EXPERIENCES FROM DETECTION TO DIAGNOSIS; LESSONS LEARNED FROM PATIENTS WITH HIGH-RISK ORAL LESIONS

by

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ABSTRACT

Oral cancer is the 6th most common cancer in the world, with a poor prognosis and frequent late-stage diagnosis, which significantly impacts survival and quality of life. The key to better control of this disease is early detection, preferably at a precancerous stage. In order to facilitate this early detection and diagnosis, it is critical to identify the factors potentially impacting on the time lag from initial detection to diagnostic biopsy.

The overall goal is to develop effective strategies for early identification of oral cancers in order to achieve better control over this disease. There are 2 components in this thesis: the objectives of part I (personal interview) were 1) to develop an interview-style questionnaire, 2) to collect data from patients with high-risk oral lesions (HRL’s) and 3) to characterize the experiences of these individuals that may have impacted the time interval leading up to diagnosis. The objectives of Part II (focus group discussion) were 1) to gather feedback regarding the questionnaire developed in Part I, 2) to obtain recommendations for future planning and delivery of province-wide questionnaire and 3) as a group, to share information on patients’ experiences to diagnosis and patients’ perspectives on their interactions with health professionals (HP’s) throughout this journey.

An interview-style questionnaire was developed to collect both qualitative and quantitative data on patients’ experiences. Forty patients with HRL’s diagnosed within 12 months were recruited and interviewed in the Dysplasia Clinic of the BC Oral Cancer Prevention Program. Two focus groups were conducted and feedback from participants regarding the questionnaire and patients’ experiences was recorded.
Among 40 patients interviewed, 21 (53%) initially self-identified their lesions (SIG) and 19 (47%) were identified by health professional screening (PSG; 84% by dental professionals). The SIG showed higher rates of invasive SCC at diagnosis as compared to those in the PSG (76% vs. 32%, $P = 0.01$) and SIG took twice as long to have the initial biopsy performed as the PSG (23 ± 52 vs. 11 ± 28 months). Notably, the main symptom of patients in SIG was pain or presence of non-healing ulcers (18/21; 86%). In contrast, all lesions in PSG were asymptomatic.

The mean time from detection to diagnosis was 17.5 ± 42.3 months (range: 0-240 months). Fourteen patients (35%) experienced a time lag of greater than 6 months from first detection of an oral lesion until the first diagnostic biopsy was performed. Both patient and professional factors impact on the time lag. The main contributing factors for this time lag include both patient factors (a lack of concern, fear, and a lack of oral cancer awareness) and the professional factors (lack of knowledge in differentiating high-risk lesions, delay in initiating the referral or ‘watch and wait’, and delay in scheduling of referral appointments to the specialists).

Focus group results supported the format and content of the questionnaire, provided input in designing of future province-wide survey and emphasized that patients require continued post-diagnostic and treatment care. A general lack of awareness of oral cancer in general population and in HP’s in addition to a lack of screening activities have been brought forward as critical factors that result in delay to diagnosis.

In conclusion, these results suggest HP’s, especially dental professionals, can play a critical role in early identification of HRL’s at an asymptomatic, pre-invasive stage
through regular screening. Strategies in raising awareness of oral cancer in both the general population and among HP’s are essential for early identification of oral cancers in order to achieve better control over this disease.
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LIST OF ABBREVIATIONS

BCCA: British Columbia Cancer Agency
BCCRC: BC Cancer Research Centre
BCOCPP: BC Oral Cancer Prevention Program
CIS: Carcinoma in situ
DDS: Dental surgeon
DMD: Doctor of dental medicine
DTD: Detection to diagnosis
ENT: Ear, nose and throat specialist
FV: Fluorescence visualization
FVL: Fluorescence visualization loss
FVR: Fluorescence visualization retained
GP: General practitioner
GDP: General practice dentist
GVHD: Graft versus host disease
HGL: High grade lesion
HIV: Human Immunodeficiency virus
HP: Health Professional
HPV: Human papilloma virus
HRL: High risk lesion
IG: Invasive lesion group
LOH: Loss of heterozygosity
MD: Medical doctor
NIG: Non-invasive lesion group
OLP: Oral lichen planus
OPL: Oral premalignant lesion
PPV: Positive predictive value
PSG: Professionally-screened group
RDH: Registered dental hygienist
SD: Standard Deviation
SCC: Squamous cell carcinoma
SIG: Self-identified group
SOM: Second oral malignancy
TB: Toluidine blue
TMD: Temperomandibular disorder
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1. INTRODUCTION

Cancer has become one of the most incipient and destructive diseases in the history of humanity. According to the World Health Organization (WHO), cancer cases are expected to increase by 50%, marking 15 million new cases worldwide by 2020 (World Cancer Report, 2003). As such, the cancer burden experienced by populations in both Canada and internationally continues to catalyze efforts in research, treatment and prevention.

Oral cancer has been identified as the 8th most common cancer worldwide, and the 9th most common in Canada (Parkin et al., 2005). This devastating disease claims the lives of about 1,150 Canadians every year while about 3,400 new cases were discovered in 2008 alone (Canadian Cancer Society, 2008). When diagnosis is delayed, tumour size and staging have been shown to be more advanced, limiting the potential for successful treatment and thus increasing morbidity and mortality. Most commonly a squamous cell carcinoma, oral cancer is understood to develop initially as an oral premalignant lesion (OLP) which may advance further to become a malignancy (Rosin et al., 2000). This process of transformation from OLP to malignant lesion may take many years which provides an opportunity through conscientious screening to ensure timely detection and successful treatment of this disease.

The following sections will review the risk factors, challenges in early detection and diagnosis, value of oral cancer screening and current knowledge regarding the factors impacting the time from initial detection to first diagnostic biopsy. At the end of
this section, I will also briefly review qualitative research with a focus on personal interview and focus group methodology that was used in this thesis.

1.1 Oral Cancer- Epidemiology

Global incidence trends have shown concerning increases in incidence and mortality rates for oral cancer (WHO, 2005). For cancers of the oral cavity and oropharynx combined, the worldwide incidence is approximately 310,000 new cases per year, with 220,000 in men (5% of all cancers) and 90,000 in women (2% of all cancers) (Franceschi et al., 2000). The incidence of oral cancer in South-Central Asia remains the highest in the world, ranking it among the three most common forms of the disease. In India, the age standardized incidence rate of oral cancer is 12.6 per 100,000 individuals as compared to 1-10 per 100,000 in many other countries (Petersen 2005). Several other more developed countries have recently seen a marked increase in the incidence of oral cancers including Germany, Denmark, Scotland, France, and areas of Central and Eastern Europe. In countries such as the United States, nearly 30,000 new cases of oral cancer are diagnosed each year, indicating a continued concern for the incidence of this disease even in highly developed regions (Patton et al., 2005). In the UK, over 2,500 cases of oral cancer are identified annually and it is estimated that 50% will die of this disease each year (Warnakulasuriya et al., 1999).

Gender and ethnicity have also been found to be important factors impacting on oral cancer incidence and mortality. In the US, men have an age standardized incidence rate (ASIR) of 15.5 per 100,000 men and women have an ASIR of 6.1 per
100,000 women (SEER National Cancer Stats 2001-2005). Blacks in America show a
higher incidence of oral cancer (17.2) than Caucasians (15.7) for men with mortality
rates of 6.7/100,000 for blacks and 3.8/100,000 for Caucasians. Asians, American
Natives and Hispanics all express a notably lower incidence and mortality rates for both
men and women than their Caucasian or Black counterparts (SEER National Cancer
Stats 2001-2005).

Five-year relative survival rates for oral cancer have been reported by age and
gender in the US from 1994-2004. The five-year survival rates for an oral cancer
diagnosis are 61% for Caucasian men, 62.9% for Caucasian women, 36.1% for black
men and 52.1% for black women (SEER National Cancer Stats 2001-2005). Staging
upon diagnosis has been linked to survival rates and outcome with 33% of oral cancers
being diagnosed in a localized stage, 51% are diagnosed with lymph node involvement
and 10% are diagnosed after distant metastasis has occurred. The corresponding 5-
year relative survival rates for these diagnoses are: 82% for localized, 52.7% for
regional (lymph node involvement) and a meager 28.7% for distant metastases (SEER
National Cancer Stats 2001-2005). This strongly underscores the importance of early
detection and diagnosis of this disease to improve prognosis and survival rates.

As of 2005, oral cancer prevalence in the American population equaled
approximately 240,176 individuals who had a history of an oral cancer diagnosis and
continued to live with the disease. This included 154,159 men and 86,017 women who
either had been cured by the disease or were still being treated and monitored (SEER
National Cancer Stats 2001-2005). There are no comparable statistics by ethnicity and staging in Canada.

Based on the reported incidence, mortality and meager 5-year survival rate of oral cancers worldwide, there is a vivid demand for the early detection and preventative efforts of professionals and general populations alike.

1.2 Risk Factors

It has been determined that most oral SCC’s develop over time as the result of chronic exposure to various carcinogens. As a result, most individuals who develop oral SCC are over the age of 50 given this often prolonged development period. The following is an overview of the risk factors associated with oral cancer etiology.

1.2.1 Chronic Consumption of Tobacco and Alcohol

Chronic consumption of tobacco and alcohol are the trademarks of the foremost high-risk population for oral cancer with tobacco use and excessive drinking responsible for 75% of all oral cancer cases in the Western world (Mashberg et al., 1993). Based on research of the cancer-related effects of both these products, alcohol and tobacco each reveal a dose-related response to the development of cancer. Strong evidence from various case control and cohort studies support this association (Silverman and Gorsky 1990; Kato et al., 1992). Smokers who are also heavy drinkers have been found to be 6-15 times more likely to develop oral SCC than non-smokers and non-drinkers according to van der Waal et al. (van der Waal et al., 1997). Results from a large
population study in Sweden indicated that both smoking tobacco and alcohol consumption are risk factors for oral and oropharyngeal SCC (Rosenquist 2005). More than 350 ml of alcohol per week (OR 2.6; 95% CI 1.3-5.4) and 11-20 cigarettes per day (OR 2.4; 95% CI 1.3-4.1) were dose-dependent risk factors. Interestingly, the results also showed a tendency for women to have a greater risk (OR 1.8) than men at any given level of tobacco consumption.

1.2.1.1 Impact of Tobacco on Oral Cancer

The WHO recently published a document entitled ‘WHO Report on the Global Tobacco Epidemic, 2008’ in which some grave new facts on tobacco were released. According to this document, tobacco kills a third to half of all people who use it, 15 years prematurely on average (World Health Organization 2008). Currently, tobacco use causes 1 in 10 deaths worldwide which equates to more than 5 million people a year. If current trends continue, it is estimated that approximately 500 million people alive today will be killed by tobacco. This product is clearly not only a risk factor to many cancers, but to a whole host of illness and complications which lead to premature death.

According to the World Health Organization, tobacco use is growing most rapidly in low income countries due to the dramatic population increase combined with the intensive targeting of these populations by the tobacco industry. By 2030, it is estimated that more than 80% of the world’s tobacco-related deaths will be in low and middle-income regions (WHO, 2008). In China, where tobacco use is currently increasing, as many as 100 million young Chinese men (under age 30) will die from tobacco use. In India, approximately 25% of deaths of middle-aged men are the result of smoking.
Today, current tobacco use in European countries is declining among men but is increasing in women, especially in Eastern Southern and Central regions of the continent. Similar trends are found in Canada. In the developing world, tobacco rates remain lower overall for women than for men however the trend is increasing among teenage girls. In South-East Asia, the smoking incidence for males is reported to be ten times higher than for females; however, among teenagers (13-15 years of age), the male smoking rate is only two and a half times greater (WHO, 2008).

Smoking remains the most important risk factor for oral cancer. The risk of developing oral cancer increases with the concentration and frequency of tobacco use. Oral cancer patients who continue to smoke despite their diagnosis are at a high risk of developing second primary malignancies (Reichart 2001).

The 2008 WHO report states that “smoked tobacco in any form causes up to 90% of all lung cancers and is a significant risk factor for strokes and fatal heart attacks.” Smoking more than 20 cigarettes per day has been associated with an elevated oral cancer risk (Jaber et al., 1999). A heavy smoker is considered to be one who smokes 20-40 cigarettes per day.

Although cigarettes are the most common form of tobacco use in the developed world, various other types of smoked tobacco can be found which include bidis, small hand-rolled cigarettes preferred by South East Asian populations. These products produce three times more carbon monoxide and 5-fold more tar than conventional
cigarettes. As a result, bidi smokers have a threefold higher risk of oral cancer as compared to non-smokers (WHO, 2008).

The risk of tobacco use is not limited to the primary malignant event. Research indicates that the risk of developing a second oral malignancy (SOM) is related to the duration and amount of tobacco smoked. As previously mentioned, oral cancer patients who do not quit smoking or drinking are at an increased risk of developing a SOM (Silverman and Gorsky 1990). In a study that examined the smoking and drinking habits of individuals who developed a secondary cancer of the upper aerodigestive tract, the length of time since the patient quit smoking was inversely proportionate to the risk of the second malignancy (Day et al., 1994). Carstensen et al. examined a cohort of 25,000 Swedish men and determined a recurrence rate of 1.3/100,000 in former smokers as compared to non-smokers (death rate of 4.3/100,000 person years). In current smokers the recurrence rate was 1.1 for 1–7 g/day of tobacco, 2.5 for 8–15 g/day and 5.4 for >15 g/day (Carstensen et al., 1987). The amount of tobacco smoked was expressed in quantities smoked (number of cigarettes, cigars, etc.). The units of grams-of-tobacco-smoked-per-day were based on one cigarette as equivalent to 1g of tobacco, small cigars as 3g and large cigars as 5g.

The ingredients of tobacco products form a list of toxic and carcinogenic substances. Of the 4000 ingredients in cigarettes, hundreds are toxic and potentially lethal. Of the most concerning, polycyclic hydrocarbons such as benzo(a)pyrene (a known carcinogen) are absorbed by the mucosal tissues due to an increased
permeability associated with the presence of nicotine. Other additives such as tar and formaldehyde compound the toxicity and carcinogenicity of tobacco products.

The geographic sites of oral cancer vary with the form of tobacco and how it is used. Generally, oral cancer in the US is associated with the floor of mouth and lateral borders of the tongue whereas in India, the buccal mucosa is the most common site for SCC due to the widespread use of smokeless tobacco (Silverman 2001).

In the collection of smokeless tobacco, a wide range of forms are available. The most common forms are known as ‘snuff’ or chewing tobacco. Snuff can be found in dry leaf form, in sachets or in moist form. Dry snuff is typically inhaled through the nose whereas moist forms of chewing tobacco are generally places inside the oral cavity, along the muco-buccal folds or between the buccal mucosa and attached gingiva. Lesions associated with the use of chewing tobacco can be found in the region which the tobacco has most often been placed. The clinical appearance of the lesion is white, thickened and wrinkled. N-nitrosamines are the main carcinogenic component of smokeless tobacco (Scully 1995). In a cohort study of 7,830 youth aged (11 - 19 years old), it was shown that approximately 824,000 young people in the USA experiment with smokeless tobacco of which 304,000 become regular users (Tomar and Giovino 1998). This increase in the use of smokeless tobacco has led to an increase in OPLs and oral malignancies in American youth (Lippman and Hong 1989).

The primary cause of the high incidence of oral cancer in South Asia is the widespread habit of chewing betel nut or paan and related areca nut use. Betel quid, or
paan chewing dates back some 2000 years and is an activity that has become steeped in tradition. It is estimated that 200-400 million people worldwide practice the habit of chewing betel nut which has resulted in the highest incidence of oral cancer in areas such as South Asia (Gupta and Warnakulasuriya 2002). The main components of betel quid may vary by region but generally include the leaf of the vine Piper betel, areca nut, slaked lime (calcium hydroxide) and spices to flavor (Warnakulasuriya et al., 2002). The areca nut is carcinogenic to humans and the risk of oral cancer increase with duration and frequency of use.

1.2.1.2 Impact of Alcohol on Oral Cancer

Second only to smoking, alcohol is considered the next most serious risk factor for oral cancer with 75-80% of oral cancer patients reporting frequent alcohol consumption (Rodriguez et al., 2004). In Europe, increasing trends in alcohol consumption have been linked to a similar increase in oral cancer incidence and mortality, according to a Denmark study (Moller 1989). In France, a reduction in alcohol consumption has been linked to a decrease in oral cancer incidence, further emphasizing the correlation between alcohol intake and oral cancer (Blot et al., 1994)

Two types of research link alcohol and cancer. Epidemiologic research indicates that a dose-dependent relationship exists between alcohol and cancer. More rigorous results have come from research that investigates the mechanism by which alcohol may contribute to cancer development. The strongest epidemiological link between cancer and alcohol implicates cancers of the upper digestive tract, including esophagus, mouth,
larynx and the pharynx (IARC 1989). Individuals who chronically consume excessive amounts of alcohol over time have an increased risk of cancer as compared to non-drinkers (Talamini et al., 1990). Epidemiologic data however provides very little insight into the mechanisms of how alcohol is implicated in carcinogenesis.

Alcohol is believed to be an independent risk factor of oral cancer. It has been suggested that acetylaldehyde, which is a product of the metabolism of alcohol, may impair a cell’s natural ability to repair its DNA, resulting in a greater likelihood to initiating the mutation process (Espina et al., 1988). It has been suggested that prolonged alcohol exposure may lead to overexpression of certain oncogenes in human cells and thereby trigger cancer promotion (Kharbanda et al., 1993). Evidence also suggests that alcohol may act as a co-carcinogen when paired with tobacco-related carcinogens (Garro and Lieber 1990) as the risk for oral cancer is 35 time greater for those who smoke and drink than those who abstain from both (Blot et al., 1988). It is thought that alcohol may also act as a solvent enhancing the penetration of oral epithelium by organic carcinogens such as tobacco smoke (Silverman and Sugerman 2000). Additionally, alcohol may induce the induction of microsomal enzymes that catalyze the activation of carcinogens in tobacco products.

There has been some debate over which form of alcohol poses the greatest threat of oral cancer. Some studies have implicated beer and hard liquor as having more carcinogenic risk over wine (Merletti et al., 1989) and in one study, whiskey was found to have a threefold greater risk when consumed excessively than wine (Keller 1981). Conversely, Mashberg et al. implicated wine and beer over whiskey in terms of
oral cancer risk (Mashberg et al., 1981). From another perspective, it had been suggested that it is not the type of alcohol (wine, beer or hard liquor) but rather the amount of ethanol that imposes the risk factor (Boyle et al., 2003). As for the amount of alcohol that poses a threat that 56 glasses of wine per week or more constituted an elevated risk (Ng et al., 1993).

The various forms of alcohol available have been found to have differing concentration equivalents which can be used for standardization. For example, 1 oz of distilled spirit, 4 oz of dry wine and 12 oz of beer are considered equivalent. The reported relative risk for developing oral cancer from consumption of alcoholic beverages alone is calculated at 2.7 for 2 whiskey equivalents per day, increasing to a range of 4.1-15.2 for seven or more equivalents per day (Mashberg et al. 1981). Blot et al. presented relative risk for oral cancer as based on strictly the number of drinks per day; more than 4.3 drinks per day (30 drinks per week) translates to a relative risk of 6.0-12.3 which varies by age and gender (Blot et al. 1988).

Despite the strong evidence that is available to support the link between alcohol and oral cancer, it is still difficult to rule out other associated risk factors. Since drinkers tend to also use tobacco products, it is difficult to identify alcohol as a single independent variable. Also, heavy drinkers tend to have poor dietary habits. As such, their deficient nutritional status may also be a confounding contributory risk factor. To further complicate matters, alcohol consumption is difficult to accurately measure as drinkers tend to underreport their consumption.
While it may be difficult to measure the distinct amount and forms of alcohol that may lead to an increased risk of oral cancer, it is reasonable to conclude that based on the extensive research linking alcohol and oral cancer, any elevated consumption may lead to elevated risk.

1.2.1.3 Synergism of Tobacco and Alcohol

The combined use of these two known carcinogens not only impacts the risk of oral cancer but does so synergistically. The use of both alcohol and tobacco has been shown to result in odds ratios (ORs) for developing oral cancer of up to 38 for men and 100 for women (Blot et al. 1988). When considering the risk of smoking alone, the risk of oral cancer is two- to four-times greater for smokers who do not drink than for non-smokers and non-drinkers. For smokers who also drink however, the risk is 6-15 times greater than for abstaining non-smokers (van der Waal et al. 1997). The mechanism by which alcohol and tobacco act synergistically is thought to be that the combined use of nicotine and alcohol significantly increases the penetration of the nitrosamines into the oral tissue with the alcohol acting as the solvent (Du et al., 2000).

1.2.2 Other Risk Factors of Oral Cancer

Although smoking and alcohol are widely understood to be primary risk factors of oral cancer, many other factors have been found to play a role in the development of this disease. Conditions that impact the systemic health such as infections, immunosuppression and nutrition factors have been determined to provide an opportunity for the development of OPLs and oral cancers.
1.2.2.1 Infections Associated with Oral Cancer

The impact of infections including *Candida albicans* and Human Papillomavirus (HPV) will be described below in terms of their impact on oral cancer.

1.2.2.1.1 Candida Albicans

*C. albicans* has been found to be present in a high percentage of leukoplakias with morphological signs associated with malignant transformation. It may be that the increased incidence of malignancy in these lesions is due to the fact that these lesions merely provide a fertile ground, thus *Candida* may be just a passenger as opposed to acting on its own (Gerson 1990). Of interest, *Candida* has been found to generate nitrosamines, a carcinogen, although the association between this activity and oral cancer has not been demonstrated (Silverman and Sugerman 2000).

1.2.2.1.2 Human Papilloma Virus (HPV)

HPV is a large family of viruses which have been found to be associated with oral squamous cell carcinoma, cervical cancer and malignancies of other mucosal surfaces. The association between HPV and various malignancies has catalyzed further investigations in this area. HPV infections, specifically HPV-16, are believed to be involved in the carcinogenesis of anogenital epithelial cancers and are also suspected of causing oral cancers (Mork et al., 2001).

HPV-16 and HPV-18 have most commonly been associated with cervical malignant transformation (zur Hausen 1991) as well as with oral malignancies. In 22% of oral cancers, oncogenic HPV has been identified either independently or in
combination with other types of risk factors (Sugerman and Shillitoe 1997). The genotypes most often found in oral carcinoma are HPV-16 and HPV-18 (Palefsky et al., 1995). However, HPV-18 is present in up to 14% of oral cancer cases, while HPV types 16 and 18 are present together in approximately 6% of cases. This suggests that HPV infection may be a co-factor in oral carcinogenesis and that latent HPV infection of the oral mucosa is common (Sugerman and Shillitoe 1997).

There are more than 100 variations of the HPV virus that have been isolated from both benign and cancerous lesions. HPV is expressed in various benign forms including warts, condylomas, and papillomas involving a number of different organs (Silverman and Miller 2003). The most commonly identified strains identified in OPLs and oral malignancies are HPV 16, 18 and 33 which are not found in normal mucosa (Bouda et al., 2000). These results were supported in another study that showed that the odds ratio for squamous cell carcinoma of the head and neck in patients that were seropositive for HPV-16 was 2.2 (95% confidence interval, 1.4 to 3.4). No increased risk was observed for other HPV types in oral cancers. In a study by Herrero et al. in 2003, HPV DNA was found in 18.3% of patients with cancer of the oropharynx and in 3.9% of patients with oral cancers. Ninety-five percent of HPV-positive patients in this study were found to have the variant HPV-16 which is also the most common type in genital cancers (Herrero et al., 2003). Interestingly, HPV DNA was found statistically significantly less often in tobacco users than non-users.

Sugerman et al. suggests that there are several feasible links between oral SCC and HPV. Oral keratinocytes which become infected with either HPV-16 or HPV-18 may deactivate the tumor suppressor proteins by viral oncoproteins, block tumor suppressor
gene transcription as a result of HPV oncogene insertion or stimulate cellular oncogene transcription (Sugerman and Shillitoe 1997). As these theories remain conceptual, further investigation is needed to determine the exact mechanism of carcinogenesis associated with oral infections such as HPV.

1.2.2.2 Immunocompromised Conditions

With an increasing number of transplants being performed to replace dysfunctional organs or to treat leukemia/lymphoma, a large number of patients exist in a state of induced immunosuppression. This repression of the immune system prevents the recipient’s immune system from rejecting the transplanted organ. When a bone marrow transplant is performed, there is a risk of the patient developing a condition known as graft-versus-host disease (GVHD). GVHD is a common complication of allogeneic bone marrow transplantation in which functional immune cells in the transplanted marrow recognize the recipient as “foreign” and mount an immunologic attack. Patients who develop GVHD have been shown to have an increased risk for developing oral cancer (Otsubo et al., 1997). These patients must be closely monitored (Zhang et al., 2002) as immunosuppression after organ transplantation has been shown to be correlated with a higher incidence of subsequent cancer development, particularly of the lower lip (de Visscher et al., 1997).

Another common form of immunocompromised condition is the patients infected by Human Immunodeficiency Virus (HIV). These patients increase every year, so do the numbers of immunocompromised individuals. It has been noted that patients with immunodeficiency acquired by medication are more likely to be diagnosed with lip
cancer but no relationship has been determined with an increase in oral cancer (Scully 1983). It has been reported that young adult males with AIDS or AIDS-related complex and who are therefore immune deficient, have a higher rate of oral cancer than controls in the same age range (Silverman, 1986). However, more recent studies have shown that oral squamous cell carcinoma in patients with HIV-infection or AIDS is generally rare (Langford, 1995).

1.2.2.3 Diet

The consumption of fresh fruits and vegetables has become widely accepted as a strong cancer preventative. Without the essentially nutrients provided by this food group, the body can quickly become malnourished. A poor diet has been identified as the third most important risk factor for oral cancer (Rodriguez et al. 2004). Beta carotene and Vitamins A, C and E all have been shown to be effective cancer preventive components of a healthy diet. These three vitamins are effective in depleting damaged cells of free radicals and thus are effective in helping to prevent cancer. Patients who ingest high concentrations of Vitamin C and fiber have been shown to have half the risk of oral cancer as compared to those who ingested the least of these (Garewal 1994). The relationship between Vitamin A and C consumption and a reduced risk for oral cancer is further supported in a study by Marshall et al. (Marshall et al., 1982) and later by this same group, the high intake of Vitamin C, fruits, vegetables and fibres was associated with reduced risk of cancer in the upper aerodigestive tract (Marshall et al., 1992).
Another nutrient which has been found to pose a risk for oral cancer is a deficiency of iron. Through their work, Binnie et al. proposed that the condition of iron deficiency may lead to a thinning of the oral epithelium, thereby increasing the potential for uptake of carcinogens through this membrane (Binnie et al., 1983). They also proposed that the lack of iron may lead to a higher turnover of epithelial cells, increasing the opportunity for carcinogens to alter DNA, or lastly, an impairment of the immune system related to low levels of iron.

Some research has also pointed to a deficiency in zinc and copper posing an increased risk for oral cancer (Varghese et al., 1987).

1.2.2.4 Lichen Planus

Oral lichen planus (OLP) is a chronic inflammatory disease of unknown etiology, found in 1-1.2% of the general population (Pindborg et al., 1972; Scully et al., 1985). This common dermatological disorder is most often associated with the oral soft tissues (Mattsson et al., 2002). Clinically, OLP may present in many forms including plaque-like, erosive and reticular variations. This condition is more commonly identified in women than in men and can be distinguished from other oral pathologies by its white striated appearance or papules. The consensus is that biopsy must be performed to rule out other conditions such as oral cancer especially when lesions occur at high-risk sites such as the lateral borders of the tongue and the floor of mouth (Silverman and Miller 2003).
The potential for malignant transformation remains of primary concern when identifying and diagnosing OLP. Researchers have followed the malignant transformation rates over time and have determined that OLP may transform to a malignancy 0-9% of the time (Mattsson et al. 2002). The WHO considers OLP to be a premalignant condition (1978). There remains extensive debate as to whether OLP is truly a premalignancy or more often misdiagnosed as a dysplastic lesion with lichenoid features (Krutchkoff and Eisenberg 1986). As such, patients with lichenoid dysplasia may demand independent consideration and suitable diagnostic methods as compared to those with OLP showing no elevated risk of malignant transformation (Mattsson et al. 2002). It has been suggested that the presence of any degree of dysplasia should not be overlooked due to an associated presence of OLPs (Zhang et al. 2000).

It has often proven difficult to distinguish and manage oral lichen planus without dysplasia and oral dysplasias with lichenoid presentations. This challenge may also lead to underreporting of OLPs with malignant transformations. To complicate matters, some lichenoid lesions may be due to lichenoid contact reactions from the components of amalgam fillings or lichenoid drug reaction from medications. These lesions are difficult to distinguish from OLP histologically and have no known risk of malignant transformation therefore their inclusion in statistic may reduce the reported transformation rate of OLP (Bolewska et al., 1990; Bratel et al., 1996).

In order to most effectively manage these conditions and ensure early detection of dysplasia, it is recommended that patients with OLP should be monitored closely and should be re-evaluated 2-4 times annually (Scully et al., 1998).
1.2.2.5 Poor Dental Health

Originally, poor oral health, improperly fitting dentures, defective restorations and misaligned teeth were not associated with any increased risk of oral cancer (Silverman et al., 1984; Silverman and Gorsky 1990). More contemporary research however, has begun to identify a correlation between the inflammation associated with poor oral hygiene and an increased risk of oral cancer (Sudbo et al., 2001; Lissowska et al., 2003). There have been no studies indicating a correlation between removable prostheses (dentures) and an increased risk of oral cancer. More research is need in this area as dentures often cause inflammation and irritation that may be masking premalignant features.

1.2.3 Genetic Implications of Oral Cancer

The development of human oral cancer has been associated with certain proteins known as ‘oncogenes,’ which may become activated and trigger malignant cell growth. Since oncogenes regulate cell cycle growth and differentiation, they are responsible for uncontrolled cell growth when a change to oncogene occurs. In such a case, the proto-oncogene is altered by a mutagen and becomes an oncogene. Tumor suppressor genes also play a role in carcinogenesis. When a tumor suppressor gene is altered by a carcinogen, loss or mutation of this gene occurs, resulting in changes to cell proliferation and increased malignancy. The mutation of the p53 tumor suppressor gene, for example, has been determined to be one of the most common mutations leading to human cancers (Greenblatt et al., 1994).
When genetic material is lost in one pair of chromosomes, it is referred to as a loss of heterozygosity (LOH). When LOH occurs on portions of the chromosome which contain the tumor suppressor genes, it is suspected that malignant process is catalyzed (Renan 1993). LOH in the 3p and 9p regions of the chromosome arms has been related to an increased malignant potential of Oral Premalignant Lesions (OPL)s (Califano et al., 1996). Rosin et al. also determined additional sites to 3p and 9p where LOH implicated elevated risk of malignant transformation (Rosin et al. 2000). Genetic research has found that mutations or allelic loss occur in over 70% of head and neck tumors; this was also found to be true for pre-invasive lesions (Nawroz et al., 1994). A loss of genetic information on chromosome 9p is an early event in head and neck squamous cell carcinogenesis. Those lesions with LOH limited to 3p and 9p showed a 3.8-fold increased risk, while those with loss at any of the chromosomes 4q, 8p, 11q, 13q, and 17p in addition to loss at 3p and 9p had a 33-fold increased risk for progression to cancer compared with lesions that retained those arms (Rosin et al., 2000).

Research continues to explore how oncogenes and tumor suppressor genes fit into the multi-step carcinogenetic process for oral cancer and to determine their role as prognostic factors for disease-free or overall survival. The use of molecular biologic markers for predicting malignant transformation of OPLs have shown great potential for application as a future diagnostic tool.
1.3 Oral Premalignant Lesions (OPL’s) and Associated Challenges

Oral premalignant lesions include a number of histological precursors to squamous cell carcinoma (SCC) and are most often detected clinically by the presence of a “white patch” referred to as leukoplakia or a “red patch” referred to as erythroplakia (Sullivan 1978). The malignant potential of these lesions is primarily determined by the presence and degree of dysplasia histologically. In this section, I will discuss the current challenges in risk assessment of these lesions.

1.3.1 Leukoplakia

Leukoplakia by definition is a “white patch or plaque that does not rub off and cannot be characterized clinically or pathologically as any other disease, and has increased cancer risk” (Sullivan 1978). Although it is quite common to clinically identify white patches intraorally, those of a potentially invasive nature must not be confused with benign entities such as hyperkeratosis. As such, a histopathological assessment of the nature of the leukoplakia is considered the ‘gold standard’ for discerning between harmless lesions resulting from trauma or occlusion and more concerning progressive malignancies. Prevalence rates of oral leukoplakia vary from 0.1% to 10.6% depending on the anatomical site (Petersen 2003).

1.3.2 Erythroplakia

Oral erythroplakia is the clinical term for a chronic red mucosal lesion which cannot be given any other specific diagnostic name and cannot be attributed to
traumatic, inflammatory or infectious causes. Erythroplakia is much less common than leukoplakia with an incidence of less than 1% (Petersen 2003). Although these types of lesions tend to be more concerning, there is still little evidence to show how readily they will undergo malignant transformation (Sudbo and Reith 2003). Therefore, there remains a need for further predictive tools for clinicians to assess which lesions are more likely to progress to malignancy.

**1.3.3 Assessment of Risk of Oral Cancer Lesions**

In order to determine the risk of an OPL advancing to malignancy, both clinical and histological assessments must be made.

**1.3.3.1 Clinical Risk Assessment**

The location of the lesion in the oral cavity has been shown to be a strong predictor of risk for oral cancer. The clinical areas of the oral cavity at the greatest risk for developing oral cancer include the lateral/ventral borders of the tongue, the floor of the mouth and the soft palate. The most common sites among these high risk areas are the lateral and ventral borders of the tongue expressed in 2.5 cases per 100,000 (Shiboski et al., 2000).

Additionally, lesions are large in size and non-homogenous in appearance are predominantly higher risk for dysplasia and progression to cancer. A previous history and family history of cancer also contribute to this risk profile. Once the clinical risk has
been established, a biopsy is conducted to determine the presence and the degree of dysplasia.

**1.3.3.2 Histological Risk Assessment**

Known as the “Gold Standard” of assessment, histological evaluation of an oral lesion involves taking a small portion of the lesion (a biopsy), which is then examined under a microscope to determine the presence and extent of dysplasia involved. The World Health Organization (Pinholt *et al.*, 1997) has established the following characteristics as dysplasia: 1) loss of polarity of the basal cells, 2) the presence of more than one layer having a basaloid appearance, 3) increased nuclear-cytoplasmic ratio, 4) drop-shaped rete ridges, 5) irregular epithelial stratification, 6) increased numbers of mitotic figures, 7) mitotic figures that are abnormal in form, 8) the presence of mitotic figures in the superficial half of the epithelium, 9) cellular and nuclear pleomorphism, 10) nuclear hyperchromatism, 11) enlarged nucleoli, 12) loss of intercellular adherence, and 13) keratinization of single cells or cell groups in the prickle cell layer.

Dysplastic lesions are further divided into mild, moderate, and severe forms depending upon how much of the tissue is dysplastic. Mild dysplasia is a lesion in which the dysplastic cells are confined to the lower one third of the epithelium. Moderate dysplasia is a lesion in which the dysplastic cells are evident in up to two-thirds of the thickness of the epithelium. Severe dysplasia is a lesion in which the dysplastic cells have filled more than two-thirds but less than the entire thickness of the epithelium. In carcinoma *in situ* (CIS), the dysplastic cells occupy the entire thickness of
the epithelium (bottom to top changes) although the basement membrane is still intact (Lumerman et al., 1995). Invasion of dysplastic cells through the basement membrane into the underlying stroma and the dissemination of these cells to other sites through the lymphoid and circulatory systems are events associated with development of invasive SCC.

Research has shown that leukoplakias which demonstrate a level of dysplasia when assessed histologically are more likely to progress to malignancy than leukoplakias with no visible dysplastic architecture. High-grade dysplasias are believed to progress more readily to invasive carcinomas and are therefore treated aggressively. Most low-grade dysplasias show little if any tendency to progress to invasive cancers when monitored over time (Wright 1999). Since many of these lesions present as a clinical leukoplakia, there is a need for more sensitive predictive tools for the risk of malignant transformation (Rosin et al. 2000).

1.3.4 Problems in Early Detection

Despite the recent advances in technology and knowledge of oral cancer screening and detection, there remain several problems in early detection of this disease. Clinically, histologically and geographically, oral cancers are often difficult to identify, locate and access which may often result in late stage diagnosis and related treatment challenges. These challenges are detailed in the following sections.
1.3.4.1 Clinical Problems in Early Detection

The oral tissues are subject to a variety of soft tissue variations such as hyperkeratosis, occlusal trauma and hyperkeratinization which may be easily confused with leukoplakias or commonly seen oral inflammatory and infectious conditions which may be confused with erythroplakias. The variation in coloration of anatomical soft tissues can also obscure lesions and pose difficulties in detection. There is a need for special training for distinguishing lesions at risk from inflammatory and infection. Furthermore, some lesions cannot be readily seen by the unaided eye (e.g. clinically occult lesions). There is therefore a need for new tools to be developed to assist in the clinical assessment of risk.

1.3.4.2 Histological Problems in Diagnosis

Challenges associates with the histological aspect of diagnosis revolve around the histological progression model of dysplasia to SCC as presented earlier. It has been noted that this model has a better predictive value for higher grade dysplasias (severe dysplasia and CIS) (Banoczy and Csiba 1976; Schepman et al., 1998). Notably, high grade dysplasias and CIS are considered at high risk for malignant progression if left untreated (Hayward and Regezi 1977) and are thus treated very aggressively. It is the histological identifier that initiates this decision for aggressive treatment. The limitation in histology lies in the fact that it is unable to differentiate between those low-grade dysplasias that will progress to cancer and those that will not. Therefore, the low-grade dysplasias that do end up as malignancy are the result of ineptitude in differentiating
lesions at risk. As such, there remains a marked need for more accurate predictors of malignant progression in low-grade dysplasias.

1.3.4.3 Access to Care Problems in Early Detection

OPLs and SCCs may be successfully detected and treated if patients seek medical or dental care in a regular or timely manner. The geographical challenge associated with detection, diagnosis and ultimately treatment is based on both the characteristics of high-risk populations and the barriers of certain geographical regions. High-risk individuals, like elderly and heavy users of tobacco and alcohol, are most likely to not ambulate to a health professional on a regular basis, thus these individuals often miss the opportunity for early detection. High-risk individuals and those in remote areas may not have the opportunity to be examined as access to medical and dental care is often a barrier.

1.4 BC Oral Cancer Prevention Program (BCOCPP)

The BC OCPP, located in Vancouver, BC, is comprised of a team of leading researchers who are paving the way for progressive worldwide research in their study of high-risk oral lesions (Rosin et al., 2008). The vision of the British Columbia Oral Cancer Prevention Program is to reduce the incidence and mortality of oral cancer through the development, validation and adoption of new techniques for early detection, risk assessment and management of premalignant and malignant oral diseases. An integrated management structure links community health professionals in a step-wise referral pathway, to ensure seamless management of the disease from early dysplasia
to frank malignancy. The initial focus is a province-wide strategy for BC with the following main objectives:

- To prevent the development of oral cancer, or to detect it at the earliest possible stage.
- To achieve a greater cancer cure rate through more clinically effective treatment.
- To improve the early detection of local and regional recurrences after treatment.

Globally, there is collective recognition that a new strategy for management of oral cancer is in great demand. The BC OCPP has been answering this call by developing universal models for transferring the BC vision to the national and international communities (www.orcanet.ca).

The BC OCCP has identified and focused on the major reasons for late diagnosis of high-risk lesions: (1) problems in the clinical differentiation of high-risk oral lesions; (2) problems in the histological diagnosis of low-grade but high-risk lesions; and (3) difficulty in accessing high-risk populations. To accommodate for these challenges, the BC OCPP has developed a number of molecular, histological and clinical tools to help the identification of the high-risk OPLs and early SCC.

1.5 Early Detection of Oral Cancer - Value of Oral Cancer Screening

Screening is the process of using various methods to detect disease in the most cost effective, least invasive and patient-friendly way possible. Screening programs should be designed in such a way as to maximize sensitivity and minimize false
positives, if possible in order to be most effective in early identification of disease. It has been recognized that early detection of oral cancer via screening programs may provide the most effective strategy for controlling this disease, especially in the high-risk communities. Early diagnosis and treatment improves quality of life of the patient by reducing the physical, functional and psychosocial disabilities attributable to the disease, and at the same time reduces the economic burden associated with the costs of treatment. Oral cancer screening programs have been implemented worldwide with varying degrees of success due to variations in design, implementation and target populations.

1.5.1 Early Detection is Key to Improving Morbidity and Mortality

It has been previously shown that in British Columbia, regular dental care is associated with early diagnosis of oral cancer and less advanced staging of the disease at biopsy (Elwood and Gallagher 1986). This data however was produced 20 years ago and requires further investigation to update and possibly redefine the relationship between dental care and early oral cancer detection.

The largest and most current evaluation of an oral cancer screening program was conducted in Kerala, India from 1996 to 2004 and included 191,873 subjects (Sankaranarayanan et al., 2005). This cluster-randomized controlled trial purposed to assess the effect of visual screening on oral cancer mortality in high-risk individuals. The study outcomes indicated a 34% reduction in mortality and a 50% increase in the 5-year survival rate of the intervention group (high-risk screened individuals).
With the meager 5-year survival rate (20%) of a late stage oral cancer diagnosis, time is valuable on every level of disease intervention; from detection to diagnosis to treatment. Even with the best possible treatment, many patients are later diagnosed with second primary tumours of the head and neck, necessitating further treatment and a more concerning prognosis. In addition, late detection requires aggressive treatments such as surgical resection, irradiation therapy and/or chemotherapy, which increase morbidity and decrease quality of life. Facial appearance may be altered; individuals may experience infections of the oral and dental structures and difficulties with eating, speaking and tasting. As a result of extensive treatment of advanced SCC the patient may suffer significant psychosocial impacts, further reducing quality of life. Early detection has been shown to be the most effective way to reduce the impact of the disease, in terms of morbidity, mortality and quality of life. Screening programs provide an essential platform for early detection and diagnosis of this disease, enabling a reduction in the physical, functional and psychosocial disabilities attributable to the disease and its treatments.

1.5.2 Oral Cancer Screening Program Design

Although various international studies have been conducted on oral cancer screening techniques, there is a distinct lack of standardization in determining which populations should be screened and which techniques should be employed. Based on the magnitudes of the studies (numbers of patient screened) and the geographic locations represented, through the PubMed search engine, a literature review of international screening programs was performed to compare and evaluate oral cancer
screening programs in the world. The intent was to obtain a selection of research that reflected a wide range of oral cancer screening programs both in size and design. The results showed individuals at high risk for oral cancer were mainly identified as smokers and excessive alcohol consumers, individuals aged over 30 years, male gender, low socio-economic status, compromised health status (HIV/AIDS etc) and a previous history of cancer (Biggar 2007). Key issues surrounding program approaches (Opportunistic versus Invitational), target populations, screening techniques employed, qualifications of examiners, compliance with referrals, biases, outcomes and limitations as well as sensitivity, specificity and positive predictive values were identified and compared among the selected screening programs. Preceding an exploration of these issues, a brief summary of six of the most prominent global oral cancer screening programs will be presented.

1.5.2.1 Summary of Oral Cancer Screening Programs in the World

In Italy, Talamini et al. conducted a screening program for oral cancer which included 627 subjects and spanned from 1991 to 1993 (Talamini et al., 1994). The main objective of the study was to quantify the relationship between the characteristics of the individuals and their compliance with a free examination by an ear, nose and throat specialist (ENT). The most significant finding of this research indicated that identifying high-risk individuals is expensive and compliance with a head and neck cancer early detection program is low, especially among smokers, females and those with no ENT symptoms.
Bouquot et al. conducted a relatively large scale oral cancer screening program in Minnesota, USA from 1957 to 1972 in which 32,000 subjects were screened (Bouquot 1986). The program was intended to enable researchers to characterize the prevalence of the most common oral lesions among this population. The 30 most common lesions, which represented more than 93% of all reported lesions, were ranked according to gender-specific prevalence rates. Leukoplakia (29.1 per 1,000) was the most common mucosal lesion and oral carcinoma (1.1 per 1,000) was 24th overall.

A screening program in Aichi, Japan was conducted by Ikeda et al. from September 1986 until June 1988 in which 3,131 individuals participated (Ikeda et al., 1991). The objective of the program was to determine the epidemiological status of oral mucosal lesions, specifically leukoplakia, in this selected population and to estimate the validity of the diagnosis of oral leukoplakia by general practitioners. Results suggested that to carry out an efficient oral health program in Japan, it would be better to limit mass screening for leukoplakia to men 30 years and older and to women aged 40 years or older.

Field et al. designed a screening program in the United Kingdom in which individuals were invited to participate in an oral cancer screening as part of their routine dental care program provided at their company headquarters (Field et al., 1995). The purpose of this study was to determine the feasibility of such a design as well as to describe the target population, measure the participation rate and determine initial results. It was determined that a methodical and thorough examination of the oral mucosa can be realistically carried out as part of a routine dental inspection. Feasibility
was determined and the program was then expanded to screen all employees in the company.

In Cuba, an extensive oral cancer screening program was mandated by the government in 1984 for all individuals 15 years or older as part of their annual dental examination (Frenandez Garrote et al., 1995). 12,990,977 examinations were performed from 1984 until 1990 during which time 30,244 individuals were referred and 8,703 complied with this referral. The purpose of Garrote’s review of this program was to determine whether the screening program had any impact on oral cancer incidence and mortality in Cuba. There were many weaknesses identified in this screening program however the greatest shortfall was the poor compliance with referrals (only 28.8%). It was determined that there was no change in oral cancer incidence and mortality that could be ascribed to this screening program.

The largest and most current oral cancer screening program was conducted in Kerala, India from 1996 to 2004 and included 191,873 subjects (Sankaranarayanan et al. 2005). This cluster-randomized controlled trial purposed to assess the effect of visual screening on oral cancer mortality in high-risk individuals. The study outcomes indicated a 34% reduction in mortality and a 50% increase in the 5-year survival rate of the intervention group (high-risk screened individuals).

1.5.2.2 Approaches- Opportunistic versus Invitational Programs

In general, screening programs employ either an opportunistic or invitational approach in recruiting participants. Although both formats are relatively common, each
has positive and negative elements that must be considered when developing a screening program.

Opportunistic programs utilize a pre-existing health program or clinic (which the subjects are already actively attending) in order to access the target population (Mehta et al., 1986; Frenandez Garrote et al. 1995) while invitational programs ‘invite’ the voluntary attendance of individuals from the target population via mail, posted advertisements or house-to-house invitations (Downer et al., 1995; Field et al. 1995; Mathew et al., 1997; Nagao et al., 2000; Nagao and Warnakulasuriya 2003).

Opportunistic screening programs commonly encompass a larger number of examinations; however, the compliance with referrals after screening is variable, from 28.8\% in a Cuban study (Frenandez Garrote et al. 1995) to 67\% in one study in India (Mehta et al. 1986). This limited compliance of referral following screening in opportunistic screening studies may be due to subjects’ mandatory participation and lack of ownership.

Invitational programs, by contrast, usually have a smaller sample size and individuals who consent to a voluntary screening tend to be low-risk, more health conscious and more compliant with referrals (Mathew et al. 1997; Nagao et al. 2000; Nagao and Warnakulasuriya 2003). One invitational study in India found a compliance rate with referrals as high as 85\% (Mathew et al. 1997).

In addition, it has been suggested that high-risk subjects (smokers, heavy drinkers, males and the elderly) are often medically or dentally underserved and less likely to participate in an invitational study, resulting in a sampling bias, which is crucial
to analyzing the screening outcome (Downer et al. 1995; Frenandez Garrote et al. 1995; Warnakulasuriya and Johnson 1996; Epstein et al., 2002; Ramadas et al., 2003). Opportunistic programs may be deemed to be preferable in terms of involving a larger sample size while using pre-existing infrastructure however they will not include patients who are not attending the clinic or treatment modality being used, resulting in a selection bias. Invitational program may also suffer from selection bias due to targeting a smaller group of individuals who have already volunteered to participate. Based on these pros and cons, the selection of approach should depend largely on the purpose of the studies and the targeted population.

1.5.2.3 Sensitivity, Specificity and Positive Predictive Value

Sensitivity is the probability that a referable lesion is present (or screening test is positive), given that the person has the disease in question (oral cancer). Specificity is the probability that a referable lesion is not present (or screening test is negative) given that the person does not have the disease, known as the ‘true negative rate’ (Rosenberg and Cretin 1989). Positive predictive value (PPV) is the probability that a person has the disease, given a positive test result. When sensitivity is low, there are a high number of false negatives, whereas when specificity is low, there is a high rate of false positives. Notably, when a screening program produces a high rate of false negatives (low sensitivity), patients may be falsely reassured and passively advocated to continue carcinogenic behaviors (Lavelle and Scully 2005). Conversely, when a high rate of false positives (low specificity) occurs, there may be an increase in patient fear and anxiety for potential treatment in the absence of true disease. With the advent of molecular assessment, histology remains the current gold standard in confirming oral cancer
diagnoses. If a diagnosis is not confirmed through a biopsy, there is no way to estimate the correct sensitivity, specificity or positive predictive value, which has been the most commonly absent information in the reviewed programs. In a small study of 292 participants in a British screening program, relatively high values for sensitivity (71%), specificity (99%) and PPV (86%) were reported (Downer et al. 1995). These results indicate a moderate to low rate of false positives among individuals screened, a low rate of false negatives and a strong probability that patients who screened positive for oral cancer were accurately diagnosed.

1.5.2.4 Screening Techniques and Adjunctive Tools

A review of the current literature indicates that the information available on the screening techniques implemented in global oral cancer screening programs is widely varied and inconsistent. Direct visual oral inspection is the most commonly used technique; however, the forms of inspection are highly varied or unclear among programs regarding the use of lighting, retraction devises, and/or palpation. Often, specific details of the examination are not provided in the research methodology, leading to notable inconsistencies between studies. Screening for oral cancer is the examination of asymptomatic people for the detection of oral pre-cancer and early cancer. Specifically, it should include a thorough head, neck and intra-oral examination, with palpation of the cervical lymph nodes and visual examination and palpation of the oral mucosal surfaces, especially the lateral borders of the tongue and the floor of the mouth. The social, family and medical history should be reviewed along with the documentation of any risk behaviors (tobacco and alcohol usage). In addition to these standard clinical techniques, adjunctive clinical tools are available which may be
employed by the trained clinician to improve the visibility of oral lesions and provide a
determination of the need for further diagnostic investigation.

1.5.2.4.1 Toluidine Blue

Although the Gold Standard of diagnosis remains the biopsy of an oral lesion,
other clinically non-invasive tools have been developed to help determine the need for a
biopsy. Toluidine blue is a metachromatic, acidophilic vital thiazine dye that is soluble in
water and alcohol (also known as tolonium chloride), which is used to enhance the
identification of suspected mucosal lesions (Mashberg and Barsa 1984; Rosenberg and
Cretin 1989; Franceschi et al., 1997). Toluidine blue has a high affinity to nucleic acid
dtherefore dysplastic changes associated with a higher concentration of nucleic acid
(DNA and RNA) demonstrate higher frequency of positive staining. A recent study
provides strong evidence that a toluidine blue positive oral dysplastic lesion is six times
more likely to become cancerous and was found to have a strong association with a
high-risk molecular pattern using loss of heterozygosity (Poh et al., 2006). Hence, the
referral for further investigation of positively stained lesions after excluding possible
inflammation and infection is well supported (Rosenberg and Cretin 1989).

Toluidine Blue (TB) can be applied by direct application or by rinsing. Direct
application involves applying a 1% TB solution directly to a lesion with a cotton tip
applicator, waiting for 30-45 seconds, and then wiping off the non-specific staining from
the painted area with a cotton tip applicator soaked in 1% acetic acid. This method can
be preceded with an initial acetic acid wipe of the lesion prior to TB application. With
the rinse method, the patient swishes with 1% acetic acid for 20 seconds, followed by a
1% TB rinse for 20 seconds, another rinse of 1% acetic acid and finally, a water rinse.
A stained lesion is considered positive when it retains a dark blue color once the lesion has been wiped with the acetic acid and rinsed with water. If the lesion stains weakly it is called ‘equivocal’, and if no stain remains on the lesion it is considered negative. It has been suggested that equivocal results should be considered positive unless proven otherwise (Mashberg 1980).

It is also worth noting that toluidine blue has been found to be a highly sensitive technique, with a sensitivity of 79.5% and a specificity of 62%, which may produce a large proportion of false positives due to the inflammatory conditions of many lesions (Mashberg and Barsa 1984; Rosenberg and Cretin 1989; Warnakulasuriya and Johnson 1996). To improve the specificity and to reduce the false positivity, a trained and experienced dental professional is required to rule out possible confounding factors.

1.5.2.4.2 Fluorescence Visualization

A novel oral cancer screening technique developed by the researchers at the BC Cancer Agency is the Direct Fluorescence Visualization (FV) using a blue light. This simple hand-held device employs tissue optics to highlight mucosal abnormalities in the oral cavity (Lane et al., 2006; Poh et al., 2007). Normal tissue will retain fluorescence and appear green (FV retained, FVR) while abnormal tissue has loss of fluorescence and appears dark brown/black (FV loss, FVL). A pilot study of 44 patients has demonstrated encouraging results with a high sensitivity and specificity (98% and 100% respectively) when comparing normal mucosa with histological confirmation of severe dysplasia or invasive carcinoma (Lane et al. 2006). This tool has also been used in patients with a history of oral dysplasia or cancer and is currently being introduced in communities, such as the high-risk community of Vancouver’s Downtown Eastside.
initial findings indicate that this tool could serve as an easy-to-use, very promising and valuable clinical adjunct in oral cancer screening.

1.5.2.5 Qualification of Individuals Performing Screening

There is a long-standing debate as to the qualifications necessary for individuals performing the oral examinations for screening programs. This debate revolves around reproducibility, training, calibration and cost effectiveness. In many international studies, it is most common for dentists to be responsible for conducting oral examinations; however, the cost restraints are often prohibitive. As a result, trained personnel in some studies varied from 10th grade education with specific health care training to university graduates (Mehta et al. 1986; Mathew et al., 1995). However, limited experience, training/education and lack of calibration make it difficult to draw conclusions as to the feasibility and reproducibility of examinations conducted by these individuals (Mehta et al. 1986; Frenandez Garrote et al. 1995; Mathew et al., 1995; Sankaranarayanan et al., 2000; Ramadas et al. 2003; Sankaranarayanan et al. 2005).

Due to a shortage of human resources in one India study by Mathew et al., the feasibility of oral self-examination was explored as part of an oral cancer screening program (Mathew et al. 1997). The lesions being detected in this high-risk population with a high prevalence of OPLs and oral cancers are known to be generally overt and easily recognizable. Due to the extensive use of known carcinogens such as betel nut and a limited access to regular screening in this area, oral lesions may become large and disfiguring tumors before they are diagnosed. Therefore, oral cancer self-examination was found to be feasible and beneficial for this specific population. In
populations where oral lesions are much smaller and only clinically apparent, the efficacy of self-examination remains inconclusive.

In developed countries such as Canada and the United States, dental hygienists are trained to perform oral cancer screening as part of regular dental hygiene care (Forrest et al., 2001; Forrest et al., 2001; Clovis et al., 2002; Ashe et al., 2006). Based on the knowledge and training of dental hygienists and their accessibility to patient care, dental hygienists indeed play an important role in oral cancer screening and referral.

1.5.2.6 Target Population

Given the very low incidence of oral cancer in individuals in developed countries who are non-smokers and who are under the age of 30, mass population screenings for oral cancer have not been widely indicated (Mashberg and Barsa 1984; Field et al. 1995). As a result, oral cancer screening programs generally target high-risk populations in both developed and developing countries based on the issue of cost effectiveness.

The majority of oral cancer screening programs have been initiated in developing countries such as India, Sri Lanka and Cuba where high-risk populations are most accessible. In developed countries, high-risk populations do exist; however, the compliance rate for screening is reportedly poor for these types of individuals. Low compliance in high-risk individuals has been associated with low socio-economic status and a lack of symptoms (Talamini et al. 1994).

The mean age of subjects recruited for screening in the reviewed studies was calculated to be 39.5 years (excluding the Cuba study outlier where no age limits were
set), the median was 35 years and the range was 30-60 years. The ages of subjects who screened positive were only determined in four studies due to a lack of complete reporting details in the majority of studies regarding age ranges of positively screened subjects. In a study by Ikeda et al., which only investigated the presence of oral leukoplakia and mucosal diseases, 81% of leukoplakia lesions were found in patients ≥30 years (Ikeda et al. 1991). Ramadasa et al. identified that 86% of individuals with positive screening results were calculated to be ≥45 years of age (Ramadas et al. 2003).

In the Cuba study (Frenandez et al.), the highest incidence of oral cancer was found to be in males ≥50 years old. In Field et al.’s study (1995), the only subject diagnosed with squamous cell carcinoma was 55 years of age while 3 subjects (aged ≥49 years) were diagnosed with leukoplakia. In summary, the definition of high-risk populations has been agreed to consist of individuals over 30 years of age, tobacco-users, heavy drinkers and males (Downer et al. 1995; Frenandez Garrote et al. 1995; Warnakulasuriya and Johnson 1996; Epstein et al. 2002; Ramadas et al. 2003).

Low socio-economic status has been reported to be a risk factor in the development of oral cancer. This is a complicated factor that might result from a limited access to medical care for late diagnosis, poor nutrition and poor general health (Talamini et al. 1994; Ramadas et al. 2003). It is noteworthy that socio-economic status is population-specific and cannot be equally applied to both developed and underdeveloped countries. Further investigation is necessary in order to substantiate the precise effect of social factors on the development of oral cancer.
1.5.2.7 Compliance with Referrals

Achieving acceptable compliance rates is a challenge in most subject-based research. This barrier to screening was noted repeatedly among the screening programs reviewed where compliance rates varied significantly or were not mentioned at all. It is understood that compliance may be related to a multitude of factors such as gender, age, health awareness, socio-economic status and known oral risk habits. Compliance is often poor in men over the age of 60 as well as in smokers and drinkers. Further to this, men are often less compliant than women (Nagao et al. 2000; Sankaranarayanan et al. 2000; Nagao and Warnakulasuriya 2003). Decreased compliance has also been attributed to negative advertisements for oral cancer screening programs that employed “scare tactics” to recruit subjects (Downer et al. 1995). Interestingly, compliance has been noted to be enhanced in cases where the screening program was made convenient for the subjects such as when it was offered in close proximity to subjects’ location of employment (Field et al. 1995).

1.5.3 Feasibility of Screening (Cost versus Benefit)

The total cost of illness in Canada in 1998 was estimated at $159.4 billion: $83.9 billion (52.7%) in direct costs and $75.5 billion (47.3%) in indirect costs (Health Canada 2001). Direct costs are associated with the care provided in hospitals, physician services, drugs and other expenses (including other health professional, public health and research cost). Indirect costs are those related to loss of life due to premature death (mortality costs) and the value of activity days lost due to disability (morbidity costs). A report from Health Canada entitled “Economic Burden of Illness in Canada,
"1998" was released to provide an outline of the illness-related expenses in this Country by illness, gender, age and province. This report states that cancer, for all sites, accounted for $2.5 billion in direct costs with hospital care accounting for $1.8 billion or 74% of the total costs. Physician costs were $333 million, or 14% of direct costs of cancer treatment. This represents 3% of the total costs in Canada of all medical services provided by physicians. This clearly points to the significant economic burden of cancer in Canada.

In other parts of the world, the economic burden of cancer treatment is similarly astounding. In the US, the total cost of cancer in 2005 was $209.9 billion USD. US spending on cancer has dramatically increased yet its proportion of health expenditures has remained virtually constant. In France, cancer hospitalizations within the public health systems cost $6.2 billion USD in 1999 (23% for chemotherapy alone). In the UK, expenditure on cancer treatment by the National Health Service in 2000-2001 was $3.2 billion USD and in the Netherlands, the cost of cancer care was $1.2 billion USD in 1999 (Cancer Atlas, Atlas 2005).

For costs related specifically to oral cancer treatment, Funk et al. calculated an average cost of $32,500 USD per patient after evaluating 73 patients with a primary oral cancer tumor (Funk et al., 1998). A Greek study reported how costs increase over the various stages of oral cancer diagnosis. Stage I cancer treatment costs were reported as $3,662 USD, Stage II at $5,867 USD, Stage III at $10,316 USD, and Stage IV direct costs at $11,467 USD (Zavras et al., 2001). These costs clearly illustrate that value of early detection in terms of the mounting economic burden that is associated with later stage diagnoses.
With oral cancer screening programs providing the most effective tool in identifying early stage disease, it is evident that this is the most cost effective way to reduce the economic burden of this disease.

1.6 Time From Detection to Diagnosis

When delayed in diagnosis, oral cancer has a significant impact on survival and quality of life. It has been determined that a diagnostic delay may contribute to more advanced diseases at diagnosis and a less favorable prognosis (Pitiphat et al., 2002; Brouha et al., 2005). In light of this, the timing of diagnosis is crucial. It has been previously shown that in British Columbia, regular dental care is associated with early diagnosis of oral cancer and less advanced staging of the disease at biopsy (Elwood and Gallagher 1986). This data however was produced 20 years ago and requires further investigation to update and possibly redefine the relationship between dental care and early oral cancer detection.

The time interval which extends from first awareness of something unusual in the oral cavity until a diagnostic biopsy is made can be evaluated and characterized in various ways. Andersen et al. describe a ‘model of total patient delay,’ which outlines the pre-diagnostic period according to six stages that may incur delay (Andersen and Cacioppo 1995). Each stage is dichotomous and the progression from one stage to the next is dependent upon the decisions and interpretations of the previous stage. The first stage is referred to as appraisal delay and incorporates the time interval from first detection of an unexplained symptom until illness is inferred. In other words, a person
must interpret a symptom as serious enough to require attention. The second step is the *illness delay* stage in which the patient makes a choice between seeking medical attention and self-treating the illness. Illness delay occurs when a person decides to postpone seeking help in favor of self-medicating. An example of this is the patient delay identified by Kerdpon *et al.* (2001) in Thailand which was associated with the use of herbal medications prior to seeking professional help (Kerdpon and Sriplung 2001). The *behavioral delay* stage begins when the patient realizes they require professional help and continues until an appointment is scheduled with a health professional. The time between making an appointment with a health professional and the actual time of the appointment is referred to as the *scheduling delay*. This form of delay can be the result of the health professional's availability or the patient's availability. The final stage of delay is known as the *treatment delay* stage which refers to the time from a patient's first consult with a health professional until treatment begins. This model of total patient delay is therefore linked to the treatment outcome rather than the diagnostic biopsy as in other models of delay.

Pitchers and Martin (2006) have proposed an alternate concept in characterizing the stages of delay. This model is based on the delay that may occur throughout the referral process for an oral cancer patient and involves 5 stages (Pitchers and Martin 2006). Stage 1 is the patient’s delay in seeking medical advice. Stage 2 occurs when the primary health care provider incurs delay in referring to a specialist. This time interval extends from the patient’s first symptomatic presentation to a health professional until the date of the referral letter to a specialist. Stage 3 is the time from the date of the referral letter to the time of the specialist’s appointment. Stage 4 involves
the delay following the specialist’s appointment until the results of the investigations are received (histology, etc). The time interval that extends from the availability of the results until treatment begins is known as Stage 5.

A third and more simplistic model of characterizing delay was presented by several researchers in which diagnostic delay is comprised of a combination of both patient and professional delay. ‘Diagnostic delay’ can be defined as the time from initial lesion detection to diagnostic workup. More specifically, diagnostic delay is essentially the combination of patient delay (time from initial lesion detection to first professional consult) and professional delay (time from first consultation to biopsy) (Guggenheimer et al., 1989; Kowalski et al., 1994; Diz Dios et al., 2005). Various factors have been identified in the literature, which may contribute to either patient delay or professional delay.

1.6.1 Patient Factors

Upon first identifying an abnormality in the mouth, there is a measurable time interval between initial detection and the first professional consultation. This time interval, whether one day or many years in length, is referred to as ‘patient delay.’ Patient delay has been noted to comprise the largest portion of the diagnostic delay period (Hollows et al., 2000) and estimates indicate that 30% of patients delay in seeking professional help for more than 3 months following initial detection of an oral lesion (Onizawa et al., 2003). Importantly, patient delays are not only restricted to the time prior to the first health consult however, once the referral process has begun, patients may also further delay in making or keeping appointments. Many studies have been conducted to
examine the nature of patient delay in attempts to qualify the factors that contribute to this key time period. With diagnostic delay potentially leading to advanced staging upon diagnosis, it is important to be able to identify and understand the contributing factors that may ultimately play a role in the prognosis of this disease.

1.6.1.1 Gender

The association between gender and patient delay remains debatable. This association has been reported by some researchers as reflecting a significant relationship between gender and patient delay whereas others have found no association at all. Yu et al. (2008) presents the most current and compelling evidence to suggest that women have a significantly greater total delay than men ($P < 0.01$) (Yu et al., 2008). This study consisted of 102 patients with oral and oropharyngeal cancer who were interviewed over a 1-year period with a mean patient delay of $21.7 \pm 51.7$ weeks. Conversely, a study by Kowalski et al. (1994) found that there was a moderate risk reduction associated with the female gender for an advanced stage diagnosis associated with delay (Kowalski et al. 1994). This finding seems to agree with Scott’s findings that women have more than a 60% decrease in risk of having advanced stage disease at diagnosis when compared to men (Scott et al., 2005). Although there is no strong evidence to explain this finding, it had been suggested that women may notice signs of oral cancer at an earlier stage. Some research has shown that women have higher somatic awareness and have a tendency to selectively attend to bodily cues (Cecile 1997).
Despite these conflicting findings, many other studies have found no relationships at all between the female gender and delay (Guggenheimer et al. 1989; Amir et al., 1999; Onizawa et al. 2003; Llewellyn et al., 2004; Tromp et al., 2004).

### 1.6.1.2 Tobacco Use

As with other factors contributing to delay, the relationship between tobacco use and total delay has been inconsistently reported. Kowalski et al. found a positive dose-related relationship for the cumulative consumption of tobacco and oral cancer status (Kowalski et al. 1994). On the other hand, it has been repeatedly published that increased delay is associated with non-smokers or those who smoke considerably less (Pitiphat et al. 2002; Llewellyn et al. 2004; Yu et al. 2008). This inverse relationship between amount of smoking and length of delay may be due to the perception of non- or light-smokers that their risk is low, thus leading to mislabeling of signs and symptoms as non-significant. Underestimation of the seriousness of symptoms then leads to a delay in seeking professional advice.

Tobacco use has also been found to have no relationship on delay which contradicts the aforementioned studies (Onizawa et al. 2003; Brouha et al. 2005; Scott et al. 2005).

### 1.6.1.3 Alcohol Consumption

The consumption of alcohol as a contributing factor to diagnostic delay presents a fairly convincing argument. On two occasions, alcohol intake was positively associated with delay based on excessive consumption (Guggenheimer et al. 1989; Tromp et al. 2004) and in one case, excessive alcohol consumption was related to
delay in the male gender (Guggenheimer et al. 1989). Tromp et al. (2004) noted that their findings were contrary to other studies as they determined that patients who drank 5 or more drink daily tended to exhibit greater patient delay that those who drank less or not at all. Their investigations related excessive alcohol consumption to increased psychological stress before treatment, which underscores the previously determined notion that alcohol intake is associated with anxious and depressive symptoms (Tromp et al. 2004). As such, patients who drank 0-2 drinks daily reported more health hardiness and reported more religious coping (benevolent religious appraisals) than moderate and heavy drinkers (3+ drinks daily). This finding may also implicate a difference in lifestyles and values, thereby somewhat confounding these results.

In a few other studies, however, alcohol has not been found to have a significant impact on delay as reported by Onizawa (2003), Brouha (2005) and Scott (2004).

1.6.1.4 Age

Although it might be hypothesized that increased age may be associated with increased delay, the research does not show strong support for this relationship. Only one investigation found that increased patient delay is associated with individuals over the age of 65 (Tromp et al. 2004). This study examined 277 patients, 62% of which were under the age of 65 years. Interestingly, only patients who self-detected their oral lesion and sought help were included in this project, which excluded a notable degree of the population who may have had a lesion detected by a health professional and simply delayed in the scheduling process of appointments. Aside from this example, the balance of the reviewed publications indicates that age is unrelated to delay.
(Guggenheimer et al. 1989; Amir et al. 1999; Onizawa et al. 2003; Llewellyn et al. 2004; Scott et al. 2005).

1.6.1.5 Marital Status

Marital status has been found in some instances to be associated with decreased patient delay leading to diagnosis. Being married and female was determined to be significantly associated with early stage disease at diagnosis ($P < 0.01$) in one study (Scott et al. 2005) while patients who were living with a partner or family (and thus possibly also married) showed less delay in another study (Tromp et al. 2004). It is conceivable that married individuals or those living with a partner may seek care earlier due to discussing their symptoms with loved ones and being encouraged to seek help in a timely manner. Pitiphat et al. (2002) found that the longest diagnostic delays were associated with being unmarried since these individuals experienced delays estimated at as much as 383 days longer than their married, widowed or separated counterparts (Pitiphat et al. 2002). It has been shown that unmarried people may be less likely to have dental care coverage (Manski 1995) and less likely to make use of dental services (Osterberg et al., 1998) which might influence their likelihood of seeking dental advice for oral symptoms potentially related to oral cancer.

Not all research however has identified a relationship between marital status and delay as determined by Brouha et al. (2005). In this case, neither living situation (alone or with family) nor marital status (married or divorced/widowed) were associated with patient delay for pharyngeal or oral cavity cancers (Brouha et al. 2005).
1.6.1.6 Tumor Size and Staging

Perhaps one of the most influential factors in delay research is the link between diagnostic delay and advanced staging at diagnosis. This continues to be a strongly-debated issue as patients with advanced stage oral cancer have shown significantly greater delay than those with early-stage disease in some cases (Brouha et al. 2005) while in others, small tumour size has been related to longer patient delays (Onizawa et al. 2003). The argument for smaller tumours (early stage) being diagnosed following a long delay is based on the difficulty in obtaining a clinical diagnosis of small-sized tumours. Conversely, patients with lymph node involvement of N1 or N2 may receive a diagnosis without delay compared with N0 because most patients with a positive N category of oral cancer have an advanced tumour that is easily identified and diagnosed (Onizawa et al. 2003).

Some researchers still maintain that diagnostic delay is unrelated to the stage of oral cancer at diagnosis based on two lines of reason. Firstly, tumours may present with intrinsic differences in aggressiveness which will determine the tumour size and stage upon diagnosis (Kaufman et al., 1980; Guggenheimer et al. 1989; Vernham and Crowther 1994). This concept outlines that biologically aggressive tumours may grow to an advanced stage in only a short period of time due to the intrinsic pace of the tumour growth. In contrast, individuals with slow growing tumours may have early stage disease at diagnosis even after a lengthy period of delay.

The second line of reason suggests that although the stage of disease at diagnosis may be dependent upon the time interval between disease onset and
diagnosis, some oral cancers may be ‘silent’ and exhibit no symptoms even into the early stages of disease progression (Guggenheimer et al. 1989; Vernham and Crowther 1994). As the pre-neoplastic stage can extend for a significant length of time, prolonged diagnostic delay may have minimal impact on the stage at diagnosis. This would explain why many patients continue to be diagnosed with early stage disease despite prolonged diagnostic delay.

1.6.1.7 Oral Cancer Awareness

Researchers have consistently identified that patients’ misunderstanding of the signs and symptoms of oral cancer can lead to prolonged delay in seeking professional consultation (Guggenheimer et al. 1989; Onizawa et al. 2003; Llewellyn et al. 2004). Patients with oropharyngeal tumours were unable to distinguish between ominous and innocuous manifestations according to Guggenheimer et al. (1989) thereby leading to increased patient delays. A lack of patient awareness of oral cancer is closely linked to the widespread lack of education regarding oral cancer signs and symptoms.

An alarming exposé of the widespread lack of awareness of oral cancer among British residents was published in 1999 which has underscored the need to pay closer attention to this contributory factor of diagnostic delay. Only 65% of the 1894 survey respondents reported that they were aware of oral cancer whereas 85% of respondents were aware of cancers that afflict other bodily organs and sites (Warnakulasuriya et al. 1999). There was also determined to be a high awareness of smoking as a risk factor in oral cancer (76%); however, only 19% reported an awareness of a link between alcohol consumption and oral cancer. These findings support consistent recommendations that
public awareness of oral cancer must be increased and that there is a need for raising awareness in the general population regarding the signs and symptoms of this disease in order to reduce patient delay.

1.6.1.8 Psychosocial Factors

In an extensive investigation, Tromp et al. (2004) examined the relationship between patient delay and psychosocial variables such as optimism, health hardiness, defensive functioning and coping mechanisms (Tromp et al. 2004). Five specific psychosocial tests were used to qualify the variables of patient delay in the care-seeking process of 427 consecutive patients with SCC. Optimism was measured such that the higher the score, the more optimistic the patient was regarding expected outcomes of life. Health hardiness measured the degree to which individuals were committed to and involved in health-related activities, perceive health as controllable and approach potential health stressors as an opportunity for growth. Defensive functioning was determined according to the level of mature defenses (ie. humour, anticipation) versus immature defenses (ie. idealism, denial, unrealistic projection) identified in the patient. Coping styles were categorized into one of 5 coping styles including active coping, seeking support, avoidance coping, palliative coping and religious coping with the use of scale scores. Anxiety and depressive symptoms were measured using a uni-dimensional measure of psychological distress. Based on these tests, Tromp et al. found that patient delay was negatively related to optimism, health hardiness and overall defensive functioning but positively related to avoidance coping. In other words, patients who delayed in seeking professional consultation were less optimistic, reported less health hardiness and made less use of active coping and
seeking support as coping styles. Patients with overall lower defensive functioning scores also exhibited a trend of increased patient delay.

Interestingly, this research identified a trend for excessive drinkers to show more delay than non-drinkers. Incidentally, excessive drinkers also showed more psychological distress than moderate or heavy drinkers which may provide an explanation for how psychological factors impact patient delay related to alcohol consumption. This further supports the notion that alcohol is also a key contributory factor to delay based on the association between alcohol intake and anxiety/depressive symptoms.

In other research, the risk of delay was found to be 7-fold higher for patients reporting stress in the period prior to diagnosis (Llewellyn et al. 2004). Furthermore, patients with worrying symptoms were found to be engaging in avoidance coping, which occurs when individuals try to distract themselves in the face of a stressful event. This may also have led to feelings of stress and anxiety and thus increased patient delays.

1.6.1.9 Frequency of Dental Visits

Elwood et al. made a significant contribution to our understanding of the importance of regular dental visits in the detection of oral cancer when they identified that 70% of individuals diagnosed with Stage I or II disease saw a dentist regularly during past 5 years as compared to only 40% who did not (Elwood and Gallagher 1985). From this early finding, authors have continued to highlight the importance of frequent dental exams in promoting early detection of oral cancer and in reducing diagnostic delays (Onizawa et al. 2003; Yu et al. 2008). Most recently, it was
reemphasized that patients who did not visit their dentist on a regular basis were more likely to experience increased delay periods ($P < 0.05$) (Yu et al. 2008).

### 1.6.2 Professional Factors

As a component of total (diagnostic) delay, professional delay is defined as the time interval that passes from the first consultation with a health professional until a diagnostic biopsy is taken. According to some researchers, professional delay may consist of a number of variables which contribute to the overall time interval. For example, of the 5 stages of delay outlined by Pitchers and Martin, potentially four of these stages were directly linked to the actions of the health care professional (HP) (Pitchers and Martin 2006). These would include Stage 2- the time from first presentation at a HP until a referral letter is written, Stage 3- the delay from referral letter time to specialist appointment, Stage 4- the delay from specialist’s appointment to results of tests (i.e., biopsy taken) and Stage 5- the delay from receipt of results to start of treatment. Hence, the rate of referral, the scheduling availability of specialists and expertise of the HP are key elements that will directly influence the overall delay a patient may be subject to leading up to diagnosis.

#### 1.6.2.1 Scheduling Availability

The concept of scheduling delay can be defined as the period between when a patient makes an appointment with an HP and when the patient actually sees the HP. This influence of the accessibility to the health care system has received little investigation and therefore is rarely published. In 2004, Diz Dios et al. designed a study aimed at evaluating the scheduling delay in oral cancer diagnosis in dental surgeries in
Galicia, Spain. The aim was to assess the influence of the professional whose role it was to allocate the appointment whether it be the receptionist or the dentist (Diz Dios et al. 2005). Two standardized patients contacted 156 dental surgeries each, one requesting an appointment to have a lingual ulceration examined and the other requesting fixed prosthodontics (dental crown and bridge). The patient with the ‘lingual ulceration’ was given an appointment the same day in 25% of the clinics and within 5 days at the other 75% of clinics. The patient needing prosthodontic work was given an appointment within 13 days at 75% of the clinics contacted. Interestingly, when the professional scheduling the appointment was considered, the scheduling delay was significantly shorter for the appointments scheduled by the dentist concerning the lingual ulceration. This indicates that the HP’s knowledge of the potential risk associated with a tongue lesion is considerably more than the knowledge of the administrative staff and that despite the prompt scheduling; there is a need for better education of all dental personnel in the urgency of examining oral lesions.

In a Danish study on the impact of delay on a lung cancer diagnosis, it was identified that waiting time for scheduling investigatory appointments were a determinant in increased delay to diagnosis (Bjerager et al., 2006). Although the frequency of scheduling delays is underreported, this remains a concerning contributory factor to professional delays and demands further investigation. Scheduling delay may also be a contributory factor to patient delay (missed appointments, rescheduling, etc) however this concept is also underreported and demands further exploration.
1.6.2.2 Appropriate Referral Pathways

The referral pathway has been found to play a direct role in staging outcomes of oral cancer upon diagnosis. It has been estimated that for every 1 week delay in referral to a specialist, the stage of presentation will progress by 0.045 of a ‘stage’ \( (P < 0.011) \) (Pitchers and Martin 2006). This strong positive relationship between staging and referral highlights the importance of the role of HP’s in reducing diagnostic delay by improving their knowledge and use of appropriate referral pathways. ‘Inappropriate referrals’ have been identified as problematic by Hollows et al. where only 54% of oral cancer cases were referred to the appropriate unit. These ‘indirect referrals’ were a significant cause of delay (Hollows et al. 2000). The following images represent the varying treatment outcomes relative to the staging at diagnosis:

![Post-surgical outcome of three oral cancer patients with varying diagnostic stages.](image)

**Figure 1:** Post-surgical outcome of three oral cancer patients with varying diagnostic stages.  
A: A faint scar at right lateral tongue post-surgery of small (<1 cm) stage I tongue cancer, B: A postsurgical soft tissue defect at left lateral tongue from a larger (2 cm) stage I tongue cancer, C: A post-surgical skin graft/scar at right lateral tongue from a 4-cm stage II tongue cancer.
The referral delay caused by HP’s has been outlined by numerous researchers worldwide. Scully et al. found median referral delays of 31 days from general medical practitioners (GMP) and 40 days from general dental practitioner (GDP)’s in the UK (Scully et al., 1986). Kowlaski et al. found that 17.4% of Brazilian GDP’s and 8% of GMP’s were responsible for delays of over a month to admission to the head and neck unit (Kowalski et al. 1994). In 2000, the Department of Health in the UK established a set of guidelines outlining a ‘2-Week Standard,’ which states that any person with a case of suspected oral cancer must be able to see specialist within two weeks (NHS Executive 2000). This was a noble step in the direction of reducing scheduling delays and improving referral times for patients in a diagnostic period where time is everything.

The referral habits of GDPs in the United Kingdom were examined in 2006 and it was determined that 65% of GDP’s referred potential oral cancer cases to oral and maxillofacial surgeons, 14% referred to oral surgeons and 19.5% referred to oral medicine specialists (Kujan et al., 2006). This would indicate that in this region, dentists are making the appropriate referral decisions; however there remains a great lack of evidence to support this in other parts of the world. As such, the need for timely and appropriate referrals will be a significant step towards reducing professional delays in the referral pathway to diagnosis.

1.6.2.3 Professional Expertise

Professional delay has been attributed to various factors however the lack knowledge and expertise of HP’s may be the most concerning of all. In a survey of
dentists in North Carolina, it was determined that only 31% of respondents had consistent medium-to-high levels of knowledge regarding risk factors and clinical diagnostic concepts (Patton et al. 2005). Another study identified that inappropriate clinical management of oral cancer patients prevailed as antimicrobial medication prescriptions and denture adjustments were the most commonly performed treatments for individuals who presented with an oral lesion (Dimitroulis et al., 1992). A failure to recognize early lesions is the dangerous outcome of HP’s who lack the clinical expertise in identifying and treating soft tissue pathologies. Dimitroulis et al. identified that the extent of delay by clinicians in establishing a diagnosis of SCC was closely linked to the degree of suspicion and diagnostic skill of the clinician. Furthermore, 22% of the asymptomatic cases of oral cancer were discovered accidentally while 33% of oral cancer cases were misdiagnosed (Dimitroulis et al. 1992). The importance of professional training in early diagnosis therefore cannot be overemphasized.

The value of regular oral cancer screening is widely recognized as a key step in early detection and positive prognosis. It is alarming to learn that in a 2002 statewide random-digit-dial telephone survey in North Carolina, only 29% of respondents reported ever having an oral cancer screening when the process was described to them (Patton et al., 2004). Although 85% of respondents reported having seen a dentist in the past 3 years, only 23% reported having an oral cancer exam in the previous year. These findings expose a worrisome knowledge gap in the awareness of oral cancer and application of preventive measures.
1.6.3 Delay Time from Detection to Diagnosis Can Impact Prognosis

Despite the controversy regarding diagnostic delay and advanced staging upon diagnosis of oral cancer, the consensus remains that early detection and prompt treatment remain the most advisable means of dealing with this disease. The meager survival rates of advanced stage diagnosis (Stage III or IV) are only 20% however early stage diagnosis (Stage I or II) boasts survival rates of 80% (NCI SEER Results, 2001). Overall, the 5-year survival rate for oral cancer in British Columbia is 62% (BCCA 2005). Bearing in mind the many factors that contribute to delay, there is an urgent need to better understand these fundamental issues in order to reduce delay, thereby providing oral cancer patients with more hope for successful treatment and a positive prognosis.

1.7 Qualitative Research

Qualitative research methods are designed to investigate human behavior and its meanings and the impact of the sociocultural context in which the behavior occurs (Bauman 1992). The term qualitative implies an emphasis on the qualities of entities being observed including the processes and meanings which are not experimentally measured in terms of quantity, amount, intensity or frequency (Denzin 2000). Qualitative researchers are interested in how social experience is created and given meaning. In contrast, quantitative research focuses on the measurement of causal relationships between variables rather than processes. Thus, qualitative research must often preempt quantitative research as it provides an observational platform which reveals the questions that quantitative research will ask.
There are many qualitative research tools which enable researchers to learn more about human behavior; personal interviews and focus groups are two such tools which are used in this thesis and described below.

1.7.1 Personal Interviews

Personal interviews are generally conducted on a one-to-one basis with the interviewer posing a set of predetermined questions to the interviewee. Questions may be open-ended or closed-ended, both having their strengths and weaknesses. For example, in closed-ended questions, respondents tend to confine their answers to the choices offered, even if the researcher does not wish them to do so (Bishop 1988; Presser 1990). That is, people generally ignore the opportunity to volunteer a response and simply select among those listed, even if the best answer is not included. Therefore, a closed-ended question can only be used effectively if its answer choices are comprehensive. However, this is difficult to assure. Closed-ended questionnaires are most commonly used in quantitative research and not qualitative research.

There has been concern that open-ended questions would not work well for respondents who are not especially articulate, because they might have difficulty explaining their feelings. However, this has been discounted by studies investigating the issue (Geer 1988). Other concerns were that respondents would be likely to answer open-ended questions by mentioning the most salient possible responses, not those that are truly most appropriate. But this, too, has been discounted (Schuman 1986). As such, open-ended questions are more viable research tools in this format.
1.7.2 Focus Group Discussions

A focus group discussion is a group interview where individuals are encouraged to discuss a specific topic so that their personal beliefs, values and perspectives on the topic might be better understood (Bloor 2001). Participants are asked to engage in focus groups because they have something in common with each other and something which the researcher is interested in — for example, a lifestyle circumstance or condition. According to Carey and Smith, the focus group technique is described as “using a semi-structured group session, moderated by a group leader (the facilitator), held in an informal setting, with the purpose of collecting information on a designated topic. The collection of personal experiences and beliefs related to the designated topic is the purpose of the focus group” (Carey 1994). Information that is shared in the first person enables the researcher to understand the depth of a patient’s experience and allows the patient to recommend strategies that would be most appropriate for them. Focus group data can provide assistance to the qualitative researcher in designing further investigations using quantitative instruments based on the feedback provided by the participants.

In focus group discussions, the interview questions are open-ended to encourage participants to respond from their own perspective, thereby giving richness and diversity to the quality of the information obtained. Detailed information is collected and documented from a small group (seven to nine persons), or individual participants. Focus groups generate discussions of similarities and differences among participants. Focus groups are generally 1-2 hours in length and operate within predetermined procedural rules (Bogart 1998).
Qualitative methods such as focus group discussions are used to explore subjective experiences and allow insight into individuals’ understandings, interpretations and beliefs. Therefore, the focus group discussions in this study permitted an investigation into the groups’ perceptions of the interview questionnaire they had participated in and elicited recommendations for future interview strategies.

2. STATEMENT OF THE PROBLEM

Oral cancer is a deadly disease which claims thousands of lives every year in Canada and worldwide. The prognosis of this disease is poor (50 – 60% five-year survival rate) and has remained unchanged for over 3 decades, largely due to late stage detection in the majority of cases. When delayed in diagnosis, oral cancer has a significant impact on survival and quality of life as it has been determined that diagnostic delay may contribute to more advanced staging at diagnosis and a less favorable prognosis. Late stage detection is also responsible for disfigurement, loss of function and extensive treatments, long periods of convalescing and an increased potential for local recurrence and distant spread of the disease.

The key to better control of this disease is early detection, preferably at precancerous stage. A 2003 British Columbia report has shown that strikingly, 42% of oral cancers are diagnosed at a late stage (stage III and IV). The literature suggests that several factors may contribute to diagnostic delay; however, in BC, there is currently no data indicating whether diagnostic delay exists and if it does, which factors contribute most to its existence.
3. HYPOTHESIS

The hypotheses of this study are twofold:

1) There is a delay in diagnosis for oral cancer patients in BC, which results in a more advanced-stage disease at diagnosis.

2) A series of contributory factors in this diagnostic delay can be identified in terms of the patient’s own experience and in working with the health professionals.
4. OBJECTIVES

The end-product of this thesis is to design a survey questionnaire to collect population-based information regarding patient experiences leading to diagnosis of oral cancer and to identify the factors associated with late diagnosis. The ultimate goal of these efforts is to develop effective strategies for early identification of oral cancers in order to achieve better control over this disease. There are 2 components in this thesis:

Part I: Personal Interviews

The objectives of Part I of this study are 1) to develop an interview-style questionnaire, 2) to collect detailed information from patients currently attending the Dysplasia Clinic at Vancouver Cancer Centre, and 3) to characterize the experiences of these individuals that may have impacted the time interval leading to diagnosis.

Part II: Focus Group Discussions

The objectives of Part II of this study involved using focus group discussions 1) to gather feedback regarding the questionnaire developed in Part I, 2) to obtain recommendations for future planning and delivery of province-wide questionnaire, and 3) as a group, to share information on patients’ experiences to diagnosis and patients’ perspectives on their interactions with health professionals during this journey. We will discuss these objectives individually in the following sections.

The following is a flow chart outlining the overall study approach: the development of the interview questionnaire and collection of data from 40 interviewees
in Part I and the conduct of two Focus Group discussions in Part II for the refinement of the questionnaire.

Figure 2: Flow chart of the study approach
5. Part I: Personal Interviews

5.1 Objectives

The objectives of Part I of this study are: 1) to develop a questionnaire for personal interviews, 2) to collect both quantitative and qualitative information from patients with newly-diagnosed high-grade oral lesions in BC (including demographics, experiences with healthcare personnel and the time interval from the initial identification of the oral lesion to the diagnostic workup), and 3) to characterize the patients' experiences in seeking the assistance of health professionals and in working with health professionals to a diagnostic workup.

5.2 Methods

5.2.1 Study Population

Individuals diagnosed with oral cancer and oral premalignant lesions (OPL) are referred to the Dysplasia Clinic at the BC Cancer Agency (BCCA) for management. The BC Oral Cancer Prevention Program (see section I.4) conducts a large-scale longitudinal study referred to as the Oral Health Study which aims to reduce the incidence and mortality of oral cancer through the development, validation and adoption of new techniques for early detection, risk assessment and management of OPLs and cancers. Individuals who received a biopsy within the 12 months prior to their interview date and had a biopsy result of high-grade dysplasia, carcinoma \textit{in-situ} and squamous
cell carcinoma (high-grade lesions; HGL’s) were eligible for the study. It was also determined that subjects had to be able to speak English in order to comfortably understand and respond to the questions being asked. Prior to participating in the interview, patients were provided with a written description of the study background, objectives and methods then asked for written consent to participate.

5.2.2 Questionnaire Development

An interview-style questionnaire was developed based on questions relating to the experiences of patients with HGL’s from first detection of an oral lesion until the first diagnostic biopsy of the HGL was taken. The questionnaire included 21 questions to collect both quantitative and qualitative data (see Appendix A.1 and A.2), which were developed from a review of the literature and expert collaboration. Questions on frequency of visits to various health professionals included: Which of the following healthcare professionals do you see regularly? When was your last dental visit? When was your last medical visit? Questions regarding the individual to first detect the patient’s oral lesion, lesion location and symptoms included: Who first detected the change (lesion) in your mouth? (If the lesion was first identified by the patient) Where was the change (lesion) located? When did you first notice something unusual in your mouth? What were the first symptoms you noticed? Questions were also asked regarding the patient’s reactions to their symptoms and their motivation to seek initial HP consultation including: What was your initial reaction to discovering your symptoms? What did you do after you noticed the change in your mouth? How long after you first noticed something unusual in your mouth did you seek professional consultation?
Questions were then asked about each experience relating to a HP visit leading up to diagnosis. These questions included: *When did you visit this HP? What was the reason for this visit? What did this HP recommend to you? What did you do next? What symptoms did you experience?* Questions were asked regarding patient’s awareness of oral cancer prior to their diagnosis, which included: *Before first noticing your symptoms, which types of cancer would you say you had heard of? Had you ever heard of oral cancer? Which symptoms of oral cancer would you say you had heard of?*

### 5.2.3 Interviews

Potential participants were identified using the BCCA patient database and if eligible, were invited to participate in this study during their regular visits to the Dysplasia Clinic. All patients who were invited and agreed to participate also provided written consent (Appendix A.3.). They were interviewed either before or after their visit. Responses to the quantitative sections (Questions 1-17) were recorded by H. Biggar and the qualitative section (Questions 18-21) was digitally audio-recorded and later transcribed verbatim for accuracy. Each interview lasted from 15-30 minutes and was conducted in a private operatory to ensure patient privacy and confidentiality. At the conclusion of each interview, patients were asked if they would be receptive to being invited to a focus group to further discuss the content and quality of the interview (see Section V.4 for Part II).
Demographic information was collected from the patient charts including: gender, age, smoking status (never, former, current), and ethnicity. The information regarding the first diagnostic biopsy was collected from pathology reports including: lesion site, size, biopsy date, submission physician, and diagnosis. Attention was given to identifying the dates of lesion detection and follow-up appointments in order to later calculate the time period from detection to diagnosis. The initial physician or dentist seen by each patient was contacted by telephone to confirm the dates reported by the patient. Subsequently, the biopsy dates were confirmed by cross-checking with the pathology report in each patient’s chart. Information was also collected on the recommendations made by HP’s and the subsequent actions taken by patients.

5.2.4 Data Analysis

Data was analyzed using the Student t-Test to compare numeric values for parametric results. The Fisher’s Exact Test was used to compare nominal values for the data collected.

5.3 Results

5.3.1 Demographics

Between February, 2007 and June, 2008, 40 patients currently enrolled in the Oral Health Study at the BCCA were found to be eligible and were interviewed. The response rate was 100 % as all eligible patients who were invited agreed to participate and were interviewed. This high response rate is likely due to these patients having been previously recruited to participate in the Oral Health Study and being familiar with
as well as appreciating the importance of on-going studies. None of the invited patients declined participating in the interview questionnaire. Of the 40 eligible patients who participated, twenty seven (67.5%) were male and thirteen (32.5%) were female (See Table 1). The mean age at time of interview was 61 ± 12.3 years (range: 37-90 years). Only three patients (7.5%) were less than 45 years of age. 28 patients (70%) were ever-smokers with current (N=10) and former smokers (N=18) and 12 (30%) non-smokers. Thirty-six patients (90%) were of Caucasian ethnicity while two (5%) were Asian and two (5%) were of South Asian descent.

5.3.2 Frequency of Visits to Health Professionals (HP’s)

Thirty-seven of the forty patients interviewed (92.5%) reported seeing a health professional (HP) at least once per year which included any dental or medical practitioner or specialist (see Table 1). Thirty-one (77.5%) reported seeing a dental practitioner at least once per year (including dental specialist visits) and 31 (77.5%) reported having a medical visit at least once per year (including medical specialist visits). Interestingly, 18 (49%) of the 37 patients who regularly saw HP’s had their lesion first detected by the patients themselves.
Table 1: Demographics and lesion characteristics of all participants interviewed

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total N=40</th>
<th>Invasive Lesions (SCC) N=22</th>
<th>Non-Invasive Lesions (Dysplasia, CIS) N=18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Female</td>
<td>13</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Age (± SD*)</td>
<td>61.2 (12.3)</td>
<td>62.5 (14.4)</td>
<td>59.6 (9.4)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever-Smokers</td>
<td>28</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Non-Smokers</td>
<td>12</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>36</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td>Asian</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>South Asian</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Frequency of HP* Visits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; once/year</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>≥ once/year</td>
<td>37</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>Dental Professionals (RDH*, DDS*, DDS Spec*)</td>
<td>31</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Medical Professionals (MD*, MD Spec*)</td>
<td>31</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Initial Identification of Lesion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HP (N=19)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDH</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>DDS</td>
<td>9</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>DDS Specialist</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>MD</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>MD Specialist</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Self (N=21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time from Detection to Dx*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Time (±SD)</td>
<td>17.5 (42.3)</td>
<td>14.6 (26.3)</td>
<td>21.0 (56.9)</td>
</tr>
<tr>
<td>≤ 6 months</td>
<td>26</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>&gt; 6 months</td>
<td>14</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Lesion Site (N=42)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>22</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Floor of Mouth</td>
<td>10</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Soft Palate/Oropharynx</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Buccal Mucosa</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Gingiva</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Lesion Size (N=29)**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greatest Dimension (mm)</td>
<td>75</td>
<td>75</td>
<td>68</td>
</tr>
<tr>
<td>Mean Area (mm²)</td>
<td>488 (713.3)</td>
<td>589 (870.6)</td>
<td>364 (457.8)</td>
</tr>
</tbody>
</table>

*SD: Standard Deviation, HP: Health professional, RDH: Registered Dental Hygienist, DDS: Dentist, DDS Spec: Dental specialist, MD: Medical Doctor, Dx: Diagnosis, CIS: Carcinoma in situ, SCC: Squamous cell carcinoma

**Lesion sizes were not available for all cases as some patients were interviewed post-operatively and the lesions were completely excised.
5.3.3 Time from Detection to Diagnosis

The mean time from detection to diagnosis was determined to be 17.5 ± 42.3 months (range: 0-240 months). Fourteen patients (35%) experienced a time lag of greater than 6 months from first detection of an oral lesion until the first diagnostic biopsy was completed.

5.3.4 The Invasive Lesion Group (IG) vs. Non-invasive Lesion Group (NIG)

Among the 40 patients interviewed, 22 (55%) were diagnosed with an invasive lesion identified as SCC and 18 (45%) were non-invasive HGL’s (see Table 1). There is no statistically difference between 2 groups in terms of gender ($P = 0.51$), average age at diagnosis ($P = 0.47$), ever smokers ($P = 0.49$) and ethnicity ($P = 0.27$).

Annual visits to a HP was reported by all (18/18; 100%) patients in NIG and 86% (N=19) in IG ($P = 0.24$). Of interest, 13 (72%) patients in the NIG had their oral lesion initially detected by a HP, compared to 6 (27%) in the IG ($P = 0.01$). See Table 1 for detailed personnel who involved in the initial identification of the lesions in each group.

There was no statistical difference in average time from detection to diagnosis between IG (14.6 ± 26.3 months) and NIG (21.0 ± 56.9 months, $P = 0.46$) and there was no difference in terms of the time lag from initial lesion detection to first diagnostic biopsy greater than 6 months (36% in IG vs. 33% in NIG, $P = 1$).

In IG, there were 20 lesions located at high-risk sites (tongue, floor of mouth, soft palate/oropharynx) and 2 located at low-risk sites (buccal mucosa and gingiva; see Table 1). Similarly, there were 17 lesions located at high-risk sites in the NIG.
Some patients (N=11, 27.5%) were first seen after surgery and we do not have the lesion size at diagnosis recorded. With those available for analysis (16 in IG and 13 in NIG), the mean area of the lesions in IG was $589 \pm 870.6 \text{ mm}^2$. This is 62% greater than those in NIG (at $364 \pm 457.8 \text{ mm}^2$). However, there is no statistical difference on the mean area or the mean largest dimension between 2 groups ($P = 0.41$).

5.3.5 Person to First Identify the Lesion

Of the 40 patients in this study, 21 (52.5%) patients reported having initially self-identified their oral lesion (Self-Identified Group, SIG) while 19 (47.5%) reported that a HP first identified their oral lesion (Professional Screening Identified Group, PSG). Of the HP’s who first identified the oral lesion, 16 (68%) were dental professionals, including 9 dentists, 5 registered dental hygienists, and 2 dental specialists.

The literature suggests that diagnosis delay is a complex combination of patient delay, which is based on the patient’s actions prior to and following the first consult with a HP, and professional delay, which can be attributed to the actions and decisions of health professionals along the referral pathway. Results from current studies have shown that patients whose oral lesion was detected through a screening exam (PSG) had different characteristics than patients who had identified their own lesion (SIG). The following section (V.3.6.) will explore and compare the characteristics of these two unique groups of patients (see Table 2).
Table 2: Demographics and lesion characteristics of SIG and PSG

<table>
<thead>
<tr>
<th></th>
<th>Total No. of Informative Cases</th>
<th>Self-Identified Group (SIG)</th>
<th>Professionally-Screened Group (PSG)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD* (years)</td>
<td></td>
<td>60.0 ± 13.6 (N=21) %</td>
<td>62.6 ± 11.0 (N=19) %</td>
<td>0.5084</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>40</td>
<td>7/21 33</td>
<td>7/19 37</td>
<td>1</td>
</tr>
<tr>
<td>Ethnicity (Caucasian)</td>
<td>40</td>
<td>18/21 86</td>
<td>17/19 89</td>
<td>0.3109</td>
</tr>
<tr>
<td>Smoking (Ever-smoker)</td>
<td>40</td>
<td>13/21 62</td>
<td>15/19 79</td>
<td>1</td>
</tr>
<tr>
<td>Remote (Outside Greater Vancouver)</td>
<td>39*</td>
<td>7/20 35</td>
<td>3/19 16</td>
<td>0.2733</td>
</tr>
<tr>
<td>Education (Less than grade 12)</td>
<td>34*</td>
<td>2/16 13</td>
<td>5/18 28</td>
<td>0.4054</td>
</tr>
<tr>
<td>Anatomical site (High risk vs. Low risk)</td>
<td>40</td>
<td>18/21 86</td>
<td>17/19 89</td>
<td>1</td>
</tr>
<tr>
<td>Mean clinical lesion size (± SD; mm²)</td>
<td>30*</td>
<td>619 ± 933</td>
<td>366 ± 419</td>
<td>0.3488</td>
</tr>
<tr>
<td>Diagnosis (SCC* vs. CIS*/Dys*)</td>
<td>40</td>
<td>16/21 76</td>
<td>6/19 32</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean number of visits prior to dx* (± SD)</td>
<td></td>
<td>4 ± 2</td>
<td>3 ± 2</td>
<td>0.029</td>
</tr>
<tr>
<td>Mean time for DTD* (± SD; months)</td>
<td></td>
<td>23 ± 52</td>
<td>11 ± 27</td>
<td>0.3605</td>
</tr>
</tbody>
</table>

*SD: Standard Deviation, SCC: Squamous cell carcinoma, CIS: Carcinoma in situ, Dys: Dysplasia, DTD: Detection to Diagnosis
+ Not all patients have information on clinical lesion site and one is without a known residential area

5.3.6 The Self-Identified Group (SIG) vs. Professionally-Screened Group (PSG)

There were no statistically significant differences between SIG and PSG in terms of mean age, gender, ethnicity, smoking habit, living outside of Greater Vancouver, education level, and anatomical site of the lesion (see Table 2). Although there is no statistical difference in mean clinical lesion size between 2 groups, the PSG presents with almost half of the clinical lesion size, compared to those in SIG. More importantly, the majority (N = 16, 76%) were invasive lesions in SIG, whereas only 6 (32%) were invasive lesions in PSG (P = 0.01). Additionally, the average number of visits to a HP prior to the diagnostic biopsy for the SIG was 4 ± 2 visits as compared to 3 ± 2 visits for the PSG (P = 0.029). Although this finding did not reach statistical significance, it is noteworthy to point out that the mean time from detection to diagnosis is more than twice as long for SIG patients as for PSG patients (23 ± 52 months for SIG vs. 11 ± 27 months for PSG).
months for PSG). In summary, these findings underscore the relevance of whether a lesion was detected through a screening exam or by the individual themselves.

5.3.7 Symptoms and Reactions with Respect to Initial Identification in SIG

Patients who initially self-identified their lesions (N=21) reported several different symptoms which alerted them to the presence of something unusual in their mouths (Table 3). Although the majority (62%) of the patients identified only one symptom, 8 patients reported multiple (2 ~ 3) symptoms associated with their oral lesion(s). Most patients reported having a painful lesion or ulcer (N=18; 86%) while five (24%) noticed a change in colour, three (14%) could feel a lump and two (10%) reported difficulty chewing. When questioned about their initial reaction to noticing these symptoms, surprisingly, 12 (57%) reported that they were not concerned about their symptoms or the presence of an oral lesion whereas only 6 (28.5%) indicated that they felt fearful or concerned.

Patients who reported a level of anxiety associated with their symptoms (N = 6) proceed to do some of the following: discuss their situation with loved ones (1), seek HP consultation (1), watch and wait (1), eat garlic (1) or do nothing at all (2). Those who were initially unconcerned about their oral lesion and associated symptoms (N = 12) were more likely to do nothing (6; 50%), to alter their oral hygiene habits (2; 17%), to use topical treatments (2; 17%), to avoid acidic beverages (1; 8%) or to seek HP consultation (1; 8%).
Table 3: Symptoms and reactions with respect to delay in SIG

<table>
<thead>
<tr>
<th></th>
<th>Total Informative Cases</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported Symptoms*</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain/Ulcer</td>
<td>18</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Colour Change</td>
<td>5</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Lump</td>
<td>3</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Difficulty Chewing</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Initial Reaction to Symptoms</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fear and Concern</td>
<td>6</td>
<td>28.5</td>
<td></td>
</tr>
<tr>
<td>Unconcerned</td>
<td>12</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Time Delay to 1st HP* Consultation</td>
<td>21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 3 Months</td>
<td>15</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>4 - 24 Months</td>
<td>3</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>&gt; 24 Months</td>
<td>3</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

*Many reported multiple symptoms
HP: Health professional

Despite this lack of concern, most (15/21; 71%) consulted with a HP within 3 months of first noticing the presence of something unusual in their mouth. Six patients (29%) however delayed consulting with a HP for 4 months or longer with 3 of these delayed professional examinations for over 24 months (see Table 3).

Some interesting characteristics of these 6 patients should be noted. Demographically, all patients were male; all were over 45 years of age, Caucasian and had a history of smoking. Four of these individuals reported being unconcerned by their symptoms or the presence of an oral lesion and of these, three undertook no actions. When queried about their motivation to seek professional consultation, the majority reported that the main reason was ‘the lesion was not resolving’ while two responded that they sought HP consultation for another medical or dental issue.
5.3.8 Timeline from Initial Identification to First Biopsy of a High Grade Lesion (HGL)

The following four figures (Figures 3 to 6) are event calendars with different DTD time lags showing a) the individual who first detected an oral lesion (by patient ■ or HP ■), b) the length of time between each HP seen along the referral pathway c) each type of HP seen leading up to diagnosis, d) the HP who performed the diagnostic biopsy and e) the diagnosis of the biopsy. Each (HP) is labeled using a colored shape to identify whether it was a dentist ★ (DDS), registered dental hygienist ♦ (RDH), dental specialist ★, medical doctor ● or medical specialist ●. The diagnostic outcome of each case was labeled as invasive ▲ (SCC) or non-invasive ▲ lesions. The time was reflected either in days (for Figure 3) or months (Figures 4-6) based on the length of the time from detection to diagnosis (DTD). Examples were made to highlight the representative cases in each group, depending on their DTD time lag.
The event calendar illustrated in Figure 3 represents the referral patterns and timelines of twelve patients interviewed and having DTD periods of between 0 and 30 days. Below are some examples which highlight the process. In the case of patient #20, the oral lesion was detected by a DDS and due to the patient’s history of being a former smoker, the lesion was biopsied immediately at the dental office with a resulting diagnosis of severe dysplasia. Patient #30 was a former smoker and had a previous history of cancer at another site. During a consultation with his Oncologist, the oral lesion was detected and biopsied immediately, yielding a diagnosis of carcinoma \textit{in situ}. Patient #12 was an 83-year old former smoker whose hygienist identified an oral lesion on the right floor of mouth and recommended that the patient consult with a physician. The patient’s family doctor examined the lesion the next day and referred the patient to
a medical specialist who biopsied the lesion a week later. The final diagnosis was CIS. Patient #22 self-detected an oral lesion on the left posterior tongue and due to his history of smoking (FS), was worried about the risk of cancer. The patient ambulated to a walk-in clinic where the physician recommended a consultation with the patient’s family doctor. The patient saw the GP the following day and upon referral to an oral surgeon, had a diagnostic biopsy 2 weeks later. The diagnosis was SCC. In the case of patient #11, a former smoker, an oral lesion was detected on the right lateral tongue by a dental hygienist during a routine hygiene and recall appointment. The patient was scheduled to have the lesion in rechecked in two weeks and when it was still present, the patient was booked for a biopsy appointment with the DSS in the same practice. The biopsy results indicated the presence of SCC. For patient #6, a visit to an MD for a chest exam resulted in the detection of an oral lesion on the right lateral tongue. The MD referred the patient to an Ear, Nose and Throat (ENT) specialist who biopsied the lesion immediately. The resulting diagnosis was carcinoma in situ. Patient #19 noticed a burning sensation on the left side of the tongue. Afraid that it could be serious, the patient booked an appointment the next day with a GP who suggested the lesion be re-checked two weeks later. Upon returning for a second exam, the patient was referred to a dermatologist two days later who then referred the patient on to an ENT. The ENT examined the tongue and recommended a biopsy one week later. The entire process from detection to diagnosis spanned approximately one month and resulted in a diagnosis of SCC.
Patient experiences reflected in Figure 4 are representative of DTD time spanning 1 to 6 months. For example, patient #39 was a smoker who self-detected a sore lesion on the right floor of mouth which thought to be the result of an ill-fitting denture. After seeing two physicians, the patient was finally referred to an ENT who performed a biopsy which resulted in a diagnosis of SCC. Patient #31, a former smoker, self-detected an oral lesion which was located at the left oropharynx. After a succession of medical and dental visits, with various recommendations including topical ointments, antibiotics and dental restorations, a referral was finally made to an oral surgeon for a biopsy approximately 2 months after the first detection. The diagnosis was SCC. Patient #26 was a former smoker who found a lesion on the floor of mouth himself and visited a walk-in clinic for an exam about a month later when it did not resolve. The patient was
immediately referred to an ENT who biopsied the lesion a month later. The histology showed evidence of SCC. For patient #21, a non-smoker, a lesion appeared on the lateral border of the tongue and persisted for 2 months despite self-medicating with polysporin and systemic antibiotics (patient’s wife was a retired MD). The patient finally consulted with an MD and was immediately referred to a dermatologist for a biopsy the same day. The biopsy results showed evidence of carcinoma in situ. For patient #34, a non-smoker presented with a sore throat which did not resolve. After a series of medical exams and antibiotic treatment, the patient finally saw a DDS who provided a referral to an ENT. The ENT recommended an ultrasound to further examine the ‘lump’ which had by then developed in the patient’s throat. A biopsy was then conducted, two and a half months from the first symptom and the outcome was SCC. A former smoker, patient #17 identified a lesion on the right ventral tongue following a cold. When the lesion was still present after 3 weeks, the patient saw three physicians over the period of one and a half months before finally being referred to an ENT for a biopsy. The final results of the biopsy disclosed the presence of SCC. Patient #7 was a non-smoker and self-identified an ulcer on the left tongue. The lesion persisted for a month before the patient presented to a walk-in clinic for an exam. The patient was given a “dental paste” to apply topically but when the lesion continued to persist, a second MD was seen. At this appointment, the patient was referred to a dermatologist and was prescribed steroidal topical medication. At a subsequent dental appointment, the patient was finally referred to an oral medicine specialist who biopsied the lesion immediately and a diagnosis of SCC was determined. The time from detection to diagnosis was 3 months. Patient #38 was also a non-smoker who self-identified a tongue lesion. After 3 months, with
symptoms of pain on swallowing, the patient consulted with an MD recommended that
the patient see a dentist. The patient then saw a dentist who provided a referral to an
oral surgeon. The specialist examined the lesion at two subsequent appointments
before performing the biopsy, nearly one month after the patient’s first HP visit. The
biopsy results showed the presence of SCC. Patient #5, a long-term smoker, also self-
identified a lesion on the lateral tongue. Despite having mentioned the lesion in passing
to various physicians over a 5-month period, no one examined the lesion. Finally, the
patient presented to an MD with a persistent finger infection and asked that the tongue
lesion also be examined. The MD referred the patient to a cosmetic surgeon a few days
later and a biopsy was performed at a subsequent appointment. The biopsy result was
SCC; however following a partial glossectomy, the cancer was found to have
metastasized and unfortunately, this patient is now deceased.
Figure 5 illustrates patient experiences from DTD with a diagnostic delay of 6 to 30 months. In the case of patient #4, a former-smoker self-identified a lesion on the right ventral tongue. At a restorative dental appointment one month later, the patient asked the dentist to examine the lesion but the DDS made no recommendations. At a subsequent dental appointment, the dentist referred the patient to a temperomandibular disorder (TMD) specialist approximately one month later. The specialist was unconcerned by the lesion presentation and prescribed topical gel. One month later, the patient saw the specialist who performed a biopsy the same day. The diagnosis was determined to be SCC. Patient #18, also a former smoker had a lesion detected on the floor of mouth by an ENT during an exam related to throat polyps. The ENT scheduled
an appointment to recheck the lesion 6 months later and performed a biopsy at that
time. The biopsy results showed evidence of severe dysplasia. A non-smoker, patient
#14 noticed a lesion on the left lateral tongue which persisted for 2 months. At a routine
medical exam for an inhaler prescription renewal, the patient showed the lesion to the
MD. The patient was then referred to an oral surgeon who monitored the lesion for
nearly 8 months before a biopsy was performed. The diagnosis was severe dysplasia.
Patient #28 was a former-smoker whose dentist detected a lesion on the floor of mouth
at a routine hygiene appointment. The dentist recommended a referral to an oral
surgeon however it took 7 months before an appointment was available. The biopsy
was performed shortly thereafter. The biopsy results showed the presence of SCC. In
the case of patient #15, a smoker, a lesion on the anterior ventral tongue was identified
by a Registered Dental Hygienist. The patient was referred for immediate biopsy
however the patient rescheduled the biopsy appointment as her dental insurance was
being discontinued and she expressed financial concerns. Six months later, the patient
visited the DDS for restorative work, at which time the DDS made a second referral for
an immediate biopsy. The patient attended this appointment a couple of weeks later and
received a diagnosis of CIS.
Figure 6 illustrates the experiences of patients from DTD with a diagnostic delay of 30 months to 240 months (20 years). For example, patient #1 had an oral lesion detected on the left ventral tongue by a DMD. The dentist informed the patient (who was a former smoker) of the lesion and instructed him to advise the dentist if it changed. Nothing further was done for 2.5 years until the dentist determined that the lesion had begun to change and decided to refer the patient to an oral surgeon. The oral surgeon examined the lesion and performed a biopsy two weeks later. The diagnosis was SCC. The longest diagnostic delay was experienced by patient #24 who was a former smoker who first noticed a sensitive area on the left lateral tongue approximately 20 years ago. The patient felt that the lesion was either a canker sore or an allergic reaction and reported being unconcerned by her symptoms. The patient attended a dental exam in
1996 (11 years ago) where the dentist noted the lesion and recommended that the patient consult with an MD for a possible biopsy, which was not completed. Six months later, the patient had an annual physical exam with an MD who recommended that the oral lesion be monitored over time. The patient visited the same MD twice more over a 9-year period and on the third visit in 2005, the MD recommended a referral to an ENT. The patient consulted with an ENT a few months later whose primary recommendation was to refer the patient to the BCCA Dysplasia clinic; however the patient reported being unreceptive to this and cancelled the subsequent biopsy appointment made by the ENT. The patient saw the ENT again and finally agreed to a biopsy procedure on the third visit to this specialist. The diagnostic biopsy revealed carcinoma in situ on the floor of mouth and severe dysplasia on the lateral tongue. Another notable case is that of patient #27. This patient had a lesion detected on the right buccal mucosa by an RDH during a routine hygiene appointment in 1997. It was suspected to be lichen planus, a chronic inflammatory condition sometimes mimicking precancerous or cancerous lesions. No further recommendations were made although the patient was a current smoker. Three years later, at a hygiene appointment in a different dental practice, the lesion was examined using toluidine blue and smoking cessation recommendations were made. No further comments were made regarding the lesion until 2006 when the lesion was again examined using toluidine blue stain. The dentist recommended continued monitoring until the next annual recall at which point, a biopsy appointment was made and subsequently performed by the DDS. The diagnosis was SCC.
5.4 Discussion

5.4.1 Demographics and Regular HP Visit and Stage of Initial Diagnosis

There is no difference in terms of age, gender, ethnicity, place of residence, level of education or anatomical site of the lesion between invasive and non-invasive lesion groups. This was consistent with many reports in the literature (Amir et al. 1999; Kerdpon and Sriplung 2001; Onizawa et al. 2003). However, some researchers found age might have different impact on the disease aggressiveness. For example, Allison et al. found that increased age exerted a significant influence on delay (Allison et al., 1998; Tromp et al. 2004) while others found in contrast that increased age provided a marginally significant reduced risk of being diagnosed with an advanced stage of oral carcinoma (Kowalski et al. 1994). A recent study of oral cancer patients conducted in Toronto, Ontario found significant associations between increased total delay and the following: female gender, frequency of dental examinations and being a non-smoker (Yu et al. 2008). The positive correlation between being a non-smoker and being diagnosed with advanced stage disease or having increased diagnostic delay was also confirmed by others (Kowalski et al. 1994; Pitiphat et al. 2002) but was not found to exist in the present study. Also in contrast to the present study were the findings from a study in the UK that further education (post-secondary) was significantly associated with increased patient delay as well as the amount of tobacco smoked per day (Llewellyn et al. 2004).

Interestingly the results have suggested that annual visits to an HP have been associated with less aggressive disease. This is consistent with findings in BC from 20 years ago, which identified that oral cancer patients who received regular dental care
were more likely to have Stage I or II disease (Elwood and Gallagher 1985). However, among the 37 patients in the current study with regular annual check-ups by either dental or medical professionals, still, almost half of them had a lesion identified by the patients themselves. These data underscore the needs for regular screening in action.

5.4.2 Lack of Oral Cancer Awareness

Less than half of the patients (N=19) reported being aware of oral cancer prior to their diagnosis. Oral cancer knowledge has been well published as being alarmingly low even among the general public in developed countries. In a 1995 survey of 1894 randomly selected adult residents in Great Britain, only 56% reported that they were aware of oral cancer as compared to 97% who were aware of lung cancer and 96% who were aware of skin cancer (Warnakulasuriya et al. 1999). In this same study, it was determined that 76% of respondents were aware of the link between oral cancer and smoking while only 19% were aware of the link with alcohol misuse. In another survey conducted in North Carolina in 2002, 1096 respondents were polled and 14% had never even heard of oral cancer (Patton et al. 2004). Furthermore, only 53% could identify one symptom of oral cancer and 25% could not state any signs or symptoms of the disease. These statistics highlight the need for awareness building among the public as they clearly lack sufficient knowledge of many important facts relating to oral cancer.

5.4.3 Earlier Detection in Professional Screening Group

Two distinct groups were identified according to who first identified the oral lesion: 21 patients who were responsible for self-identifying their oral lesion (SIG) and 19 patients who had their oral lesion first identified through a screening conducted by a
HP (PSG). There is a significant difference of the stages of disease between SIG and PSG. In PSG, 68% (13/19) of cases were in NIG (T0 or below), as compared to the SIG in which only 24% (5/21) had a pre-invasive lesion diagnosed ($P = 0.01$) (see Table 2).

Also of significance was the average number of visits to a health professional prior to diagnosis. The SIG patients tended to see 4 ($\pm 2$) HP’s before a diagnosis was made whereas the PSG patients saw an average of 3 ($\pm 2$) HP’s prior to having a biopsy ($P = 0.029$) (see Table 2). In a study of 100 consecutive cases of oral SCC, Hollows et al. found that significant delay occurred when patients were not referred directly to the hospital maxillofacial unit, a primary care facility for head and neck cancers in South Yorkshire. Indirect referrals resulted in more HP visits prior to biopsy and increased diagnostic delay ($P = 0.012$) (Hollows et al. 2000). In a similar fashion, it is possible that as the SIG overall had more HP visits prior to biopsy that this may be a contributing factor to the overall greater diagnostic delay as compared to the PSG cases. This is supported by the results that reveal the mean time from detection to diagnosis was twice as long for individuals in the SIG as for those in the PSG group (Table 2). This increased time lag suggests that patient delay prior to the initial HP visit is one of the most significant contributors to the total diagnostic delay.

When the clinical size of the lesion was considered, SIG lesions were approximately twice the mean clinical size of lesions from PSG (Table 2). This might be related to the increased time from detection to diagnosis associated with this group, which would allow the lesion a greater amount of time for growth. The size of the lesion has been shown to be the most influential determinant of whether a lesion was at a high
risk for developing SCC (Napier et al., 2003). It is possible that an increased time delay from detection to diagnosis would allow more opportunity for growth and advancement in stage as well as an increased opportunity for more “hits” from oncogenic agents, resulting in a larger lesion and a worse prognosis.

5.4.4 Dental Professionals May Play Important Roles in Screening

Of note, the majority (84%) of patients in the PSG was initially examined by a dental professional. This is likely due to the increased knowledge and frequency of oral cancer screenings performed by dentists as compared to physicians. A 2006 survey of 338 general practice dentists (GDP’s) in the UK found that 92% of GDP respondents reported carrying out a systematic oral examination for oral cancer at initial patient appointments for patients over 40 years of age (Kujan et al. 2006). An American survey comparing the screening activity between physicians and dentists found that only 18% of MD’s reported conducting a routine annual oral cancer exam on at least 50% of patients as compared to 83% of dentists who report doing so (Yellowitz and Goodman 1995).

Our results are consistent with others in that patients referred from a dental office were of significantly lower stage at diagnosis than those from a medical office and a dental office (rather than a medical office) is the most likely source of detection of an oral lesion due to screening (Holmes et al., 2003). It must be noted that a selection bias may be present due to the majority of patients in this study attending BCCA due to a referral from an existing oral biopsy service or dental network. There remains however a continued need for additional education of medical professionals relating to oral cancer
and screening practices in order to increase their confidence and frequency in both screening and early identification of potentially malignant lesions. Additionally, this indicates that dental professionals may play an important role in early identification of oral lesions at risk.

**5.4.5 Common Initial Symptoms and Reaction of Patients with HRL’s**

As outlined in Table 3, 86% (18/21) of the first symptoms reported by the SIG patients were the sensation of pain or the presence of an ulcer. The literature reports a wide variation of results with respect to the first symptoms reported by oral cancer patients. This is consistent with other studies. Pain/ulcer was reported as the first symptom in 81% of patients in a study by Llewellyn *et al.* which examined 53 newly diagnosed oral cancer patients in the UK (Llewellyn *et al.* 2004). Other reports include a range of frequencies of pain/ulcer reports varying from 19 -62% (Yu *et al.* 2008; Onizawa *et al.* 2003; Guggenheimer *et al.* 1989; Amir *et al.* 1999). Despite this variation in numbers of similar reports, the literature consistently found no significant relationship between the first symptoms of pain/ulcer and patient delay. This was also the case in the current study.

One surprising finding was the significant number of patients who reported a lack of concern upon first identifying their oral lesion. As noted in Table 3, 67% (14/21) of SIG patients reported feeling unconcerned at the prospect of finding a lesion in their mouth. This attitude further impacts the timing leading up to seeking HP consultation. Six (28%) of these patients had a delay of over 6 months prior to seeking the first HP consultation. The correlation between this lack of concern regarding symptoms and
ensuing delay is of significant interest. In a 1996 study, 367 women with a definitive breast cancer diagnosis were interviewed to explore the factors contributing to delay occurring between the first consultation with a HP and when the diagnosis was made (Caplan et al., 1996). Of the 157 women who reported that the delays were due to the patient themselves (as opposed to some portion of the health system), 37.6% indicated that the cause of the delay was that they felt their problem was not important or not urgent. Caplan et al. reported that their initial presumption was that fear would be a contributing factor to delay; however it became clear that in fact a lack of fear or concern was a greater deterrent to patients than fear. This is consistent in the present study as a lack of fear or a report of “unconcerned” was found to contribute to the patient delay. The notion that an oral lesion (which might be painful and/or ulcerative) is of little or no concern to patients indicates that more awareness on this disease is needed to impress upon the public the potential risks associated with ignoring these lasting symptoms. It is noteworthy that many of the early lesions are asymptomatic. In the PSG, none of the patients experienced pain or ulcer; however, nearly one third (N=6) of the lesions in this group were already invasive lesions.

5.4.6 Health Professional Who Performed Biopsy

Interestingly, in the SIG, most patients (13/21; 62%) had their biopsy performed by a medical specialist while fewer had a biopsy conducted by a dental specialist (8/21; 38%, see Table 4). Among the PSG patients, most patients (14/19; 74%) had their diagnostic biopsy performed by a dental specialist. This data is consistent with the finding that the majority of the SIG patients sought a medical professional for the first
consultation regarding their oral lesion which would sensibly lead to having a biopsy performed by a member of the medical community. Since most PSG patients first saw a dental professional as a result of receiving an oral cancer screening in a dental office, it is also logical that this group would have a biopsy performed by a dentist or dental specialist.

5.4.7 Factors that Impact the Time Lag

The majority of patients interviewed (N= 28, 70%) received a diagnostic biopsy in less than 6 months after the first detection of the lesion; however, the mean time from detection to diagnosis in SIG was twice as long to have the initial biopsy performed as the PSG (23 ± 52 vs. 11 ± 27 months) (see Table 2). This is the evidence to support the potential patient factor impacting on the diagnostic delay, especially in the patients in SIG. Mean total delay times reflected in the literature include 3 to 11 months (Pitiphat et al. 2002); (Onizawa et al. 2003); (Kerdpon and Sriplung 2001; Yu et al. 2008). As such, the mean total delay reflected in the present study in the SIG group was notably longer than in comparable studies. The majority of patients in the SIG group (71%) however had a diagnostic time lag of less than 6 months which is within the range of 2.75 months to 10.7 months presented in the literature.

Also noted was only 68% of the PSG group were less than 6 months from detection to diagnosis. This indicates the potential professional factors impacting on the diagnostic delay. During the interview (see section V.3.8 event calendars), we found out there are both patient and professional factors in both SIG and PSG. The patient factors include a lack of concern and fear (N=15), a lack of oral cancer awareness (N =
13) and financial limitation factors (N = 1). The professional factors include lack of knowledge in differentiating high-risk lesions (N = 8), delay in initiating the referral or ‘watch and wait’ (N = 8), delay in scheduling of referral appointments to the specialists (N = 5) and improper management of lesions (N = 1).

5.4.8 Strengths and Limitations of Part I: Personal Interviews

Personal interview surveys are useful when the desired sample consists of respondents in a very specific target population. In a personal interview, the interviewer has the ability to probe respondents for clarification of responses and observe the individual’s behavior, which allows for the exchange of material and/or information between respondent and interviewer. Personal interviews have many advantages such as good response rates, enabling respondents to tolerate longer interviews and allowing researchers to test and observe attitudes and behaviors. The format of open interaction in this form of survey may encourage story-telling and allows for gathering of valuable qualitative data. Additionally, personal interviews allow information to be collected from those who are visually impaired and may be unable to complete a written questionnaire. Personal interview methods also present certain limitations such as being time-consuming and resource-intensive, being non-representative if the respondent’s location does not match the desired target population, imposing a recall bias due to patients’ inability to accurately recall dates and events and potentially introducing an interviewer bias.

It must be noted that the current study drew participants from a pool of patients already attending the BCCA Dysplasia Clinic. As such, these individuals are not
representative of the general population of oral cancer patients in BC as they have certain unique demographic characteristics including: having access to dental and medical care, having had a biopsy that made them eligible to attend a dysplasia clinic (dysplasia, CIS or SCC), did not have advanced tumours of the head and neck, were of age and mobility that they allowed them to ambulate to a clinic for follow-up care and had been under the expert care and treatment of specialists in a cancer-specific facility. Careful consideration must be given in generalizing the results of this study due to these specific patient characteristics which impose a sample bias. Furthermore, the response rate of this study is not representative of what would be achieved in a province-wide study due to the nature of patients in continuing cancer care who are highly motivated to participate in research that is associated with a facility that has provided excellent care and treatment. The limitation of only providing an interview in English is an additional factor that must be considered when attempting to generalize these results. Many cultures have been under-represented in this sample due to the limitation of not speaking English. Although there were no patients who were eligible to participate in this study but were dismissed due to a language barrier, it can be argued that many other areas of the city and province would be populated by individuals who would be excluded based on this factor alone.

Patient responses regarding the date of first detection of an oral lesion were difficult to confirm. Patient responses regarding the first health professional consultation were confirmed through phone calls to the first health professional visited where the lesion was examined. It was noted that in most cases, although patients were often
unable to recall exact dates, generally the month of the first visit was accurate within ± 1 month.

**Table 4: Factors Contributing to Diagnostic Delay of SIG and PSG after their initial HP visits**

<table>
<thead>
<tr>
<th></th>
<th>Self-Identified Group (SIG) (N=21)</th>
<th>Professionally-Screened Group (PSG) (N=19)</th>
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<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td><em><em>First HP</em> Seen</em>*</td>
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<tr>
<td>Dental Professional</td>
<td>5</td>
<td>24</td>
<td>16</td>
</tr>
<tr>
<td>Medical Professional</td>
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<tr>
<td><strong>Number of HP's Seen Before Biopsy</strong></td>
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<tr>
<td>0-3</td>
<td>11</td>
<td>52</td>
<td>17</td>
</tr>
<tr>
<td>&gt; 3</td>
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<td>48</td>
<td>2</td>
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<td><strong>Site of Lesion</strong></td>
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<td>3</td>
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<td><strong>Awareness Of Oral Cancer</strong></td>
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<tr>
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<td>9</td>
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<tr>
<td><strong>Time from 1st HP to Biopsy</strong></td>
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<td>0-6 Months</td>
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<td>71</td>
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<td>&gt; 6 Months</td>
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<td>6</td>
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<td>Invasive</td>
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<td>76</td>
<td>6</td>
</tr>
</tbody>
</table>

* HP: Health Professional  
DDS: Dentist  
MD: Medical Doctor
6. Part II: Focus Group Discussions

6.1 Objectives

The objectives of Part II of this study were to use focus group discussions to: 1) gather feedback on the questionnaire developed in Part I, 2) to obtain recommendations from participants regarding future planning for delivery of this questionnaire on a province-wide basis from the patients' point-of-view and 3) to share patients' experiences from detection to diagnosis and treatment, including their views on patient awareness and experiences interacting with health professionals during this journey.

6.2 Methods

6.2.1 Participant Recruitment

During interviews, patients who participated in Part I were invited and verbally consented to potentially participate in the focus group discussions (N=7). These seven patients were then contacted by telephone and formally re-invited to attend a focus group to discuss the questionnaire and to share some of their personal views on their experience leading to diagnosis. Additionally, some participants (N=5) currently attending the BCCA for ongoing care following treatment of oral cancer (who were ineligible for the Part I study due to the time of their diagnosis to interview period being longer than 12 months which can cause recall bias) were invited and signed a consent
to attend the focus group. Their participation provided an external perspective on the questionnaire and they also provided information on interactions with other patients and HP's between the time from initial detection of their oral lesion to diagnosis and treatment. They were identified and invited during their visits to BCCA and confirmed through phone calls. On the day of focus group, they provided written consent.

6.2.2 Conduction of Focus Group Discussions

Each focus group lasted 60-80 minutes and was led by a facilitator (H. Biggar), a co-facilitator (C. Poh) and 2-3 supporting staff. The supporting staff provided help in organizing, recording participant responses and monitoring the involvement of each participant. The discussion sessions were audio taped and transcribed verbatim. The transcriptions from the 2 focus groups were then analyzed to find the common themes.

At the beginning of each session, all the participants were given the opportunity to review the questionnaire (see Appendix A.4 for the guiding questions used in the FG discussions) then were asked for their feedback on format, length, content and clarity of the questions. In light of the current format of the questionnaire, the group was asked for input as to their opinions on the best format of a questionnaire to be delivered to a province-wide group (i.e. email, telephone, written correspondence, in person, etc). Participants were then asked about the quality of their experiences with health professionals from first detection to diagnosis of their oral lesion in terms of positive or negative interactions and potential for improvement of these interactions. The focus group was also asked how they felt public awareness of oral cancer could be improved upon. Finally, the group was queried as to what types of information they had received
throughout the course of their experience that they had found the most useful. The two sessions were 1.5 hours in length and was held at the BC Cancer Research Centre (BCCRC). The questions for both focus groups are given in Appendix A.4.

6.2.3 Demographics of the Participants of the Focus Group Discussions

The two Focus Group discussions were conducted in April and June, 2008. The characteristics and demographic data of participants in both focus groups are presented in Table 5. The first focus group consisted of seven participants, six of which were previously interviewed participants from Part 1 and the second focus group consisted of 5 participants, 2 of which had participated in the interviews from Part I (please see section VI.2.1. for details).
Table 5: Demographics and Characteristics of Focus Groups 1 and 2

<table>
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*SD: Standard Deviation
SCC: Squamous cell carcinoma
CIS: Carcinoma in situ
DTD: Detection to diagnosis

6.2.4 Data Analysis

Data was analyzed, sorted and coded using a Microsoft Excel spread sheet. This method was used as the structure of the Excel spreadsheet allowed for easy classification and more direct comparisons of individual responses. The transcripts were repeatedly read in order to become familiar with the data, and identify major recurrent themes. Once the major themes were identified and coded, this data was
extracted and regrouped according to the appropriate thematic reference on a Microsoft Excel spreadsheet thus allowing comparisons between and within groups. In addition, the data was sorted in a systematic manner to allow comparisons and interpretations of key themes within the participant’s original context.

6.3 Results

6.3.1 Main Themes

As the result of the analysis of the focus group discussions, 3 main themes and several sub-themes were identified and used to represent the views of participants:

1. Feedback Regarding the Questionnaire
   a. Format of Questionnaire
   b. Recommendations for Province-Wide Questionnaire

2. Patient Experiences Leading to Diagnosis
   a. Patient Awareness of Oral Cancer
   b. Patient Perspectives on Interactions with Health Professionals

3. Patient’s Experience from Diagnosis to Post-Treatment

Quotations from the focus group discussions are used to highlight the responses from the participants and are quoted verbatim. Overall findings from both focus groups are discussed in the following sections.
6.3.2 Theme 1: Feedback Regarding the Questionnaire

Focus group respondents were asked to provide feedback regarding the format of the questionnaire in terms of length, clarity, use of an interval scale and the overall comprehension of the survey tool. Participants then discussed the potential for delivery of the tool on a province-wide scale and made recommendations for the format, delivery method and timing of such a survey. Details of their responses to these questions are outlined in the following sections.

6.3.2.1 Format of Questionnaire

The feedback from participants on the overall format of the questionnaire was positive. The general comments indicate that the questions were thorough, logical and appropriately sequenced to ensure that the concepts were well understood by the interviewees.

“You ask the questions and the sequence of questions here brings out exactly what the response was meant to be…”

The Length of the Questionnaire

Many commented on how the questionnaire appeared long when they reviewed it at the beginning of the discussion; however, when it was delivered verbally, the length seemed to be justified.

“It looks long on paper but it isn’t.”

“I mean there are a lot of questions but that is what you are looking for…”

“It’s a little more lengthy than what I would have expected it to be, however it’s very clear.”
“I think it’s very good especially verbally – like if you’re asking the questions”

Recall of the Time and Dates for all the Events

Focus group participants were asked for their opinions on how the questions could be asked in order to improve people’s ability to accurately recall dates and events. There was a strong agreement among the group that patients should be informed in advance that they would be participating in an interview questionnaire or receive a copy of questionnaire in advance of the interview so that they could be more prepared to answer the questions accurately. Conversely, it could be completed prior to the actual interview in order to improve the accuracy of the responses. This is consistent with the observation from the interviewing process that patients often had difficulty recalling dates and events from first detection of their oral lesion and leading up to the diagnostic biopsy.

“So perhaps a paper (questionnaire) ahead of time and come and have the interview and if there were some questions that the person didn’t understand, you would be able to tell them what they are looking for in that question. So a combination.”

The Interval Scale

Participants were also asked about the format of the interval scale (see Appendix A.3) which was used to identify patients’ satisfaction levels throughout interactions with various health professionals. Although the tool has been recognized and used frequently in evaluation of scale of satisfaction, there were several suggestions as to how the scale could be revised to accommodate individuals who might prefer word or visual images to represent satisfaction levels.
“I think possibly some people are comfortable for putting a numerical value to things because we are doing it on a scale from 1 to 10 on how you feel today, but for some people a word is better sometimes.” “…… like ‘excellent’ or ‘terrible’.”

Other feedback from the groups suggested that it would be helpful to have a space on the interval scale where patients could make comments to clarify or expand on why they responded in a certain way.

“You had some comments that were down in part of the scale, you might have a section down here with comments as to why. Well I just mean if someone was unhappy with a surgeon or their GP, or some part of this process…”

6.3.2.2 Recommendations for Province-Wide Questionnaire

Preference of Written Format for Date Recall

Focus group participants were asked what format of questionnaire would be easiest to respond to if delivered to oral cancer patients across British Columbia. There was no concrete unanimous agreement on whether the format should be verbal or written and some suggested a combination of both. However, general consensus is that a written format would provide time for deliberation and better recall of dates.

“If it’s verbal, you obviously haven’t thought of perhaps all the things you wanted to say and you’ll miss something.”

“…most people are able to speak right out and don’t mind right away telling you the answer and then given a written (set of the) same questions, they might even go look up some of the answers and be more accurate.”

Posted Mail

One individual felt that a questionnaire could be sent out in postal mail as long as it was made easy to send it back, such as “in a preaddressed envelope”.

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“No Phone”

The prospect of reaching patients by telephone incited a consistent response from the focus group participants as they indicated that in this generation, people are plagued by telephone surveyors and a common first reaction is to hang up. Many vocalized that they would not be receptive to any kind of telephone survey when it involved sharing personal information

“I feel that when I’m giving personal information, the telephone is not a place I want to be doing it on, that’s all. I stay away from it.”

A potential solution was suggested by one participant that if the patients were informed in advance that they should expect to receive a call from a BCCA representative regarding the survey, they would be very likely to be receptive to the call. Another suggestion was to have a switchboard intermediate who could confirm the validity of the call.

Email

When asked about the effectiveness of a questionnaire delivered via email, one group unanimously agreed that this would be the least effective method while the second focus group disagreed. According to the participants in the first focus group, extensive length of many email surveys, the frequency of spam, the high number of poorly designed surveys and the potential for misunderstanding questions were cited as some of the reasons an email survey would be the last preferable format.

“…the internet surveys can go on screen after screen and pretty soon you say I don’t care what the answer is anymore.”

“…… if I don’t know what's coming, I delete it.”
“I think you are more open to misunderstanding……if people didn’t understand the question.”

In contrast, some of the second focus group participants felt that an email-delivered questionnaire would be more cost effective and easier to manage, allowing patients to complete the survey on their own time. Others however, felt that email is still not commonly used among some ethnic or age groups and as a result would disadvantage these populations by not being accessible to them.

“Email I’m against because I’m computer illiterate still and there are a lot of ethnic people and to me, you’re using a certain portion of the population and older people.”

Compulsory Questionnaire and the Timing of Delivery

Several participants indicated that they felt the questionnaire should be a mandatory step in process of patient care. They felt that this would increase the response and asserted that once given a diagnosis of cancer, a person is more likely to comply with a given process of patient treatment, care and research.

“….if you want to make it work as far as response is concerned, you have to take the voluntary aspect out of it. That is has to be mandatory that once, it has to be part of the process.”

“Make it mandatory as was indicated here that is part of the, once the biopsy comes back positive then this is part of it, you have to do it.”

Despite these assertions, requirements of ethics boards mandate that participation in research is voluntary. Therefore, future surveys must continue to to be voluntary in order to comply with ethics requirements.
Most agreed that it would be most appropriate to request an interview or deliver a questionnaire as soon as the biopsy results are shared with the patient so that all the events leading up to this date would be easy to recall.

6.3.3 Theme 2: Patient Experiences Leading to Diagnosis

In order to better understand the experiences that patients face from first detection of an oral lesion until diagnostic biopsy, focus group participants were asked to share their personal experiences. Respondents indicated that factors such as a widespread lack of oral cancer awareness and notable variation in the expertise and screening practices of health professionals contributed to the diversity of their experiences. The feedback on these factors will be discussed in the following sections.

6.3.3.1 Awareness of Oral Cancer

Lack of Awareness in General Population

Participants indicated that they felt there was a general and concerning lack of oral cancer awareness and even complacency in terms of the seriousness of the disease. Participants stressed the importance of prompt consultation with a health professional on detecting an oral lesion and felt this is a critical piece of knowledge that is missing in public awareness.

“There’s just a general ignorance on the whole subject.”

“Cancer is so pervasive but oral cancer, what do we know about it (oral cancer)?”
It is noteworthy that both focus groups commented extensively on the common incorrect assumption that people without traditional known risk factors, especially smoking are resistant to cancer. The lack of knowledge about oral cancer risk factors lead to people overlooking concerning symptoms due to a false sense of security in being a non-smoker.

“…and like I wasn’t aware of that before so I am a non-smoker and I would have never expected to get oral cancer.”

“One thing I would like to say is that what fits the criteria. I don’t smoke, I am not that unhealthy, I mean not totally healthy but you know I am a vegetarian, I don’t eat a lot of stuff that could cause health reasons. I didn’t know that could happen.”

It was also identified that beyond the known risk factors, other risk factors may be poorly understood or under reported, allowing lesions originating from these sources to go unnoticed. A lack of awareness and knowledge of risk factors was felt to result in more instances of oral cancer progressing without early detection.

“People think oh I don’t smoke I won’t get cancer which isn’t always the case. So it’s almost like people need an education.”

How to Raise Public Awareness

When participants were asked about ways that public knowledge and awareness of oral cancer could be increased, they indicated that they felt the HP held a major responsibility in public education. HP’s, especially dental professionals, can use examination appointments to communicate and educate patients about oral cancer and its risk factors. The participants also felt that the media played a significant role in educating the public, including both audiovisual and printed information. Some
participants also felt that printed material, such as brochures, magazine articles and newspaper articles would be valuable in educating the public on oral cancer.

“I think media is the answer. Very important one.”

“Articles – like an interview in the newspaper that it’s something that people need to be aware of.”

It was emphasized however that printed information needs to be very brief and succinct in order to convey a strong message.

“Just one page. If you have this one page in the newspaper, airtight……”

Interestingly, it was also suggested that perhaps the health care professionals would benefit from reading informative articles in order to increase their own oral cancer knowledge and awareness. It was also pointed out that certain sectors of the population, which are disadvantaged and high-risk, may not value oral cancer awareness or education and thus be more difficult to help. Community outreach was cited as an important component of increasing public knowledge for those who have little access to the health care system or other forms of oral health education.

Participants felt that having been through the experience of oral cancer, they had learned the importance of early detection and prompt consult when a lesion arises. They expressed that this experience and knowledge gave them a responsibility to help inform others.

“I think we’re walking help for other people because they’ve seen us go through it and they are more diligent about getting things checked out for themselves.”
6.3.3.2 Patient Perspectives on Interactions with Health Professionals

When the participants were asked to comment on their interactions with health care professionals leading up to diagnosis, a wide variety of experiences were shared, including both positive and negative commentary. Among the negative feedback on experiences with health professionals were concerns about a lack of oral cancer awareness and an overall lack of oral cancer screening being conducted among HP’s.

Positive Interactions – Prompt Attention, Diagnosis and Referral

The focus group participants had many positive experiences to share regarding very prompt attention, accurate and speedy diagnoses and thorough oral cancer screening. Participants shared examples of when health professionals were very prompt to recognize when a lesion was serious and made timely and appropriate recommendations for patient referral.

“I appreciated the way that he (the dentist) responded to expedite the process once the red flag went up and he was in the loop for that…He has been very supportive after the fact too.”

“They gave me an accurate diagnosis and I was very impressed and also this important key factor to interest the later prognosis.”

“The timing was very fast, yeah. Very satisfying.”

In several cases, participants were impressed at the thorough screening of the oral health professional which detected an oral lesion in the absence of any symptoms.

“In my case, I did not have any symptoms that I was aware of. The dentist picked up on it.”
“...it was pre-cancer – it was underneath my tongue which I never noticed. It was caught by the dental hygienist.”

Interestingly, one participant expressed that the younger health professionals seem to be much more current in terms of oral cancer knowledge and awareness than some of their contemporaries.

**Negative Interactions - Lack of Awareness in HP’s**

On the other hand, many participants expressed their frustration in the lack of expertise of HP’s in terms of identifying concerning oral lesions and taking appropriate action.

“I went to see a Doctor 3 times, two different Doctors and a Dentist twice before I was sent for the test. Can’t they recognize something?”

One individual noted that it was only because of his own persistence in convincing HP’s of the seriousness of his condition that he was granted a biopsy and a diagnosis was made.

“...my condition could have been a lot more serious than it was because I was being persistent, knocking on doors and saying okay, this is not going away.”

Several participants were critical of dental HP’s, indicating that they focused their practice more on cosmetic and periodontal outcomes than on oral health education and screening. Some were concerned about the overall lack of knowledge and expertise in the dental field and whether this was the reason many oral cancers were being missed or biopsies were not being performed. Many felt that health practitioners often dismissed oral lesions that they could not easily diagnose or recognize. They were disappointed by how little many health professionals seemed to know about oral cancer.
“...I would suspect like anything else that they would send you somewhere to have a look at it if he didn't know instead of dismissing it. I mean that's the normal process of things I think – they send you off to a specialist if they don't know.”

“...how many people were dying from it before because nobody was paying attention to it. Nobody was picking up on it.”

**Negative Interactions – Lack of Oral Cancer Screening Activity**

Participants shared a mutual concern regarding the lack of frequent oral cancer screening being performed in dental offices.

“What shocked me the most was hearing from my dentist that not every dentist looks at patient’s tongues when they go for a visit – even today.”

“I don’t know what the percentage is out there of dentists who don’t check the tongue.”

Participants commented that they felt screening was valuable and a responsibility of the dentist during regular check-up appointments.

**6.3.4 Theme 3: Patient Experiences from Diagnosis to Post-Treatment**

**Lengthy Waiting time for Biopsy Results**

Several participants expressed frustration with the length of time that passed following the biopsy until diagnostic results were shared with the patient by the health professional. These individuals felt that the timing of the results was crucial as their lives were put on hold until the results were made available.

“When a Doctor sits on the results for 2 weeks and the results are bad and that cuts down 2 weeks you could be in the line-up for getting fixed. So I had a real issue with that... then you are losing valuable time, could be life and death.”
“I kept pushing and knocking on the doors and saying this is going on for too long.”

Experiences in Receiving Cancer Diagnosis

Participants expressed in various ways the fear and anxiety they experienced in receiving their oral cancer diagnosis. They also described feelings of stress and dread over the potential of a reoccurrence despite a positive prognosis following their treatment.

“The dental surgeon should understand that the patient is under stress. The word cancer, the first time it was mentioned was in his office. From then on it was stress.”

“…once you are told that you have got that C word, you ultimately, because of the knowledge you have got we know of other kind of cancers out there but the oral one, we are not knowing the kind of the impact it can have and how dangerous it can be.”

“I was with a new doctor after surgery. He said surgery is done and you are fine. Well I am not fine because it can come back.”

Pre- and Post-Surgical Uncertainty

Many participants had strong feelings about negative interactions they had with HP’s regarding poor communication of the post-surgical outcomes. Participants expressed frustration at the lack of understanding they had going into surgery and the shock they experienced when they realized the post-surgical convalescent period could often be quite extensive.

“My big thing was post-(treatment)care. I was not informed of what was going to happen.”

“I figured the swelling would go down, I’d go back to normal and everything. I phoned and they told me anywhere up to three months…”

“I was not prepared. Not prepared at all.”
Patients also indicated the significant lifestyle compromise they faced following treatment and how little advance warning had been offered by the medical staff. They stressed how unprepared they were for the surgical outcome of their treatment.

“No, they took half my tongue – they’ve taken the whole side out and underneath. …… I’m lisping, I lisp really badly and it’s just…it’s very annoying. So the post care could be improved upon.”

“I mean even the pictures are graphic, but at least if you have some indication of how much they’re going to take off or what it’s going to look like…..”

One participant expressed her annoyance at the lack of sensitivity displayed by some of the medical personnel when she inquired about the expected convalescent period. She relayed how the medical staff had neglected to inform her of what to expect prior to the surgery and then laughed when she indicated she thought she would be able to return to work promptly. Patients stressed that they needed more than basic continuing care following their cancer treatment; they needed emotional and psychological support as well as continued communication.

“I need that support and the communication continuation. Not just the monitoring but the support. Because once it (oral cancer) has touched you, you are never the same.”

Communication Deficiencies

The communication deficit with health professionals was echoed by several participants and one individual also pointed out that even the written communication was unhelpful. She was referring to the pathology report she received and expressed her annoyance at being unable to decipher the meaning of the report due to the
complex terminology used and a lack of assistance from the health professional in translating the meaning of the report.

“…when I got the letter, it was all medical terms. Now I am not a practitioner or anything. I don’t understand terminology.”

**BC Cancer Agency Experience**

Unanimously, the focus group participants agreed that their treatment and continuing care at the BC Cancer Agency has been a very positive experience. Patients felt at ease and confident in their care when attending the BCCA and felt that the communication was very positive.

“How well we have been treated (at BCCA)! I cannot believe how well, friendly, helpful, positive it has been. Every visit and I have been here 30 odd times.”

 “…attention that has been demonstrated by the staff and doctors (at BCCA) is exceptional. It really gives the patient a sense of confidence…”

 “Since I’ve been with the Cancer Clinic getting checked regularly, I feel like I’m in really good hands.”

**6.4 Discussion**

**6.4.1 Benefits of Using Focus Group Discussions**

Focus groups serve to extract valuable and rich information in an organized discussion setting. This type of group interviewing is particularly suited for obtaining several perspectives on the same topic and allows the researcher to draw upon participants’ attitudes, feelings and beliefs in a way that would otherwise not be feasible using other research methods (Gibbs 1997). Focus groups are helpful in encouraging contribution from people who would otherwise be reluctant to be interviewed, who may
not be able to read or write or feel they have nothing of value to say (Kitzinger 1995). In supplementary uses of focus groups, these discussions can be used to generate survey questionnaires or to confirm and validate the initial outcomes of the same (Morgan 1997). The information drawn from these focus groups was beneficial in gaining a more in-depth understanding of the individuals’ experiences.

The focus group discussions conducted in this study provided an opportunity for the author to gain valuable feedback on the format and clarity of the interview questionnaire developed and implemented in Part I from both prior interviewees and oral cancer patients who had never seen the questionnaire before. It is important to gain the perspective of the patients on these issues in order to improve future response rates to the questionnaire and to maximize patient understanding and accuracy of results. The focus group also investigated the emotional and psychosocial aspects of the patients’ experiences leading up to diagnosis in terms of their communication with HP’s, reactions around biopsy results and the issue of poor oral cancer awareness among the public. These issues may not easily come to light in a personal interview situation; however, in a focus group context; the peer support and relatedness increase the comfort level of patients in discussing these important topics.

6.4.2 Confirmation of the Quality of the Questionnaire

6.4.2.1 Format of Questionnaire

The questionnaire used in Part I was delivered to patients in an interview-style format as this method was deemed to increase the response accuracy and provide patients with an opportunity to elaborate on their responses, thereby achieving a more
comprehensive understanding of their experiences leading up to diagnosis. According to the literature, interview questionnaires tend to produce the best response rates and allow the interviewer the opportunity to correct misunderstandings and to make observations throughout the interview (Oppenheim 1992). Personal interviews are often more successful with respondents who have reading or language difficulties. The disadvantages of personal interviews are the notable expense and time investment required to survey a large sample size which limits the sample size potential. Examiner bias is also a consideration when balancing the advantages and disadvantages of this style of questionnaire (Oppenheim 1992).

The focus group discussions revealed that the interview-style questionnaire which was developed was of an appropriate length to be delivered orally. In a survey conducted by the British Medical Journal on stroke survivors, both the response rate and proportion of completed forms were higher for a shorter questionnaire (approximately 6 questions) as compared with a longer questionnaire of 34 questions (Dorman et al., 1997). Focus group respondents indicated that the interview questionnaire appeared long for a written format; however, it didn’t seem unduly long when delivered orally. Future revisions of the questionnaire to a written format should consider shortening the length of the questionnaire so as to maximize response rates.

Focus group participants shared their opinions on the interval scale, which was used to determine patients’ levels of satisfaction with each various recommendations made by their HP’s. An interval scale is a scale of measurement where the distance between any two adjacent units of measurement (or ‘intervals’) is the same but the zero
point is arbitrary. Points on an interval scale may be expressed numerically or with the use of images or words. Focus group respondents indicated that the use of adjectives or pictures would be preferable to a numerical scale. It was noteworthy that it would be preferable to have a section where comments could be made to clarify the response given.

It became evident throughout the process of the personal interviews in Part I that recalling dates and events relating to their experiences leading to diagnosis was difficult for patients in an on-spot interview setting. Focus group respondents also expressed their difficulty in recalling important information during the personal interviews. Research has confirmed that one of the main challenges in obtaining an accurate health history (or record of health-related dates and events) from a patient relates to specifying the relevant time interval for the patient. To avoid this, we have limited our eligibility of participant within 12 months of their biopsy of significance.

The most common error is for the patient to assign a date to an event that is more recent than the actual occurrence due to the ambiguity of the concept of “the past” (Redelmeier et al., 2001). This bias, known as the “telescoping effect,” results in a tendency to overestimate the frequency of repeated events and to exaggerate the acuteness of the events. For example, a patient who was referred to multiple HP’s prior to finally receiving a biopsy might overestimate the number of times each HP was seen and the difficulty in obtaining a concrete diagnosis beyond that of actual reality. One suggested way of limiting this bias is to avoid relating events to calendar dates and to refer to salient dates such as holidays and birthdays instead (Redelmeier 2001). A
patient’s memory may also fail due to the loss of relevant information or the creation of misinformation. As such, it is possible to coax a patient into remembering events that did not actually happen. Interviewers must be very careful not to pose leading questions that may incite incorrect information. Furthermore, memories of emotional events are also easily distorted through discussions with friends and family, leading the embellishments to become incorporated into the memory of the experience (Quas et al., 1999). These false or embellished memories can often be identified by the interviewer when a sequence of events seems overly perfect and careful steps should be taken to further investigate the reality of the statements.

Evidence suggests that events and dates will be most accurately recalled by patients if they induce strong emotions, retain their original significance, remain relatively unusual and mark transitional periods in life (Linton 1982). This is a reasonable explanation for why patients seemed to recall the events surrounding the reporting of their diagnosis and the sequence of events that followed as opposed to the experiences leading up to diagnosis.

On the other hand, issues of “self-presentation” are discussed by Redelmeier and colleagues as being responsible for distortions of the truth by patients in order to impress others. These distortions are more pronounced in face-to-face interviews than in written surveys and are more prominent when the interviewer is an authority figure rather than a peer. Distortions of reality are also exacerbated when the patient feels they share blame for a situation (Redelmeier et al. 2001). For example, an oral cancer patient may distort the reality about how long he or she waited before seeking
professional consultation for an oral lesion because of how they incorrectly perceive a
delay in help-seeking could be viewed by the interviewer as being a contributor to the
stage of diagnosis. In the current study, HP’s were contacted to confirm important dates
and referrals in order to validate patient responses from the interviews.

Focus group suggestions of providing a written format of the questionnaire to be
completed prior to the interview seemed to stem from patients not wanting to be “caught
off guard” or to feel “stupid” during an interview when recall was a challenge. Informing
patients in advance of the upcoming interview would allow them the opportunity to
gather information regarding dates of appointments with HP’s prior to the interview.
Suggestions were made regarding providing a written version of the questionnaire prior
to their visit for interview. It was felt that this would also procure better results as
patients would not feel pressured by having to provide dates on the spot and could look
up sequencing on their personal calendars.

In the focus groups, participants felt that HP’s should be responsible for sharing
the dates and referral pathways of patients with one another. Respondents expressed
frustration at having to fill out new forms at each appointment when this information
could be relayed more efficiently among health professionals. In many provinces in
Canada (Manitoba, Alberta, Saskatchewan and Ontario), provincial privacy legislation
prohibits health care providers from disclosing health information without consent. All of
the acts however permit disclosure of health information without consent to other health
practitioners for research purposes, for evaluation purposes by quality of care
committees, in court proceedings, for police investigations, for investigations by
provincial Ministries of Health for fraud detection purposes, and to health regulatory bodies if required for investigation (Peekhaus 2006). Based on this legislature, referring HP's should exercise their rights to share appropriate health information as necessary with other HP’s in the referral pathway in order to reduce the burden of information gathering from patients.

6.4.2.2 Recommendations for Province-Wide Questionnaire

Survey questionnaires may be delivered using a variety of techniques including mail-out written surveys, face-to-face interviews, telephone interviews and email surveys. The results of the focus group provided mixed feedback on this matter as some respondents indicated a preference for a written questionnaire, which would allow more time to consider the questions before responding while most of the participants suggested that a combination of both written and verbal would be preferable.

With regard to the delivery method of the interview, mail-out survey methods have been shown to have various advantages and disadvantages according to the literature. The main advantages of mail-out surveys are the cost effectiveness of the data collection and processing, the ability to reach respondents in isolated areas and the avoidance of interviewer bias (Oppenheim 1992). Conversely, postal questionnaires generally provide poor response rates and are unsuitable for respondents who have difficulty with literacy, poor eyesight and those who are either of elderly age or below the age of 10. In a post-delivered questionnaire, respondents also have no opportunity to ask for clarification in case of misunderstanding of the questions or intent of the questionnaire. The researchers also have no opportunity to provide explanations or
assistance and have no control over the order in which questions are answered, incompleteness of the questionnaire or the involvement of other in the responses (Oppenheim 1992).

Focus group participants were queried about their receptiveness to telephone surveys. The consensus of the focus groups was that telephone surveyors have plagued the public to such an extent that they incite a reactionary negative response from potential respondents. It was suggested that the only way of enabling a more positive response from patients would be to inform them in advance that the interview would be conducted via telephone and to arrange a time when the call would be expected. Oppenheim states that increased response rates can be achieved in a variety of ways, including advance notice, explanation of how the patient was selected for the interview, ensuring confidentiality and anonymity and even providing incentives for participation (Oppenheim 1992).

Email delivery of surveys was found to produce a conflicting response from focus group participants as some were in favor of this method and others were adamantly opposed to it. Research on response rates to email surveys is scant however one study which compared response rates of 31 email surveys from 1986 to 2000 produced interesting results (Sheehan 2001). The author found that email surveys produced the most favorable response rates in their early years of use (61.5% in 1986 and 72% in 1992) but these declined notably as the frequency of internet use increased (24% in 2000). The author hypothesized that as the novelty of internet and email wore off, response rates dwindled accordingly. It was also suggested that the increased
frequency of surveying in the United States and the increased frequency of unsolicited emails among internet users likely impacted the decline in response rates to email surveys. Several other factors have been found to impact email survey response rates including the length of the survey, use of pre-notification, follow-up contacts and issue salience. These factors will be examined independently as follows.

The length of email surveys has been shown by some research to have an impact on the response rates however this is not consistently agreed upon. Several studies indicate that the length of surveys does not influence the response rate (Mason 1961; Bruvold 1988) while others argue the opposite. Response rates have been shown to negatively impact survey length in that longer surveys tend to have lower response rates (Yammarino 1991; Steele 1992).

Pre-notifying respondents of an upcoming email survey has shown conflicting results in terms of response rate influences. Some studies have found that pre-notification increases response rates (Haggett 1994) while others argue that email pre-notification has a negative impact on potential respondents (Mehta 1995) and might be perceived as unsolicited email. Follow-up contact has also been identified as a factor which may influence the response rates of email surveys. It has been shown that a follow-up email reminder can increase response rates by as much as 25% (Sheehan 1997).

Despite the ease and cost effectiveness of email questionnaires as a method of surveying oral cancer patients in British Columbia, poor response rates may be only one of several reasons this may not be the preferred method of delivery. Additional barriers
associated with email surveys are the reduced access to seniors who are unfamiliar with internet use, individuals with impaired sight and those with literary deficits as internet use may be difficult if not impossible for many of these groups of individuals.

Issues salience, which can be defined as the perceived importance or timeliness of a specific topic has been shown to have a strong correlation to both email and postal response rates (Sheehan 1997; Watt 1999). A particular topic may have higher salience to a certain population than to another. For example, oral cancer patients would have a higher salience to an oral cancer survey than would a group of high school students. It has been suggested that topic salience may have a greater impact on response rates than any other factors such as survey length, respondent contact and monetary incentives (Roberson 1990; Martin 1994).

The language choice for the survey is also of consideration. If the questionnaire is available only in English, this will create limitations for those whose first language is not English. It will also not be possible to generalize the outcomes of the survey to individuals whose first language is not English or who speak English only as a second language. If translations are used, problems may arise in maintaining the true intent of the questions as subtle inferences are often lost in the translation process. Additional research would also be necessary to determine which languages are predominant in a given area in order to ensure the appropriate translations are made available. In the case of using live translation rather than written forms, it is necessary to ensure that back translation is used in order to verify that the true meaning of the questions is being understood by the participants.
6.4.3 Patient Experiences Leading to Diagnosis

6.4.3.1 Patient Awareness of Oral Cancer

A widespread lack of oral cancer awareness has become a universal concern and significant barrier in attempting to increase early detection and improve the prognosis of this disease. It is known that there is an alarming lack of public awareness regarding the signs and symptoms of oral malignant and premalignant lesions (Boyle et al., 1993). Even more worrisome is the lack of awareness regarding oral cancer in general. In a 1999 survey of 1,894 residents of the United Kingdom over the age of 16 years, only 56% of respondents indicated that they had heard of oral cancer as compared to 97% who were familiar with lung cancer and 96% who were familiar with skin cancer (Warnakulasuriya et al. 1999). These statistics confirm the notions expressed in the focus group sessions that the general public is ignorant to the topic of oral cancer and greater efforts must be made to educate the public and health professionals alike on this topic.

Focus group participants pointed out that there is a common misconception that in the absence of known risk factors such as smoking and drinking, oral cancer will not develop. This is also an indication of a lack of education among the general public regarding the etiology of oral cancer. Focus group respondents felt that the increased prevalence of anti-tobacco campaigns are partly to blame for this misconception as they tend to infer that only smoking causes oral cancer, misguiding people to assume that if one does not smoke, one will not develop oral cancer.
Further outcomes from the focus group discussions reflected a belief that there is a great need for oral cancer education among the public. Increasing oral cancer awareness requires a multi-faceted approach which focus group respondents felt should begin with the responsibility of the health professional. In a study which surveyed both health professionals (103 dentists and 172 physicians) and 540 members of the community who were current smokers, 75% of the smokers said they would quit smoking if told to do so by their physician (Brink et al., 1994). Two thirds reported having been asked about smoking by their dentist or physician, less than half were informed of the dangers of smoking and only 20% were given a pamphlet that outlined this information. This illustrates the confidence that individuals have in the opinions of their HP’s but also the lack of education being provided by HP’s which has the potential to increase cancer awareness among patients.

Other forms of oral cancer education may be provided through media vehicles such as television, radio, the internet or a combination thereof. Awareness campaigns often employ one or more of these forms of media to inform the public on certain health issues. During the 1991 National Skin Cancer Awareness Week in Australia, it was determined that skin examinations increased by 56% with nearly 90% of these exams being initiated by patients themselves (Lowe 1994). In Utah, two separate health awareness campaigns were launched in April 2003 providing information and cautionary messages regarding skin cancer and colon cancer (Broadwater et al., 2004). The media campaigns utilized internet exposure, radio, tie-ins with entertainment and sporting events as well as weather forecasting sponsorships. Residents were surveyed both in January (prior to the start of the campaigns) and again in May (4-6 weeks after the
campaigns) as to whether they reported having heard skin cancer or colon cancer announcements. In January, only 18% of respondents reported hearing skin cancer announcements but by May, 76% reported hearing the announcements and 78% could repeat the basic information cited in the campaigns. Similar statistics were reported for increased awareness of colon cancer over the duration of the campaigns (Broadwater et al. 2004). These studies provide evidence that awareness campaigns which employ various forms of media are effective both in drawing public attention to a particular disease and increasing consultation with health professionals.

6.4.3.2 Patient Perspectives on Interactions with Health Professionals

The process of identifying an oral lesion, consulting with HP’s and finally receiving a diagnosis of oral cancer can be a very emotional and difficult experience. Patients may experience a wide variety of emotions throughout this process which may be the result of either positive or negative interactions with HP’s. Focus group discussions brought to light some of the most notable interactions from both perspectives.

Many patients expressed their gratitude for the perceptiveness of their attending dentists, dental hygienists and physicians in being able to quickly identify a potential malignancy and initiate the appropriate referral pathway. The contrasting views and reflections of patients further emphasize the wide variety of experiences that may be encountered from first detection of an oral lesion until a diagnostic biopsy is performed. It is therefore essential that HP’s strive to deliver timely biopsy results, maintain client-centered communication and continue to perform regular oral cancer screenings in
order to preserve and improve the satisfaction of oral cancer patients throughout these experiences.

However, several focus group participants expressed frustration with the perceived delay in receiving a diagnosis following the initial biopsy. A delay in receiving a diagnosis wasted valuable time, which to them was perceived as the difference between “life and death”. They also expressed feeling as though their lives were put ‘on hold’ until the biopsy results were disclosed. The timing of diagnostic disclosure has been reported to be a key element in the patients’ perceptions of their interactions with the diagnosing HP, as an extended wait time increases anxiety and fear of an unknown outcome.

Patients receiving a cancer diagnosis are in a position of extreme vulnerability and uncertainty (Sardell and Trierweiler 1993). Since HP’s are almost invariably responsible for sharing this news, they are accountable for providing the appropriate information and comfort to the patient in attempts to reduce fear and anxiety. From the point of diagnosis throughout the treatment and recovery period, patients need support and open communication with their health care providers. This support and mentoring can be viewed as one way of preserving patient hopefulness and enabling better treatment outcomes.

Additionally, many complained of not receiving adequate information outlining what they could expect to face following invasive oral surgery. As a result, they felt unprepared for the loss of oral function, speech impediments and extensive convalescent periods that are common post-surgical outcomes. This lack of information
contributed heavily to patient anxiety, fear and confusion. In a survey of newly-diagnosed melanoma patients, Schofield and colleagues determined that patient satisfaction with their health professional's communication was significantly greater if they perceived the information given by their doctor was 'everything' or if the amount of information received was in line with their comfort level (Schofield 2003). Current research supports the concept of patient-centered communication in which the health professional tailors the interactions to the expectations and desires of the patient as an individual (Little et al., 2001; Schofield 2003). A large study aimed at assessing patient preferences for patient-centered communication identified that those with a very strong preference for patient-centeredness are often vulnerable socioeconomically or are feeling particularly unwell or worried (Little et al. 2001). These latter two qualifiers could be descriptive of a newly-diagnosed oral cancer patient. Hence there is a need for HP’s to be conscious of their communications with patients regarding sensitive issues such as diagnosis and treatment and to make efforts to utilize patient-centered communication to improve satisfaction and reduce anxiety.

Further patient concerns highlighted the lack of oral cancer awareness exhibited by some health professionals throughout patients’ experiences to diagnosis. Many expressed serious concern that their HP’s were unable to recognize a worrisome oral lesion as potentially malignant and therefore did not make appropriate or timely referral and biopsy recommendations. A lack of health practitioner knowledge has been repeatedly identified in the literature and in some cases has been shown to contribute to inadequate detection of early cancers and delays in treatment ((Schnetler 1992; Kujan et al. 2006; Carter and Ogden 2007). In a 2005 survey of dentists in North Carolina,
only 31% were determined to have a medium-high level of oral cancer knowledge (Patton et al. 2005). The literature is consistent in calling for further education of HP’s in oral cancer detection, diagnosis and treatment. Patients also expressed frustration at the lack of oral cancer screening that was being conducted in general dental practices as they felt that screening was a valuable and necessary component of a typical dental exam.

As for the oral cancer screening activities, there were conflicting findings from HP’s’ and patients’ perspectives. In a 2006 survey of 338 general dental practitioners in the UK, 92% of the dental practitioners surveyed reported conducting an oral cancer screening for new patients in their practice (Gajendra et al., 2006). In a 2005 survey of dentists and hygienists in New York State, 82% of dentists and 72% of hygienists reported providing oral cancer examinations to patients 40 years or older in their practices (Cruz et al., 2005). In British Columbia and Nova Scotia, 70% of dentists reported conducting an oral cancer exam for new patients 40 years or older and 10% reported not doing so (Clovis et al., 2002). However, patients who have been surveyed about the frequency of receiving oral cancer exams have reported much different results. In a 2006 survey of veterans diagnosed with oropharyngeal cancer in North Carolina, only 53% reported having undergone an oral cancer examination within the past 3 years (Kim et al., 2006). When 1,096 adults in North Carolina were surveyed about their oral cancer knowledge, only 29% reported ever having an oral cancer exam when this procedure was described to them (Patton et al. 2004). These conflicting statistics indicate a discrepancy between how frequently HP’s report conducting oral cancer exams and how infrequently patients report having received them. An
explanation may be a tendency not to inform patients when an oral cancer screening exam has been performed.
7. CONCLUSION & FUTURE DIRECTIONS

Diagnostic delay is a real and concerning contributor to advanced staging at diagnosis and a reduced opportunity for successful treatment. This study has shown that diagnostic delay exists among patients with high-risk oral lesions attending the BCCA Oral Oncology clinic and that certain factors can be associated with increased delay. The main contribution factors for this time lag are a general lack of awareness regarding oral cancer in both patients and health professionals.

Patients who self-identify an oral lesion tend to experience longer diagnostic delay, exhibiting larger clinical lesions and more advanced staging, as compared to patients whose lesions are detected through screening by a HP. These factors demand further investigation and attention in order to reduce the potential for delay to diagnosis and to improve prognosis and survival rates.

A general lack of awareness was also found to contribute to professional delay. Dental professionals are more likely to conduct regular screening exams and make appropriate referrals as compared to medical practitioners however all HP’s have been found to contribute to diagnostic delay to some degree. Further education of HP’s relating to oral cancer detection and diagnosis is needed in order to improve HP confidence in identification of oral lesions, to promote appropriate referrals and to reduce professional delay.
Future goals include the expansion of the study population to include a more representative sample of patients with HRL’s across the province of BC. A posted mail-out survey would likely be the most cost-effective format however it would be prudent to consider various delivery formats for varying segments of the population based on their limitations and needs. A combination of mail-out surveys for hard-to-access populations and personal interviews for use in centres with oral cancer clinics (Vancouver and the Okanagan); and/or questionnaires that can be included with patient health histories in dental/medical offices are a few examples.

A strong need was identified to better understand patients’ support needs post-operatively. There is currently insufficient evidence to show what forms of support would be most beneficial to patients throughout the treatment and convalescing stages of their disease experience as well as which support systems patients would actually utilize.

Ultimately, further research is necessary to provide more substantial data of the factors contributing to diagnostic delay among BC oral cancer patients. Additional education of both the public and health professionals is also important in order to promote early detection and improve the prognosis of this deadly disease.
8. BIBLIOGRAPHY


9. APPENDICES

Appendix A.1 Interview Questionnaire

Oral Health Study: Experiences Leading to Diagnosis
Interview

NAME: ______________________      ID#:____________OHS ID#: ____________

Date of Birth: ___________ (YYYY/MM/DD)     Date: ________________ (YYYY/MM/DD)

Age:_______ Sex:________

1. Which of the following healthcare professionals do you see regularly?

<table>
<thead>
<tr>
<th>Healthcare Professional (Please check all that apply)</th>
<th>Frequency of visits (Please check one):</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Dentist/Dental Hygienist</td>
<td>once per</td>
</tr>
<tr>
<td>□ Dental Specialist</td>
<td></td>
</tr>
<tr>
<td>□ Family Doctor</td>
<td></td>
</tr>
<tr>
<td>□ Medical Specialist</td>
<td></td>
</tr>
<tr>
<td>□ Nurse</td>
<td></td>
</tr>
<tr>
<td>□ Alternative Medicine Practitioner</td>
<td></td>
</tr>
<tr>
<td>□ Other (Please specify)</td>
<td></td>
</tr>
</tbody>
</table>

□ ½ - 1 yr □ 2 yrs □ 5 yrs □ > 5yrs
□ Never

□ ½ - 1 yr □ 2 yrs □ 5 yrs □ > 5yrs
□ Never

□ ½ - 1 yr □ 2 yrs □ 5 yrs □ > 5yrs
□ Never

□ ½ - 1 yr □ 2 yrs □ 5 yrs □ > 5yrs
□ Never

□ ½ - 1 yr □ 2 yrs □ 5 yrs □ > 5yrs
□ Never
2. When was your last dental visit? Date: ___________(mm/yyyy)

3. When was your last medical visit? Date: ___________(mm/yyyy)

Now, I am interested how you found out you had this oral lesion. Can you start with when the problem first noticed and then tell me how things went after that?

4. Who first detected the change (lesion) in your mouth?

(Check one): 1. ____Self

2. ____Dental Hygienist

3. ____Dentist

4. ____Medical Doctor

5. ____Dental Specialist (______________)

6. ____Medical Specialist (______________)

7. ____Nurse

8. ____Other: __________________

5. Where was the change (lesion) located?

6. When did you first notice something unusual in your mouth?

Date: ________________ (dd/mm/yyyy)

7. Where was the lesion located in your mouth?

8. What were the first symptoms you noticed?

9. What was your initial reaction to discovering your symptoms?

10. What did you do after you noticed the change in your mouth?
11. Did you discuss your symptoms with anyone? If yes, with whom?

12. How long after you **first** noticed something unusual in your mouth did you seek professional consultation?
   _____ days   _____ weeks   _____ months

13. Can you tell me more about the decision to seek help initially and from whom?

14. **Timeline:** Can you tell me more about your visit to health professionals?

<table>
<thead>
<tr>
<th>Timeline → visit/HP seen</th>
<th>1st visit:</th>
<th>2nd visit:</th>
<th>3rd visit:</th>
<th>4th visit:</th>
<th>5th visit:</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Which HP did you visit?</td>
<td>Name:</td>
<td>Clinic:</td>
<td>Ph:</td>
<td>Address:</td>
<td></td>
</tr>
<tr>
<td>b) When did you visit this HP? (mm/yyyy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c) What was the reason for the visit?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) What did this HP recommend to you?</td>
<td>1=Bx 2=Recheck 3=W&amp;W 4=Nothing 5=Topical and 6=Refer 7=Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) How did you feel about this experience? (refer to interval scale)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f) What did you do next?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g) Did you discuss this experience with other people? With whom and what was their response?</td>
<td>1=No 2=Spouse 3=Family 4=Friend 5=Coworker 6=Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h) What symptoms did you experience?</td>
<td>1=none 2=pain 3=colour change 4=ulcer 5=lump 6=difficulty chewing 7=other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
15. **Before noticing your first symptoms**, which **types of cancer** would you say you had heard of? (List types.)

   Heard of oral cancer? 1.____yes 2.____no

16. **Before noticing your first symptoms**, which **symptoms of oral cancer** would you say you had heard of? (Check all that apply.)

   1.____none 2.____pain 3.____colour change 4.____ulcer 5.____lump
   6.____difficulty chewing 7.____other

17. In your best estimation, how much time passed from the first time the lesion was detected in your mouth until the first tissue sample was taken? ________days ________months ________years

18. Based on your experience, what would you suggest to health professionals who want to reduce any delays patients might experience in finding out if they have significant oral lesions?

19. What are the suggestions you have for other people who think they might have a problem in their mouth?

20. Is there anything else you would like to tell me about your experience, that I have not asked about?

21. Now that you have completed your treatment, what can you tell me about the overall experience and how it has impacted your life? (impact on lifestyle? Oral function? Concerns or worries?)

This completes our interview. Thank you once again for taking the time to participate in this study. Your contribution is both valuable and greatly appreciated.
Appendix A.2 Interval Scale

*Experiences Leading to Diagnosis Interview*

Interval Scale for Question 14 e:

*Please indicate on this line a number which represents how satisfied you were with the recommendation (treatment, referral, watchful waiting) of this health professional.*

Not at all Satisfied | Fair | Very Satisfied
--- | --- | ---
0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10
Appendix A.3 Interview Questionnaire Consent Form

Experiences Leading to Diagnosis

Subject Information and Consent Form

BCCA REB # H07-01942

BCCA Principal Investigator: Dr. Miriam Rosin
Cancer Control Research
Telephone: 604-675-8061

Project Principal Investigator: Dr. Catherine Poh
Faculty of Dentistry/UBC
Telephone: 604-675-8078

Project Co-Investigators:

Heather Biggar (Master student) Faculty of Dentistry/UBC
Telephone: 604-675-8057

Dr. Greg Hislop Cancer Control Research/BCCA
Telephone: 604-675-8060

Dr. Lewei Zhang Faculty of Dentistry/UBC
Telephone: 604-822-7344

Dr. Pam Gardner Fraser Valley Cancer Centre/BCCA
Telephone: (604) 930-2098 ext. 4549

Non-Emergency contact numbers are noted at the end of this document under the section heading “Contact”.

Background

You are being invited to participate in this study to learn more about your experiences leading to the diagnosis of your recent oral condition that was biopsied. With a better understanding of this experience, we hope to be able to make the diagnostic process quicker and more efficient.
Your standard of care at BCCA will involve regular monitoring, testing and treatments as deemed necessary to best manage your condition. This study will in no way interfere with your standard of care. You participation is voluntary and you will continue to receive this standard of care whether or not you agree to participate in this study.

**Purpose**

The *purpose* of this study is to collect detailed information about your experiences with healthcare personnel from the time that a change in your mouth was first identified until a tissue sample (biopsy) was collected.

Your experiences will provide valuable insight into the diagnostic process.

**Who Can Participate In This Study?**

You may participate in this study if:

- You fully understand the study and give your informed consent to participate as demonstrated by signing this consent form.
- You can clearly speak and understand English.
- You have had a tissue sample (biopsy) for an oral condition collected within the past 12 months.

**Study Procedures**

Your participation will involve an interview in which you will be asked questions regarding your experience during the time period from first identifying the condition in your mouth to biopsy. This will include information about the various health professionals you have seen and your overall experience leading up to the biopsy. The interview will last approximately 20 minutes and will take place at one of your scheduled oral medicine exam visits. With your consent, this interview will be audio recorded. If any information is missed during the interview, you may be contacted by telephone.

Your participation would also include giving permission to access your medical and dental records regarding your oral conditions to supplement information about your diagnostic work-up. You might also be invited to participate in a focus group where you will be asked to provide feedback on the study findings.

**Benefits & Risks**

There are no direct benefits to yourself from participating in this study. However, we hope that the information learned from you may improve the health care provided to your community in the future. You will not incur any personal expenses as a result of your participation in this study.
Confidentiality

Your confidentiality will be respected to the extent permitted by applicable laws and regulations, and your medical and study records will not be publicly available. No information that discloses your identity will be released or published without your specific consent. Your identity will not be used in any reports about the study. In records that leave this centre you will be identified by a study code only. All information associated with this study will be kept behind locked doors or in secure computer files.

The information gathered from this study, with personal identifiers removed, will be used to better understand and improve the diagnostic process.

Your rights to privacy are legally protected and guaranteed by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor or the UBC BCCA Research Ethics Board.

Compensation:

You will not be paid for participating in this study.

You do not waive any of your legal rights for compensation by signing this form.

Contact

We will be glad to answer any questions you may have regarding this research in order to ensure that you fully understand the process.

If you have any questions or desire further information with respect to this study, you may contact the project principal investigator, Dr. Catherine Poh or Heather Biggar at 604-675-8057, or Eunice Rousseau with the BC Oral Cancer Prevention Program at (604) 675-8078.

If you have any concerns about your rights as a research subject, you may contact the Research Subject Information Line in the UBC office of Research Services at 604-822-8598.

Subject Consent

I understand that participation in this study is entirely voluntary. I authorize access to my medical record as described in this consent form. I may choose not to participate or I may withdraw from the study at any time and I will continue to be offered the best available medical care. I understand that I may ask questions about this study in the future.
I will receive a signed copy of this consent form including all attachments, for my own records.

I consent to participate in this study.

________________________  ___________________________  ________
Subject’s Signature  Printed name  Date

________________________  ___________________________  ________
Witness’ Signature  Printed name  Date

________________________  ___________________________  ________  ________
Signature of Person Obtaining Consent  Printed name  Study Role  Date

Was the consent form read to the subject? (If this is not mandatory, we can delete this one)

☐ Yes  ☐ No
Appendix A.4 Focus Group Questionnaire

Experiences Leading to Diagnosis Study

Focus group questions

Introductory script:

Thank you for participating in our focus group. The objective of this discussion will be to review the questions from the interview you have all participated in over the past few months. We look forward to receiving your feedback in order to refine the questions in order to better investigate the experiences from first detection to diagnosis of an oral condition. I will be asking a series of questions and with your consent, your responses will be audio-recorded. Please take a few minutes to read through the questionnaire to re-familiarize yourself with the questions you responded to during your previous interview. (Questionnaire will be handed out to all attendees to review.)

1. At the beginning, we would like to ask your help to improve the questionnaire:
   (Read questions A and B then give 5 min to review questionnaire)(30 min)
   
   A) Please tell us your opinion of the format of the questionnaire in terms of clarity and the length of the questionnaire.

   B) In the questionnaire, you were asked about your satisfaction with some of the experiences during the process of consulting with various health professionals (question 14e). Please share your thoughts on the interval scale that was used.

   C) What questions do you feel should have been asked that were not asked?

   D) I noticed during the interviews that it was often difficult for you to recall specific dates. How could we ask the questions in order to help you better recall dates?
E) **What format of questionnaire (written, telephone, email, in person) do you feel would be easiest to respond to? Why? Any previous experience with various types of interviews- helpful or not? (If this questionnaire was delivered to individuals across the province?)

2. During your interaction with health professionals leading up to the diagnosis of your mouth condition, can you please share with us the situation that impressed you most? How could this situation have been strengthened or improved? (Were there any parts of your experiences with health professionals that you were unsatisfied or particularly happy with and why?) (10min)

3. We found out that many people have never heard of oral cancer or any of its symptoms. In your opinion, what are the types of information do you think the public would like to know about oral cancer (symptoms, risk factors, others)? Any way in your opinion, we could help to raise public awareness of oral cancer? (Info at dental office/medical office, media, internet, etc)(10 min)

4. During the time that the problem/lesion in your mouth was noticed and then diagnosed what information did you find most useful to you? What information do you need the most? (What concerns or questions did you have that were not adequately addressed by those you sought advice or help from during that time?) ** Focus on time from Detection to Dx **

Now that you have completed your treatment, what concerns/questions do you still have? (10min)