psychosocial issues, such as perceptions of symptoms and illness; behavioural responses; accessibility to health care, including financial; and structural and personal barriers such as beliefs, culture, and language.¹³¹ Esmaelbeigi et al. (2014) conducted a case-control study to explore factors that affect total diagnostic delay in oral cancer, and showed that out of 206 patients in an Iranian population, those with primary-level education had a 70% lower risk of delay compared to the illiterate patients (OR = 0.3, 95% CI 0.1–0.7), and the risk was lower again among patients with diploma-level education (OR = 0.04, 95% CI 0–0.7) and college level education (OR = 0.1, 95% CI 0–0.4).¹³² The delayed patients were diagnosed at a more advanced stage than were the patients without delay (OR = 2.1, 95% CI 1.0–4.4).¹³³ A recent study investigating barriers to oral cancer screening among rural African-Americans showed three primary patient barriers to screening.¹³³ Lack of knowledge (not knowing about oral cancer and not knowing oral cancer symptoms) accounted for 31.8% of all barriers mentioned, lack of resources (e.g., lack of money and health insurance) for 25.0%, and fear (e.g., fear of screening and diagnosis) for 22.9%. Howell et al. (2013) placed these barriers within the Theory of Planned Behaviour and concluded that interventions aimed at increasing oral cancer screening should focus first on changing individual's attitudes toward screening by increasing knowledge about oral cancer and reducing fear.¹³³

Causes of professional delay provide an opportunity for interventions, which may lead to increase in opportunistic screening of the higher-risk population. Research has shown that lack of knowledge regarding the main locations of oral cancer, low suspicion of oral cancer, and low levels of skill and confidence to perform a full head and neck examination with appropriate equipment are prevalent in the general medical and dental community to varying degrees.^{131, 134-136} The presence of co-morbidities in patients has also been shown to result in clinicians focusing their attention on the existing disorders.¹³⁷⁻¹³⁹ Prescription of medicines, such as analgesics, in the primary care setting (OR = 5.3, 95% CI 2.2–12.9), history of dental procedure (OR=6.8, 95% CI 1.7–26.9), and history of loose teeth increased the risk of delay by four times (OR = 4.0, 95% CI 1.6–9.8) and were associated with a higher risk of delay compared to patient who were biopsied from the beginning.¹³² Two studies suggest a strong relationship between professional delay and decreased survival rates, specifically when professional delay is longer than a month.^{140, 141} Two

further studies reported a significant association between professional delay and the tumour stage at diagnosis across a spread of different populations.^{137, 142}

Esmaelbeigi et al. (2014) showed that of out of 206 Iranian patients, 71.4% were diagnosed with oral cancer at an advanced stage (III-IV).¹³² The medians of the patient, professional, and total delays were 45, 86, and 140 days, respectively.¹³² In a systematic review by Gomez et al. (2009), total diagnostic delay was associated with a more advanced tumour stage at diagnosis and the pooled relative risk (RR) was 1.47 (95% CI: 1.09–1.99).³³ However, in a separate systematic review expanded to include all head and neck cancers, no association was found between diagnostic delay in head and neck cancers and tumour stage at diagnosis.¹⁴³ Seoane et al. (2010) further challenged the strength of the relationship with a statistical analysis of 83 OSCC cases, which showed that when the analysis was adjusted for tumour stage at diagnosis (I-II vs. III-IV), proliferative activity became an independent prognostic factor for survival, whereas diagnostic delay did not influence survival significantly.¹⁴⁴ To complicate the issue further, research on professional delay and mortality in tongue cancer is even more paradoxical, as less professional delay trends toward worse survival rates, which appears to be an unreasonable statistical outcome.^{140, 145} This paradoxical response whereby diagnostic delay, tumour stage, and prognosis are inversely related has also been described in breast, cervical, lung, colon, renal, and urethral cancer.¹⁴⁶ This suggests that stage at diagnosis and survival are affected more by the biology of the tumour (for example, rapid growth or poor differentiation) than by diagnostic delay.¹⁴⁶

Rather than focusing on delay as a major contributor to tumour stage at diagnosis and survival, the focus should be shifted to identifying lesions in the asymptomatic period. An overwhelming volume of literature shows that many patients are diagnosed in the symptomatic phase, often at an advanced stage (III-IV) of disease. As research on diagnostic delay by definition deals with the symptomatic phase, if an early stage diagnosis is to be achieved, then future research efforts should focus on improving oral cancer screening in the asymptomatic phase through appropriate screening strategies. A reasonable conclusion is that, regardless of the body of research focusing on diagnostic delay from time of first symptoms, the true clinical aim is to diagnose a lesion in the asymptomatic phase as either an OPML, an OED, or a small-size tumour at diagnosis; that is, less than 2cm in diameter and less than 4mm in invasion depth.²⁰

2.4 Screening Strategies

The WHO defines screening as the presumptive identification of unrecognised disease or defects by means of tests, examinations, or other procedures that can be applied rapidly.¹⁴⁷ The overall benefit should also outweigh any harm that results from screening. In addition, when community resources are used to fund screening, there should be a community consensus that the benefits of screening justify the expense.¹⁴⁸

In Australia, the Australian Health Minister's Population Based Screening Framework sets out clear guidelines, based on the WHO principles of screening, to define when a disease is suitable for population-based screening versus opportunistic case-finding, herein referred to as opportunistic screening.⁷⁸ Based on these guidelines, oral cancer does not fulfil the requirements for a population-based screening programme.¹⁴⁹

A Cochrane systematic review evaluated screening strategies for reducing oral cancer mortality and revealed that there is insufficient evidence to recommend inclusion or exclusion of screening for oral cancer using a visual and tactile examination in the general population.^{25, 27} According to the WHO and NIDCR, an oral cancer screening examination should include a visual examination of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the mouth, tongue, and palate with mouth mirrors to help visualise all surfaces.³⁰ The tactile examination includes palpating the regional lymph nodes, tongue, and floor of the mouth.³⁰ The Cochrane collaboration concluded by encouraging opportunistic screening and stating that GMPs and GDPs should continue to carry out visual and tactile examination of the oral cavity as an integral part of their routine daily work, and particular attention should be paid to high-risk individuals.²⁷

An expert European consortium formed in 2014 to systematically review the oral cancer and pre-cancer screening programmes in Europe. As there are no randomised controlled trials (RCTs), the findings were essentially the same as the Cochrane collaboration in 2013.^{24, 25} In 2015 at the 11th Asian Congress of Oral & Maxillofacial Surgery (ACOMS), an expert consensus was reached to highlight the importance of oral cancer screening by various conventional and novel methods based on scientific research into their populations.²⁶ In Asia the emphasis is on addressing the relatively high prevalence rate of oral cancer due to tobacco and betel nut consumption.²⁶

Monteiro et al. (2015) carried out separate invitational and opportunistic oral cancer

screening interventions in the city of Oporto in Portugal. The first part of this study was an invitational screening programme where residents of Oporto City were invited to attend on a designated screening day advertised via a mass media campaign.¹⁵⁰ Pre-information regarding the oral cancer screening day were provided by screen shots on the Portuguese television, notices in newspapers and also by radio announcements.¹⁵⁰ Additionally, the announcements of the screening day and central city location were by posters on local billboards and by distribution of leaflets at public places.¹⁵⁰ The second part of the study was an opportunistic screening programme offered to consenting patients visiting for dental consultation (first appointment) in a public hospital of Oporto City.¹⁵⁰ A total of 727 individuals responded (277 males and 450 females) with a mean age of 54 years (range 18-94), and an oral cancer screening tactile and visual examination was performed.¹⁵⁰ A total of 267 (36.7%) were from the invitational oral cancer screening day. Twenty-two OPMLs, 9 cases of lichen planus, no erythroplakia, and no erythroleukoplakia were detected.¹⁵⁰ In addition, two oral carcinomas were detected early, with both in the T1 stage of the disease and identified in the asymptomatic phase.¹⁵⁰

Initial outcomes recently published from an integrated outpatient-based screening programme for oral cancer in Taipei, Taiwan also support the need for screening in the asymptomatic phase. High-risk patients attending an outpatient facility at Far Eastern Memorial Hospital were identified using an automated system based on their response to questions regarding tobacco and betel nut usage, and then they were offered the opportunity to be screened with a standard visual and tactile oral cancer screening examination.³² A total of 8037 high-risk patients were recruited as participants to the screened cohort from the automated system; 1664 patients were identified with positive lesions, and 302 patients underwent a biopsy. Five patients were diagnosed with oral cancer and 121 with dysplastic OPMLs.³² The stage of disease at diagnosis of this asymptomatic cohort was compared to a symptomatic cohort presenting to the same outpatient facility for investigation of a symptomatic oral lesion.³² The symptomatic cohort comprised 157 patients with oral cancers and 61 with OPMLs, and, as expected, the automated screening programme identified earlier stages of oral cancers than the symptomatic cohort.³²

There is only one study investigating high-risk populations and oral mucosal disease in Australia. The Lesion Evaluation, Screening and Identification of Oral Neoplasia Study (LESIONS) aims to understand factors that may influence all oral mucosal disease in a

high-risk population with a particular focus on oral cancers and OPMLs.¹⁵¹ LESIONS has targeted two communities at high risk of oral cancer and OPMLs. The first was a low socio-economic region characterised by documented higher rates of tobacco and alcohol consumption.¹⁵¹ The second was an indigenous Australian population known to present with a higher rate of cancer-related modifiable risk factors, namely tobacco consumption and excessive alcohol use, which were 20% and 10% higher, respectively, than the general Australian population.¹⁵¹ The authors recently reported on the recruitment experiences and outcomes from the programme across ten screening sites within public and private dental clinics, indigenous health clinics and a community pharmacy.¹⁵¹ A visual and tactile oral mucosal screening examination was completed on 1498 participants by one of 11 trained and calibrated dentists or oral health therapists.¹⁵¹ In these high-risk populations, oral mucosal lesions were detected in over half the cohort examined, but only 16% were clinically non-homogenous and more likely to contain dysplasia or early malignant change.¹⁵¹ The results of biopsy and specialist review are not presented in the current report, however, the bivariate and multivariable analysis concludes that increased age, moderate/heavy tobacco consumption and high socioeconomic disadvantage are strongly associated with the prevalence of non-homogenous oral mucosal lesions.¹⁵¹

Huang et al. (2015) have recently published their nation-wide analysis of 22024 cases of oral cancer in Taiwan after follow-up for 10 years.¹⁸ In their retrospective analysis they conclude that early diagnosis and early intervention before stage II can significantly improve life expectancy and decrease expected years of life lost to oral cancer.¹⁸ The results will be used to encourage the public to participate in oral cancer screening programmes.¹⁸ In Western populations where betel nut usage is minimal, population-based annual or semi-annual screening for oral cancer is not cost-effective.²³ Instead, targeting high-risk groups such as tobacco and alcohol consumers over 40 years of age to be opportunistically screened using a visual and tactile examination should be encouraged in the primary care setting.²³

2.5 Opportunistic Screening: Opportunities and Threats

2.5.1 Patient Factors

In Australia, for opportunistic screening to occur, asymptomatic patients need to attend a GMP or GDP and receive an oral cancer screening examination. Specific educational interventions to raise awareness of oral cancer and knowledge of the risk factors for

developing it is predicted to increase the number of patients requesting an oral cancer screening examination. In the UK, patients' knowledge of oral cancer is low compared to that of other types of cancer.¹⁵² A theory-based study found that a group at high risk for oral cancer wanted not only more information on the symptoms of oral cancer, but also more guidance on how to evaluate symptoms.¹⁵³ Clear evidence of successful educational interventions includes the increased numbers of oral cancer screening examinations that have been performed over the years following the introduction of Oral Cancer Awareness Week (now Month) in the UK and Oral Cancer Awareness Month in the USA in 2000.¹⁵⁴

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Many factors contribute to patient delay, such as perception of symptoms and illness and the behavioural responses they elicit, in addition to the major issue of accessibility to health care, including financial, structural, and personal barriers.¹⁴⁴ These same factors present a threat to opportunistic screening strategies and opportunities for improvement. In Australia, each citizen has access to a free public health system with access to many GMPs under the government-funded Medicare scheme. However, citizens do not have access to a free dental health system. Australian citizens in the lowest income percentage, who are healthcare cardholders, are entitled to free dental treatment but are usually subject to long waiting lists unless emergent treatment is required. Research has shown that patients with oral lesions often consult their GMPs rather than their GDPs, even in the UK where there is greater access to free dental treatment.^{156, 157} A recent systematic review of patient acceptance of screening for oral cancer outside the dental setting showed that GMPs can be confident that acceptance of and satisfaction with oral cancer screening is high, particularly when patients have previously been educated about oral cancer.¹⁵⁸ It is assumed, but not proven, that most patients with oral cancer in Australia would act similarly and present to GMPs in the symptomatic phase, given the lack of general subsidised access to GDPs under the Medicare scheme.

This assumption will be tested in Chapter Three of this thesis, which investigates patients who have been diagnosed with oral cancer through the head and neck cancer clinic at the RBWH.

2.5.2 General Medical and Dental Practitioners

In order to achieve an early stage at diagnosis, a patient should ideally be diagnosed in the asymptomatic phase. This requires a GMP, GDP or other health professional to

perform an oral cancer screening examination. This takes approximately 90 seconds to perform after adequate training and includes extra-oral and intra-oral examinations in white light and manual palpation of related specific sites.^{159, 160} The examination should be accompanied by a review of the patient's medical and dental history.^{159, 160} GMPs and GDPs should also be confident in the clinical signs of a malignant lesion and OPML, as this is key to reducing the anxiety associated with inappropriate referrals of benign pathologies.¹⁶¹ In December 2000 the UK Department of Health introduced Oral Cancer Awareness Week and also attempted to reduce professional delay by implementing the two-week rule system with regard to referrals of head and neck cancer. Under this system GMPs and GDPs would utilise a standard referral form and have the patients reviewed by a specialist within two weeks. Several audits of this intervention have shown it to be successful in reducing professional delay, but a high proportion of non-malignant lesions have been referred, with no significant improvement in stage of disease at diagnosis.¹⁶²⁻¹⁶⁵ This highlights a low sensitivity among GMPs and GDPs and stresses the need for further education and training in assessing malignant lesions and OPMLs.¹⁶²⁻¹⁶⁵ Whilst newer techniques, such as toluidine blue staining, chemiluminescence, and autofluorescence, are becoming more established clinical tools for differentiating dysplastic from non-dysplastic lesions and malignant from non-malignant tissue, the most suitable, accessible, and practical screening tool for a GMP or GDP remains a methodical extra-oral and intra-oral examination in adequate white light.^{166, 167}

When oral cancer awareness among GMPs and GDPs is compared, there is significant divergence in most populations studied. A study in the UK found that GMPs were less likely to examine patients' oral mucosa routinely, were less likely to advise patients about risk factors for oral cancer, identified fewer risk factors for oral cancer, and felt less confident about diagnosing it from clinical appearance than their dental counterparts.¹⁶⁸ In the USA a similar study concluded the GDPs were much more likely to feel adequately trained and regularly provide oral cancer screening examinations, but much less likely to discuss tobacco and alcohol cessation or to palpate the neck nodes.¹⁶⁹ Similar studies in Saudi Arabia, Qazvin, Ireland, and Scotland reported similar key findings. In summary, GMPs are less intent on performing oral cancer screening, less skilful in performing oral cancer screening examinations, and less confident in diagnosing pathologies in the oral cavity than GDPs.¹⁷⁰⁻¹⁷³ A recent study of 640 GDPs in Australia showed that over 90% regularly perform oral mucosal screening examinations for all patients.³¹ Australian GDPs reported lack of training, confidence, time, and financial incentives as barriers to

performing mucosal screening to at least some degree.³¹ While most Australian GPs manage referrals for oral mucosal pathology appropriately and promptly, only half believe in following up with the referred patients and only half believe they could influence a patient to quit smoking.³¹

The intent of GMPs to conduct oral cancer screening has been investigated utilising the Theory of Planned Behaviour and this has identified barriers to conducting oral examinations for screening purposes in general medical practice. The results suggest considerable potential for improving intention to perform oral cancer screening in general practice.¹⁷⁴ Suggested interventions include: 1) theory-based interventions, such as further training to enhance confidence, expertise, knowledge, and ease of examination, 2) provision of adequate equipment in the surgery (light and dental mirrors), and 3) introducing guidelines on opportunistic screening that increase motivation to comply, with more peers performing screening or an oral cancer awareness month.¹⁷⁴

In regard to GMP skill in oral cancer screening examinations, there is a statistically significant association between undergraduate and postgraduate teaching on examination of the oral cavity and whether practitioners felt confident in their ability to detect oral cancer.¹⁷³ GMPs display decreased diagnostic confidence in detecting malignant or OPMLs. In fact, in a study of Irish GMPs, a statistically significant association was found between undergraduate and postgraduate teaching on the diagnosis of oral malignant disease and whether practitioners felt confident in their ability to detect oral cancer and OPMLs clinically.¹⁷³ The authors concluded that the level of knowledge of GMPs needs to be addressed with appropriate initiatives both at undergraduate level and via continued medical education (CME).¹⁷³ This raises the question of what is being taught at medical schools to improve these poor findings regarding the oral cancer awareness, intent to opportunistically screen, and skill in examination and diagnosis of GMPs when compared to GPs. In addition, a potentially greater threat to improving opportunistic screening amongst GMPs was identified in a Scottish study in which a high proportion (66%) of GMPs felt strongly that oral cancer detection is the remit of the dental team.¹⁷² At present there is no data to suggest Australian GMPs are similar to their Scottish counterparts in knowledge, attitudes, and behaviour regarding oral cancer screening; however, if this attitude does pervade among Australian GMPs then it may prove difficult to change behaviour pertaining to opportunistic screening. At present the Royal Australian College of General Practitioners (RACGP) teaches that there is insufficient evidence to recommend

screening by visual inspection or by other screening methods.¹⁷⁵ The RACGP identifies increased-risk individuals as smokers aged greater than 50 years, heavy drinkers, users of chewing tobacco or areca/betel nuts, and those exposed to excessive UV in the lip area.¹⁷⁵ If an individual is identified as having an increased risk, the RACGP encourages opportunistic examination of mouth and lips every 12 months but does not provide an examination description matching the desired nine-step visual and tactile oral cancer screening examination.^{30, 175}

2.5.3 Medical and Dental Student Education

Studies comparing UK undergraduate medical and dental students showed that the students gave responses similar to those of their senior colleagues, suggesting there will be no improvement in the next generation of doctors regarding oral cancer screening.¹⁷⁶ Again, these results are echoed in studies from Iran, Nigeria, and the USA, and suggest a need to review the curriculum of medical and dental schools to improve awareness of and behaviour toward increased screening.¹⁷⁷⁻¹⁸¹

In fact, two significant studies investigated the curriculum for oral cancer teaching in the USA and UK. In 2011, the majority of the responding USA medical schools offered very little oral health education, with approximately 80% offering less than five hours of oral health curriculum over the entire course.¹⁸² Alarmingly, similar research 15 years earlier in the USA also concluded that oral cancer training lacked both adequacy and comprehensiveness.¹⁸³ A logical conclusion is that there has been no improvement in training over this 15-year period. Similarly, in a 2011 UK study, undergraduate oral cancer teaching varied widely in terms of duration, format, and content, and the authors concluded that there is a need to develop a curriculum to address the important aspects of oral cancer from an evidence-based approach that can be integrated into the already-crowded undergraduate medical curriculum.¹⁸⁴

2.5.4 Contribution of Bias

Whilst diagnosis in the asymptomatic phase from opportunistic oral cancer screening is worth achieving, it should be noted that the success of any screening intervention could be affected by length-time and lead-time bias.

Length-time bias occurs when the possibility of detecting aggressive (rapid-growing) oral

cancers by screening is low due to the fact that the period until symptoms arise is short. In contrast, less aggressive (slow-growing) cancers have longer periods until symptoms arise and are easier to detect by screening.¹⁴⁶ This phenomenon may lead a researcher to think that an early diagnosis improves prognosis, when in fact the screening approach simply detects tumours that are biologically less aggressive.²³

Lead-time bias occurs when survival following an oral cancer diagnosis seems better when cases are diagnosed early, when in fact the patient did not live any longer than he or she would have if the cancer had been diagnosed in the symptomatic period.²³

The contribution of both of these potential sources for bias must be considered when analysing data on the success of screening programmes. To date there is insufficient evidence to conclude that screening alters disease-specific mortality in an asymptomatic person seeking GMP or GDP care.² Of course, insufficient evidence only means that there no methodologically sound studies are available to support the given screening approach.¹⁴⁶

CHAPTER THREE: AUSTRALIAN PATIENTS WITH ORAL CANCER

3.1 Introduction

Oral cancer has one of the highest mortality rates among all malignancies worldwide.³ Over the last twenty years the incidence of oral cancer has increased throughout developed regions globally, including Australia, New Zealand, North America, Europe, and parts of East Asia.^{185, 186} Overall, the five-year survival rate is approximately 50% for all anatomical sites and stages.¹¹ The most important prognostic marker for oral cancer remains tumour stage at diagnosis.^{6, 12} Unfortunately, most oral cancers lack early symptoms, and hence by the time symptoms do develop and stimulate a patient to seek a diagnosis, the disease has already reached advanced stage, resulting in more than 60% of patients being diagnosed with stage III and IV disease.^{13, 14} The reported five-year survival rate for stage III or IV oral cancer ranges between 15% and 55%.¹⁵⁻¹⁸ Survival rates are significantly improved if the disease is treated at an early stage, ideally when the patient is asymptomatic with a tumour less than 2cm in diameter and with less than 4mm of invasion.²⁰ Therefore, early detection of malignant lesions and oral potentially malignant lesions (OPMLs) is an important goal for reducing morbidity and mortality.^{14, 15, 21, 22}

Huang et al. (2015) recently published an analysis of 22,024 pathologically verified cases of oral cancer in Taiwan after follow-up for 10 years.¹⁸ In their retrospective analysis, they concluded that early diagnosis and intervention before stage II can significantly improve life expectancy and decrease expected years of life lost to oral cancer.¹⁸ These results will be used to encourage the public to participate in oral cancer screening programmes.¹⁸ The Cochrane collaboration and an expert European consortium agreed that whilst population-based annual or semi-annual screening for oral cancer is not cost-effective, targeting high-risk groups—such as tobacco and alcohol consumers over 40 years of age—with opportunistic screening using a visual and tactile examination should be encouraged in the primary care setting.²³⁻²⁵ Opportunistic oral cancer screening should remain an integral part of routine daily work for GMPs and GDPs, with particular attention paid to high-risk individuals.²⁷

In Australia the most significant risk factors for the development of oral cancer are increased age, tobacco, and alcohol consumption.^{28, 29} While it is rare to diagnose oral cancer (excluding lip) under the age of 40 years in Australia, an increasing number of

cases show no prior alcohol or tobacco use; often these are women under 45 years of age.^{2, 15, 54, 106} Ongoing research has suggested a role for HPV in such cases, although this has not been confirmed.^{2, 15, 54, 106} The incidence of male and female HPV-related oropharyngeal cancers in Australia has significantly increased annually across both genders in line with global trends.⁹¹

To date only one Australia cohort of patients has been investigated regarding patient awareness, risk factors and components of diagnostic delay, however this study was limited to patients attending a private specialist oral medicine clinic, and most of the pathology noted was OPMLs, with only 8 cases of OSCC.¹⁸⁷ No Australian cohort of patients with newly diagnosed and pathologically confirmed oral cancer has been investigated regarding patient awareness, knowledge of risk factors, actual risk factors, patient delay, professional delay, diagnostic delay and access to health practitioners in the Australian health system in the asymptomatic phase prior to diagnosis. Much research has focused on review of patient and professional delay, but this research precedes the patient delay phase and focuses on the asymptomatic phase where the oral cancer may be present and detected at an earlier stage of disease.³² A key aim is to identify missed opportunities for early diagnosis of malignant lesions or OPMLs by investigating patient interactions with GMPs and GDPs in the asymptomatic phase.

3.2 Hypotheses

1. Oral cancer patients at the RBWH had poor awareness of oral cancer prior to their diagnosis.
2. Oral cancer patients at the RBWH had poor knowledge of risk factors prior to their diagnosis.
3. Oral cancer patients at the RBWH had one or more known risk factors for oral cancer at the time of diagnosis.
4. Oral cancer patients at the RBWH had exposure to health practitioners in the asymptomatic phase in the preceding months or years before awareness of symptoms or diagnosis occurred.
5. No oral cancer patient at the RBWH had ever been opportunistically screened for oral cancer by a GMP in the asymptomatic phase.

3.3 Aims

1. To assess participants' awareness of oral cancer prior to diagnosis.
2. To assess participants' knowledge of risk factors prior to diagnosis.
3. To identify participants' risk factors for oral cancer at diagnosis.
4. To assess patient, professional, and total diagnostic delay.
5. To identify whether participants had opportunities in the Australian health system to receive an opportunistic oral cancer screen in the asymptomatic phase.

3.4 Methods and Materials

Ethical Approvals

The study protocol was approved by the University of Queensland Dental Science Research Ethics Committee (1217) and the RBWH Human Research Ethics Committee (HREC/14/QRBW/82).

Study Design

Following extensive review of the literature, a questionnaire was designed to address the study aims. A cohort of Australian patients diagnosed with pathologically verified oral cancer (excluding lip) through the RBWH Head and Neck Clinic under the Metro North Hospital and Health Service of Queensland Health were invited to participate in the year-long study. The validity and reliability of the questionnaire was established with a small pilot group of six patients, utilising the test and re-test method.

Participant Recruitment

The research study pack contained an introductory cover letter on Queensland Health letterhead signed by the site coordinator, a participant information form, a form for informed consent, the questionnaire, and a professionally addressed and stamped return envelope for return of the questionnaire. As recruitment in a retrospective manner, the research study pack was mailed, utilising the modified Dillman method known to increase response rates, to patients who were recently diagnosed with an oral cancer (excluding lip) three months prior to the ethical clearance date (April 2014).^{31, 187-189} In a prospective manner, new patients attending the RBWH Head and Neck Clinic until January 2015 who were diagnosed with an oral cancer (excluding lip) were invited to participate on the day of their attendance by the approved site coordinator or their delegate employee of Queensland Health; this was independent from the researchers. The participants were

able to freely consent and either complete the questionnaire at the clinic or return it via pre-paid mail. The questionnaire responses were initially identifiable to allow a follow-up phone call for clarification of responses if required, and to award the incentive (“a new iPad”), which was randomly drawn by the chief investigator at the conclusion of data collection.

Questionnaire

The questionnaire consisted of 36 open, multiple-choice, or closed questions investigating demographics; awareness of oral cancer before diagnosis; knowledge of risk factors before diagnosis; asymptomatic or symptomatic diagnosis; symptoms developed; referral pathway; dates for calculation of patient, professional, and diagnostic delay; analysis of interactions with GMPs, GDPs, and any other health professionals in the asymptomatic phase before diagnosis; and any risk factors the participant had prior to diagnosis. A full copy of the questionnaire is given in Appendix A.

Data Analysis

Completed questionnaires were de-identified, manually coded and recorded into Microsoft Excel (Microsoft Corporation, Washington, USA) to allow statistical analysis of binary and non-binary responses. Insufficient numbers of patients were recruited in the year to allow subset analysis of patient groups with any significance. The results were expressed as proportions and frequency count charts calculated using Microsoft Excel (Microsoft Corporation, Washington, USA)

3.5 Research Results

Unless otherwise stated, all percentages reported are the percentage in agreement.

3.5.1 Response Rate and Demographics

22 of 27 questionnaires mailed to the retrospective group and 81 of 85 questionnaires mailed to the prospective group were returned, giving a total of 103 questionnaires returned and an overall response rate of 92%. The median age of participants was 65 years, and 74 (72%) were male and 29 (28%) were female; these were the only demographics collected via Questions 1 and 2.

3.5.2 Patient Awareness of Oral Cancer

Table 3.1 presents the responses to Questions 3 to 10 regarding patients' awareness of oral cancer before receiving a diagnosis. Of interest is that 6% of participants had a previous diagnosis of oral cancer and 25% had a friend or relative with a previous diagnosis of oral cancer, and yet in spite of that exposure, only 17% stated that they had ever read anything about oral cancer prior to their own diagnosis. If a participant had answered 'no' to Questions 3 through 9, then they were left with a positive response to Question 10, highlighting, after clarification of responses by the chief investigator, that 46% had never heard of oral cancer until their diagnosis.

Table 3.1: Patient Awareness of Oral Cancer

n=103	Yes		No	
	n	%	n	%
Have you worked with patients with oral cancer in a health care role?	3	3%	100	97%
Have you had a previous diagnosis of oral cancer?	6	6%	97	94%
Have you had a previous diagnosis of oral cancer in your extended family?	12	12%	91	88%
Have you had a previous diagnosis of oral cancer in a friend?	13	13%	90	87%
Have you heard of a previous diagnosis of oral cancer in someone not known to you but you had heard about it from others or from talking or online?	31	30%	72	70%
Have you ever read anything about oral cancer prior to your diagnosis?	17	17%	86	83%
Had you never heard of oral cancer until you were diagnosed?	47	46%	56	54%

3.5.3 Patient Knowledge and Risk Factors

Table 3.2: Patient Knowledge of Risk Factors vs. Actual Risk Factors

n=103	Patient knowledge		Risk factor present	
	n	%	n	%
Tobacco	54	52%	69	67%
Alcohol	15	15%	68	66%
Betel Nut	0	0%	2	2%
HPV	2	2%	5	5%
Poor Diet	0	0%	11	11%
Age > 40 years	0	0%	98	95%
Male	0	0%	74	72%
Family History	3	3%	3	3%
OPML	3	3%	3	3%
Poor Dental Hygiene	1	1%	Not assessed	NA

Table 3.2 presents the responses to Questions 11 and 34, highlighting the fact that approximately half (52%) of participants identified tobacco consumption (smoking or smokeless) as a risk factor, despite 67% using tobacco themselves. In addition, only 15% were aware that alcohol consumption is a risk factor, in contrast to 66% being regular consumers of alcohol. Three participants (3%) identified an OPML as a risk factor, due to all three being repeatedly monitored for their own OPML via clinical review. Overall, participants are low in knowledge of other risk factors, such as human papilloma virus (HPV), betel (areca) nut consumption, age, sex (male), and a diet poor in fresh fruit and vegetables. 95% were over 40 years of age at diagnosis, and 67% and 66% were regular consumers of tobacco and alcohol, respectively.

3.5.4 Patient Diagnostic Process

Table 3.3 represents the responses to Questions 12-15 and 17, and reveals that only 7% of all participants were diagnosed in the asymptomatic phase, and all these were by health practitioners with a dental qualification. The remaining 93% of participants were only diagnosed once symptoms had developed, with the large majority (73%) electing to see a GMP rather than a GDP (14%) for explanation of their symptoms. The three most common symptoms that led participants to present to a health practitioner were pain (60%), a lump/lesion (52%), and an ulcer/sore (43%).

Table 3.3: Patient Diagnostic Process

	n	%
Asymptomatic Diagnosis (Yes responses= 7, n=103)	7	7%
Diagnosed by Dental Practitioner	4	4%
Diagnosed by Dental Specialist (Oral Medicine/Oral Pathologist)	2	2%
Diagnosed by General Medical Practitioner	0	0%
Diagnosed by OMF Surgeon (monitoring OPML)	1	1%
Symptomatic Diagnosis (Yes responses = 96, n=96)	96	93%
Diagnosed by Dental Practitioner	14	14%
Diagnosed by Dental Specialist (Oral Medicine/Oral Pathologist)	0	0%
Diagnosed by General Medical Practitioner	75	73%
Diagnosed by Medical Specialist	4	4%
Diagnosed by Emergency Physician	3	3%
What symptoms did you develop before diagnosis? (n=96)		
Altered Neurology	5	5%
Altered Speech	2	2%
Bleeding	4	4%
Erythema	2	2%
Lump/Lesion	50	52%
Pain	58	60%
Ulcer/Sore	41	43%
Weight Loss	4	4%

95 of 96 participants were able to recall the date of symptoms and date of attending their initial health practitioner. Questions 16, 18, and 19 allow calculation of the patient and professional delay (Figure 3.1) and the overall diagnostic delay (Figure 3.2). The median patient delay was 14 days. The median professional delay was 34 days. The median of total diagnostic delay was 62.5 days, or 9 weeks.

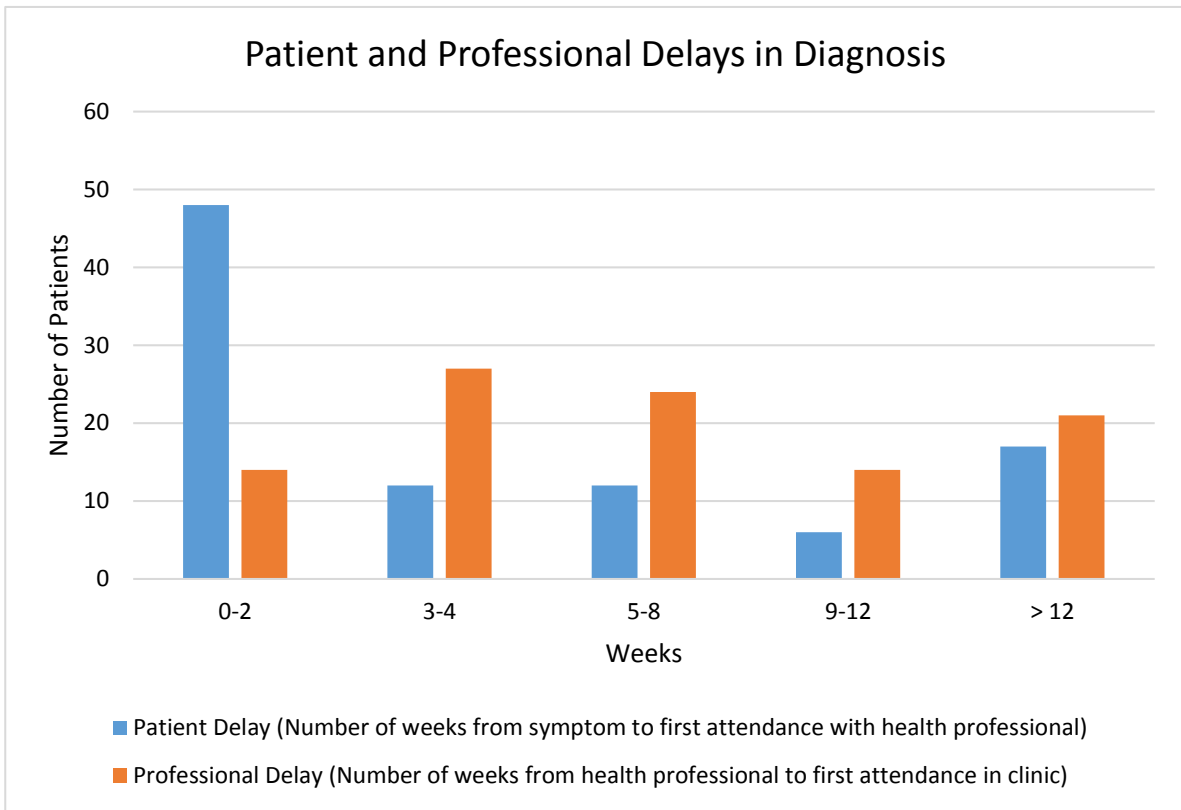


Figure 3.1: Patient and Professional Delay

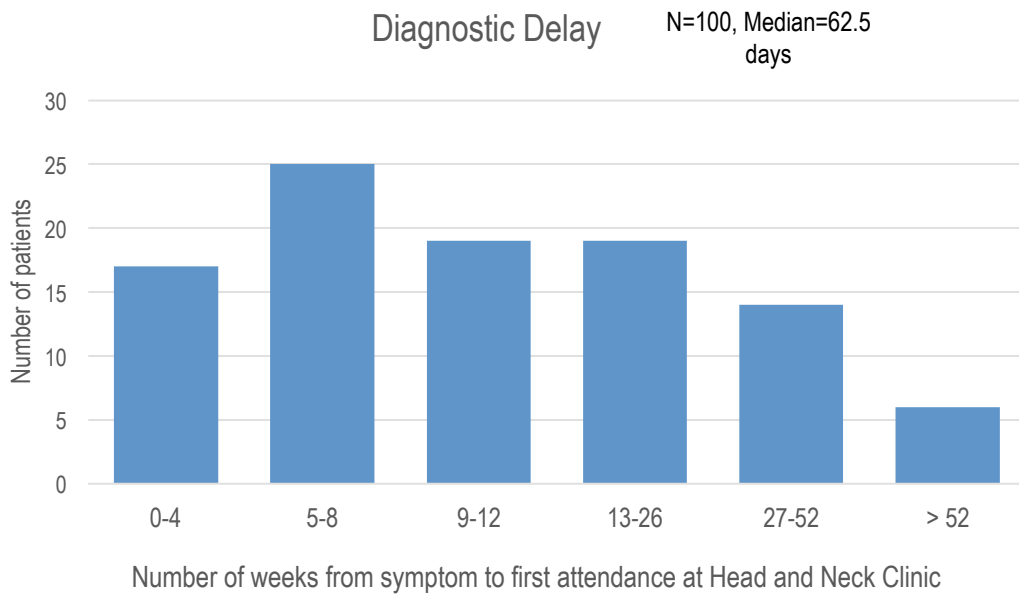


Figure 3.2: Diagnostic Delay

3.5.5 Encounters with Medical Profession in Asymptomatic Phase

Table 3.4 displays the responses to Questions 20-26 and highlights the fact that 92% of participants had seen their GMP in the preceding two years before diagnosis, 80% had seen their GMP within the last six months (37% less than one month, 28% between one and three months, and 15% between three and six months) and 63% saw their GMP at least three times a year. These responses show there are many attendances where opportunistic oral cancer screening could have been performed. Of concern is that while 84% of participants state they have a regular GMP, only 3% of their GMPs had ever discussed the risk factors for oral cancer, and only 6% responded that their GMPs had ever performed an oral cancer screening examination on them.

Table 3.4: Patient Encounters with General Medical Practitioners

n=103	Yes		No	
	n	%	n	%
Did you access a GMP in Australia in the preceding two years for any other reason?	94	91%	9	9%
Do you have a regular GMP in Australia that you would call "your GP"?	86	83%	17	17%
At any time, has a GMP in Australia discussed oral cancer or its risk factors with you?	3	3%	100	97%
At any time, has a GMP in Australia performed oral cancer screening examination on you?	6	6%	97	94%
Prior to symptoms or diagnosis (for those participants with an asymptomatic diagnosis), when was the last visit to a GMP? (N=103)				
< 1 month before symptoms	38	37%		
1 - 3 months before symptoms	29	28%		
3 - 6 months before symptoms	15	15%		
6 - 12 months before symptoms	8	8%		
> 12 months before symptoms	6	6%		
Unknown	7	7%		
Participant has a regular GMP and lists average number of visits per year to their regular GMP (n=86)				
0	3	3%		
1	9	9%		
2	9	9%		
3	10	10%		
4	18	17%		
5+	37	36%		
Participant has no regular GMP and lists average number of visits per year to any GMP (n=16)				
0	10	10%		
1	2	2%		
2	1	1%		
3	1	1%		
4	2	2%		
5+	0	0%		
Unknown	1	1%		

3.5.6 Encounters with Dental Profession in Asymptomatic Phase

Table 3.5 presents the responses to Questions 27-33 and reveals that fewer participants (65%) had seen a GDP in the preceding two years before they developed symptoms, and only 47% had a regular GDP. Of those who had a regular GDP, most attended their dentist only once or twice per year. The remaining 53% did not have a regular GDP and predominantly would only see a dentist for an emergent dental problem, with the vast majority stating zero times per year as their average rate of dental visits. These questions also revealed that 6% of participants had their risk factors for oral cancer discussed with them by a GDP and a GDP had performed an oral cancer screening examination on 9%.

Table 3.5: Patient Encounters with General Dental Practitioners

n=103	Yes		No	
	n	%	n	%
Did you access a GDP in Australia in the preceding two years for any other reason?	67	65.0%	36	35.0%
Do you have a regular GDP in Australia that you would call "your dentist"?	48	46.6%	55	53.4%
At any time, has a GDP in Australia discussed oral cancer or its risk factors with you?	6	5.8%	97	94.2%
At any time, has a GDP in Australia performed oral cancer screening examination on you?	9	8.7%	94	91.3%
Prior to symptoms or diagnosis (for those participants with an asymptomatic diagnosis), when was the last visit to a GDP?	n	%		
< 1 month before symptoms	12	11.7%		
1 - 3 months before symptoms	10	9.7%		
3 - 6 months before symptoms	14	13.6%		
6 - 12 months before symptoms	18	17.5%		
> 12 months before symptoms	24	23.3%		
Unknown	25	24.3%		
Participant has a regular GDP and lists average number of visits per year to their regular GDP (n=48)				
0	2	1.9%		
1	22	21.4%		
2	17	16.5%		
3	4	3.9%		
4	2	1.9%		
5+	1	1.0%		
Participant has no regular GDP and lists average number of visits per year to any GDP (n=55)				
0	48	46.6%		
1	5	4.9%		
2	0	0.0%		
3	0	0.0%		
4	1	1.0%		
5+	1	1.0%		
Unknown	0	0.0%		

3.6 Discussion

Prevention and early stage of diagnosis are promising for oral cancers because of known risk factors and the relative ease of identifying oral cancers and OPMLs by a simple oral cancer screening examination. For an oral cancer screening examination to be performed in the primary healthcare setting requires either the patient to be sufficiently aware of oral cancer and risk factors to request one, or the GMP or GDP to be aware of oral cancer and the patient's risk factors and initiate an oral cancer screening examination. The first study aim was to assess participants' awareness of oral cancer. Unfortunately, this study—of patients with newly-diagnosed oral cancer presenting to a public hospital head and neck clinic—reports one of the lowest scores in the literature regarding awareness of oral cancer, with 46% stating they had never heard of oral cancer until their diagnosis. This is in contrast to reports from the USA in which only 14-15.5% of adults had never heard of oral cancer.^{190, 191} The low awareness of oral cancer in this Australian cohort is highlighted by the response from 67% of current participants that they had been regular consumers of tobacco in Australia where plain packaging of tobacco products is legislated. This packaging contained graphic images of lip, mouth, tongue, and lung cancer for many years preceding this study. This suggests that even plain packaging of tobacco products has failed to raise awareness of oral cancer in a high-risk population. Another Australian study investigated 101 patients referred with a suspicious oral lesion to a private oral medicine clinic.¹⁸⁷ These patients reported being far more aware of oral cancer, with 91.8% having heard about someone with oral cancer.¹⁸⁷ Patients in this study expected that both GDPs and GMPs should check for and be able to explain oral mucosal pathology, raising the question of whether the general public might expect similar standards of care.¹⁸⁷ The demographics of these two Australian cohorts are very different, making comparison between the two groups difficult; however, there is an obvious wide divide in awareness of oral cancer when private and public patients are compared.

The second and third study aims were to identify participants' knowledge of risk factors and their actual risk factors (Table 3.2). With regard to actual risk factors for oral cancer, this Australian cohort is consistent with results reported from other cohorts from developed nations, in that the most significant risk factors identified are increased age, tobacco use, and alcohol consumption.^{28, 29} 95% were over 40 years of age at diagnosis, and 67% and 66% were regular consumers of tobacco and alcohol, respectively. There was poor knowledge of these important risk factors and almost no knowledge of HPV as a risk factor. A recent international large pooled study estimated the population attributable risks

for tobacco and alcohol use to be 64% (95%CI:45-75%), showing these two risk factors alone are responsible for a large number of cases.²⁸ The poor knowledge of risk factors for oral cancer logically follows from the cohort's generally poor awareness of oral cancer. Over the last 20 years the anti-tobacco campaign in Australia has been very strong, so it is not surprising that approximately half (52%) of participants identified tobacco consumption (smoking or smokeless) as a risk factor for oral cancer. However, considering the volume of anti-tobacco campaign material in the Australian community, and that 67% of participants reported using tobacco themselves, a much higher figure of 90-100% was expected. Additionally, only 15% were aware that alcohol consumption is a risk factor, while 66% were regular consumers of alcohol. In contrast to the strength of the anti-tobacco campaign, there is very little promotion of the health risks of alcohol in Australia.

The lack of awareness and knowledge in our Australian cohort can be improved with specific educational interventions, either in the general population or targeted to high-risk groups. The Lesion Evaluation, Screening and Identification of Oral Neoplasia Study (LESIONS) aims to understand factors that may influence all oral mucosal disease in a high-risk population with a particular focus on oral cancers and OPMLs.¹⁵¹ LESIONS targeted two Australian communities at high risk of oral cancer and OPMLs, mostly in the dental setting but also at a community pharmacy location. The first was a low socio-economic region characterised by documented higher rates of tobacco and alcohol consumption.¹⁵¹ The second was an indigenous Australian population known to present with a higher rate of cancer-related modifiable risk factors, namely tobacco consumption and excessive alcohol use, which are 20% and 10% higher, respectively, than the general Australian population.¹⁵¹ Whilst the exact numbers were not captured, the authors noted a high rate of patient refusal when approached opportunistically before or after scheduled dental appointments.¹⁵¹ Common patient barriers identified were perceived time pressure, embarrassment regarding the condition of the dentition (when screening attempted at community pharmacy), unwillingness to know if disease was detected, lack of concern and lack of pain.¹⁵¹

Many interventions have been tested and reported in the literature, and some have been shown to increase the number of patients requesting an oral cancer screening examination. Recently published results of an invitational and opportunistic oral cancer screening intervention in Oporto, Portugal reported on a total of 727 participants with a mean age of 54 years. After a visual and tactile oral cancer screening examination was

performed, many OPMLs were diagnosed, but of most significance is that two oral cancers were detected, both asymptomatic and in the T1 stage.¹⁵⁰ Awareness and knowledge of oral cancer is key for patients to accept an invitation of oral cancer screening. This is most notable in the recently published data from a novel approach to oral cancer screening at Far Eastern Memorial Hospital in Taiwan. High-risk patients attending an outpatient facility were identified using an automated system based on their responses to questions regarding tobacco and betel nut usage, and they were then offered the opportunity to be screened with a standard visual and tactile oral cancer screening examination.³² A total of 38 693 patients were identified as high-risk, yet only 8037 (20.8%) were recruited as participants in the screened cohort from the automated system.³² This means that approximately 80% were advised that they were at high risk for developing oral cancer yet declined a free oral cancer screening examination. The reasons these Taiwanese patients declined the invitation are most likely multifactorial, as with all health behaviours and outcomes, but a significant component is likely to be poor awareness and knowledge of oral cancer. This was evident in UK pilot research exploring ways to improve understanding of individuals at risk of oral cancer and their attitudes toward early detection interventions. In particular, the target population for opportunistic screening activities was shown to require further persuasion that their lifestyle choices (tobacco and alcohol) contributed to an increased risk of oral cancer.¹⁵³ Over the last decade following the introduction of an oral cancer awareness week (now month) in the UK and the Oral Cancer Awareness Month in the USA in 2000, increasing numbers of oral cancer screening examinations have been performed each year.^{154, 155} It is still difficult to elucidate whether the high-risk target population are being reached, though, or whether the general population is gaining increased awareness and knowledge and becoming more accepting of screening activity.

Our fourth study aim was to assess patient, professional, and total diagnostic delay. In addition to the challenge of finding and diagnosing these lesions in the early stages of disease, some literature also reports that a significant determinant of oral cancer survival is diagnostic delay. Diagnostic delay generally refers to the time between the patient's first awareness of symptoms and a definitive diagnosis following specialist review, during which a tumour can become locally invasive or disseminate via lymphovascular or perineural spread.^{25, 128, 129} In turn, diagnostic delay is commonly divided into patient delay, which refers to the time between the beginning of symptoms and when the patient first meets with a professional for a consultation regarding diagnosis,¹³⁰ and professional delay,

or the time that has elapsed from this initial consultation, often in the primary care setting, until a definitive diagnosis is made, often after referral to a specialist setting. Total diagnostic delay averages from three to six months and is fairly evenly distributed between patient and professional delay.²³

A study by Esmaelbeigi et al. (2014) of delay in oral cancer showed that 71.4% of Iranian study participants were diagnosed at the advanced stage (III-IV),¹³² and the medians of the patient, professional, and total delays in this Iranian cohort were 45, 86, and 140 days, respectively.¹³² A 2009 systematic review reported that total diagnostic delay was associated with a more advanced tumour stage at diagnosis, with a pooled relative risk (RR) of 1.47 (95% CI: 1.09–1.99) for oral cancers and a diagnostic delay greater than one month resulting in a pooled RR of 1.69 (95% CI: 1.26-2.77).³³ In the same year a conflicting systematic review including all head and neck cancers, not purely oral cancers, reported no association between diagnostic delay in head and neck cancers and tumour stage at diagnosis.¹⁴³ Seoane et al. (2010) further challenged the strength of the relationship via a statistical analysis of 83 OSCC cases, which showed that when the analysis was adjusted for tumour stage at diagnosis (I-II vs. III-IV), proliferative activity resulted to be an independent prognostic factor for survival, whereas diagnostic delay did not influence survival significantly.¹⁴⁴ Research on professional delay and mortality in tongue cancer is even more paradoxical, as shorter professional delay trends toward worse survival rates, an unreasonable statistical outcome.^{140, 145} This paradoxical response whereby diagnostic delay, tumour staging, and prognosis are inversely related has also been described in breast, cervical, lung, colon, renal, and urethral cancer, and the data suggest that stage at diagnosis and survival are affected more by tumour biology (rapid growth, poorly differentiated etc.) than by diagnostic delay.¹⁴⁶ Despite this controversy, diagnostic delay and its components remain useful for characterising a typical patient's journey through the health system toward treatment. Before this thesis there were no Australian data from a head and neck clinic that enabled calculation of patient, professional, and diagnostic delay in oral cancer. We have provided this data (Figures 3.1 and 3.2) and found a median total diagnostic delay of 62.5 days, or 9 weeks, which is better than most reports from other countries in the literature. This indicates that there may be opportunities to improve the efficiency of the referral and investigation pathway, especially when the patient delay component has a median value of two weeks.

Causes of patient delay relate to psychosocial issues, such as perception of symptoms and illness, and the behavioural responses they elicit, in addition to the major issue of accessibility to health care, including financial, structural, and personal barriers, such as beliefs, culture, and language.¹³¹ In the Iranian cohort, patients with primary-level education had a 70% lower risk of delay compared to illiterate patients, and the risk was lower again among patients who had diploma-level or college-level education.¹³² A recent study investigating barriers to oral cancer screening in rural African-Americans showed three primary patient barriers to screening: lack of knowledge of oral cancer and its symptoms accounted for 31.8% of all barriers mentioned, lack of financial resources or health insurance for 25.0%, and fear of screening and diagnosis for 22.9%.¹³³ Howell et al. (2013) placed these barriers within the Theory of Planned Behaviour and concluded that interventions aimed at increasing oral cancer screening should first focus on changing people's attitudes about screening by increasing knowledge about oral cancer and reducing fear.¹³³

Identifying causes of professional delay provides an opportunity to develop interventions which may lead to increased opportunistic screening of the higher-risk target population. Research has shown that lack of knowledge regarding the main locations of oral cancer, low suspicion of oral cancer, and low levels of skill and confidence to perform a full head and neck examination with appropriate equipment are prevalent in the general medical community.^{131, 134-136} The presence of patient co-morbidities has also been shown to result in clinicians focusing their attention on the existing disorders.¹³⁷⁻¹³⁹ Prescription of medicines (such as analgesics) in the primary care setting (OR = 5.3, 95% CI 2.2–12.9), history of dental procedure, (OR = 6.8, 95% CI 1.7–26.9), and history of loose teeth increased the risk of delay four times (OR = 4.0, 95% CI 1.6–9.8) and were associated with a higher risk of delay compared to patients who were biopsied from the beginning.¹³²

Rather than focusing on delay as a major contributor to tumour stage at diagnosis and survival, the focus should be shifted to identifying lesions in the asymptomatic period. There is no disputing the overwhelming volume of literature showing that many patients are diagnosed in the symptomatic phase, often at an advanced stage (III-IV) of disease. As research on patient delay by definition deals with the symptomatic phase, if an early stage diagnosis is to be achieved, then future research efforts need to focus on improving oral cancer screening in the asymptomatic phase through appropriate novel screening strategies.

Our final study aim was to identify whether participants had opportunities in the Australian health system to receive an opportunistic oral cancer screen examination in the asymptomatic phase. According to the WHO and NIDCR, an oral cancer screening examination should include a visual examination of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the mouth, tongue, and palate, with mouth mirrors to help visualise all surfaces.³⁰ The tactile examination includes palpating the regional lymph nodes, tongue, and floor of the mouth.³⁰ In this patient questionnaire an abridged version of the above definition was provided in the section asking participants to answer questions about their encounters with GMPs and GDPs in the asymptomatic phase. The responses (Tables 3.4 and 3.5) reveal that opportunistic oral cancer screening could have been performed at many attendances.

In Australia, every citizen has access to a free public health system with access to many GMPs under the Medicare scheme. In contrast, access to the dental health system is not free; only Australian citizens in the lowest income percentage are eligible and entitled to free public dental treatment, and access is usually subject to long waiting periods unless emergent treatment is required. Research has shown that patients with oral lesions often consult their GMP rather than their GDP, even in the UK where there is greater access to free dental treatment.^{156, 157} The preference for presentation to GMPs has held true in this study, with 80% having seen a GMP within the last six months and 63% seeing their own regular GMP at least three times a year. In contrast, only 35% had seen a GDP within the last six months and only 6.8% visited their own regular GDP at least three times a year. While less than half (47%) of patients have their own regular GDP, 84% have their own regular GMP. Despite the latter high figure, only 3% of these patients, who were mainly high-risk, reported that their regular GMPs had ever discussed their risk factors for oral cancer, and only 6% had ever received an oral cancer screening from them. These results present an opportunity to target new education interventions to GMPs toward increasing opportunistic oral cancer screening in the primary medical care setting.

A previous study of Australian GDPs reported that 94.5% checked all new patients for oral mucosal pathology and 85.7% checked all recall/review patients for oral mucosal pathology.³¹ In conflict with this, participants in our study responded that only 9% had a GDP ever perform an oral cancer screening examination on them and only 6% had a GDP ever discuss their risk factors for oral cancer with them. Perhaps the definition provided for an oral cancer screening examination would make these participants think that no GDP

had palpated their neck or face and therefore they had never been formally screened. Perhaps the study of Australian GDPs should have asked if GDPs are performing visual and tactile oral cancer screening examinations as per the definition given by the WHO and NIDCR. It is questionable whether 94.5% of GDPs are performing all nine steps of the visual and tactile oral cancer screening examination on every new patient, as the evidence suggests that GDPs are much less likely to palpate the neck nodes.¹⁶⁹ All future questionnaires relating to oral cancer screening should define the standard visual and tactile examination steps described in that definition as a way of standardising the research in this field.

Only 47% of participants have a regular GDP, and most only attend once or twice per year. The remaining 53% do not have a regular GDP, and predominantly only see a dentist for an emergent dental problem, the average rate of dental visits being zero times per year for the vast majority. The evidence suggests that GDPs are more skilled and confident in performing the oral cancer screening examination than their medical counterparts.^{168, 170-173} However, the low attendance rate for GDPs in Australia suggests that targeting education interventions toward increasing oral cancer screening with GDPs would be less productive than that with GMPs, where the target population is more likely to attend. A recent systematic review of patient acceptance of screening for oral cancer outside the dental setting showed that GMPs should be confident that acceptance of and satisfaction with oral cancer screening is high, particularly when patients have previously been educated about oral cancer in the waiting room.¹⁵⁸ In short, the results clearly show that participants had many opportunities in the Australian health system to receive an opportunistic oral cancer screening examination before their diagnosis.

Table 3.6 presents a tabulated summary of outcomes to the five hypotheses tested in this study. It is clear that in Australia, there is a deficiency in both patients and GMPs regarding oral cancer. It is also clear that the target population for oral cancer screening is attending the primary medical healthcare setting in Australia. Asymptomatic diagnosis of early-stage disease is definitely possible in the primary medical healthcare setting in Australia, and future interventions should be targeted to increasing awareness and knowledge of oral cancer for both patients and GMPs.

Table 3.6: Hypotheses Results (Oral Cancer Patients)

Hypotheses Tested	Outcome
Oral cancer patients at the RBWH had poor awareness of oral cancer prior to their diagnosis.	Null hypothesis true 46% never heard of oral cancer
Oral cancer patients at the RBWH had poor knowledge of risk factors prior to their diagnosis.	Null hypothesis true 52% identify tobacco as risk factor 15% identify alcohol as risk factor
Oral cancer patients at the RBWH had one or more known risk factors for oral cancer at the time of diagnosis.	Null hypothesis true All patients had at least one risk factor
Oral cancer patients at the RBWH had exposure to health practitioners in the asymptomatic phase in the preceding months or years before awareness of symptoms or diagnosis occurred.	Null hypothesis true All patients had accessed a health practitioner in the asymptomatic phase
No oral cancer patient at the RBWH had ever been opportunistically screened for oral cancer by a GMP in the asymptomatic phase.	Alternative hypothesis true 6% reported screening by GMP (9% reported screening by GDP)

3.7 Conclusion

Australian oral cancer patients at the RBWH reported very poor awareness of oral cancer and poor knowledge of risk factors prior to their diagnosis. Improving patient awareness of oral cancer and knowledge of their own risk factors is important if patients are to request an oral cancer screening examination or respond to an invitation to receive one in the primary healthcare setting. Health promotion messages should convey information that helps patients know when to consult their health care professional.¹⁹² For example, to increase screening of asymptomatic individuals, media messages should focus on encouraging patients over 40 who use tobacco products or drink alcohol regularly to see a local GMP or GDP for a quick and painless oral cancer screening examination. To increase screening of symptomatic individuals, media messages should focus on advising that any oral lesion lasting for more than two weeks, after local causative factors are removed, should be biopsied or referred without delay.¹⁹³

Most often, Australian oral cancer patients had one or more known risk factors for oral cancer at the time of diagnosis. This is similar to other cohorts from western nations where betel nut consumption is not prominent. Research that has already been conducted in the

USA and UK is likely to be relevant to our higher-risk target population. Australia is behind both the USA and UK and their respective oral cancer awareness month campaigns in promoting awareness for oral cancer and encouraging screening.

Asymptomatic diagnosis of oral cancer at early stages of the disease is possible in the primary medical setting in Australia. Australian oral cancer patients are much more likely to see a GMP for other issues if they are asymptomatic with an oral lesion, indicating an opportunity for the GMP to suggest a visual and tactile oral cancer screening examination. They are also more likely to see a GMP than a GDP even if a symptomatic oral lesion is present, suggesting that interventions toward increasing oral cancer screening in Australia must be focused around the primary medical healthcare setting and GMPs.

Current rates of visual and tactile oral cancer screening examination in Australia are very poor, and both GMPs and GDPs should be targeted to reach competency in diagnostic skill and performance of a thorough opportunistic screening examination of patients over 40 who use tobacco products or drink alcohol regularly.

CHAPTER FOUR: AUSTRALIAN GMPs COMPARED TO GMSs

4.1 Introduction

Most oral cancers lack early symptoms; hence, by the time symptoms develop and stimulate a patient to seek a diagnosis, often the disease has already reached an advanced stage.^{13, 14} This results in more than 60% of patients being diagnosed with stage III or IV disease.^{13, 14} The reported five-year survival rate for stage III or IV oral cancer ranges between 15 and 55%.¹⁵⁻¹⁸ The most important prognostic marker for oral cancer remains the tumour stage at diagnosis.^{6, 12} Survival rates are significantly improved if the disease is treated at an early stage, ideally when the patient is likely to be asymptomatic with a tumour less than 2cm in diameter and with less than 4mm of invasion.²⁰ Therefore, early detection of malignant lesions and OPMLs is an important goal for increasing the probability of improved morbidity and mortality.^{14, 15, 21, 22}

The Cochrane collaboration and other expert consortia have agreed that whilst population-based annual or semi-annual screening for oral cancer is not cost-effective, targeting high-risk populations to be opportunistically screened using a visual and tactile examination should be encouraged in the primary care setting.²³⁻²⁶ According to the WHO and the NIDCR, an oral cancer screening examination should include both visual and tactile components. The visual component requires examination of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the mouth, tongue, and palate with mouth mirrors to help visualise all surfaces.³⁰ The tactile examination includes palpating the regional lymph nodes, tongue, and floor of the mouth.³⁰ Opportunistic oral cancer screening by GMPs and GDPs should remain an integral part of their routine daily work, and particular attention should be paid to high-risk individuals.²⁷ The results from our study of Australian patients with oral cancer suggest, in line with the Cochrane collaboration, that the most significant risk factors in the development of oral cancer are increased age (over 40 years) and tobacco and alcohol consumption.^{28, 29} The increasing role of human papilloma virus (HPV) as an additional risk factor is consistent with the rising incidence of male and female HPV-related oral cancers in Australia and globally.⁹¹

These known risk factors, and the relative ease of identifying oral cancers and OPMLs by a simple visual and tactile screening examination, point to significant potential for the prevention and early-state diagnosis of oral cancers. In theory, asymptomatic diagnosis at

an early stage of disease is achievable in the primary medical healthcare setting; however, the results from our cohort of patients with oral cancer indicate that very few opportunistic oral cancer screening examinations are actually being performed in Australia. Performance of an oral cancer screening examination requires either that the patient is sufficiently aware of oral cancer and his or her risk factors to request an oral cancer screening examination, or that the GMP or GDP is sufficiently aware of oral cancer and the patient's risk factors to initiate a screening examination.

The results from Chapter 3 highlight that patient awareness of oral cancer is very poor. Asymptomatic patients are therefore unlikely to attend a GMP or GDP and request oral cancer screening at the current level of awareness and knowledge. As discussed in Chapter 3, only 7% of the patients studied were diagnosed in the asymptomatic phase, and all of these by health practitioners with a dental qualification. This finding suggests that GDPs or specialists with dental qualifications were more active than GMPs in opportunistic oral cancer screening, a finding supported by a recent study of Australian GDPs which showed that 90% regularly perform oral mucosal screening examinations for all patients.³¹ Of the 93% of patients in our cohort who were diagnosed in the symptomatic phase, the majority preferred to attend a GMP (74%), rather than a GDP (14%), for investigation and explanation of their symptoms. This study also reported significant missed opportunities for oral cancer screening, as 80% of patients had seen their GMP within the last six months and 63% visited their GMP at least three times per year. Of concern is that whilst 84% of participants stated they have a regular GMP, only 3% of those GMPs had ever discussed risk factors for oral cancer and only 6% of the patients stated that their GMPs had ever performed an oral cancer screening examination on them.

When awareness of oral cancer is compared between GMPs and GDPs, there is significant divergence in most populations studied. In a UK study, GMPs were less likely to examine patients' oral mucosa routinely, were less likely to advise patients about risk factors for oral cancer, and identified fewer risk factors for and felt less confident about diagnosing oral cancer from clinical appearance than their dental counterparts.¹⁶⁸ A similar study in the USA concluded that GDPs were much more likely to feel adequately trained and regularly provide oral cancer screening examinations, but much less likely to discuss tobacco and alcohol cessation or to palpate the neck nodes.¹⁶⁹ Additional studies in Saudi Arabia, Qazvin, Ireland, and Scotland have yielded similar results; some general conclusions were that GMPs are less intent on performing oral cancer screening, less

skilful in performing oral cancer screening examinations, and less confident in diagnosing pathologies in the oral cavity than GPs.¹⁷⁰⁻¹⁷³

These results were echoed by a comparison of UK undergraduate medical and dental students, which suggests that there will be no improvement in the next generation of health professionals, particularly medical practitioners, regarding oral cancer screening.¹⁷⁶ Further results along these lines from studies in Iran, Nigeria, and the USA indicate a need to review the curriculum of medical and dental schools to improve awareness and behaviour toward increasing opportunistic oral cancer screening.¹⁷⁷⁻¹⁸¹ In 2011 two significant studies investigated medical school curricula for oral cancer teaching in the USA and UK, respectively. The majority of the responding USA medical schools offered very little oral health education, with approximately 80% offering less than five hours of oral health curriculum over the entire course.¹⁸² Oral cancer training lacked both adequacy and comprehensiveness, and showed no improvement relative to a similar study from 15 years earlier.^{182, 183} The UK study highlighted that undergraduate oral cancer teaching varied widely in terms of duration, format, and content across British medical schools.¹⁸⁴ Its authors recommended the development of a curriculum addressing important aspects of oral cancer from an evidence-based approach that can be integrated into the already-crowded undergraduate medical curriculum.¹⁸⁴

There are no data on the awareness, knowledge, and attitudes toward opportunistic oral cancer screening in the Australian GMP population. Similarly, there is no Australian study investigating these same attributes in graduate medical students as they exit medical school and enter the workforce. The primary purpose of the following research is to establish this Australian dataset via a survey of new GMSs and established practicing GMPs in Brisbane. It is hoped that this dataset will provide valuable insights leading to educational and training interventions, and thereby improve the rates of visual and tactile opportunistic oral cancer screening in the primary medical healthcare setting in Australia.

4.2 Hypotheses

1. Both groups do not routinely examine oral mucosa.
2. Both groups have received limited education and training in oral cancer and visual and tactile oral cancer screening examination
3. Both groups do not routinely advise patients about risk factors for oral cancer.
4. Both groups are not confident diagnosing malignant and pre-malignant lesions from clinical appearance.
5. Both groups do not perform all nine steps of a visual and tactile oral cancer screening examination.
6. Both groups are not sufficiently confident in their techniques to complete all nine steps of a visual and tactile oral cancer screening examination.
7. Both groups are not confident in identifying pathology in all nine steps of a visual and tactile oral cancer screening examination.

4.3 Aims

This study aims to identify:

1. whether either group routinely examines oral mucosa;
2. whether either group had sufficient training in oral cancer and visual and tactile oral cancer screening examination;
3. whether either group knows the risk factors and communicates these to patients;
4. what changes in the oral mucosa both groups would associate with malignant and pre-malignant oral lesions;
5. which of the nine steps of the visual and tactile oral cancer screening examination are performed by either group;
6. whether either group is confident in performing the technique in each of the nine steps of the visual and tactile oral cancer screening examination;
7. whether either group is confident in identifying pathology in each of the nine steps of the visual and tactile oral cancer screening examination; and
8. where patients are referred if an oral cancer or OPML is identified.

4.4 Methods and Materials

Ethical Approvals

The study protocol was approved by the University of Queensland Dental Science Research Ethics Committee (1217) and the RBWH Human Research Ethics Committee (HREC/14/QRBW/82).

Study Design

Following a literature review that investigated similar issues in populations of graduate medical students (GMS) and general medical practitioners (GMPs) in other locations worldwide, a questionnaire was designed and validated with a pilot group of GMPs and GMSs utilising the test and re-test method.^{168, 176} 553 GMPs were selected randomly for the sample from a database developed on GMPs working in locations that would be expected to refer suspected oral cancer patients to the RBWH Head and Neck Clinic. A similar questionnaire was designed to collect data from a sample of 151 Graduate Medical Students (GMS) commencing work as intern medical officers at the RBWH in Brisbane, Australia.

Participant Recruitment

Each research study pack contained an introductory cover letter on Queensland Health letterhead signed by the site coordinator, a participant information form, a participant informed consent form, the questionnaire, and a professionally addressed and stamped envelope for return of the questionnaire. These packs were mailed, utilising the modified Dillman method known to increase response rates, to those GMPs randomly selected by practice address within the catchment of referral to the RBWH Head and Neck Clinic.^{31, 187-189} The GMSs were invited to participate during intern training days on commencement with Queensland Health, and were able either to consent to, complete, and return the questionnaire at this training meeting, or to return the questionnaire via pre-paid mail. The questionnaire responses were initially identifiable to allow a follow-up phone call for clarification of responses if required and to award the incentive (“the new iPad”), which was randomly drawn by the chief investigator at the conclusion of data collection.

Questionnaires

The GMP questionnaire consisted of 49 open, multiple-choice, or closed questions investigating the stated aims of the study. The GMS questionnaire asked an additional four questions to investigate GMS exposure to OPMLs, oral cancers, learning regarding oral cancer, and appropriate screening during medical school. The full copy of the questionnaire given to GMPs is available in Appendix B. The full copy of the questionnaire given to GMSs is available in Appendix C.

Data Analysis

Completed questionnaires were de-identified, manually coded and recorded into Microsoft Excel (Microsoft Corporation, Washington, USA) to allow statistical analysis of binary and non-binary responses. The results were expressed as proportions and frequency count charts calculated using Microsoft Excel (Microsoft Corporation, Washington, USA) When comparing responses between groups, Pearson's Chi-Squared Test was calculated using Stata (Statacorp, Texas, USA) and differences were considered statistically significant at a p-value of < 0.05 .

4.5 Research Results

Unless otherwise stated, all percentages reported are the percentage in agreement.

4.5.1 Survey Response Rate and Demographics

Questionnaires were returned by 144 GMPs and 141 GMSs, a response rate of 27% and 93% respectively. The proportions of male and female participants were comparable. The majority of GMPs (83%) had graduated from medical school over 15 years ago, in comparison to all GMSs, who had just entered the work force out of medical school. Table 4.1 displays the response rates and demographics collected.

Table 4.1: Survey Response and Demographics

	GMPs	GMSs
Total Surveyed	553	151
Total Responses	144	141
Response Rate	27%	93%
Male	71 (49%)	66 (47%)
Female	73 (51%)	75 (53%)
Years Since Graduation		
< 15	24 (17%)	141 (100%)
15-29	51 (35%)	0 (0%)
30-45	62 (43%)	0 (0%)
45+	7 (5%)	0 (0%)

4.5.2 Awareness, Behaviours and Training in Oral Cancer

Table 4.2 summarises the responses to questions regarding awareness of oral cancer, undergraduate and postgraduate teaching on the examination of the oral cavity, and diagnosis of pre-malignant and malignant disease. Over 90% of both groups reported regularly advising patients about risk factors for other cancers and encouraging risk reduction for these; however, only a third of both groups regularly advised patients about risk factors for oral cancer. GMPs reported significantly more knowledge than GMSs (44%vs18%, $p < 0.001$) regarding prevention of oral cancer, but less than 50% of both groups reported performing oral cancer screening examinations, even on high-risk patients. After reading the nine steps of a visual and tactile oral cancer screening examination that were displayed and explained in the questionnaire, only 34% of GMPs

and 11% of GMSs felt they had sufficient knowledge to detect a pre-malignant lesion or an early asymptomatic oral cancer. About one-fifth of both GMPs and GMSs stated they had received sufficient training during either GP training or medical school to identify high-risk groups and perform thorough opportunistic oral cancer screening examinations.

Table 4.2: Awareness and Knowledge for Oral Cancer (GMPs vs. GMSs)

(# - GMPs not asked this question)	GMPs n=144		GMSs n=141		χ^2 p-value
Have you had an oral cancer screening examination performed on yourself?	27	(19%)	12	(9%)	0.013*
Have you ever seen an oral cancer during medical school?#	#	#	65	(46%)	
Have you ever seen a pre-malignant oral lesion during medical school?#	#	#	55	(39%)	
Did you learn about oral cancer during medical school?#	#	#	104	(74%)	
Did you learn about opportunistic oral cancer screening during medical school?#	#	#	15	(11%)	
Do you regularly advise patients about risk factors for other cancers?	139	(97%)	129	(92%)	0.109
Do you regularly encourage reduction in risk factors for other cancers	143	(99%)	135	(96%)	0.052
Do you regularly advise patients about risk factors for oral cancer?	46	(32%)	48	(34%)	0.675
Do you feel you have sufficient knowledge concerning prevention of oral cancer?	64	(44%)	25	(18%)	<0.001**
Do you perform oral cancer screening routinely?	9	(6%)	30	(22%)	<0.001**
If not routinely, do you perform oral cancer screening if patients are in high-risk groups?	64	(47%)	46	(42%)	0.417
Do you have sufficient training, knowledge and technique to perform oral cancer screening examination? (Before screening examination steps shown)	46	(32%)	10	(7%)	<0.001**
Do you feel you have sufficient knowledge to detect a pre-malignant lesion or an early asymptomatic oral cancer? (After screening examination steps shown)	49	(34%)	15	(11%)	<0.001**
Do you feel you received sufficient training in either GP training or medical school to identify high-risk groups and perform thorough opportunistic oral cancer screening examinations? (After screening examination steps shown)	29	(20%)	27	(19%)	0.833

4.5.3 Knowledge of Risk Factors for Oral Cancer

Table 4.3 presents the responses to the open text question asking both groups to list as many risk factors for oral cancer as they could recall. Both groups strongly identified tobacco as a risk factor. Approximately half of each group (GMPs 57%, GMS 54%) identified alcohol as a risk factor. Other known risk factors, such as age, HPV infection, areca nut (betel nut) chewing, and poor diet were not identified strongly by either group. Overall, when the groups were compared regarding knowledge of the main risk factors for oral cancer (age, tobacco, alcohol, betel nut chewing, HPV status, and poor diet), there was no significant difference between the inexperienced GMSs and experienced GMPs.

Table 4.3: Knowledge of Risk Factors for Oral Cancer (GMPs vs. GMSs)

	GMPs		GMSs		χ^2 p-value
Age	19	(13%)	21	(15%)	0.626
Alcohol	82	(57%)	75	(54%)	0.661
Betel Nut	31	(22%)	24	(17%)	0.381
Ethnicity	5	(3%)	5	(10%)	0.072
Family History	21	(15%)	47	(34%)	< 0.001 **
HIV/Immunosuppression	23	(16%)	26	(19%)	0.525
HPV	29	(20%)	37	(27%)	0.186
Male Gender	3	(2%)	4	(8%)	0.049 *
Oral Sex	0	(0%)	10	(7%)	
Oral Pre-Malignant Lesion	16	(11%)	1	(2%)	0.050 *
Poor Dental Hygiene/Chronic Irritation	34	(24%)	23	(17%)	0.147
Poor Diet	4	(3%)	7	(5%)	0.320
Previous Head and Neck Cancer	17	(12%)	42	(30%)	< 0.001 **
Tobacco	144	(100%)	134	(97%)	0.040 *
UV/Radiation	24	(17%)	4	(8%)	0.129

4.5.4 Knowledge of Pre-Malignant and Malignant Clinical Changes

Table 4.4 presents the responses to open text questions regarding knowledge of clinical changes in pre-malignancy and oral malignancy. In regard to pre-malignancy, both groups identified, in rank order: leukoplakia, non-healing lesions, and lump/swelling/induration. In regard to oral malignancy, GMPs identified, in rank order: non-healing lesions, lump/swelling/induration, and leukoplakia. The GMSs were similar, with lump/swelling/induration and non-healing lesions, followed by bleeding. Overall, neither

group was confident in diagnosing pre-malignant and malignant lesions from clinical appearance, but GMPs were significantly more confident than GMSs (GMPs 53% vs. GMSs 88%, $p < 0.001$).

Table 4.4: Knowledge of Pre-malignant and Malignant Clinical Changes

	GMPs		GMSs		χ^2 p-value
What changes in oral cavity would you associate with pre-malignant disease?					
(Open Text Responses Grouped As Follows)					
Leukoplakia	116	(82%)	81	(60%)	<0.001**
Erythroleukoplakia	11	(8%)	3	(6%)	0.595
Erythroplakia	24	(17%)	10	(19%)	0.747
Non-Healing Lesions (Ulcer/OLP)	88	(62%)	54	(41%)	<0.001**
Lumps/Swelling/Induration	51	(36%)	52	(39%)	0.586
Pain/Dysphagia/Hypo/Hyperaesthesia	10	(7%)	4	(3%)	0.125
Pigmentation	19	(13%)	8	(15%)	0.795
Bleeding	12	(8%)	14	(11%)	0.557
What changes in oral cavity would you associate with malignant disease?					
(Open Text Responses Grouped As Follows)					
Leukoplakia	42	(30%)	33	(25%)	0.355
Erythroleukoplakia	6	(4%)	0	(0%)	
Erythroplakia	10	(7%)	5	(10%)	0.552
Non Healing Lesions (Ulcer/OLP)	122	(86%)	71	(53%)	< 0.001**
Lumps/Swelling/Induration	108	(76%)	95	(71%)	<0.001**
Pain/Dysphagia/Hypo-/Hyper-aesthesia	19	(13%)	15	(11%)	0.581
Pigmentation	12	(8%)	24	(18%)	0.020*
Bleeding	27	(19%)	38	(28%)	0.067
Dental Hygiene/Odour	0	(0%)	9	(7%)	
In regard to clinical appearance, do you feel confident diagnosing pre-malignant and malignant lesions from clinical appearance?					<0.001**
Very Confident	4	(3%)	0	(%)	
Confident	63	(44%)	16	(12%)	
Not Confident	71	(50%)	102	(74%)	
Very Not Confident	5	(3%)	20	(14%)	

4.5.5 Nine-Step Oral Cancer Screening Examination

The section presents results in relation to questions about performing each step of the recommended nine-step visual and tactile oral cancer screening examination. Table 4.5 presents the results of assessing whether the recommended equipment is accessible to the GMP or GMS in their clinical setting; that is, whether there are equipment barriers to performing opportunistic screening examinations. The main barrier appears to be poor access to dental or ENT mirrors.

Table 4.5: Tools Required for Oral Cancer Screening Examination

Do you have all the equipment required to perform an oral cancer screening examination? (% in agreement)	GMPs	GMSs	χ^2 p-value
Bright White Light Source	138 (96%)	56 (53%)	< 0.001 **
Dental or ENT Mirror	29 (20%)	7 (7%)	0.003 *
Gauze Squares	133 (92%)	116 (93%)	0.891

Tables 4.7, 4.8, and 4.9 report the results for each step of the screening examination, asking whether the step is performed and assessing confidence with the technique of the required examination step and confidence in identifying pathology in that specific step. Each step on the questionnaire contained a picture of the step and an explanation in text of the technique involved. The GMPs indicated that, in their routine, the only steps performed more often than not were Step 1 (extra-oral), Step 2 (lip examination), and Step 8 (palate and oro-pharynx). The GMSs had even fewer steps in their routine, with only Step 1 (extra-oral) performed more often than not. Confidence in performing the step for both groups mirrored whether they actually performed the step in their routine. It follows that in all other steps, neither group was confident performing the technique required. Likewise, confidence in identifying pathology mirrored whether they actually performed the step. In all steps other than Step 1 (extra-oral), GMSs were significantly less confident in the technique and pathology identification than the GMPs. Table 4.6 highlights the poor overall proficiency of each group, with GMPs performing 4.3 steps on average compared to 3.8 for GMSs. Overall, while GMSs were significantly worse than the GMPs, neither group was confident with techniques and pathology identification in the screening examination.

Table 4.6: Summary of Proficiency in Oral Cancer Screening Examination

Average number of steps (standard deviation)	GMP	GMS	χ^2 p-value
Performed	4.3 (2.3)	3.8 (2.4)	0.075
Confident with technique	4.6 (2.6)	2.9 (2.3)	< 0.001 ***
Confident with identifying pathology	4.2 (2.8)	2.2 (2.4)	< 0.001 ***

**Table 4.7: Oral Cancer Screening Steps 1-3
Performed, Confidence in Technique, and Confidence in Pathology Identification**

Step 1: Extra-oral examination	GMP		GMS		χ^2 p-value
Perform	130	(90%)	129	(91%)	0.722
Do not perform	14	(10%)	12	(9%)	
How confident are you with your technique of extra-oral examination?					
Very Confident	24	(17%)	19	(14%)	0.079
Confident	107	(74%)	95	(68%)	
Not Confident	12	(8%)	25	(18%)	
Very Not Confident	1	(1%)	0	(%)	
How confident are you with identifying pathology in extra-oral examination?					
Very Confident	19	(13%)	1	(1%)	< 0.001 ***
Confident	102	(71%)	78	(56%)	
Not Confident	23	(16%)	50	(36%)	
Very Not Confident	0	(%)	10	(7%)	
Step 2: Lip Examination	GMP		GMS		χ^2 p-value
Perform	117	(81%)	65	(46%)	< 0.001 ***
Do not perform	27	(19%)	76	(54%)	
How confident are you with your technique of lip examination?					
Very Confident	23	(16%)	1	(1%)	< 0.001 ***
Confident	97	(67%)	58	(41%)	
Not Confident	22	(15%)	70	(50%)	
Very Not Confident	2	(1%)	12	(9%)	
How confident are you with identifying pathology in lip examination?					
Very Confident	17	(12%)	1	(1%)	< 0.001 ***
Confident	91	(63%)	44	(31%)	
Not confident	35	(24%)	84	(60%)	
Very Not Confident	1	(1%)	12	(9%)	
Step 3: Labial Mucosa Examination	GMP		GMS		χ^2 p-value
Perform	55	(38%)	38	(28%)	0.057
Do not perform	89	(62%)	100	(72%)	
How confident are you with your technique of labial mucosa examination?					
Very Confident	5	(3%)	1	(1%)	0.017 *
Confident	56	(39%)	36	(26%)	
Not Confident	77	(53%)	88	(64%)	
Very Not Confident	6	(4%)	13	(9%)	
How confident are you with identifying pathology of the labial mucosa?					
Very Confident	6	(4%)	1	(1%)	0.002 *
Confident	49	(34%)	24	(18%)	
Not Confidant	84	(58%)	102	(74%)	
Very Not Confident	5	(3%)	10	(7%)	

**Table 4.8: Oral Cancer Screening Steps 4-6
Performed, Confidence in Technique, and Confidence in Pathology Identification**

Step 4: Buccal Mucosa Examination	GMP		GMS		χ^2 p-value
Perform	35	(24%)	45	(32%)	0.132
Do not perform	109	(76%)	94	(68%)	
How confident are you with your technique of buccal mucosa examination?					
Very Confident	2	(1%)	0	(%)	0.014 *
Confident	47	(33%)	25	(18%)	
Not Confident	80	(56%)	99	(71%)	
Very Not Confident	15	(10%)	15	(11%)	
How confident are you with identifying pathology of the buccal mucosa?					
Very Confident	4	(3%)	0	(%)	0.008 *
Confident	44	(31%)	24	(17%)	
Not Confident	84	(58%)	103	(74%)	
Very Not Confident	12	(8%)	12	(9%)	
Step 5: Gingival Examination	GMP		GMS		χ^2 p-value
Perform	51	(35%)	50	(36%)	0.958
Do not perform	93	(65%)	90	(64%)	
How confident are you with your technique of gingival examination?					
Very Confident	3	(2%)	0	(%)	0.039 *
Confident	50	(35%)	32	(23%)	
Not Confident	81	(56%)	97	(69%)	
Very Not Confident	10	(7%)	11	(8%)	
How confident are you with identifying pathology of the gingiva?					
Very Confident	3	(2%)	0	(%)	0.028 *
Confident	43	(30%)	25	(18%)	
Not Confident	87	(60%)	103	(74%)	
Very Not Confident	11	(8%)	12	(9%)	
Step 6: Tongue Examination	GMP		GMS		χ^2 p-value
Perform	48	(33%)	73	(52%)	0.002 *
Do not perform	96	(67%)	68	(48%)	
How confident are you with your technique of tongue examination?					
Very Confident	4	(3%)	0	(%)	0.114
Confident	65	(45%)	54	(38%)	
Not Confident	68	(47%)	80	(57%)	
Very Not Confident	7	(5%)	7	(5%)	
How confident are you with identifying pathology of the tongue?					
Very Confident	4	(3%)	0	(%)	0.025 *
Confident	63	(44%)	45	(32%)	
Not Confident	67	(47%)	86	(61%)	
Very Not Confident	10	(7%)	10	(7%)	

**Table 4.9: Oral Cancer Screening Steps 7-9
Performed, Confidence in Technique, and Confidence in Pathology Identification**

Step 7: Ventral Tongue and Floor of Mouth	GMP		GMS		χ^2 p-value
Perform	62	(43%)	52	(37%)	0.309
Do not perform	82	(57%)	88	(63%)	
How confident are you with your technique of floor of mouth examination?					
Very Confident	4	(3%)	0	(%)	0.002 *
Confident	59	(41%)	34	(24%)	
Not Confident	75	(52%)	96	(68%)	
Very Not Confident	6	(4%)	11	(8%)	
How confident are you with identifying pathology of the floor of mouth?					
Very Confident	4	(3%)	0	(%)	0.001 *
Confident	49	(34%)	24	(17%)	
Not Confident	84	(58%)	103	(74%)	
Very Not Confident	7	(5%)	13	(9%)	
Step 8: Palate and Oro-pharynx	GMP		GMS		χ^2 p-value
Perform	80	(56%)	62	(44%)	0.058
Do not perform	64	(44%)	78	(56%)	
How confident are you with your technique of tongue examination?					
Very Confident	3	(2%)	0	(%)	< 0.001 ***
Confident	71	(49%)	43	(30%)	
Not Confident	66	(46%)	86	(61%)	
Very Not Confident	4	(3%)	12	(9%)	
How confident are you with identifying pathology of the tongue?					
Very Confident	4	(3%)	0	(%)	< 0.001 ***
Confident	60	(42%)	30	(21%)	
Not Confident	76	(53%)	100	(71%)	
Very Not Confident	4	(3%)	11	(8%)	
Step 9: Bimanual palpation of Floor of Mouth	GMP		GMS		χ^2 p-value
Perform	39	(27%)	20	(14%)	0.008 *
Do not perform	105	(73%)	120	(86%)	
How confident are you with your technique of bimanual palpation?					
Very Confident	4	(3%)	0	(%)	< 0.001 ***
Confident	38	(27%)	6	(4%)	
Not Confident	89	(62%)	96	(69%)	
Very Not Confident	12	(8%)	38	(27%)	
How confident are you with identifying pathology using this method of palpation?					
Very Confident	3	(2%)	0	(%)	< 0.001 ***
Confident	34	(24%)	8	(6%)	
Not Confident	91	(64%)	92	(66%)	
Very Not Confident	15	(10%)	40	(29%)	

4.5.6 Referral Destination for Pre-Malignant and Malignant Lesions

Table 4.10 presents the responses to questions regarding referral destination. Participants could select more than one destination if desired. The groups were similar in responses, with the referral destination most likely to be oral and maxillofacial surgeons, followed by ear, nose, and throat (ENT) surgeons and oral medicine/oral pathologist, irrespective of suspected pre-malignancy or malignancy in the oral cavity.

Table 4.10: Referral Destination for Pre-Malignant and Malignant Lesions

Where would you refer a patient if you suspected a pre-malignant lesion in oral cavity?	GP (n=144)	Student (n=141)
Oral and Maxillofacial Surgeon	86 (60%)	81 (57%)
ENT Surgeon	69 (48%)	51 (36%)
Oral Medicine/Oral Pathologist	23 (16%)	9 (6%)
Dentist	15 (10%)	8 (6%)
Plastic Surgeon	5 (3%)	2 (1%)
No Referral (manage by self)	3 (2%)	0 (0%)
RBWH Head and Neck Clinic	1 (1%)	0 (0%)
Where would you refer a patient if you suspected a malignant lesion in oral cavity?	GP (n=144)	Student (n=141)
Oral and Maxillofacial Surgeon	103 (72%)	86 (61%)
ENT Surgeon	65 (45%)	50 (35%)
Oral Medicine/Oral Pathologist	10 (7%)	7 (5%)
Plastic Surgeon	3 (2%)	7 (5%)
RBWH - Head & Neck Clinic	1 (1%)	1 (1%)
Dentist	1 (1%)	0 (0%)
Other (specify)	0 (0%)	1 (1%)

4.6 Discussion

There is significant potential for prevention and early-stage diagnosis of oral cancers because their risk factors are known and it is relatively easy to identify them via a simple visual and tactile oral cancer screening examination. The results from our Australian cohort of oral cancer patients in Chapter 3 indicate that very few opportunistic oral cancer screening examinations are being performed in the high-risk population in Australia. Only 7% of the patients studied were diagnosed in the asymptomatic phase, and these were all by health practitioners with a dental qualification. Of the 93% of patients studied in our cohort who were diagnosed in the symptomatic phase, the majority preferred to attend a GMP, rather than a GDP, for investigation and explanation of their symptoms. The study also highlighted significant missed opportunities for oral cancer screening, as the majority of patients visited their GMP regularly but fewer than 10% had ever received an oral cancer screening examination or discussion of risk factors.

Previous studies have shown that GMPs are more likely to see the high-risk target population for oral cancer than their dental counterparts.¹⁹⁴ Of concern is that while 84% of the oral cancer participants had a regular GMP, only 3% of those GMPs had ever discussed the risk factors for oral cancer, and only 6% of patients had an oral cancer screening examination performed on them by the GMP. The importance of GMP awareness of oral cancer, knowledge of the risk factors, ability to competently perform a visual and tactile oral cancer screening examination, and confidence in identifying pathology during that examination should not be underestimated. Likewise a GMS entering the workforce should be aware, knowledgeable, and confident in identifying a high-risk individual, suggesting and performing an opportunistic oral cancer screening examination.

Our first study aim in this chapter was to identify whether either group routinely examines oral mucosa. Our finding that 6% of GMPs routinely perform oral cancer screening (Table 4.2) is surprisingly consistent with the 6% of oral cancer patients that reported ever being screened for oral cancer by their GMP. 22% of GMSs reported performing oral cancer screening routinely; however, when asked if they would do so for a high-risk patient, the responses of both groups increased to over 40%, suggesting that they had some awareness of high-risk populations and a willingness to perform the screening examination in the medical healthcare setting.

Unfortunately, our second study aim identified that both groups had insufficient training in oral cancer and performing the visual and tactile oral cancer screening examination. GMSs were asked four additional questions relating to their recent medical school experience. 74% had learnt about oral cancer in medical school and almost half (46%) had seen an oral cancer, yet only 11% recalled ever learning about opportunistic oral cancer screening. Initially about one-third of GMPs reported that they had sufficient training, knowledge, and technique to perform oral cancer screening. Whilst over 40% of both groups initially stated that they would screen if the patient was high-risk, once the nine steps of a screening examination were shown in the next part of the questionnaire, only 20% of both groups felt they had sufficient training to identify a high-risk patient and perform a thorough opportunistic nine-step screening examination.

Our third study aim was to identify whether either group knew the risk factors for oral cancer and communicated these to patients. We found no statistically significant difference between the groups with regard to their knowledge of the main risk factors for oral cancer (Table 4.3). Both groups strongly identified tobacco as a risk factor, consistent with studies from both developed and developing countries.^{168, 176, 195-197} Approximately half of each group (GMPs 57%, GMS 54%) identified alcohol as a risk factor, again consistent with other studies reporting a less well-known association of oral cancer with alcohol consumption.¹⁹⁸ Other known risk factors, such as age, HPV, betel nuts, and poor diet, were not identified strongly by either group. The evidence for the role of HPV as an aetiologic agent in oral cancer has grown rapidly, and two recent meta-analyses found HPV to be an independent risk factor for a subset of oral cancers.^{81, 82} More than 70% of the participants in the present study did not list HPV as a risk factor, similar to reported findings in other studies.^{195, 198} Most GMPs (97%) regularly advised patients about risk factors for other cancers, and nearly all GMPs (99%) regularly encouraged risk factor reduction for other cancers. 32% of GMPs self-reported advising patients about their risk factors for oral cancer, which contradicts the 3% figure generated by the oral cancer patient cohort when asked if a GMP had ever discussed their risk factors for oral cancer with them. These findings suggest that Australian GMPs and GMSs are deficient in knowledge regarding risk factors for oral cancer, which is likely to limit their ability to identify at-risk patients and perform opportunistic screening.

The fourth aim for this study was to identify what changes in the oral mucosa both groups would associate with malignant and pre-malignant oral lesions, via responses to open text

questions regarding knowledge of clinical changes in pre-malignancy and oral malignancy (Table 4.4). With regard to pre-malignancy, both groups identified leukoplakia, non-healing lesions, and lump/swelling/induration, in that order. Unfortunately, this shows a poor understanding of the clinical appearance of OPMLs, a collective term used for the wide range of clinical presentations of oral lesions that may harbour oral epithelial dysplasia (OED). Clinically OPMLs can appear as leukoplakia, erythroplakia, or erythro-leukoplakia (speckled erythroplakia).²² Although various other factors, such as smoking history, patient age and gender, and lesion size and location may contribute to the suspicion of malignant potential, clinical appearance is often the primary driving factor toward the decision to biopsy or offer intervention.³⁵

Clinical leukoplakias, the most common OPMLs, show a low rate of malignant progression irrespective of the histopathologic diagnosis of mild, moderate, or severe dysplasia.³⁶ In contrast, erythroplakias and erythro-leukoplakias have been shown to have a much higher risk of malignant transformation (14-50%).³⁷ We can confidently state that lesions exhibiting redness or a non-homogenous texture were strongly associated with OED and should be considered for biopsy at presentation.³⁸⁻⁴⁰ Unfortunately, these clinical features at presentation may allow estimation of the rate of OED in OPMLs, but there is no way of differentiating OPMLs into dysplastic and non-dysplastic on clinical findings alone, because OED can manifest clinically in any number of presentations.⁴²⁻⁴⁴

With regard to changes related to malignant disease, 86% of GMPs correctly identified non-healing lesions as suspicious. A significant proportion of GMPs (30%) and GMSs (25%) reported leukoplakia as a clinical change associated with malignancy. Most often these leukoplakia are not homogenous. Malignancy can present as lumps/swelling/induration, be painful or painless, be pigmented, or bleed. Overall both groups reported being 'not confident' in diagnosing pre-malignant and malignant lesions from clinic appearance (GMPs 53% vs. GMSs 88%, $p < 0.001$). This p-value indicates that GMPs are significantly more confident than GMSs. It appears necessary to improve teaching on OPMLs and oral malignancy in the undergraduate medical curriculum and provide continuing medical education opportunities for GMPs to improve current deficiencies in knowledge of oral cancer. The key message for both groups is that any oral lesion lasting longer than 2 weeks, after local possible causative factors are removed, should be biopsied or referred without delay.¹⁹⁹ GMPs and GMSs should also be educated

to look for leukoplakia, erythroplakia, and erythroleukoplakia during the oral cancer screening examination.

The next three aims of our study all relate to the nine steps of the visual and tactile oral cancer screening examination specified by the WHO and NIDCR.³⁰ The first objective was to identify which of the nine steps of the visual and tactile oral cancer screening examination either group performed. When individual steps were assessed, GMPs indicated that the only steps performed more often than not (meaning over 50% of GMPs indicated that they did perform the step) were Step 1 (extra-oral), Step 2 (lip examination) and Step 8 (palate and oro-pharynx). The GMSs had even fewer steps in their routine, with only Step 1 (extra-oral) performed more often than not. When the nine steps were assessed together, each group exhibited poor overall efficiency (Table 4.6), with GMPs performing 4.3 steps on average compared to 3.8 for GMSs. Of most concern is that both groups often overlooked common sites of oral cancer development, such as the floor of the mouth, venterolateral surface of the tongue, and retromolar trigone. The second and third objectives were to identify whether either group was confident in performing the technique of each step and identifying pathology at each step. Confidence in performing each step for both groups mirrored whether they actually performed the step more often than not, with GMPs confident in performing Steps 1, 2, and 8, and GMSs only Step 1. In all other steps neither group was confident performing the technique required. Likewise, confidence in identifying pathology for each group mirrored performance of the step; in all steps except Step 1 (extra-oral), GMSs were statistically significantly less confident in the technique and identifying pathology than the GMPs (Table 4.6).

The results of this study clearly indicate that GMPs in Australia lack the awareness, knowledge, equipment, and skills to adequately perform opportunistic screening for oral cancer in high-risk patients attending their practice. When these results are compared to other results from similar studies across the world, Australian GMPs are similar to their peers in the developed nations. GMPs are unlikely to examine patient's oral mucosa routinely, unlikely to advise patients about risk factors for oral cancer, likely to identify few risk factors, technically poor at performing the nine steps of oral cancer screening examinations, and overall not confident in diagnosing OPMLs or oral cancers.¹⁶⁸⁻¹⁷³ In addition, medical students entering the workforce have been trained with even less awareness, knowledge, confidence, and skills for performing opportunistic screening for oral cancer than their more experienced colleagues.

Intent of GMPs to conduct oral cancer screening has been investigated utilising the Theory of Planned Behaviour, and this has identified barriers to conducting oral examinations for screening purposes in general medical practice. The results suggest that there is considerable potential for improving intention to perform oral cancer screening in general practice.¹⁷⁴ Suggested interventions include: 1) theory-based interventions, such as further training to enhance confidence, expertise, knowledge, and ease of examination, 2) provision of adequate equipment in the surgery (light and dental mirrors), and 3) introducing guidelines on opportunistic screening that increase motivation to comply with goals, such as more peers performing screening or an oral cancer awareness month.¹⁷⁴ One potential threat to improving opportunistic screening amongst GMPs was identified in a Scottish study that reported a high proportion of GMPs (66%) felt strongly that oral cancer detection is the remit of the dental team.¹⁷² If this same opinion pervades the GMPs in Australia, then it may prove difficult to change behaviour regarding opportunistic screening. At present the RACGP teaches that there is insufficient evidence to recommend screening by visual inspection or by other screening methods.¹⁷⁵ The RACGP identifies increased-risk individuals as smokers aged greater than 50 years, heavy drinkers, patients chewing tobacco or areca/betel nuts, and those exposed to excessive UV in the lip area.¹⁷⁵ If an individual is identified as increased risk, the RACGP encourages opportunistic examination of mouth and lips every 12 months but does not provide an examination description matching the desired nine-step visual and tactile oral cancer screening examination.^{30, 175}

With regard to GMP skill in performing an oral cancer screening examination, there is a statistically significant association between undergraduate and postgraduate teaching on examination of the oral cavity and whether practitioners felt confident in their ability to detect oral cancer.¹⁷³ GMPs also display decreased diagnostic confidence in detecting malignancies or OPMLs. In fact, in a study of Irish GMPs, a statistically significant association was found between undergraduate and postgraduate teaching on the diagnosis of oral malignant disease and whether practitioners felt confident in their ability to detect oral cancer and OPMLs clinically.¹⁷³ The authors concluded that the knowledge level of GMPs needs improvement with appropriate initiatives at both the undergraduate and graduate levels via continued medical education (CME).¹⁷³ CME is encouraged worldwide for healthcare professionals and is compulsory in Australia. Internet-based CME programmes have demonstrated that they are also an effective medium for transfer of

knowledge for health care practitioners.²⁰⁰ Engaging with GMP training colleges, such as the RACGP in Australia, may be of benefit for review of the postgraduate training curriculum and updating of guidelines regarding prevention and early detection of oral cancer. The question of what is being taught at medical schools across Australia in relation to oral cancer also remains. The GMS results point to a need to develop an undergraduate curriculum to address the important aspects of oral cancer from an evidence-based approach that can be integrated into the already crowded undergraduate medical curriculum.¹⁸⁴

Table 4.11: Hypotheses Results (GMPs vs. GMSs)

Hypotheses Tested	Outcome
	GMPs vs GMSs (p-value)
Both groups do not routinely examine oral mucosa.	Null hypothesis true 6% vs 22% (<.001***)
Both groups have received limited education and training in oral cancer and visual and tactile oral cancer screening examination	Null hypothesis true 20% vs 19% (0.833)
Both groups do not routinely advise patients about risk factors for oral cancer.	Null hypothesis true 32% vs 34% (0.675)
Both groups are not confident diagnosing malignant and pre-malignant lesions from clinical appearance.	Null hypothesis true 53% vs 88% (<0.001***)
Both groups do not perform all nine steps of a visual and tactile oral cancer screening examination.	Null hypothesis true Average steps performed 4.3 vs 3.8 (0.075)
Both groups are not sufficiently confident in their techniques to complete all nine steps of a visual and tactile oral cancer screening examination.	Null hypothesis true Average steps confident in technique 4.6 vs 2.9 (<0.001***)
Both groups are not confident in identifying pathology in all nine steps of a visual and tactile oral cancer screening examination.	Null hypothesis true Average steps confident in pathology 4.2 vs 2.2 (<0.001***)

In summary, Table 4.11 presents a tabulated summary of outcomes to the seven hypotheses tested in this study. The p-value indicates there is a statistically significant difference between the groups in some hypotheses tested, however, we argue although different, both groups were still poor in the outcome measured and hence the null

hypothesis held true in all seven. The present study has several limitations. The characteristics of the responding GMPs may not fully reflect the knowledge and practices of all GMPs in Australia, particularly given that the response rate was 27% and the only district sampled was North Brisbane. Similarly, the characteristics of the responding GMSs entering the workforce at two large metropolitan hospitals in Brisbane may not reflect the variance in medical school curriculums across Australia or the knowledge and practices of all GMSs across Australia.

4.7 Conclusion

The present study demonstrated that Australian GMPs and GMSs had an inadequate level of knowledge of oral cancer, OPMLs, and risk factors, as well as skill in performing opportunistic oral cancer screening examinations. Although oral cancer is relatively uncommon in Australia, oral cancer patients often present to GMPs multiple times a year in the asymptomatic phase prior to their diagnosis. This suggests an opportunity for early-stage diagnosis via opportunistic screening of high-risk individuals in the primary medical healthcare setting in Australia. Early-stage diagnosis is achievable and has significant morbidity and survival benefits for patients with oral cancer.

For rates of opportunistic oral cancer screening by Australian GMPs to increase, interventions need to improve the knowledge and confidence of both GMSs and GMPs toward oral cancer and screening of high-risk individuals. Improvements to undergraduate medical school curriculums, development of CME programmes, and review of the postgraduate training curriculum of GMPs are suggested. Engagement with the RACGP in Australia is suggested in order to influence the content of the oral cancer prevention section in the next edition of RACGP published guidelines for preventive activities in general practice.

CHAPTER FIVE: GENERAL DISCUSSION AND CONCLUSION

5.1 Introduction

Most oral cancers lack early symptoms that would prompt a patient to seek diagnosis; hence, at presentation most patients are diagnosed with stage III or IV advanced disease. Prevention and early stage of diagnosis are promising for oral cancers because of known risk factors and the relative ease of identifying oral cancers and OPMLs by a simple oral cancer screening examination. However, due to the relatively low prevalence of oral cancer in developed communities, evidence is currently insufficient to support population-based screening. There is significant evidence that the recommended visual and tactile opportunistic oral cancer screening examination, performed by trained health practitioners on the general and high-risk populations when asymptomatic, detects many OPMLs and some early-stage (Stage I) oral cancers.^{32, 150, 151} A large volume of evidence also links early stage of disease at diagnosis with significantly reduced morbidity and mortality.^{11, 14, 15, 18, 19, 21, 22, 25} Together, these two bodies of evidence suggest that diagnosis in the asymptomatic phase via evidence-based screening initiatives is likely to have a significant impact on mortality and morbidity from oral cancer. Therefore, early detection of oral cancer and OPMLs in the asymptomatic phase via an opportunistic screening examination is important. It is unlikely that there will ever be a rigorously designed and implemented, randomly controlled trial with long-term follow-up that will prove this connection in oral cancer without questions of lead-time and length-time bias. Adoption of opportunistic screening will only be effective if patients access it and it is offered in the primary healthcare setting or via novel public health initiatives. The core objective of this thesis is to determine whether asymptomatic diagnosis of oral cancer at an early stage of disease is achievable in Australia, particularly in the primary medical healthcare setting. We achieve this by evaluating the awareness of, and attitudes toward, oral cancer and opportunistic screening held by recently-diagnosed oral cancer patients, experienced general medical practitioners, and recently-graduated medical students.

5.2 Oral Cancer Patients

This thesis evaluated an Australian cohort of patients with newly diagnosed oral cancer, presenting to a public hospital head and neck clinic, to identify opportunities for increasing early diagnosis of oral cancer. Particular emphasis was placed on investigating patient

interactions with GMPs and GDPs in the asymptomatic phase where the oral cancer may be present and detected at an earlier stage of disease.³²

Unfortunately, this study reports one of the lowest scores in the literature regarding awareness of oral cancer, with 46% stating they had never heard of oral cancer until their diagnosis. This alarming lack of awareness is even more concerning when added to the fact that 67% of participants reported being regular consumers of tobacco in Australia, where plain packaging of tobacco products contains graphic images of lip, mouth, tongue and lung cancer, and has done so for many years preceding our research. At least 67% of our participants should have seen oral cancer on this packaging at some point and reported such. Perhaps also our questionnaire should have used the term mouth or throat cancer as interchangeable with oral cancer and the reported awareness might not have been so low. Studies from the USA report that only 14-15.5% of adults had never heard of oral cancer.^{190, 191} Another Australian study investigated 101 patients referred with a suspicious oral lesion to a private oral medicine clinic.¹⁸⁷ These patients reported being far more aware of oral cancer, with 91.8% having heard about oral cancer.¹⁸⁷ Of interest is that private patients in this private oral medicine clinic expected that both GDPs and GMPs should check for and be able to explain oral mucosal pathology, raising the question of whether the general public might expect similar standards of care.¹⁸⁷ The demographics of these two Australian cohorts are very different, making comparison between the two groups difficult; however, there is an obvious wide divide in awareness of oral cancer when private and public patients are compared.

With regard to actual risk factors for oral cancer, this Australian cohort is consistent with results reported from other cohorts from developed nations, in that the most significant risk factors identified are increased age, tobacco use, and alcohol consumption.^{28, 29} 95% were over 40 years of age at diagnosis, and 67% and 66% were regular consumers of tobacco and alcohol, respectively. There was poor knowledge of these important risk factors and almost no knowledge of HPV as a risk factor. A recent international large pooled study estimated the population attributable risks for tobacco and alcohol use to be 64% (95% CI: 45-75%), showing that these two risk factors alone are responsible for a large number of cases.²⁸ The poor knowledge of risk factors for oral cancer logically follows from the cohort's generally poor awareness of oral cancer. Another recent Australian study, the Lesion Evaluation, Screening and Identification of Oral Neoplasia Study (LESIONS), has aimed to understand factors that may influence all oral mucosal disease in high-risk

populations, with a particular focus on oral cancers and OPMLs.¹⁵¹ LESIONS targeted two Australian communities at high risk of oral cancer and OPMLs, mostly in the dental healthcare setting but also at indigenous health clinics and a community pharmacy location.¹⁵¹ The authors have reported on the recruitment and initial screening outcomes of 1498 participants and they confirm that those participants with higher disadvantage were more likely to have a history of tobacco use, as expected from international studies.¹⁵¹ Those participants with low income also had significantly higher prevalence ratios of having suspicious oral mucosal lesions.¹⁵¹ Although the exact numbers were not captured, the authors noted a high rate of patient refusal when approached opportunistically before or after scheduled dental appointments.¹⁵¹ Common patient barriers identified in LESIONS were: perceived time pressure, embarrassment regarding the condition of the dentition (when screening attempted at community pharmacy), unwillingness to know if disease was detected, lack of concern and lack of pain.¹⁵¹ Another study investigating barriers to oral cancer screening in rural African-Americans showed three primary patient barriers to screening — lack of knowledge of oral cancer and its symptoms accounted for 31.8% of all barriers mentioned, lack of financial resources or health insurance for 25.0%, and fear of screening and diagnosis for 22.9%.¹³³ Howell et al. (2013) placed these barriers within the Theory of Planned Behaviour and concluded that interventions aimed at increasing oral cancer screening should first focus on changing people's attitudes about screening by increasing knowledge about oral cancer and reducing fear.¹³³

Awareness and knowledge of oral cancer are key for patients to accept an invitation for oral cancer screening. This is most notable in the recently published data from Far Eastern Memorial Hospital in Taipei, Taiwan. Utilising a novel approach, high-risk patients attending an outpatient facility were identified using an automated system based on their responses to questions regarding tobacco and betel nut usage.³² They were then offered the opportunity to be screened with a standard visual and tactile oral cancer screening examination.³² A total of 38 693 patients were identified as high-risk, yet only 8037 (20.8%) were recruited as participants in the screened cohort from the automated system.³² This means that approximately 80% were advised that they were at high risk for developing oral cancer yet declined a free oral cancer screening examination. Not only do the high-risk populations decline screening invitations, in addition, UK research reports that the target high-risk population for opportunistic screening activities was shown to require further persuasion that their lifestyle choices (tobacco and alcohol) contributed to an increased risk of oral cancer.¹⁵³

This thesis also identifies whether participants had opportunities in the Australian health system to receive an opportunistic oral cancer screen examination in the asymptomatic phase. Research has shown that patients with oral lesions often consult their GMP rather than their GDP, even in the UK where there is greater access to free dental treatment.¹⁵⁶ ¹⁵⁷ The preference for presentation to GMPs has held true in this study, with 80% having seen a GMP within the last six months and 63% seeing their own regular GMP at least three times a year. In contrast, only 35% had seen a GDP within the last six months and only 6.8% visited their own regular GDP at least three times a year. While less than half of patients have their own regular GDP, 84% have their own regular GMP. Unfortunately, only 3% of these patients reported that their regular GMPs had ever discussed their risk factors for oral cancer, and only 6% had ever received an oral cancer screening examination from them. These results present an opportunity to target new education interventions to GMPs toward increasing opportunistic oral cancer screening in the primary medical healthcare setting.

The evidence suggests that GDPs are more skilled and confident in performing the oral cancer screening examination than their medical counterparts.^{168, 170-173} Our study reported that only 47% of participants had a regular GDP, and most only attended once or twice per year. The remaining 53% did not have a regular GDP, and predominantly only saw a dentist for an emergent dental problem; therefore the average rate of dental visits in this group was reported as zero times per year for the vast majority. This low attendance rate to GDPs in Australia suggests that targeting education interventions toward increasing oral cancer screening with GDPs would be less productive than that with GMPs, where the target population is more likely to attend. A recent systematic review of patient acceptance of screening for oral cancer outside the dental setting showed that GMPs should be confident that acceptance of, and satisfaction with, oral cancer screening is high, particularly when patients have previously been educated about oral cancer in the waiting room.¹⁵⁸ In short, the results clearly show that participants had many opportunities in the Australian health system to receive an opportunistic oral cancer screening examination before their diagnosis. Asymptomatic diagnosis of early-stage disease is certainly possible in the primary medical setting in Australia, dependent on knowledge and awareness of both patients and GMPs.

5.3 General Medical Practitioners

The importance of GMP awareness of oral cancer, knowledge of the risk factors, ability to competently perform a visual and tactile oral cancer screening examination, and confidence in identifying pathology during that examination should not be underestimated. In our study of GMPs, only 6% reported routinely performing oral cancer screening. However, when asked if they do so for a high-risk patient, over 40% stated they would perform oral cancer screening, suggesting some awareness of high-risk populations and a willingness and ability to perform the screening examination in the primary medical healthcare setting. Initially about one-third of GMPs reported that they had sufficient training, knowledge, and technique to perform oral cancer screening. However, once the nine steps of the screening examination were shown in the next part of the questionnaire, only 20% of GMPs felt they had sufficient training to identify a high-risk patient and perform a thorough opportunistic nine-step screening examination.

Similarly, knowledge of risk factors for oral cancer was also poor amongst our cohort of GMPs. The cohort strongly identified tobacco as a risk factor, consistent with studies from both developed and developing countries.^{168, 176, 195-197} Only 57% of GMPs identified alcohol as a risk factor, again consistent with other GMP studies reporting a less well-known association of oral cancer with alcohol consumption.¹⁹⁸ Other known risk factors, such as age, HPV, betel nuts, and poor diet, were not identified strongly. This deficiency in knowledge of risk factors for oral cancer displayed by our cohort of Australian GMPs is likely to limit their ability to identify high-risk patients and perform opportunistic screening.

We also investigated if GMPs perform each of the nine steps of the visual and tactile oral cancer screening examination specified by the WHO and NIDCR.³⁰ GMPs performed on average 4.3 steps of the required nine-step screening examination. Of most concern is that common sites of oral cancer development, such as the floor of the mouth, ventrolateral surface of the tongue, and retromolar trigone were often overlooked. Overall the results of our study clearly indicate that Australian GMPs lack the awareness, knowledge, equipment, and skills to adequately perform opportunistic screening for oral cancer in high-risk patients attending their practice. These results are similar to those reported in studies from other developed nations. GMPs have low suspicion of oral cancer, are unlikely to examine patient's oral mucosa routinely, are unlikely to advise patients about risk factors for oral cancer, and are likely to identify few risk factors; they lack knowledge regarding the main locations of oral cancer, are technically poor at performing

the nine steps of the oral cancer screening examination, and overall are not confident in diagnosing OPMLs or oral cancers.^{131, 134-136, 168-173} The presence of patient co-morbidities has also been shown to result in clinicians focusing their attention on the existing disorders.¹³⁷⁻¹³⁹

Intent of GMPs to conduct oral cancer screening has been investigated utilising the Theory of Planned Behaviour, and the results suggest that there is considerable potential for improving intention to perform oral cancer screening in the primary medical healthcare setting.¹⁷⁴ Suggested interventions include: 1) theory-based interventions, such as further training to enhance confidence, expertise, knowledge, and ease of examination, 2) provision of adequate equipment in the surgery (light and dental mirrors), and 3) introducing guidelines on opportunistic screening that increase motivation to comply with goals, such as more peers performing screening or an oral cancer awareness month.¹⁷⁴ At present the RACGP teaches that there is insufficient evidence to recommend screening by visual inspection or by other screening methods.¹⁷⁵ The RACGP identifies increased-risk individuals as smokers aged greater than 50 years, heavy drinkers, patients chewing tobacco or areca/betel nuts, and those exposed to excessive UV in the lip area.¹⁷⁵ If an individual is identified as increased risk, the RACGP encourages opportunistic examination of mouth and lips every 12 months but does not provide an examination description matching the desired nine-step visual and tactile oral cancer screening examination.^{30, 175}

Over 50% of GMPs in this study reported that they were not confident in diagnosing OPMLs or oral cancer from clinical appearance. There is a statistically significant association between undergraduate and postgraduate teaching on examination of the oral cavity and whether practitioners felt confident in their ability to detect oral cancer.¹⁷³ The key message is that any oral lesion lasting longer than 2 weeks, after local possible causative factors are removed, should be biopsied or referred without delay.¹⁹⁹ The level of knowledge of GMPs needs to be addressed with appropriate initiatives at both the undergraduate and graduate levels via continued medical education (CME).¹⁷³ Engaging with GMP training colleges, such as the RACGP in Australia, may be of benefit for review of the postgraduate training curriculum and updating of guidelines regarding prevention and early detection of oral cancer.

5.4 Medical Student Education

A GMS entering the health workforce should be aware, knowledgeable, and confident in identifying a high-risk individual, and suggesting and performing an opportunistic oral cancer screening examination. Overall, the GMS results were mostly equivocal, but also sometimes statistically significantly worse than their more experienced GMP counterparts studied. In our study, 88% of GMS were not confident in diagnosing OPMLs and oral cancer from clinic appearance. These results were echoed by a comparison of UK undergraduate medical and dental students, which suggests that there will be no improvement in the next generation of health professionals, particularly medical practitioners, regarding oral cancer screening.¹⁷⁶ Other studies in Iran, Nigeria, and the USA indicate a need to review the curriculum of medical and dental schools to improve awareness and behaviour toward increasing opportunistic oral cancer screening.¹⁷⁷⁻¹⁸¹ In 2011, two significant studies investigated medical school curricula for oral cancer teaching in the USA and UK, respectively. The majority of the responding USA medical schools offered very little oral health education, with approximately 80% offering less than five hours of oral health curriculum over the entire course.¹⁸² Oral cancer training at medical schools lacked both adequacy and comprehensiveness, and showed no improvement relative to a similar study from 15 years earlier.^{182, 183} The UK study highlighted that undergraduate oral cancer teaching varied widely in terms of duration, format, and content across British medical schools.¹⁸⁴ Our GMS results point to a need to develop an undergraduate curriculum to address the important aspects of oral cancer from an evidence-based approach that can be integrated into the already crowded undergraduate medical curriculum.¹⁸⁴ The question of what is being taught at medical schools across Australia in relation to oral cancer also remains.

5.5 Opportunistic Oral Cancer Screening

A Cochrane systematic review evaluated screening strategies for reducing oral cancer mortality and revealed that there was insufficient evidence to recommend inclusion or exclusion of screening for oral cancer using a visual and tactile examination in the general population, as the only significant RCT was on a high prevalence oral cancer population and the study was assessed as having bias in the study design.^{25, 27} According to the WHO and NIDCR, an oral cancer screening examination should include a visual examination of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the

mouth, tongue, and palate with mouth mirrors to help visualise all surfaces.³⁰ The tactile examination includes palpating the regional lymph nodes, tongue, and floor of the mouth.³⁰ The Cochrane review concluded by encouraging opportunistic screening and stating that GMPs and GDPs should continue to carry out visual and tactile examination of the oral cavity as an integral part of their routine daily work, and particular attention should be paid to high-risk individuals.²⁷ Since publication of the Cochrane review in 2013, three significant articles have been published that further support their conclusion that opportunistic screening for oral cancer is important.

In Asia, the emphasis is on addressing the relatively high prevalence rate of oral cancer due to tobacco and betel nut consumption.²⁶ High-risk patients attending an outpatient facility at Far Eastern Memorial Hospital, Taipei, Taiwan, were identified using an automated system based on their response to questions regarding tobacco and betel nut usage, at the time of check-in to the outpatient facility.³² If they answered 'yes' to the risk factors, they were automatically offered the opportunity to be screened with a standard visual and tactile oral cancer screening examination.³² A total of 8037 high-risk patients were recruited as participants to the screened cohort from the automated system; 1664 patients were identified with positive lesions, and 302 patients underwent a biopsy.³² Five patients were diagnosed with oral cancer and 121 with dysplastic OPMLs.³² The stage of disease at diagnosis of this asymptomatic cohort was compared to a symptomatic cohort presenting to the same outpatient facility for investigation of a symptomatic oral lesion.³² The symptomatic cohort comprised 157 patients with oral cancers and 61 with OPMLs, and, as expected, the automated screening programme identified earlier stages of oral cancers than the symptomatic cohort.³²

Two other studies report from developed nations where the prevalence of oral cancer is far less than in Taiwan. Monteiro et al. (2015) carried out separate invitational and opportunistic oral cancer screening interventions in the city of Oporto in Portugal. The first part of this study was an invitational screening programme where residents of Oporto were invited to attend on a designated screening day advertised via a mass media campaign including television, newspapers, radio, billboards and posters.¹⁵⁰ A total of 267 participants responded to the general invitation to attend the oral cancer screening day. The second part of the study was an opportunistic screening programme offered to consenting patients visiting for dental consultation (first appointment) in a public hospital of Oporto, and 460 screening examinations were performed in this dental healthcare setting.

In total, 727 individuals (277 males and 450 females) with a mean age of 54 years (range 18-94) were included in the study. Twenty-two OPMLs, nine cases of lichen planus and two oral carcinomas were detected early, with both in stage one of the disease and both identified in the asymptomatic phase.¹⁵⁰

The two communities targeted by the LESIONS study in Australia were at high risk of oral cancer and OPMLs. The ten screening sites were within public and private dental clinics, indigenous health clinics and a community pharmacy.¹⁵¹ After a visual and tactile oral mucosal screening examination was completed by one of 11 trained and calibrated dentists or oral health therapists on 1498 participants, oral mucosal lesions were detected in over half the cohort examined, but only 16% were clinically nonhomogeneous and more likely to contain dysplasia or early malignant change.¹⁵¹ Although the results of biopsy and specialist review are not yet presented from this study, the volume of oral lesions detected is significant and likely to contribute to the evidence supporting opportunistic screening of high-risk populations.¹⁵¹

In Western populations where betel nut usage is minimal, population-based annual or semi-annual screening for oral cancer is not cost-effective.²³ Instead, targeting high-risk groups such as tobacco and alcohol consumers over 40 years of age to be opportunistically screened using a visual and tactile examination should be encouraged in the primary care setting.²³ Over the last decade following the introduction of an oral cancer awareness week (now month) in the UK and the Oral Cancer Awareness Month in the USA in 2000, increasing numbers of oral cancer screening examinations have been performed each year.^{154, 155} It is still difficult to elucidate whether the high-risk target population are being reached, or whether the general population is gaining increased awareness and knowledge and becoming more accepting of screening activity.

5.6 Conclusion

This thesis has provided valuable insights into the challenge of achieving asymptomatic diagnosis of oral cancer in the early stage of disease in Australia. Oral cancer patients had poor awareness of oral cancer and knowledge of risk factors prior to diagnosis. Most oral cancer patients were over 40 years of age, and most consumed tobacco, alcohol, or both, suggesting a target population for opportunistic screening in the primary healthcare setting. Patient, professional, and total diagnostic delays were better than in many other

countries. Oral cancer patients are more likely to see a GMP multiple times a year for unrelated medical issues in the asymptomatic phase prior to their diagnosis, suggesting significant opportunities for GMPs to perform opportunistic oral cancer screening. Once symptomatic, oral cancer patients are still likely to seek help from a GMP. Initiation by a patient of a consultation with a GMP or GDP for an oral cancer screening examination would require that the patient have an improved awareness of oral cancer and knowledge of his or her personal risk factors for developing it. Future research should investigate the barriers to, and triggers of, attendance at healthcare appointments by the high-risk target population, and should consider novel ways of engaging in opportunistic oral cancer screening activity.

The present study has highlighted significant missed opportunities for oral cancer screening, as the majority of patients visited their GMP regularly. Of concern is that, while 84% of the oral cancer participants had a regular GMP, only 3% of those GMPs had ever discussed the risk factors for oral cancer, and only 6% of patients had an oral cancer screening examination performed on them by the GMP. This thesis has shown that Australian GMPs and GMSs have an inadequate level of knowledge of oral cancer, OPMLs, and risk factors, as well as an inadequate level of skill in performing opportunistic oral cancer screening examinations. At the present level of knowledge and confidence, it would be very unlikely for a GMP to conduct a thorough visual and tactile oral cancer screening examination even if a high-risk individual presented to his or her clinic. To encourage increased rates of screening nationally, the guidelines published by RACGP for preventative activities in general practice need updating in line with the latest literature and systematic reviews regarding opportunistic oral cancer screening. For opportunistic oral cancer screening activity to increase on the part of Australian GMPs, interventions are needed to improve the knowledge and confidence of GMPs and GMSs toward diagnosing oral cancer, OPMLs, and the screening of high-risk individuals.

The following are recommendations for further research and interventions focused on the primary medical healthcare setting, identified during the thesis preparation and aimed at increasing the detection of asymptomatic, early-stage oral cancers and, ultimately, the survival of patients diagnosed with oral cancer.

- Investigate the undergraduate and postgraduate medical school curricula in Australian Medical Schools to establish the current scope of oral medicine and

pathology training and ensure that the teaching incorporates reaching competency in risk factors for oral cancer, diagnostic confidence, and performance of the nine-step visual and tactile examination for oral cancer screening.

- Engage the RACGP to reconsider the evidence for opportunistic screening and modify the current guidelines for preventative activities in general practice.
- Investigate the most effective ways of training GMPs and ensure that teaching incorporates reaching competency in risk factors for oral cancer, diagnostic confidence, and performance of the nine-step visual and tactile oral cancer screening examination.
- Investigate the most effective ways of raising awareness among the general public of oral cancer, its risk factors, and the availability of screening examinations at GMPs or GDPs.
- Investigate the most effective ways of raising awareness among the high-risk target population of oral cancer, its risk factors, and the availability of screening examinations at GMPs or GDPs.
- Investigate the roles that professional organisations – such as the Australian Medical Association, Australian Dental Association, Oral Medicine and Oral Pathology Societies, and Australian and New Zealand Head and Neck Cancer Societies – are taking in public awareness campaigns, health practitioner education interventions, and policy development to improve early detection of oral cancer.
- Engage the Preventative Health Taskforce with submissions at any future opportunity to include early detection of oral cancer as part of future updates or revisions to the Australian National Preventative Health Strategy.

Asymptomatic diagnosis of oral cancer in the early stage of disease is achievable in the primary medical healthcare setting in Australia. The present study and literature review shows that it has already been achieved in the primary dental healthcare setting in Australia, and lessons in undergraduate and postgraduate training can be taken from the Australian dental profession. Changing the ingrained practice behaviour of the Australian GMP population toward opportunistic oral cancer screening is a great challenge that will require determined effort both from individuals and from professional multi-disciplinary societies, such as the Australian and New Zealand Head and Neck Cancer Society. The rigorous design and implementation of further research activities following the above recommendations will enhance the early detection of oral cancer.

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APPENDICES

Appendix A: Participant with Oral Cancer Questionnaire

Appendix B: General Medical Practitioner Questionnaire

Appendix C: Graduate Medical Student Questionnaire

Appendix A: Participant with Oral Cancer Questionnaire

Participant Questionnaire

This questionnaire has been designed with the purpose of using the information obtained to consider ways of improving prevention, early detection and referral of oral cancer from both general medical and dental practitioners.

The information you provide will likely guide efforts to increase awareness of oral cancer and early detection of it throughout Australia.

Age:.....yrs Sex: Male/Female

Before you were diagnosed did you have any experience with oral cancer?

(Please answer all questions)

Have you worked with patients with oral cancer in a health care role? YES or NO

If Yes, What role?.....

Have you had a previous diagnosis of oral cancer in your mouth? YES or NO

Have you had a previous diagnosis of oral cancer in your extended family? YES or NO

Have you had a previous diagnosis or oral cancer in a friend? YES or NO

Have you heard of a previous diagnosis of oral cancer in someone not known to you but you had heard about it from others talking or online? YES or NO

Have you ever read anything about oral cancer prior to your diagnosis? YES or NO

Had you never heard of oral cancer at all until you were diagnosed? YES or NO

Before you were diagnosed what was your knowledge of any risk factors that could increase your chances of oral cancer?

(List as many as you were aware of before diagnosis)

.....

Were you diagnosed before you developed symptoms? YES or NO

If Yes, who examined you to diagnose the cancer?

(circle best option)

a) Doctor (GP) or b) Doctor (Specialist) - please specify?.....

c) Public Hospital Emergency Department Doctor

d) Dentist (GP) or e) Dentist (Specialist) – please specify?.....

f) Other Health Practitioner – please specify?.....

Did you develop symptoms before diagnosis? YES or NO

If Yes, what symptoms did you develop?

(List as many as you were aware of before diagnosis)

.....

When did you first become aware of symptoms: ____ / ____ / ____
(at least month and year)

What type of health care professional did you choose to attend first to assist you with diagnosing the cause of your symptoms?
(circle best option)

- a) Doctor (GP) or b) Doctor (Specialist) - please specify?.....
- c) Public Hospital Emergency Department Doctor
- d) Dentist (GP) or e) Dentist (Specialist) – please specify?.....
- f) Other Health Practitioner – please specify?.....

When did you first attend this health professional once you were concerned about your symptoms:
____ / ____ / ____
(at least month and year)

Date of first attendance at Head and Neck Clinic: ____ / ____ / ____

Now think back to the period prior to your symptoms before answering the next section of questions. Use the date at the top of this page as your reference.

Did you access a General Medical Practitioner (GP) in Australia prior to this date in the preceding two years for any other reason (i.e. other illness, prescriptions, medical check-up, certificate etc.)? YES or NO

When was the last visit to the General Medical Practitioner (GP)
(circle best answer)

- a) less than one month before symptoms
- b) between one and three months before symptoms
- c) between three and six months before symptoms
- d) six to twelve months before symptoms
- e) greater than twelve months before symptoms

Do you have a regular GP in Australia that you would call “your GP”? YES or NO

If Yes, how often in a year would you roughly see “your GP” ?

- a) zero b) once c) twice d) three e) four f) more than four

If No, how often in a year would you seek medical advice from any GP?

- a) zero b) once c) twice d) three e) four f) more than four

At any time in your life has any GP you attended in Australia ever discussed oral cancer with you or the risk factors you may have for oral cancer? YES or NO

Whilst it is not standard of care in Australia to have an oral cancer screen regularly, we are interested if can you recall at any time in your life if any GP in Australia ever performed an oral cancer screening examination on you? YES or NO

(An oral cancer screening examination involves feeling your face and neck for lymph nodes while doctor stands behind you, in addition to looking at the inside of your lips, around your teeth left and right with a dental mirror, up on your palate, top of tongue, under tongue and down both sides of the tongue, and finally the throat. You need a dental mirror and a light to do this and takes about 2-5minutes to complete.)

Did you access a General Dental Practitioner (Dentist) in Australia prior to this date in the preceding two years for any other reason (i.e. other oral illness or dental check-up etc.)? YES or NO

When was the last visit to the General Dental Practitioner (Dentist)?

(circle best answer)

- a) less than one month before symptoms
- b) between one and three months before symptoms
- c) between three and six months before symptoms
- d) six to twelve months before symptoms
- e) greater than twelve months before symptoms

Do you have a regular dentist that you would call “your dentist”? YES or NO

If Yes, how often in a year would you roughly see “your dentist” ?

- a) zero b) once c) twice d) three e) four f) more than four

If No, how often in a year would you seek a dental review from a dentist?

- a) zero b) once c) twice d) three e) four f) more than four

At any time in your life has any Dentist you attended in Australia ever discussed oral cancer with you or the risk factors you may have for oral cancer? YES or NO

At any time in your life has any Dentist in Australia ever performed an oral cancer screen on you?

(This involves feeling your face and neck for lymph nodes in addition to looking at the inside of your lips, around your teeth, on your palate, tongue, under tongue and down both sides of the tongue, and finally the throat. You need a dental mirror and a light to do this)

YES or NO

Please confirm if you had any of these known risk factors prior to symptoms developing in your individual situation? (circle as many as are applicable to you)

- a) Age over 40 years b) Alcohol consumption c) Human Papilloma Virus (HPV)
- d) Tobacco Consumption (chewing, smoking and passive) e) Chewing betel quid (nut)
- f) Diet low in fresh fruit and vegetables

Finally is there any other health professional who has performed an oral cancer screen on you in Australia? YES or NO If Yes, please specify what type of professional? _____

This section will be detached from your survey so as to de-identify your responses and maintain your privacy. However prior to this occurring the principal investigator, Dr John Webster may need to contact you to clarify responses so please provide your contact details below if you consent to being contacted for clarification purposes.

NAME: _____ PHONE: _____

ADDRESS: _____

EMAIL ADDRESS: _____

Appendix B: General Medical Practitioner Participant Questionnaire

General Medical Practitioner Participant Questionnaire

Age:.....yrs Sex: Male/Female

Graduating Year of Medical School:.....

Qualifications:.....

Do you perform oral cancer screening routinely? YES or NO

If you answered no to the above question, do you perform oral cancer screening if the patients are in high risk categories? YES or NO

What would you consider risk factors for oral cancer?
(list as many as you can recall)

.....
.....

Do you regularly advise patients about risk factors for oral cancer?
YES or NO

Do you regularly advise patients about risks factors for other cancers?
YES or NO

Do you regularly encourage reduction in risk factors for cancers?
YES or NO

In regards to clinical appearance do you feel confident diagnosing oral cancer or pre-malignant oral lesions from clinical appearance?

Very confident Confident Unsure Very Unsure

What changes in the mouth would you associate with pre-malignancy?

.....
.....

What changes in the mouth would you associate with oral cancer?

.....
.....

Do you have sufficient training, knowledge and technique to perform and oral cancer screening examination? YES or NO

Do you have all the tools required to perform an oral cancer screening?

- a) A source of bright white light? YES or NO
- b) A dental or ENT mirror? YES or NO
- c) Access to gauze squares? YES or NO



Step 1: Extra-oral examination

Palpate the face and neck to exclude lymphadenopathy and lesions.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of extra-oral examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology in extra-oral examination?

Very confident Confident Unsure Very Unsure



Step 2: Lip Examination

Note colour, texture and surface changes and changes at vermilion borders.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of lip examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology in lip examination?

Very confident Confident Unsure Very Unsure



Step 3: Labial Mucosa Examination

Note colour, texture and any swelling or other abnormalities in vestibular mucosa and gingiva.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of labial mucosa examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the labial mucosa?

Very confident Confident Unsure Very Unsure



Step 4: Buccal Mucosa Examination

Using dental/ENT mirrors examine with bright white light the right and left buccal mucosa from anterior labial commissure back to tonsillar pillar.

**Do you perform this step in your routine?
YES or NO**

How confident are you with your technique of buccal mucosa examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the buccal mucosa?

Very confident Confident Unsure Very Unsure



Step 5: Gingival Examination

As in step 4 look around the oral cavity with dental mirror and bright white light to examine the buccal and lingual gingiva.

Do you perform this step in your routine?

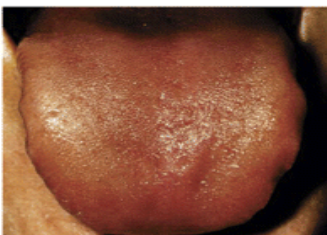
YES or NO

How confident are you with your technique of gingival examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the gingiva?

Very confident Confident Unsure Very Unsure



Step 6: Tongue Examination

Assess colour, texture, mobility and positioning. Grasp tip with gauze and assist full protrusion. Assess posterior and lateral borders with mirror while retracting cheek. Palpate the dorsum and lateral borders for hard tissue development.

Do you perform this step in your routine? YES or NO

How confident are you with your technique of tongue examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the tongue?

Very confident Confident Unsure Very Unsure



Step 7: Ventral Tongue and Floor of Mouth

Ask patient to lift tongue. Use gauze to dry floor of mouth and assess the ventral tongue and floor of mouth tissue for pathological changes.

Do you perform this step in your routine? YES or NO

How confident are you with your technique of floor of mouth examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the floor of mouth?

Very confident Confident Unsure Very Unsure

Step 8: Palate and Oro-pharynx

Use dental mirror to depress the tongue and bright white light to examine hard and soft palate and then patients says” Argh” to view oro-pharynx.



Do you perform this step in your routine? YES or NO

How confident are you with your technique of tongue examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the tongue?

Very confident Confident Unsure Very Unsure

Step 9: Bimanual palpation of Floor of Mouth

One finger in floor of mouth and hand under chin to palpate for abnormality between fingers. Palpate any other pathology noticed on examination.

Do you perform this step in your routine? YES or NO

How confident are you with your technique of bimanual palpation?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology using this method of palpation?

Very confident Confident Unsure Very Unsure



Where would you refer a patient if you suspected a pre-malignant lesion in the oral cavity?

Plastic Surgeon ENT Surgeon Oral and Maxillofacial Surgeon Dentist
Oral Medicine/Oral Pathologist Other Specialist (please specify):.....
I would observe and manage myself

Where would you refer a patient if you suspected an oral cancer?

Plastic Surgeon ENT Surgeon Oral and Maxillofacial Surgeon Dentist
Oral Medicine/Oral Pathologist Other Specialist (please specify):.....
I would observe and manage myself

Do you feel you have sufficient knowledge concerning prevention of oral cancer?

YES or NO

Do you feel you have sufficient knowledge to detect a pre-malignant lesion or an early asymptomatic oral cancer?

YES or NO

Do you feel you received sufficient training through medical school and general practice training to identify high risk groups and perform thorough opportunistic oral cancer screening?

YES or NO

Has anyone ever performed an oral cancer screen on yourself?

(This could be a general medical or a dental practitioner)

YES or NO

This section will be detached from your survey so as to de-identify your responses and maintain your privacy. However prior to this occurring the principal investigator, Dr John Webster, may need to contact you to clarify responses so please provide your contact details below if you consent to being contacted for clarification purposes.

NAME: _____ PHONE: _____

ADDRESS: _____

EMAIL ADDRESS: _____

Appendix C: Graduate Medical Student Participant Questionnaire

GRADUATE MEDICAL STUDENT PARTICIPANT QUESTIONNAIRE

This questionnaire has been designed with the purpose of using the information obtained to consider ways of improving prevention, early detection and referral of oral cancer from both general medical and dental practitioners.

Age:.....yrs Sex: Male/Female

Graduating Year of Medical School:.....

Qualifications:.....

University attended for Medical School:.....

How many years were you in attendance at Medical School:.....

During training did you ever see an oral cancer in a patient's mouth? YES or NO

During training did you ever see a pre-malignant oral lesion (PMOL) in a patient's mouth? YES or NO

During training did you ever discuss or learn about oral cancer in lecture, problem-based learning, tutorial or have clinical exposure to a patient with oral cancer? YES or NO

During training did you ever discuss or learn about opportunistic screening for oral cancer in lecture, problem-based learning, tutorial or during clinical experience? YES or NO

From your training do you feel you have sufficient knowledge and technique to perform an oral cancer screening examination? YES or NO

If asked to perform an oral cancer screening examination right now, which of the following would indicate your confidence in performing this correctly?

Very confident Confident Unsure Very Unsure

In your clinical experience do you examine patients' oral mucosa routinely? YES or NO

If you answered NO to the above question, do you screen the oral mucosa if the patients are in high risk categories or have risk factors for oral cancer? YES or NO

What would you consider risk factors for oral cancer?

(list as many as you can recall)

.....
.....

Do/will you regularly advise patients about risk factors for oral cancer? YES or NO

Do/will you regularly encourage risk factor reduction for oral cancer? YES or NO

Do/will you regularly advise patients about risks factors for other cancers? YES or NO

Do/will you regularly encourage risk factor reduction for other cancers? YES or NO

Do you feel confident diagnosing oral cancer or pre-malignant oral lesions from clinical appearance?

Very confident Confident Unsure Very Unsure

What changes in the mouth would you associate with pre-malignancy?

.....
.....

What changes in the mouth would you associate with oral cancer?

.....
.....

The following 8 steps are included in an oral cancer screening examination. Research also suggests a bright white light (not simply a torch/pupil torch), dental/ENT mirror and gauze squares are required for adequate visualization of all areas during the examination.

Do you have all the tools required to perform an oral cancer screening in your workplace?

- a) A source of bright white light? YES or NO or UNSURE
- b) A dental or ENT mirror? YES or NO or UNSURE
- c) Access to gauze squares? YES or NO or UNSURE



Step 1: Extra-oral examination

Palpate the face and neck to exclude lymphadenopathy and lesions.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of extra-oral examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology in extra-oral examination?

Very confident Confident Unsure Very Unsure



Step 2: Lip Examination

Note colour, texture and surface changes and changes at vermilion borders.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of lip examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology in lip examination?

Very confident Confident Unsure Very Unsure



Step 3: Labial Mucosa Examination

Note colour, texture and any swelling or other abnormalities in vestibular mucosa and gingiva.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of labial mucosa examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the labial mucosa?

Very confident Confident Unsure Very Unsure



Step 4: Buccal Mucosa Examination

Using dental/ENT mirrors examine with bright white light the right and left buccal mucosa from anterior labial commissure back to tonsillar pillar.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of buccal mucosa examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the buccal mucosa?

Very confident Confident Unsure Very Unsure



Step 5: Gingival Examination

As in step 4, look around the oral cavity with dental mirror and bright white light to examine the buccal and lingual gingiva.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of gingival examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the gingiva?

Very confident Confident Unsure Very Unsure



Step 6: Tongue Examination

Assess colour, texture, mobility and positioning. Grasp tip with gauze and assist full protrusion. Assess posterior and lateral borders with mirror while retracting cheek. Palpate the dorsum and lateral borders for hard tissue development.

Do you perform this step in your routine? YES or NO

How confident are you with your technique of tongue examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the tongue?

Very confident Confident Unsure Very Unsure



Step 7: Ventral Tongue and Floor of Mouth

Ask patient to lift tongue. Use gauze to dry floor of mouth and assess the ventral tongue and floor of mouth tissue for pathological changes.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of floor of mouth examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the floor of mouth?

Very confident Confident Unsure Very Unsure



Step 8: Palate and Oro-pharynx

Use dental mirror to depress the tongue and bright white light to examine hard and soft palate and then patients says "Ahh" to view oro-pharynx.

Do you perform this step in your routine?

YES or NO

How confident are you with your technique of tongue examination?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology of the tongue?

Very confident Confident Unsure Very Unsure



Step 9: Bimanual palpation of Floor of Mouth

Place one finger in floor of mouth and other hand under chin to palpate for abnormality between fingers. Palpate any other pathology noticed on examination.

Do you perform this step in your routine? YES or NO

How confident are you with your technique of bimanual palpation?

Very confident Confident Unsure Very Unsure

How confident are you with identifying pathology using this method of palpation?

Very confident Confident Unsure Very Unsure

Now that you are aware of all the steps, has anyone ever performed an opportunistic oral cancer screening examination on you? (This could be a general medical or a dental practitioner)

YES or NO

Where would you refer a patient if you suspected a pre-malignant oral lesion?

Plastic Surgeon ENT Surgeon Oral and Maxillofacial Surgeon Dentist

Oral Medicine/Oral Pathologist Other Specialist (please specify):.....

I would observe and manage myself

Where would you refer a patient if you suspected an oral cancer?

Plastic Surgeon ENT Surgeon Oral and Maxillofacial Surgeon Dentist

Oral Medicine/Oral Pathologist Other Specialist (please specify):.....

I would observe and manage myself

In Australia do you think a patient should go to a general medical practitioner (Doctor) or a general dental practitioner (Dentist) if he/she has an oral lesion?

DOCTOR or DENTIST

Overall do you feel you have sufficient knowledge concerning prevention of oral cancer?

YES or NO

Overall do you feel you have sufficient knowledge to detect a pre-malignant lesion or an early asymptomatic oral cancer?

YES or NO

Overall do you feel you received sufficient training through medical school to identify high-risk groups and perform thorough opportunistic oral cancer screening examinations?

YES or NO

This section will be detached from your survey so as to de-identify your responses and maintain your privacy. However prior to this occurring the principal investigator, Dr John Webster may need to contact you to clarify responses so please provide your contact details below if you consent to being contacted for clarification purposes.

NAME: _____ PHONE: _____

ADDRESS: _____

EMAIL ADDRESS: _____