ORAL CANCER AND DYSPLASIA TRENDS AMONG SOUTH ASIANS IN BRITISH COLUMBIA: LESION SITES, RISK HABITS, AND ACCESS TO CARE

by

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Abstract

Objectives: While oral cancer is one of the most common malignancies across the globe, the vast majority of cases arise in South Asian countries. Currently in British Columbia, nearly 10% of the population is of South Asian ethnicity. Evidence suggests that risk factors within this population play a significant role in oral cancer incidence and clinical presentation. As a significant subgroup, it is crucial to gain insight into the trends of oral precancerous and cancerous lesions in this population. This thesis aims to explore differences in oral cancer, dysplasia and hyperplasia between South Asians and the general population, as well as differences in anatomical lesion sites and access to care. This thesis also examines biopsy activity by dental practitioners across the province.

Methods: Data from the British Columbia Oral Biopsy Service (OBS) and the British Columbia Cancer Registry (BCCR) were used to identify cases of squamous cell carcinoma, carcinoma *in situ*, dysplasia, and hyperplasia in the oral cavity in British Columbia in 2007 and 2013. Name recognition software programs were utilized to determine ethnicity.

Results: Oral cancer, dysplasia, and hyperplasia trends vary between South Asians and the general population. There are more cases among South Asian males than males in the general population. South Asian cases are diagnosed at younger ages than in the general population, with a mean age at diagnosis below the age of sixty years. While common lesion sites among South Asians include the gingiva and buccal mucosa, these lesion sites are common within the general population as well. The number of biopsies received by the OBS increased by 36% from 2007 to

2013. The number of dental practitioners performing biopsies also increased, as well as the overall number of South Asian cases seen in the OBS.

Conclusion: Results from this thesis provide current information regarding trends and risk factors for hyperplasias, dysplasias, and oral cancers in the South Asian population in BC. These findings, along with spatial analysis of biopsy trends, provide a basis for tailored screening programs and oral cancer prevention initiatives in British Columbia.

Preface

This thesis is an original intellectual product of the author J. Lavallee. All components of the study design, research program, and data analysis were performed by the author.
The University of British Columbia (UBC) and British Columbia Cancer Agency (BCCA) joint Research Ethics Board approved this study, certificate number H15-01139, entitled “OBS Incidence”.

A version of Section 5.3.5 “Validation of Software in B.C.” has been submitted for publication. The author conducted all of the testing and analyses, and wrote the manuscript.

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Age-standardized rate (ASR)

British Columbia (BC)

British Columbia Cancer Agency (BCCA)

British Columbia Cancer Registry (BCCR)

Cancer Agency Information System (CAIS)

Carcinoma *in situ* (C*IS*)

College of Dental Surgeons of British Columbia (CDSBC)

Deoxyribonucleic acid (DNA)

Floor of mouth (FOM)

Fluorescence visualization (FV)

Fraser Valley Cancer Centre (FVCC)

Hospital Episode Statistics (HES)

International Agency for Research on Cancer (IARC)

Loss of heterozygosity (LOH)

Mild dysplasia (D1)

Moderate dysplasia (D2)

National Household Survey (NHS)

Negative predictive value (NPV)

Odds ratio (OR)

Oral Biopsy Service (OBS)

Oral Cancer Prediction Longitudinal study (OCPL)

Oral Cancer Prevention Program (OCPP)

Oral Health Study (OHS)

Oral potentially malignant disorder (OPMD)

Oral squamous cell carcinoma (OSCC)

Oral submucous fibrosis (OSF)

Personal health number (PHN)

Positive predictive value (PPV)

Second primary tumour (SPT)

Severe dysplasia (D3)

Simon Fraser University (SFU)

South Asian (SA)

Squamous cell carcinoma (SCC)

Toluidine blue (TB)

Transforming growth factor-β (TGF-β)

United Kingdom (UK)

University of British Columbia (UBC)

Ultraviolet (UV)

Vancouver General Hospital (VGH)

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Chapter 1: Introduction

Oral cancer is the sixth most common cancer in the world, with a broad variation across the globe. [1-3] It is the thirteenth most common cancer in Canada, but in South Asian countries like India, Pakistan, and Sri Lanka, oral cancer is the number one most common cancer. [1] The five-year survival rate is 83% when diagnosed in the early stages of disease when the cancer is localized, and drops to approximately 37% in late-stage diagnoses when the cancer has metastasized. [4]

Cancer incidence is higher in South Asian countries than anywhere else in the world, with age-standardized incidence rates (ASR) of up to 7.3:100,000, compared to worldwide ASR statistics closer to 4:100,000. [1,5] These statistics are of importance in Canada, a diverse country where 20% of the population belong to ethnic minorities, the majority of which are South Asian. [6] As such, it is important to assess differences in oral cancer trends and explore access to care within this population.

One of the aims of this thesis is to examine differences in oral cancer and dysplasia trends between the South Asian population in British Columbia (BC) and the general population; for example, differences in prevalence by sex and age at diagnosis, and the anatomical lesion sites commonly affected. Another aim of this thesis is to explore access to care within this population, and to examine the capacity of the dental network and access to care in BC.

Potential benefits of this research include increased awareness regarding differences in oral cancer and dysplasia trends in the South Asian population, updates to screening and biopsy

guidelines, development of oral cancer prevention programs tailored to meet the needs of the South Asian population, and implementation of outreach programs to increase access to care for this population.

1.1 Oral Cancer Epidemiology

1.1.1 Global

Oral cancer is the sixth most common cancer in the world. [1-3] Trends across the globe indicate a rising incidence, particularly in younger age groups. [2] Table 1.1 compares worldwide oral cancer statistics with those of Canada and South Asian countries. The average incidence of oral cancer globally is 2.1%, with a slightly higher incidence in males (2.7%) compared to females (1.5%). The annual estimated incidence for oral cancer is 275,000. [2]

1.1.2 Canada

The incidence of oral cancer in Canada is lower than the global rate, at 1.4%, with a slightly higher incidence rate in men (1.7%) than women (1.1%). [1] The incidence in developed countries is generally highest among ethnic minorities and immigrants from high-risk areas. [3] There are 4,600 oral cancer diagnoses predicted in Canada for 2016. [7]

1.1.3 South Asia

The oral cancer incidence in South Asian countries is much higher than global rates, at approximately 7.2%. [1] The incidence rates are highest for men at 10.3%, which is nearly three times the incidence rate for women of 4.4%. In certain countries, such as Sri Lanka, India, Pakistan and Bangladesh, oral cancer is the most common type of cancer; in parts of India, oral cancer accounts for more than 50% of all cancers. [8] Unfortunately, parts of the world where oral cancer is most common are often areas where data and statistics are least available, as a result of limited resources. [3] One third of all oral cancer incidence occur in South Asian countries, with over 75,000 cases diagnosed yearly in India alone. [2,9]

	Canada	South Asian	Worldwide
Incidence	1.4%	7.2%	2.1%
Sex Male	1.7%	10.3%	2.7%
Female	1.1%	4.4%	1.5%
ASR+	4.2	7.3	4.0
Mortality	0.9%	6.7%	1.8%

Table 1.1 Canadian, South Asian, and worldwide cancer statistics
+Age-Standardized Rate
Adapted from Canadian Cancer Statistics, 2013; World Health Organization, 2014. [1,5]

1.2 Oral Cancer Histology

Oral cancer is a multistep process of genetic alterations that modify the normal functions of genes and oncogenes, thereby affecting cell functions such as cell-cycle regulation, cellular differentiation, proliferation and death, DNA repair, and cellular immunity. [10] When the uncontrolled growth of abnormal cells forms a tumour, it has the potential to metastasize to lymph nodes or to other distant sites; at any stage, oral cancer can result in significant morbidity

and mortality. Oral cancer may refer to oral cavity cancer, or to both oral cavity and oropharyngeal cancer. Cancer of the oral cavity affects the tongue, floor of mouth, hard palate, gingiva, and mobile portions of the tongue and cheeks, while oropharyngeal cancer includes the soft palate, uvula, tonsils, posterior pharyngeal walls, and base of the tongue. [11] While this difference in terminology helps to differentiate between lesions' anatomical sites, it is of interest to note that these terms are sometimes used interchangeably in the literature.

Oral cancer (including both the oral cavity and oropharynx) is currently the sixth most common malignancy worldwide, accounting for approximately 300,000 deaths each year. [2,12-14] Over two thirds of these cases arise in developing countries. [2,12] Despite recent improvements in treatment modalities, the 5-year survival rate for oral cancer, which is approximately 60% globally, has not improved significantly over the last 30 years. [7] While more than 80% of early-stage oral carcinomas can be cured by therapy, about 70% of patients with late-stage disease cannot be cured. [7] These statistics highlight the need to expand on preventive measures including screening and early detection, which stand to have an impact on survival rates, as well as prevention through education and awareness regarding risk factors.

1.2.1 Histological Progression

While there exists a widely accepted model of histological progression based on Western research and findings, it is becoming increasingly evident that there exist other pathways to progression, which are currently not well understood. As a result, while there may be some

similarities between progression models, it cannot be assumed that the natural history, histology, and pathology of oral cancer are the same across different populations.

1.2.2 Oral Submucous Fibrosis

Oral submucous fibrosis (OSF) is a chronic and progressive oral potentially malignant disorder (OPMD) predominantly found in Asian and South Asian countries, and their emmigrants across the globe. [15] OSF is characterized by juxta-epithelial inflammation, fibrosis of the submucosa, and epithelial atrophy leading to rigidity of the oral mucosa, trismus, and an inability to eat. [15-17]

OSF was first investigated as a premalignant disease by Paymaster in 1956 when he noted slow-growing squamous cell carcinoma (SCC) in one third of patients presenting with the disease. Epithelial dysplasia occurs in 7 to 26% of OSF lesions, depending on the study population, while malignant transformation rates range from 7 to 13%. [15]

Clinical features of early OSF include blanched and leathery mucosa of the oral cavity and the oropharynx, petechiae, depapillation of the tongue, oral ulceration, intolerance to spicy foods, and taste disturbance. [18] Clinical features of advanced OSF include the presence of fibrous bands, keratosis, xerostomia, flattening of the palate and uvula, trismus, limited mouth opening, and limited tongue mobility. [18]

OSF is a disease of collagen metabolism, often secondary to areca nut use. Areca nut contains alkaloids, flavonoids and copper, which are believed to disrupt collagen synthesis and

breakdown. The use of substances such as areca nut and betel quid also cause localized mucosal inflammation, resulting in the activation of T cells and macrophages, and an increase in cytokines and transforming growth factor-β (TGF-β). These responses create both an increased production of collagen and an inhibition of its breakdown. [18] When OSF is diagnosed prior to the development of trismus, cessation of the areca nut habit is often curative. However, once trismus has developed and the disease has progressed beyond the early stages, OSF becomes irreversible. [18]

1.2.3 Hyperplasia and Hyperkeratosis

Hyperplasia presents as an increase in the number of cells present in tissue. In the case of stratified squamous epithelium, hyperplasia results in the thickening of the epithelium, also called acanthosis. [19] Hyperplasia can occur in different layers of tissue, including the stratum basale and the spinous layer. [19] No architectural or cellular changes are present in hyperplastic tissue, rendering it difficult to predict malignant transformation. [19] Hyperplasia is often caused by irritation or trauma, and typically subsides once the irritant is removed. [19]

The definition of hyperplasia, when loosely applied, may also include cell products such as collagen and keratin. Hyperkeratosis is characterized by an increased thickness of the keratin layer in stratified squamous epithelium, known as the stratum corneum. Hyperkeratosis if often also secondary to chronic irritation, for example biting of the mucosa or tobacco use, [20] and lesions most often resolve once the irritant is removed. The superfcial layer of the epithelium may contains either orthokeratin or hyperkeratin, and hence hyperkeratosis can be further

differentiated into hyperorthokeratosis and hyperparakeratosis.[21] Orthokeratin differs from parakeratin in that it contains nonucleated keratin, and the latter contains residual nuclei.[21] Areas of epitelial acanthosis and hyperkeratosis appear clinically as white, rough, painless patches that do not rub off.

1.2.4 Dysplasia

Dysplasia is characterized by architectural disturbances in the tissue, accompanied by variations in the size and shape of the keratinocytes, known as atypia.[19] The changes in the epithelium found in dysplasia, both cytological and architectural, are associated with an increased risk of malignant transformation.[19,22,23] Dysplasias are categorized into grades of mild, moderate, and severe depending on the presence and severity of histopathological features in the tissue.[19] The grade of dysplasia is the current gold standard for predicting malignant transformation.[24] Dysplasia is linked to an increased rate of progression to invasive SCC; the more severe the dysplasia, the greater the risk of progression.[19,28-30] However, because dysplasia involves a spectrum of change rather than distinct stages, there is subjectivity in determining the specific grade of dysplasia present in a lesion.[25,26] There is also variability in individual interpretation of the histopathological criteria, leading to challenges regarding the consistency of diagnoses.[25]

Mild dysplasia is characterized by architectural changes and proliferation of cells at the basal and parabasal layers, with no extension beyond the lower third of the epithelium.[19,27] Moderate dysplasia demonstrates a proliferation of atypical cells extending into the middle third of the epithelium, and includes early cellular changes.[19,27] In severe dysplasia, the abnormal

proliferation of atypical cells extends from the basal layer into the upper third of the epithelium, but does not reach the entire thickness of the epithelium. [19,27,28]

1.2.5 Carcinoma *in Situ*

Carcinoma *in situ* (C*IS*) is a localized form or cancer, where the abnormal cells are confined to the surface epithelium. [20] The architecture of the epithelium is almost completely disrupted in C*IS*, with atypia and hyperchromatism frequently noted in superficial cells. [19] The cellular changes are indicative of both premalignant and malignant changes, without invasion beyond the basement membrane. [27]

1.2.6 Squamous Cell Carcinoma

Oral squamous cell carcinoma (OSCC) is the end stage of this series of cellular alterations in the epithelium, and is the most common malignant neoplasm of the oral cavity. [20,21] The main histological factor that distinguishes cancer from C*IS* is invasion through the basement membrane into the submucosa, creating the potential for metastasis. [19] The level to which abnormal cells resemble normal cells is called differentiation; if the tumour is histologically similar to normal tissue, with less than 25% of undifferentiated cells, it is classified as being well differentiated. [31,32] As the tissue becomes less structured, it is graded as moderately differentiated when it contains less than 50% of undifferentiated cells, and poorly differentiated when that number rises to 75% or more. [31-34] The majority of conventional SCCs are well- to moderately- differentiated. [33]

1.2.7 Verrucous Configuration

A particularly aggressive form of oral hyperplasia, termed verrucous hyperplasia, begins with hyperkeratosis and spreads to become multifocal and verruciform in appearance, with a high tendency to progress to carcinoma.[35] These lesions also have a high rate of recurrence, up to 55.6%.[35] Verrucous lesions were first described by Shear and Pindborg in 1980,[36] and it is still not well understood today why some hyperkeratotic lesions develop into aggressive verrucous lesions. Verrucous lesions of the oral mucosa resemble large warts, and have a 'cauliflower'-like presentation.[33] They may display areas of erythematous change within white patches, and appear as verrucous or nodular leukoplakias.[35] The lesions vary and change from small, homogenous, white plaque-like lesions, to characteristically 'speckled' leukoplakia, to more extensive thickened leukoplakia.[35] The lesions may be either single or multifocal, with varying degrees of keratosis.[33] Regardless of their clinical presentation, these lesions tend to be slow-growing and persistent.[35]

The most common sites for verrucous lesions are the buccal, vestibular and alveolar mucosa, as well as the gingiva.[35-37] Prevalent risk habits associated with verrucous lesions are the placement of chewing tobacco, areca nut and betel quid inside the buccal vestibules; common sites for these lesions correspond to common sites where these substances are placed.[37]

Verrucous hyperplasia and verrucous carcinoma are separate entities, but have very similar clinical and histopathological presentations.[37,38] The distinction between them relies on detailed histological assessment.[33]

1.2.7.1 Verrucous Hyperplasia

Epithelial hyperplasia that presents with a verrucous surface is termed verrucous hyperplasia.[38] Verrucous hyperplasia is characterized histopathologically by hyperplastic epithelium with superficial to adjacent normal epithelium.[38] Clinically, most cases present as white, keratotic, verruciform lesions ranging from two to four centimeters.[37]

It is uncertain what proportion of verrucous hyperplasias progress to verrucous carcinomas, as there is a general lack of diagnostic criteria for verrucous lesions. In addition, a number of verrucous lesions rather progress to conventional SCC. Focal moderate to severe dysplasia is seen in around 60% of cases of verrucous hyperplasia, and foci of SCC are seen in approximately 10%.[33]

1.2.7.2 Verrucous Carcinoma

Verrucous carcinoma is a well-differentiated, low-grade malignant variant of SCC; it is also much less common.[38] Verrucous carcinoma is characterized histologically by the invasion of hyperplastic epithelium into the underlying connective tissue.[38] It may co-exist with or transform into SCC.[33]

1.2.8 Tumour Grade and Stage

Tumour grade describes the abnormality of the cells present in a tumour. The grade of a tumour is histologically determined by the degree of differentiation, or the proportion of abnormal cells that lack normal tissue structures.[31,32,34] This grading is also dependent on the degree of histological change.[31,32] If over 75% of the tumour cells are undifferentiated, the tumour is graded as anaplastic/pleomorphic.[31,32] Tumour grading is an important indicator of how quickly a tumour is likely to grow and spread.[34]

Staging describes the severity of cancer based on the size and extent of the primary tumour, and whether the cancer has spread to other areas in the body. Cancer staging is based on the TNM staging system, which stands for Tumour, Node, and Metastasis.[39] T represents the size of the primary tumour; N represents lymph node involvement; and M represents metastasis and tissue invasion.[39] The application of this system is key in determining prognosis, treatment, and outcomes.[40] The five-year survival rate for localized disease is about 83%, while the rate for regional spread is 61.5%, and dropping to 37.7% for distant metastasis.[7]

1.2.9 Molecular and Genetic Events Leading to SCC

In 2000, Hanahan and Weinberg identified six essential hallmarks of cancer cells that distinguish them from their normal counterparts: self-sufficiency in growth signals, insensitivity to growth-inhibitory signals, evasion of programmed cell death, immortality or unlimited replicative potential, sustained angiogenesis, and tissue invasion and metastasis.[41] This initial definition has

been updgraded to include additional hallmarks as the development of development continues to be investigated.

Individual genes, as well as larger portions of the genetic material including chromosomes, can be damaged by chronic exposure to carcinogens such as tobacco, alcohol, oncogenic viruses, and inflammation.[41] This damage can spark the development of premalignant lesions and subsequent invasive carcinomas. These genetic alterations include the presence of oncogenes that promote cell survival and proliferation, as well as the inactivation of tumour suppressor genes which inhibit cell proliferation.[41] From these alterations, tumour cells acquire autonomous self-sufficient growth and evade growth-inhibitory signals, resulting in the potential for uncontrolled growth. As carcinomas invade and metastasize, new blood vessel formation is critical to sustaining their growth. SCCs, like most tumours, can create their own blood supply by stimulating endothelial cell proliferation and forming new blood vessels.[41] Invasion into adjacent normal tissue is made possible through the loss of cellular adhesion molecules, such as integrins and cadherins, which allows cancer cells to migrate away from the primary site.[41]

Some common early genetic alterations in SCC include the loss of chromosomal region 9p21, which occurs in 70-80% of dysplastic lesions of the oral mucosa, and loss at the chromosome 3p.[41] Loss of heterozygosity (LOH) at 17p and mutation of the p53 gene are genetic alterations that occur in the later stages of progression from dysplasia to invasive SCC.[41] Loss of chromosomal material at 3p, 9p, and 17p is observed in a high proportion of dysplasias, indicating that these genetic events are early markers of oral carcinogenesis. In particular, 17p is linked with early carcinoma, and has been identified as a gateway to OSCC.[42,43] Loss at 13q and 8p are observed

more frequently in carcinomas compared to dysplasias, and are hence are associated with later stages of carcinogenesis. [41]

1.2.10 Field Cancerization

Slaughter *et. al.* introduced the theory of field cancerization in 1953, stemming from the extensive histological examination of dysplastic epithelium surrounding oral cancers. [44] This dysplastic epithelium accounts for a high incidence of second primary tumours (SPT) in patients treated for oral cancers. SPTs are generally associated with a lower rate of survival than the original tumours. [41]

Braakhuis *et al.* expanded on the theory of field cancerization by introducing a progression model for the development of SCC. [45] In the initial phase of this model, a stem cell located in the basal cell layer of the epithelium acquires a genetic alteration and subsequently gives rise to a clonal unit that shares the same DNA alteration. This patch of cells then progresses into an expanding field as a result of additional genetic alterations. [45] This mucosal field pushes the normal epithelium aside and can expand, in some cases, up to several centimeters. [45] These fields are often macroscopically undetectable, but they may also present clinically as oral lesions like leukoplakia or erythroplakia. Ultimately, clonal selection leads to the development of carcinoma within this field of pre-neoplastic cells. [41] Current data supports this theory, with findings indicating that approximately 30% of oral and oropharyngeal cancer cases are surrounded by large fields of genetically altered cells that indicate a clonal relation to the invasive carcinoma. [10] An important implication of this model is that a field of pre-neoplastic

cells may remain after the surgical removal of a lesion, and hence has the potential to give rise to new carcinomas, considered SPTs. [10,45] The multifocality of oral carcinogenesis is an important cause of treatment failure in oral cancer. [41] Although primary excision can completely remove an oral carcinoma, the field of altered tissue may remain. Patients can develop a SPT within the same field, typically within three centimeters of the initial tumour, which may be difficult to distinguish clinically from a local recurrence. [10,41]

1.2.11 Clinical Presentation

Benign, precancerous, and malignant lesions may present as leukoplakias, erythroplakias, or erythroleukoplakias. [28] A leukoplakia is a clinically white lesion that cannot further be defined. [21] An erythroplakia is a red lesion of the oral mucosa, and an erythroleukoplakia is a mixed red-and-white lesion of the mucosa. These are descriptive terms which refer to the appearance of a lesion. A biopsy is required to diagnose a lesion, and to determine if the lesion is premalignant or cancerous. Dysplasia can occur among verrucous or papillary leukoplakia, or in the margins of chronic mucosal ulcers. [28] Dysplastic tissue is consistently present in the mucosa surrounding invasive SCC. [28]

The clinical presentation of SSC in advanced stages is so characteristic that there is usually clear suspicion of malignancy. In contrast, clinical presentation in the early stages is less distinguishable, and it can be challenging to differentiate. As the clinical characteristics alone are insufficient, it is crucial to obtain a diagnosis by biopsy and histopathological examination. [46] SCC lesions vary greatly in size, ranging from a few millimetres to several centimetres in more

advanced cases.[46] The clinical presentation of early malignant lesions is often in the form of erytholeukoplastic lesions. These are well-demarcated red and white lesions that present with a rough texture. The elasticity of the soft tissue changes and becomes indurated, or more firm, upon palpation. In advanced stages of malignancy, classic features of SCC include ulceration, nodularity, and fixation to underlying tissues.[46] There is often pain associated with advanced SCC.

Dental professionals are trained to look for the following abnormaities when examining the oral mucosa and determining a differential diagnosis:[47,48]

Margins	Diffuse, discrete
Colour	Red, white, red and white, other (blue, black, brown, purple)
Appearance	Non-homogenous, homogenous
Texture	Ulcerated, verrucous, smooth, corrugated, fissured, nodular, grainy
Size	Length, width, thickness
Site	Floor of mouth, lateral and ventral tongue, soft palate
Duration	The longer the lesion has been present, the greater the risk

1.3 Oral Cancer Etiology

Numerous risk factors are implicated in the development of oral cancer. Despite the many known risk factors for oral cancer, SCC also occurs in patents with no known risk factors.[20,49] The etiology of oral cancer varies in different populations[8]; this thesis will focus on outlining known

etiology for Western and South Asian populations. For the purpose of this thesis, Western populations include those of North America and Europe, while South Asian populations include the Southern portion of the Asian continent, including the countries of India, Pakistan, Sri Lanka, Bangladesh, Afghanistan, Bhutan, Maldives, and Nepal.

1.3.1 Alcohol

The role of alcohol as an independent factor in oral carcinogenesis has been examined by numerous studies, which have identified a link between alcohol and cancers of the oral cavity, pharynx, and esophagus. [50,51] Alcohol increases the risk of oral cancer through various interactions. Ethanol metabolizes to acetaldehyde, which is a probable human carcinogen, and also generates reactive oxygen species. These can causes damage to human DNA and important proteins. [51] Alcohol also impairs the body's ability to metabolize and absorb various vitamins and nutrients that play a role in reducing cancer risk, such as Vitamins A and C, folate, and carotenoids. [51] Alcohol has a dehydrating effect on the oral mucosa, which increases its permeability and results in atrophy. This change in morphology leads to easier penetration of carcinogens into the oral mucosa. [49]

A strong dose-response relationship has been established with alcohol use, and heavy alcohol consumption (consuming over 23.2 grams of ethanol daily) alone can increases oral cancer risk five-fold. [52,53] Numerous studies have also identified a strong synergistic relationship between alcohol and tobacco, resulting in a drastically increased oral cancer risk in individuals who consume both tobacco and alcohol. [49,52]

1.3.1.1 In Western Countries

Alcohol consumption is common in Europe and North America.[51] Over 75% of alcohol consumed in Western countries includes wine and beer, with spirits making up the remaining 25%.[54] The proportion of heavy drinkers is 11-15%.[54] In developed countries, the main risk factors for oral cancer are alcohol and tobacco, and up to 75% of these cancers are attributable to these two lifestyle factors.[51]

1.3.1.2 In South Asian Countries

Trends over the last four decades in South Asian countries show steady increases in alcohol consumption rates.[51] The majority of alcohol consumed in South Asian countries is in the form of spirits.[54] While the known percentage of heavy drinkers is quite low in South Asian countries at 0.9%, it is believed that the vast majority of alcohol use in these countries remains undocumented.[54]

1.3.2 Tobacco

The relationship between smoking and oral cancer has been established by numerous epidemiological studies.[55] The most important carcinogens in tobacco smoke are the aromatic hydrocarbon benz-pyrene and the tobacco-specific nitrosamines (TSNs), namely 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and N-nitrosonornicotine (NNN).[49]

The metabolism of these carcinogens involves oxygenation by certain enzymes.[56] Genetic polymorphisms in the genes coding for these enzymes are believed to play an important role in the genetic predisposition to tobacco-induced cancers of the head and neck.[57] There is a 20-fold risk of oral cancer in heavy tobacco smokers (one pack a day or more). Due to the strong dose–response relationship, the risk of oral cancer increases as the number of cigarettes smoked per day and the duration of smoking increase.[57,58]

1.3.2.1 In Western Countries

Exposure to tobacco in Western countries is almost entirely through smoking; products used are mainly cigarettes, cigars, and pipes.[58] The IARC and the World Health Organization investigated the global prevalence of tobacco use in 2000, and found that about 26% of the North American population and 31% of the European population above the age of fifteen were smokers.[58] In Canada in 2009, 27% of men and 23% of women smoked.[58] Recent statistics in Canada indicate that smoking rates are declining.[59]

Smoked tobacco substances in Western countries (Table 1.3) include filtered and unfiltered cigarettes, as well as cigars, pipe tobacco, hookah (water pipe), and modern methods of tobacco consumption such as electronic cigarettes and vaporizers.

Name	Contents						Countries used
	Tobacco	Nicotine	Filter	Paper	Leaf Tobacco	Flavouring	
Cigarette (filtered)	X		X	X			Worldwide
Cigarette (unfiltered)	X			X			Worldwide
Cigar[+]	X		*		X		Worldwide
Pipe Tobacco	X						Worldwide
Hookah *Narghile, Shisha*	X					*	Worldwide
Vaporizer *E-cigarette*		X				*	Worldwide

Table 1.2 Smoked substances in Western countries
***** Optional
[+] Including little cigars, small cigars ("cigarillos"), regular cigars, premium cigars
Adapted from the World Health Organization (IARC), 2004 [58]

1.3.2.2 In South Asian Countries

Cigarettes, both filtered and hand-rolled, are also consumed in South Asian countries. The IARC and the World Health Organization investigated global prevalence of tobacco use in 2000, and found that 27-33% of the South Asian population above the age of fifteen were smokers. [58] Other common forms of smoked tobacco in South Asia include bidi smoking and the use of chutta, which is used for reverse smoking. A bidi is a hand-rolled cigarette, where shredded or flaked tobacco is rolled into a conical shape using a temburni leaf (of the Diospyros melanxylon plant, native to India and Sri Lanka), and tied using a thread. [58] Bidi smoking is linked with an

increased risk of oral cancer in men. [52] Chutta, which is also a hand-rolled cigarette, is primarily used by Indian women for reverse smoking, which is the process of placing the lit end of a cigarette inside the mouth. [58,60]

Name	Contents				Countries used
	Tobacco	Filter	Paper	Temburni Leaf	
Cigarette (filtered)	X	X	X		Worldwide
Cigarette (unfiltered)	X		X		Worldwide
Bidi	X			X	India
Chutta	X		X		India

Table 1.3 Smoked substances in South Asian countries
Adapted from the World Health Organization (IARC), 2004 [58]

1.3.3 Smokeless Tobacco

Tobacco that is chewed rather than smoked is referred to as smokeless tobacco. Smokeless tobacco products and their use vary extensively across the globe.

1.3.3.1 In Western Countries

In Europe and North America, the main types of chewing tobacco include plug, loose-leaf, and twist (Table 1.4). Their use is declining in these regions, although it remains a prevailing habit in

certain subpopulations. Wet or moist snuff is particularly common in North America and Scandinavia. The habit of snuff (referred to as snuff-dipping) causes oral SCC referred to as *snuff-dipper's cancer*.[49]

Name	Contents					Countries used
	Shredded Tobacco	Powdered Tobacco	Sweetener	Flavouring	Fungi Ash	
Loose-leaf / *snuff* / *dip* / *rub*	X		X	X		Scandinavia, Europe, North America
Plug	X		X			North America
Twist	X			X		North America (Eastern USA)
Dissolvable tobacco		X		X		USA
Name	Contents					Countries used
	Shredded Tobacco	Powdered Tobacco	Sweetener	Flavouring	Fungi Ash	
Snus		X				Sweden, USA
Iqmik / *blackbull*	X				X	USA (Alaska)

Table 1.4 Smokeless tobacco substances in Western countries
Adapted from the World Health Organization (IARC), 2004[58]

1.3.3.2 In South Asian Countries

The use of smokeless tobacco is a highly prevalent habit in South Asian countries, with an age of initiation as young as 9-12 years old. [61] A systematic review of six studies found that the average age of commencement was 15 years old. [62] The young age of initiation may be linked to accelerated temporal trends in oral cancer progression.

Developing Asian countries have a greater prevalence of smokeless tobacco use, as well as the use of areca nut, betel quid, and their substitutes as major carcinogenic influences. [63] The use of areca nut and betel quid is almost exclusively found in Asian and South Asian countries, and their immigrants worldwide. Their use, in a variety of forms and compositions, is widespread in Asia. [49] Both men and women consume smokeless tobacco; overall, 34.7% of men and 32.4% of women in South Asian countries use smokeless tobacco. [64] Rates of use in women range widely, from 1% to 61% in different regions. [65] There is a general lack of knowledge regarding the harmful effects of areca nut and betel quid, which perpetuates its role as a major risk factor in oral cancer in South Asians countries. Betel quid is widely associated with socializing, family traditions and cultural heritage, and it is believed to be associated with various health benefits. [62] Oral cancer prevention programs tailored to South Asian populations must consider these beliefs; awareness of these beliefs, barriers, and other cultural considerations is key to undertaking successful prevention programs in South Asian communities. [62]

A broad range of variations of smokeless tobacco and chewed substances exists in South Asian countries, including areca nut, betel quid with and without tobacco, and paan masala with and

wthout tobacco. Other chewed products include gutka, mawa, mainpuri tobacco, khaini, khiwam, and naswar (Table 1.5).

Name	Contents						Countries used
	Areca nut	Betel leaf	Slaked lime	Tobacco	Spices	Catechu	
Areca nut	X						India
Betel quid w/out tobacco	X	X	X		*	*	South Asia
Betel quid with tobacco	X	X	X	X	*	*	South Asia
Pan / Paan without tobacco	X	X	X		*	X	South Asia
Pan / Paan with tob.	X	X	X	X	*	X	South Asia, Southeast Asia
Paan Masala / *chaalia*	X		X		X	X	India, Pakistan (*chaalia*)
Gutka / *Gutkha*	X		X	X		X	South Asia
Mawa / *kharra* (variant of gutka)	X		X	X	*	*	South Asia
Mainpuri tobacco	X		X	X		X	India (Mainpuri district of Uttar Pradesh)
Khaini, *chaini*	*		X	X	X		South Asia, India (Gujarat and Maharashtra)

Name	Contents						Countries used
	Areca nut	Betel leaf	Slaked lime	Tobacco	Spices	Catechu	
Khiwam				X	X		South Asia
Naswar			X	X			Afghanistan, Iran, Russia, South Asia

Table 1.5 Smokeless tobacco substances in South Asian countries
* Optional
Adapted from the World Health Organization (IARC), 2004; Bhissey, 2013 [58,64,66]

1.3.3.3 Areca Nut

The seed of the *Areca catechu* palm, known as the areca nut, is a highly addictive substance which is widely used in Asian and South Asian communities. [63] It is the fourth most consumed drug after nicotine, ethanol, and caffeine, and is known for its psycho-stimulating and cholinergic effects. [67,68] There is a general lack of knowledge about its link with oral cancer. [63] It is sometimes referred to as 'betel nut', which is botanically incorrect. [64]

The chemical composition of areca nut includes carbohydrates, fats, proteins, crude fibre, polyphenols, alkaloids, and minerals such as sodium, calcium, manganese, and copper. [64] Four alkaloids that have been identified in areca nut include arecoline, arecaidine, guvacine, and guvacoline. [64] Betel quid and its substitutes are associated with higher genotoxic and carcinogenic potential, which is increased through interactions with nitrosamines in tobacco and alkaloids in areca nut. [63] On its own, areca nut is classified as a Group I carcinogen by the International Agency for Research on Cancer (IARC), meaning that there is sufficient evidence

of carcinogenicity to humans.[69] Betel quid, both with and without tobacco, is also classified as a Group I carcinogen.[69]

The use of areca nut and betel quid are socially and culturally acceptable habits in South Asian communities.[63] These products are easily available in cheap, attractive sachets that make them popular among all age groups, including children and young adults.[63] Areca nut is seen by many South Asians as a divine fruit, and is used during religious ceremonies, weddings, prayers and blessings. In certain religions, is believed that God blesses the areca nut, which is then distributed to the followers.[70] The use of areca nut in South Asian countries is also believed to bring various health benefits, including improved digestion and freshening of the breath.[70]

1.3.3.4 Betel Quid

The betel plant (Piper betel L.) is a vine found in many South Asian countries.[64] Betel leaf contains oil, which is composed of hydroxychevicol, euginol phenol, and chevicol, as well as Vitamin C and carotenes.[64] Betel leaf on its own has not been shown to be carcinogenic.[64]

The term *quid* refers to a mixture that is placed in the mouth.[64] Betel quid, also known as *pan* or *paan*, is a substance or mixture that is placed and retained in the mouth, chewed, and sometimes swallowed.[63,64] Betel quid typically contains betel leaf, areca nut, slaked lime, and sometimes tobacco.[64] It may also contain various spices such as cardamom, saffron, cloves, turmeric, or sweeteners.[64] As such, the components of betel quid vary, and as do the possible interactions between these components.

Calcium hydroxide ($Ca(OH)_2$), often referred to as 'slaked lime', is an inorganic compound in the form of a clear, odorless powder. It is commonly prepared from limestone or seashells. [64] The use of slaked lime in betel quid increases the pH, leading to an alkaline environment; this in turn results in increased mutagenic activity. [71,72] Catechu is another common component in betel quid, and is a resin product from the Acacia Catechu tree. Catechu has a distinct reddish brown color. [64]

Considerable research has recent been focused on the carcinogenic, mutagenic, and genotoxic potential of betel quid ingredients when used together, especially tobacco, areca nut, and slaked lime. In vitro studies have shown that some essential components of betel quid are genotoxic, cytotoxic, and also stimulate cell proliferation. Reactive oxygen species (ROS), methylating agents, and reactive metabolic intermediates from betel quid can induce DNA damage. [49,73]

1.3.4 Anatomical Lesion Site

Anatomical lesion sites for oral cancer vary by population. This may be linked to differences in risk habits.

1.3.4.1 In Western Countries

The tongue is the most common site for oral cancer among Western populations including Europe and North America, accounting for 40–50% of oral cancers. [74] Smoking poses a greater

risk of oral cancer at certain sites compared to others, particulaly the ventral and lateral surfaces of the tongue and the floor of the mouth (FOM). [75]

1.3.4.2 In South Asian Countries

The gingiva and the buccal mucosa are the most commonly affected sites for oral cancers in South Asian countries. [76] A 2016 study of nearly 1,000 South Asian cancer cases found that 40.5% of cancerous lesions were located on buccal mucosa, while only 22.2% presented on the tongue. [77] It is theorized that this difference in common lesion sites is linked to risk habits; while the tongue and floor of the mouth are high-risk sites for oral cancer in Western popuations where tobacco smoking is a common risk habit, the gingiva and buccal mucosa are sites that are associated with South Asian risk habits such as chewing tobacco and the use of areca nut and betel quid.

1.3.5 Sex

The incidence of head and neck cancers is generally higher in males than females worldwide. [1]

1.3.5.1 In Western Countries

In Western countries, rates of oral cancer are marginally higher in males. [1,3] For example, in Canada, the incidence rate in males is 1.7%, while it is slightly lower at 1.1% in females. [1] This trend might be attributed to heavier indulgence in risk habits by men, including tobacco and alcohol. [3]

1.3.5.2 In South Asian Countries

In South Asian countries, the ratio of men to women regarding oral cancer incidence is approximately 4:1. [74] This trend might be attributed to smoking habits and alcohol intake, which are often not as common among females, with the exception of areca nut and betel quid chewing which is believed to be equally common among females and males. [74]

1.3.6 Age

Increased age is linked with an increased risk of oral cancer. [74,78,79] Increased age is linked to cellular biological alterations due to long-term exposure to environmental pollutants, chemicals found in foods and other products, as well as risk habits. These affect the homeostatic stability of genes that control cell proliferation and death, thereby increasing the risk of cancer. [79]

1.3.6.1 In Western Countries

Oral cancer rates in Europe and North America increase with age; the increase becomes more rapid after the age of fifty years, and peaks between sixty and eighty years of age. [3,74,78] However, recent sudies indicate that mean age at diagnosis is decreasing in Western populations, with an increase in the number of oral cancer cases diagnosed in patients below the age of fourty years. This shift may be related to changing risk factors. [78,79]

1.3.6.2 In South Asian Countries

In South Asian countries, oral cancer most often occurs between fifty and sixty years of age. [74] This is linked to a greater exposure to risk habits in developing areas, such as India and Sri Lanka. In these countries, many patients with oral cancer are younger, and present with heavy abuse of various forms of tobacco. [74] Additionally, South Asian individuals begin using tobacco products from a very young age, contributing to the earlier development of cancerous lesions.

1.3.7 Poor Oral Hygiene

Oral dysplasias and cancers have been found to be associated with dental neglect and poor oral hygiene. [52] While poor dental status, including sharp teeth and decay, and chronic ulceration have been suggested to promote oral cancer in the presence of other risk factors, [49] there is little definitive evidence to determine the role of poor oral hygiene alone on the etiology of oral cancer.

Periodontal disease has also been linked with oral cancer; each millimeter of alveolar bone loss has been associated with a five-fold increase in the risk of tongue cancer. [80,81] Possible mechanisms for this association revolve around microbial interactions. [82] Oral bacteria may also synthesize acetaldehyde from alcohol. [52,83,84] Further research is required to investigate the relationship between periodontal disease and oral cancer risk.

1.3.8 Viruses

Viral infections may induce malignant transformation by interfering with the host's cell cycle, and affecting cell growth and proliferation. Certain viral genes are proto-oncogenes, which become oncogenes when inserted into the host's DNA and ultimately result in malignant transformation. The prototypic viruses implicated in oral cancer development include Epstein–Barr virus (EBV), human papillomavirus (HPV), and herpes simplex virus. [49,85-87] HPV is the most common virus implicated in oral carcinogenesis; strong associations have been reported by numerous studies between HPV and SCC, particularly in the oropharynx. Certain HPV types, referred to as high-risk types, are associated with both oral premalignant lesions and oral malignancies. These types include HPV 16, 18, 31, 33, 35, and 39. [49]

1.3.8.1 In Western Countries

While oral cavity cancers are generally decreasing in Western and developed countries due to a consistent decline in tobacco use, oropharyngeal cancer rates have been increasing over the last two decades. [88] HPV infection accounts for 60% to 70% of oropharyngeal cancers in Western countries. [88]

1.3.8.2 In South Asian Countries

While there is little research available on the role of viruses in oral and oropharyngeal cancer in South Asian countries, it has been shown that viral infections account for a much smaller proportion of oropharyngeal cancers in less developed countries, approximately 10% of cases. [88]

1.3.9 Other Factors

Other factors implicated in oral cancer etiology include ultraviolet (UV) exposure, nutrition, and genetic predisposition.

1.3.9.1 UV Exposure

Exposure to excessive solar radiation and UV light has been known to cause lip cancers. UV rays may also causes actinic cheilitis, which may transform to cancer. [49]

1.3.9.2 Nutrition

The International Agency for Research on Cancer (IARC) states that a low intake of fruits and vegetables is linked to an increased risk of cancer development, while regular consumption of fruits and vegetables, particularly carrots, fresh tomatoes, and green peppers, has been associated with a reduced risk of oral cancer. [49,89] Some other foods and nutrients that have a protective

effect include fish and seafood, vegetable and olive oil, bread, cereals, legumes, protein, fat, fresh meat, chicken, liver, and fiber. [49]

In developing countries, the majority of oral, oropharyngeal, and esophageal cancers are thought to be linked to micronutrient deficiencies from restricted diets low in fruits, vegetables, and animal products. [89,90] While the relative roles of various nutrients are not clearly defined, deficiencies of riboflavin, vitamin C and zinc are believed to be of particular importance. [89,90]

Excessively hot foods and beverages may increase the risk of cancers of the oral cavity, pharynx and esophagus. [50] For example *maté*, a tea-like beverage consumed in South America, has been identified as an independent cause for the development of oral and oropharyngeal cancers, though the exact pathogenesis has not been determined. [50] Some proposed causes for *maté*'s carcinogenicity include thermal injury, its role as a solvent for other chemical carcinogens, and its content of tannins and N-nitroso compounds. [49,91]

1.3.9.3 Genetic Predisposition

Genetic predisposition has been identified as an important risk factor in the development of oral cancer. [49] Certain individuals may inherit the inability to metabolize carcinogens or to repair DNA damage once it has occurred. [49] Many studies have identified markers that might be of diagnostic or prognostic value in the development of oral cancer. [49,52]

While migrant studies have shown that immigrants bring their risk of disease from their country of origin, such studies also show that they often adopt the new country's disease profile within the span of a few generations. [92,93] This indicates that while genetic factors play a role in disease rates among different populations, it is likely that the risk itself is a result of interactions with environmental factors rather than genetic factors alone. [94]

1.4 Clinical Examination

1.4.1 Screening

Screening is the process of identifying apparently healthy people who may be at an increased risk of disease. It involves checking for the presence of disease in a person who is free of symptoms, with the intention of diagnosing treatable conditions in early stages of disease. [95] Oral cancer screening is performed regularly by dental professionals, including dental hygienists, as part of a complete intraoral examination of the patient being seen for dental or dental hygiene procedures.

1.4.2 Visual Intraoral Examination

Intraoral examination under normal lighting is the most commonly accepted and applied method of screening for oral cancer. [96] While conventional visual examination can be very effective in detecting lesions in accessible areas such as the mucosa, tongue, and floor of the mouth, it is limited in identifying areas of histologic changes, which may clinically appear normal. [96] One

study determined that visual intraoral examination has a sensitivity of about 85% and specificity of 97%, [96] which supports this screening method's longstanding status as the gold standard for oral cancer screening.

Limitations of visual intraoral inspection include difficulty in differentiating between benign, oral potentially malignant disorders (OMPDs) and malignant lesions, particularly for general dental pracritioners; this may result in a delay in patient referrals, or overdiagnosis. [96] Leukoplakias are the most common form of OPMD, and have an overall transformation rate of approximately 5%. The extent and rate of progression in dysplasia varies according to individual patient and lesion characteriatics, and it is hence difficult to differentiate between OPMD lesions at high or low risk of progression to carcinoma.

1.4.3 Adjunctive Clinical Aids

Due to the potential limitations in the conventional visual intraoral examination, alternative screening methods and adjuncts may facilitate the detection of oral cancers, dysplasias, and potentially malignant disorders. These include the use of contrast agents and vital dyes, such as toluidine blue (TB), and fluorescence visualization. [95]

1.4.3.1 Fluorescence Visualization

The principles of fluorescence visualization are based on the presence of fluorophores in the epithelium. Various elements of the epithelium, including collagen, elastin, keratin, flavin

adenine dinucleotide (FAD) and nicotinamide adenine dinucleotide (NAD), typically exhibit a green fluorescence when excited by light between 375 and 440 nanometers.[95] However, during carcinogenesis, metabolic and structural changes take place that alter the concentration of the fluorophores, and result in a loss of fluorescence due to increased absorption and the scattering of light.[95] Changes in cell metabolism cause a breakdown of collagen, particularly by proteases that are upregulated in cancer.[95] Additionally, an increase in nucleus to cytoplasm ratio causes scattering of light, and an increase in microvasculature causes absorption of light. These mechanisms results in a decreased amount of light reaching the stroma.[95] Loss of tissue fluorescence is also linked to non-specific inflammation, which results in high rates of fasle-positive results.[97]

The VELscope™ (Visually Enhanced Lesion Scope; LED Dental, White Rock, BC, Canada) is a hand-held visualization device that exposes tissues to blue-violet light at a range of 400 to 460 nanometers.[95,98] Normal mucosa emits a pale green fluorescence when viewed through the VELscope, whereas neoplastic tissue exhibits a loss of normal fluorescence, appearing instead as a dark area.[95]

In a study of 175 patients undergoing histopathological assessment, 96% of cases diagnosed as SCC showed loss of fluorescence when examined under a florescent light.[99] There was also a statistically significant correlation between dysplastic tissue and a loss of fluorescence. Numerous studies support these findings, with evidence that VELscope typically demonsrates high sensitivity.[98,100-102] However, low sensitivity has been noted in regards to differentiation

between different grades of dysplasia and normal tissue. While FV does not replace histopathological assessment, it is a useful adjunctive tool in the monitoring of oral lesions. [99]

1.4.3.2 Toluidine Blue

Toluidine blue (TB), also known as tolonium chloride, is a vital dye that stains nucleic acids and abnormal tissues. [96,103-105] TB has a high sensitivity for the detection of severe dysplasias and carcinomas, but a lower sensitivity in detecting mild and moderate dysplasias. [96,104] A study by Nair *et. al*. in 2012 found that 100% of carcinomas stained positively with TB, but only 50% of dysplasias stained positively. [96]

On the other hand, some studies show that TB has the potential to aid in the visualization of faint lesions which may not be easily visible during visual intraoral examination. A study by Epstein *et al*. suggest that TB is effective in selecting a site for biopsy, as the areas with the most concentrated TB uptake demarcate the site of perceived highest risk. [106] TB staining is also related to genetic changes associated with the progression of potentially malignant lesions to SCC, including LOH and allelic loss. [104,107] A longitudinal study by Zhang *et al.* shows that cases with TB uptake in low-grade dysplasia were four times more likely to progress to cancer compared to lesions exhibiting no TB uptake. [104] While evidence suggests that the specificity of TB is low, TB staining continues to play a role in the identification of high-risk oral lesions, and is regarded as a useful adjunctive tool. [96,108]

1.4.4 Biopsy

A biopsy is a small sample of tissue obtained from a lesion or affected area, which is submitted to a pathologist for histological review. A pathologist is able to determine the exact diagnosis of the biopsy by assessing the tissues microscopically. A biopsy may be incisional (wedge or punch) or excisional. Tissue samples from a biopsy are fixed in 10% neutral buffered formalin fixative. [109] Each biopsy should be accompanied by pertinent clinical information including lesion descriptors such as location, size, duration and appearance, presence of risk factors or habits, and previous histroy of dysplasia or cancer. [109]

Diagnotic biopsies are indicated when a suspicious mucosal lesion persists for more than three weeks following the removal of any known or suspected irritants. [108] Biopsies are considered the gold standard of lesion diagnosis. [109]

1.4.4.1 Biopsy Guidelines

In 2008, the College of Dental Surgeons of British Columbia (CDSBC) published biopsy guidelines developed by a working group of the BC Oral Cancer Prevention Program (OCPP). The working group was comprised of experienced clinicians and scientists from the British Columbia Cancer Agency (BCCA).

These biopsy guidelines aimed to provide general information for clinicians, and to facilitate and inform decision-making regarding indications for biopsies of suspicious oral lesions. The

guidelines outlined oral cancer statistics in the province, and highlighted risk factors including tobacco and alcohol. Clinicians were encouraged to pay particular attention to high-risk sites for oral cancer, including the lateral and ventral surfaces of the tongue, the floor of the mouth, and the soft palate. [108] The article provided clear guidelines for the biopsy of lesions persisting beyond three weeks following the elimination of possible local irritants, and outlined patient referral pathways based on the diagnosis of the biopsy.

1.4.4.2 Limitations of Current Biopsy Guidelines

While the 2008 biopsy guidelines from the CDSBC and the BC OCPP aimed to increase awareness and provide a clear referral pathway for clinicians, these recommendations are now dated and may not reflect important considerations in the examination of suspicious oral lesions. For example, it is crucial to discuss risk factors beyond tobacco and alcohol, which may be prominent in various communities within BC. One such example is the use of chewed tobacco, which is a common risk habit among Canada's largest visible minority population. Additionally, sites considered high-risk for progression may differ by population, an important fact which was not included in the guidelines or recommendations.

It is also important to consider that the outlined referral pathways may not be suitable for the entire population in BC. Referral pathways should be easily accessible for South Asian populations and other minority populations, particularly those at high risk for oral cancer.

1.5 Ethnicity

1.5.1 Definitions of Ethnicity

Ethnicity can be defined as as a socially, politically, and historically constructed concept used to categorize populations based on characteristics like nationality, culture, language, religion, geographic location, or identity. [110,111] Ethnicity is self-defined, and is something that can change with time, location, or context. [110]

Ethnicity and race are terms that are often used interchangeably, although their meanings differ markedly. Race refers to a group of people who share similar and disctinct physical and biological characteristics. [111,112] While race describes someone's physical appearance and genetics, ethnicity describes one's cultural background and identity. There is no concensus on the appropriate use of these terms in epidemiology and research. [112]

1.5.2 South Asian Ethnicity

There exist various definitions of South Asian ethnicity. In geographical terms, South Asia represents the Southern portion of the Asian continent. According to the United Nations Geoscheme, Southern Asia includes nine countries: Afghanistan, Bangladesh, Bhutan, India, Iran, Maldives, Nepal, Pakistan, and Sri Lanka. [113] However, the Central Intelligence Agency (CIA) World Factbook and the South Asian Association for Regional Cooperation (SAARC) both exclude Iran from this definition, and state that the definition of South Asia may also

include the British Indian Ocean Territory, Mauritius, and Tibet. [114,115] In classifying visible minorities, Statistics Canada does not provide a clear definition of what constitutes South Asian ethnicity. Instead, they provide brief examples of South Asian classification, such as Bangladeshi, Punjabi, or Sri Lankan. [6] Bangladeshi and Sri Lankan refer to countries of origin, and Punjabi may refer to a place or a language.

South Asian ethnicity can also be viewed from religious and linguistic standpoints. The major religions of South Asia include Hinduism, Islam, Sikhism, Buddhism, and Christianity. [6] There are also numerous different languages and dialects spoken throughout South Asia. In the 2001 Canada Census, members of the South Asian community reported more than 75 different mother tongues. Punjabi was the most common mother tongue (29%), followed by English (27%), Tamil (10%), Urdu (8%), Gujarati (6%) and Hindi (6%). [116] Despite such a broad range of languages, religions and ancestries, South Asians are unified in sharing strong family values, social networks, and traditions. [116]

1.6 South Asian Immigrants

Immigrants from South Asian countries currently live on each continent, as well as numerous islands throughout the world. [117]

1.6.1 Globally

Large-scale emigration from India began in the nineteenth century during British colonial rule. Following the abolition of slavery, colonies such as Britain, France, Portugal and the Netherlands required labourers for sugar and rubber plantations. This prompted the British to establish an organized system of temporary labour migration from the Indian subcontinent, known as the indenture system. Poverty in South Asia served as incentive for many to leave their country. In 1834, Britain began exporting South Asian labour to East Africa, France, and the Netherlands. [117]

Workers initially signed a five-year work contract, but many chose to stay in their new country of residence permanently. [117] Workers were housed in cramped barracks, and were subjected to severe punishments for inadequate or insufficient work. As a result of intense criticism, the British Imperial Legislative Council abolished the indenture system in 1916. It is estimated that by that time, more than 1.5 million South Asians had been shipped to work in colonies in the Caribbean, Africa, Asia, and Oceania. [117] Emigration from South Asia to the United Kingdom and North America also started during colonial rule, but the number of emigrants was not significant: there were less than 10,000 South Asians in the United States, Canada, and the UK at this time. [117]

In 1930, India restricted the issuance of passports in order to limit the migration of less-educated Indians. This continued until 1967 when the right to travel became a fundamental right under the Indian constitution, following which the Passports Act of 1967 was introduced. [117] After the independence of several South Asian countries, many workers emigrated from India to the UK.

The UK's commonwealth immigration policy, which allowed any citizen of a Commonwealth country to live and work in the UK, encouraged this emigration trend, along with Britain's post-war increased demand for labour. [117] The South Asian population in the UK grew from 50,000 in 1961 to over 1 million in 2001. [117]

1.6.2 In Canada

In 1904, there were about 100 Indian immigrants in Canada, which was also part of the British Empire at that time. Most Indians were Sikh men, and worked in the logging, mining, and railroad industries. This number rose to over 5,000 before a restrictive immigration policy was introduced, known as the Continuous Journey Regulation, which required landed immigrants to Canada to make a continuous journey from their country of origin. Since no ships traveled directly from South Asia to Canada, these immigrants were no longer able to come to Canada. [117] This policy remained in effect until 1947, when the recent independence of South Asian nations like India, Pakistan, and Ceylon (present-day Sri Lanka) sparked the introduction of annual immigration quotas by the Canadian government.

By the 1960s, restrictions were lifted from Canadian immigration policies, leading to an explosive growth of South Asian communities within Canada, from a population of 6,700 which grew to nearly 70,000 within a decade. There are currently over 1.5 million South Asians living in Canada. [6]

1.6.3 Areca Nut and Betel Quid Use in South Asian Immigrant Populations

The use of chewed carcinogenic substances such as areca nut and betel quid is prevalent in South Asian countries. As an important immigrant population in numerous countries across the globe, and within Canada, it is important to consider the use of these substances among immigrant populations.

1.6.3.1 Globally

Studies of oral cancer risk habits among South Asian migrants in England and South Africa have shown that the use of areca nut is prevalent in these communities, and that the patterns of use are closely related to the chewing customs prevalent in the countries of origin. [118] A comparison of chewing habits among first- and second-generation South Asians in England suggests that areca nut and betel quid chewing habits continue long after immigration, as these habits promote close ties with cultural heritage, as well as a sense of community. [118,119]

The South Asian community is very diverse, and is comprised of many cultures with distinct beliefs and practices. The extent of areca nut and betel quid use varies among different religious groups, different regions of origin, and different generations of immigrants. [70] Sikhs generally do not indulge in tobacco or betel quid chewing, while Hindus from both first and second generations tend to continue chewing betel quid or pan masala in their new country of residence. On the other hand, second-generation Muslims and Jains are less likely to continue to chew these products. [118,119]

Rates of use of chewed substances vary by country, and within South Asian immigrant communities themselves. In Durban, South Africa, rates of betel quid use are 30.7% in women, and 5.5% in men. [118] The Bandgladeshi population in the UK is reported to have rates as high as 78-96% [118] , while a study from New York reports slightly lower but still prevalent rates of betel quid use among South Asian immigrants, at approximately 31-45%. [120] Some of these studies have small sample sizes; while they may not be representative of the entire immigrant population, they do provide crucial information regarding the use of chewed substances among immigrant populations.

1.6.3.2 In Canada

There are no studies that specifically examine the rates of use of areca nut and betel quid in Canadian immigrant populations. A study by Auluck *et. al.* in 2009 reports that betel quid use is common in immigrant workers and farmers around the Vancouver area, and that chewed products such as areca nut and betel quid are readily available in local shops. [70] It should be noted that while users of these products traditionally spit the chewed contents out of the oral cavity, social norms in Western countries render this habit unacceptable, and the contents are often swallowed instead. This tendency to swallow the contents of areca nut and betel quid causes an increased concern regarding adverse health effects, including cancer risk. [70]

1.6.4 Oral Cancer Awareness

South Asians are generally not aware that areca nut and betel quid cause oral cancer. [70,119,121] South Asian immigrants are exposed to numerous risk factors for oral cancer, yet the majority of these individuals have poor knowledge regarding the implications of these behaviours. [122,123] A recent study in England found that only 18% of South Asian immigrants had seen a dentist in the previous two years. [122]

1.7 Collection of Ethnicity Data

According to Canada's 2011 National Household Survey (NHS), approximately 19%, or close to one-fifth, of Canadians are members of visible minority groups. [6] Understanding and reducing health disparities while promoting equity in ethnic minority populations are becoming top priorities in Canadian research and public policy. However, ethnic variations in population health, service utilization and general health outcomes are not thoroughly studied in Canada, largely due to a lack of data on ethnicity. [124] While some countries such as those of the UK, the USA, and New Zealand have taken steps to begin routinely collecting ethnicity data at the individual level, there remains no requirement for Canadian institutions and agencies to collect such information. [110,125]

The collection of data on ethnicity has the potential to promote quality healthcare for all population groups by contributing to better information databases. [110] This data can be used to determine which groups are accessing care and services, identify barriers to care, and improve

outcomes by tailoring services to meet the needs of diverse groups. [110] Quantifying disparities in health status and health outcomes within different ethnic groups is an important aspect of health research, which cannot be accurately assessed without data on ethnicity. A 2006 survey in Western Canada found that nearly 85% of respondents felt comfortable with the collection of this data in healthcare settings. [124]

On the other hand, ethnicity tends to be conceptualized very narrowly, and is often defined interchangeably with race. This poses barriers in terms of data collection, given the ambiguity of these concepts. [110,126] Some argue that classifying people by race or ethnicity reinforces racial and ethnic division in society, and that patients are concerned about being judged, and ultimately receiving poor care, on the basis of assumptions and stereotypes. [110,112,126] Additionally, differences in disease rates among ethnic minorities may be addressed through the imposition of changes in practice, which often promote assimilation to Western norms. [94] Although Canada is widely perceived as egalitarian and equitable, health inequalities remain, along with experiences of discrimination which continue to impact patients' access to and utilization of health services. [110] While there are numerous potential benefits to obtaining data on ethnicity, it is important to consider and understand the potential and perceived barriers. [126]

In the absence of self-reported ethnicity data, supplementary methods of obtaining this information have been explored, such as the use of Census data, existing health records, and name recognition software programs. Name recognition software programs offer an effective methodology to identify ethnicity within health care datasets, and can successfully assist researchers, planners, and policy makers in identifying and addressing health inequalities. [127,128]

1.7.1 Internationally

In the UK, the Hospital Episode Statistics (HES) database collects ethnicity data for about 80% of patients seen in the hospital setting. Ethnicity is self-reported using various categories, which include: White, Black, Caribbean, Black African, Black Other, Indian, Pakistani, Bangladeshi, Chinese and Other. [129]

In the United States, health systems routinely collect information on race in health records and administrative data, and this information has permitted the compilation of a considerable body of knowledge on racial disparities in health and access to care. [130] Health records in the United States typically use six groups for race: American Indian, Asian, Black, Hispanic, White, and Unknown/Missing. [131]

1.7.2 In Canada

In order to adequately represent the cultural factors passed on through generations which may influence health, Canada chooses to focus on ethnicity rather than rate. [124] There is, however, a general lack of data and research on the role of ethnicity on health in Canada. As a result, researchers and policy makers cannot adequately address the health and acces to care of visible minorities. [132] Visible minorities include groups such as South Asians, Chinese, Latin Americans, and other groups (other than Aboriginal peoples) who are not Caucasian in race and not white in colour. [132] There exists a large body of research regarding health disparities between Aboriginal populations and the general Canadian population. [132] The OCPL study at the BCCA

uses a study questionnaire, which includes the following six options for self-reported ethnicity: White, East or South-East Asian, South Asian, First Nations, Black, and Other.

1.7.3 Issues with Collection of Ethnicity Data

The validity of ethnicity data is largely dependent on how it is collected. Self-reporting is considered to be the most accurate method of obtaining data on ethnicity. [124] Health care workers and clinicians may hesitate to ask patients about their ethnicity, fearing that such a question may seem discriminatory or offensive. [133,134] Additionally, immigrants may feel uneasy regarding medical and dental visits, particularly when seeing a practitioner of a different ethnic background. [70,135] Communication may be limited, and translators may not readily be available to ease communication between the patient and the clinician. These barriers may create difficulty in obtaining self-reported ethnicity data, and may affect the accuracy of the data that is obtained.

Even in settings where ethnicity data is collected routinely, this data may not be accurate or complete. For example, certain ethnic categories provided as options for patients to self-report their ethnicity might not accurately reflect the ethnicity that an individual may identify with. This can result in a lack of accuracy with the collection of ethnicity data. In a setting where this data is collected, it is also possible that not all patients will choose to report their ethnicity. This results in a lack of complete data, which as a result may not accurately represent the population from which it arises.

Chapter 2: Problem

Data on ethnicity is not routinely collected in Canadian health care institutions. Canada is a diverse country with a significant South Asian population, particularly in BC. South Asian risk habits such as the use of areca nut and betel quid remain prevalent in immigrant populations, posing an increased risk for oral premalignant disorders, oral dysplasia, and oral cancer. While assessing oral cancer trends and access to care within this population is of high importance, very little is known about these trends in the BC population, and few studies have sought to explore differences between South Asians and the general population in Canada, limiting the development of oral cancer prevention programs in this population.

Chapter 3: Objectives

1) To identify differences in oral cancer and dysplasia trends between the South Asian population and the general population, including trends in demographic data, anatomical lesion sites, risk habits and histological presentation.

2) To explore oral biopsy trends and explore access to care within the South Asian population and the general population in British Columbia.

3) To quantify changes in oral biopsy activity between 2007 and 2013 in British Columbia.

Chapter 4: Hypothesis

1) Oral cancer and dysplasia trends in the South Asian population, including demographic data, anatomical lesion sites, risk habits, and histological presentation, will be similar to those in the general population in British Columbia.

2) Biopsy trends and access to care in the South Asian population in British Columbia will be similar to those in the general population.

3) Biopsy activity in British Columbia in 2013 will be similar to that of 2007.

Chapter 5: Materials and Methods

5.1 Data Collection

Data collection for this study included data from the British Columbia Oral Biopsy Service (OBS), the British Columbia Cancer Registry (BCCR), the British Columbia Oral Cancer Prediction Longitudinal study (OCPL), as well as data provided by the College of Dental Surgeons of British Columbia (CDSBC).

5.1.1 The British Columbia Oral Biopsy Service

The British Columbia Oral Biopsy Service (OBS) was founded in 1980 at Shaughnessy Hospital and is currently maintained at Vancouver General Hospital. The OBS provides a centralized pathology review service for the dental community in BC, where biopsy samples are read by an oral pathologist and a diagnosis is provided in the form of a pathology report. Diagnoses range vastly, from amalgam tattoos and mucoceles, to carcinomas and other malignancies. The OBS continues to receive an increasing number of biopsies, currently over 6,000 biopsy reports yearly; these include both primary biopsies and recurrences. The British Columbia Cancer Agency (BCCA) maintains a database of pertinent diagnoses from the OBS including cancers, dysplasias and hyperplasias.

The information included in each pathology report includes demographic information (patient name, sex, date of birth), biopsy date, lesion site, final diagnosis, and ordering dentist (see Appendix A).

5.1.2 The British Columbia Cancer Registry

The British Columbia Cancer Registry (BCCR) was founded in 1969, and has been maintained at the British Columbia Cancer Agency (BCCA) since 1980. [136] It contains demographic information as well as information on diagnosis, treatment, and outcome for all cases of cancer diagnosed in BC residents. The BCCR serves to generate cancer statistics and provide data for cancer control, with the aim of monitoring and reducing the burden of cancer in the province. [136] This data informs the design of outreach programs aimed at reducing morbidity and mortalitty. The BCCR is able to monitor the effectiveness of such programs, and serves as an important source of information for researchers. [136]

The information included in the BCCR database is very detailed, and includes a broad range of demographic, diagnostic, treatment, mortality, and physician information. For the purposes of this thesis, the information requested from the BCCR included demographic and diagnostic data fields.

5.1.3 The British Columbia Oral Cancer Prediction Longitudinal Study

The British Columbia Oral Cancer Prediction Longitudinal Study (OCPL), formerly known as the Oral Health Study (OHS), is a multi-site collaboration involving the British Columbia Cancer Agency (BCCA), the Fraser Valley Cancer Centre (FVCC), Vancouver General Hospital (VGH), the University of British Columbia (UBC) and Simon Fraser University (SFU). The OCPL is an ongoing longitudinal study which aims to monitor progression and recurrence in patients with oral cancers and dysplasias. The study collects demographic, clinical, pathological, and molecular information to improve detection, risk assessment, and management of patients with high-risk lesions. The OCPL has been recruiting cases of oral cancers and dysplasias since 1999, and is currently one of the largest longitudinal studies of its kind worldwide. The OCPL has been supported by grants from the National Institutes of Health as well as the National Institute of Dental and Craniofacial Research.

5.1.4 Dental Practitioner Data

Data for dental practitioners in BC was provided by the College of Dental Surgeons of British Columbia (CDSBC), and includes dental practitioner location (including postal code) and total number of dental practitioners, both general dentists and dental specialists, in BC in 2007 and 2013.

5.2 Study Eligibility

This study examines a sub-group of cases from the OBS who had a biopsy in 2007 or 2013. The eligibility criteria for patients for this study included: 1) aged 18 years or older; 2) a diagnosis of SCC, C*IS*, dysplasia, or hyperplasia in 2007 or 2013; 3) a resident of B.C. at the time of diagnosis. Patients who did not meet the eligibility criteria were excluded from the study.

5.2.1 Inclusion Criteria

Diagnoses included were as follows:

- Squamous cell carcinoma
- Basaloid squamous cell carcinoma
- Papillary squamous cell carcinoma
- Verrucous carcinoma
- Carcinoma *in situ*
- Severe dysplasia
- Moderate dysplasia
- Mild dysplasia
- Verrucous hyperplasia
- Hyperplasia
- Hyperkeratosis (hyperother- and hyperpara-keratosis

5.2.2 Exclusion Criteria

Diagnoses excluded were as follows:

- Actinic cheillitis
- Adenocarcinoma
- Adenosquamous carcinoma
- Adenoid cystic carcinoma
- Apical granuloma
- Atypia
- Atypical lymphoid hyperplasia
- Basal cell carcinoma
- Benign squamous papilloma
- Cemento-ossifying fibroma
- Chronic apical periodontitis
- Chronic hyperplastic candidiasis
- Chronic sialadenitis
- Cyst (odontogenic, radicular, dentigerous, follicular, nasopalatine duct)
- Cystadenoma
- Focal fibrous hyperplasia (fibroepithelial polyp)
- Fragments of necrotic bone

- Giant cell fibroma
- Granulation tissue
- Hyperplastic dental follicle
- Infiltrating duct carcinoma
- Keratocystic odontogenic tumour
- Large cell carcinoma
- Lichen planus
- Lichenoid mucositis
- Malignant salivary gland tumour
- Melanotic macule
- Minor salivary gland tissue
- Mucoepidermoid carcinoma
- Mucus extravasation phenomenon (mucocele)
- Neoplasm
- Nodular basal cell carcinoma
- Non-small cell carcinoma
- Ossifying fibroma
- Papillary adenocarcinoma
- Papillary hyperorthokeratosis (skin graft)
- Pericoronitis
- Polymorphous low grade adenocarcinoma
- Psoriasiform mucositis

- Pyogenic granuloma
- Root tip
- Varicose vein
- Varix
- Verruca vulgaris
- Verruciform xanthoma

Lesion sites excluded were as follows:

- Salivary gland
- Parotid gland
- Pharynx
- Hypopharynx
- Nasopharynx
- Vallecula

5.3 Name Recognition Software

Name recognition software programs are technologies that classify first and last names into different ethnic and linguistic origins. These programs were designed to help understand the composition of ethnic groups in today's increasingly multicultural societies. The quality and availability of ethnicity data in health care is often limited, if at all existent, as is the case in

Canada and within BC. Analyzing names has proven to be an efficient method of determining ethnicity in the absence of ethnicity data. [128] The ability to determine ethnicity can help improve access to care, and explore differences in the etiology, clinical presentation, and risk factors associated with precancerous and cancerous lesions in a given population.

5.3.1 Nam Pehchan

Nam Pehchan, which translates to *name recognition* in Hindi, was developed by the Bradford Health Authority in England. [128] This particular software has been in use for more than twenty-five years, and has been used by numerous studies and validated by many others. [128,137-140] The program matches specific components of a name within an internal name registry for names of South Asian origin, and assigns the name as either 'South Asian' or 'non-South Asian'. [137] The program attaches a four-character, alphanumeric code to each name to indicate the type of match, language, and religion. [137]

The sensitivity of Nam Pehchan has been reported to range from 71% to 96%, with a specificity of 99%. [128,137] The variability of the program's performance may be a result of its internal name registry, as it likely performs better in communities with name origins similar to those used to populate the program's registry. For example, it has been suggested that Nam Pehchan is more effective at identifying names of Pakistani origin compared to those originating in India. [137] Therefore, it may perform better in a population that is associated with origins in Pakistan.

5.3.2 Onolytics

Onolytics, previously known as Onomap, is a software developed in 2009 at University College London in England. Onolytics analyses common patterns of first and last names, using a large database of names from 28 different countries; its classification covers over 500,000 first names and 1 million last names. Onolytics' methodology combines aspects of language, religion, geographical region, and culture to classify names. Individuals are classified into various cultural, ethnic, and linguistic groups based on the probable origins of their names. [127]

The sensitivity of Onolytics is high for South Asian ethnic groups, with less than 5% misclassifications; it has a sensitivity of 82% to 99%, and a specificity of 99.9%. [127,128] It has been used by numerous studies worldwide, in medicine as well as population research and human resources. [141-143]

5.3.3 Other

The South Asian Name and Group Recognition Algorithm, also called SANGRA, is another name recognition software program designed in England in 2001. Validation studies of the program report a sensitivity of 78-96% and specificity of 87-99% in South Asian populations. [144,145] This software program has been used in a few epidemiological studies, all of them in England. [146-148]

Previous studies of South Asian oral cancer cases in BC have used surname lists generated from self-reported ethnicities. [149,150]

5.3.4 Combined Use of Software

This study's approach to ascribing South Asian ethnciity included the combined use of Nam Pehchan and Onolytics, due to a large number of supporting studies for each program, as well as the increased sensitivity and specificity of the programs when used together.

A 2012 study showed that the combined use of Nam Pehchan and Onolytics resulted in a 90.5% sensitivity and 99.9% specificity. [128] Their combined use yielded higher sensitivity than either sofware program alone, suggesting that the best name-based predictions of ethnicity could be achieved through the use of multiple applications. [128]

5.3.5 Validation of Software in BC

While there is a general lack of ethnicity data gathered in Canadian health care institutions, ethnicity data is routinely collected as part of the OCPL. This dataset was used with known ethnicity to run a pilot study of the combined use of Nam Pehchan and Onolytics, in order to assess their accuracy in a BC population.

Nam Pehchan software was obtained from Dr. Ronan Ryan at the University of Birmingham. A limited license for Onolytics software was purchased from Onomap Inc. Nam Pehchan and

Onolytics software programs were applied to a reference dataset from the OCPL which contains ethnicity data self-reported through a study questionnaire (see Appendix C) collected in BC (n=1,128). Results of the name recognition software programs were compared with known ethnicity from the reference dataset. The use of Nam Pehchan alone showed a sensitivity of 94.7% and specificity of 98% in determining ethnicity. The software demonstrated a high negative predictive value (NPV) of 99.6%, and a lower positive predictive value (PPV) of 78%. Onolytics use alone obtained a sensitivity of 93.4% and specificity of 98.7%. The NPV was 99.5%, and PPV of 83.5%. Individual use of each software program showed high levels of sensitivity and specificity, demonstrating accuracy in determining South Asian ethnicity within a B.C. population. The combined use of Nam Pehchan and Onolytics demonstrated a sensitivity of 94.7% and specificity of 99%, which are higher than either software program used alone. The NPV in the combined use of programs was 99.6%, and the NPV was 88.9%, which was also higher than either software used individually. The combined use of software programs marginally increased sensitivity and specificity when compared to the use of either software individually. The PPV in the combined use of the programs was 5% greater than in Onolytics alone, and over 10% greater than in Nam Pehchan alone. Combined use of software programs demonstrates a higher accuracy within this population. Overall, the study demonstrated high accuracy in determining ethnicity by combining the use of Nam Pehchan and Onolytics software within a BC population.

5.4 Details of Data Collection

Cases meeting inclusion citeria were identified in the OBS database and the BCCR database. Name recognition software programs were applied to all names meeting the inclusion criteria. Figures 5.1 and 5.2 illustrate patient selection by diagnoses for this study.

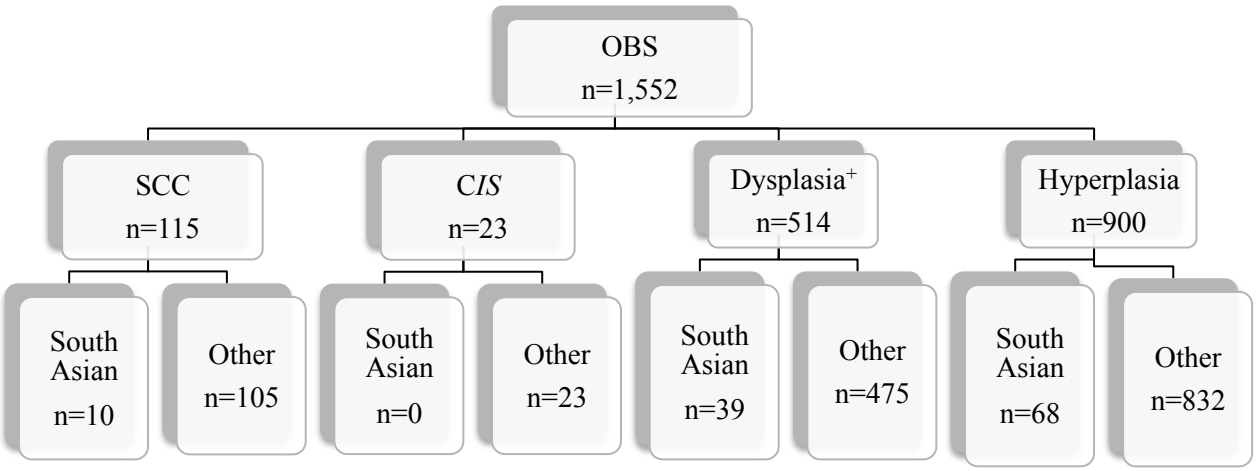

Figure 5.1 2007 and 2013 OBS data collection flowchart
SCC: Squamous cell carcinoma
C*IS*: Carcinoma *in situ*
+ Includes mild, moderate, and severe dysplasia

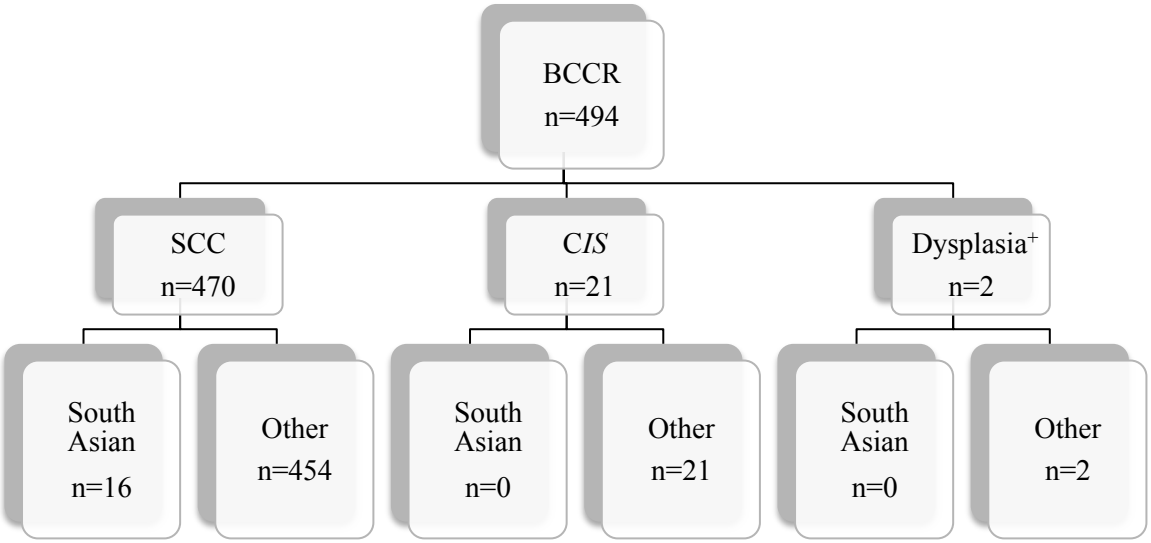

Figure 5.2 2007 and 2013 BCCR data collection flowchart
SCC: Squamous cell carcinoma
C*IS*: Carcinoma *in situ*
[+] Includes severe dysplasia

The OBS biopsy requisition forms contained information such as patient demographics, lifestyle factors and pathological history as well as clinical features of the lesion biopsied.

5.4.1 Demographic Information

Demographic data collected from each patient by the dental practitioner peforming the biopsy includes: name, gender, date of birth, and age.

5.4.2 Diagnoses

Data for diagnoses was grouped into three categories: cancer, dysplasia, and hyperplasia. For the purpose of this thesis, as many severe dysplasias are treated with intent to cure, diagnoses of

severe dysplasia were designated as “cancer” (Table 5.1). Verrucous lesions were noted in a separate, dichotomous category.

Diagnosis	Inclusion
Cancer	Squamous cell carcinoma, carcinoma *in situ*, severe dysplasia
Dysplasia	Moderate dysplasia, mild dysplasia
Hyperplasia	Hyperplasia, hyperkeratosis (hyperortho- and hyperpara-keratosis)

Table 5.1 Diagnosis descriptions

Cases of SCC, C*IS* and severe dysplasia within the OBS databse were identified within the BCCR database to ensure all diagnoses fro the Oral Biopsy Service were present in the Cancer Registry. Cases present in OBS were removed from BCCR database to prevent cases from being represented twice during data analysis. The personal health number (PHN) attached to cases from the OBS that were not identified in the BCCR datase were entered into the Cancer Agency Information System (CAIS) to check their presence within the BCCA database.

5.4.3 Lesion Sites

Data on anatomical lesion sites were grouped by category (Table 5.2). For the purposes of this thesis, the term *buccal mucosa* is inclusive of the buccal, labial, and vestibular mucosa.

Lesion Site	Inclusion
Gingiva	Gingiva, alveolar ridge, edentulous ridge, "tissue from (tooth number)", retromolar area, posterior alveolar ridge, posterior tuberosity, trigone, maxilla, mandible
Buccal mucosa	Buccal, labial, and vestibular mucosa
Floor of Mouth	Floor of mouth
Ventral / Lateral Tongue	Ventral tongue, lateral tongue, ventro-lateral tongue, posterior tongue, right tongue, left tongue, tongue
Dorsal Tongue	Dorsal tongue, tip of tongue
Soft Palate	Soft palate, junction of hard and soft palate, palate, oropharynx, tonsillar area, tonsillar fossa, base of tongue
Hard Palate	Hard palate
Other	Lip, external lip
Unspecified	Site unspecified, oral cavity, mouth

Table 5.2 Lesion site descriptions

5.4.4 Lesion Sites Categorized by Risk

Based on the available literature relating to high-risk sites for oral cancer in Western countries and South Asian countries, data on lesion sites was further categorized into Western risk and South Asian risk (Table 5.3). Western high-risk sites included the ventral and lateral surfaces of the tongue, as well as the floor of the mouth. South Asian high-risk stes included the gingiva and buccal mucosa.

	Western countries	South Asian countries
High Risk	Ventral tongue Lateral tongue Floor of mouth	Gingiva Buccal mucosa[+]
Other	All other sites	All other sites

Table 5.3 Lesion sites by Western and South Asian risk
[+] Includes buccal/labial and vestibular mucosa

5.4.5 Risk Habit Information

While the OBS requitision form (see Appendix B) includes a field for risk factors, many practitioners do not include this information when completing and submitting the requisition forms. Furthermore, while risk habit information is present on some pathology reports, the OBS database maintained by the BCCA does not contain this information.

Cases identified as South Asian were reviewed individually for the presence of risk habit information within the pathology reports.

5.4.6 Clinician Performing Biopsy

The dental practitioner performing each biopsy was identified from the OBS database and associated pathology report.

5.4.7 Biopsy Postal Code

Postal code information of ordering physician/dentist is included on each pathology report in the OBS databse. Access to the Cancer Agency Information System (CAIS) enabled the identification of ordering physicians' postal code information within the BCCA database.

5.5 Statistical Analysis

The statistical software SPSS Version 23 (Armonk, NY: IBM Corp) was used for all statistical analyses. Statistical tests are performed to determine any differences or associations between: 1) South Asian cases and the general population; and 2) demographic, lesion site, and risk habit information. Verrucous lesions were also examined separately.

Categorical data such as ethnicity, age, gender, diagnosis, and lesion site were analyzed using Pearson's chi-squared test. Fisher's Exact Test was used when the sample size was small, or with one or more cells were present with a value of zero. Odds ratio and corresponding 95% confidence intervals were calculated. All tests were two-sided and results deemed statistically significant when $p<0.05$. Multinomial logistic regression was used in cases where ordinal categrical variables could not be statistically analyzed using chi-squared tests, to allow statistical analysis of dependent variables with more than two categories.

5.6 Spatial Analysis

Once data was collected and analyzed, spatial analysis was performed on the data points. ArcGIS software version 10.1 was used for this analysis; ArcGIS is a data viewer for maps and Geographical Information Systems (GIS) data, and also provides base maps and shape-files for querying of spatial data. The first step of this process is to populate data for use in ArcGIS. Data sources included BC Local Health Area (LHA) shape-files and 2006 and 2011 Census Canada data. These were obtained online from BC Government and Census Canada websites through open access agreements. Additionally, postal codes for dentist locations were obtained from the CDSBC.

In order to determine the ethnic concentration in various LHAs, particularly the concentrations of South Asian individuals, the following languages, notes as "mother tongue spoken at home", were extracted from the Census Canada dataset: Bengali, Gujarati, Hindi, Pashto, Punjabi, Sindhi, Singhalese, Tamil, and Urdu. A percentage of South Asian density was then determined for each LHA. While this method may not provide a direct representation of ethnicity in BC, assessment of ethnicity by mother tongue is viewed as an accurate assessment of ethnicity for the purposes of this study.

Percentage totals for each LHA (*.xls) were then linked to the shape-file (*.shp) using ArcGIS. Each LHA has a specific identifying number associated with it, known as the LHAID. Both the percent totals for each LHA in spreadsheet form and the LHA shape-files contain the LHAID, thus determining the association of the linkage. Once the linkage is complete, each LHA in the

shape-file contains new meta-data which includes the percentage of South Asian ethnicity, which can then be colour-coordinated to show variations on a map.

The final step in creating the base map was to add the dentist locations. The format of the spreadsheet for dentist locations contains postal codes for each dentist, which are then spatially linked to the LHA shape-file through a process known as geocoding. Geocoding is the process of using an address locator to convert a physical address, such as a postal code, into latitude and longitude coordinates so that it may be displayed on a map. For this study, the address locator used was designed specifically for BC (Blake Walker, SFU Department of Geography). After this process, each dentist location can now be represented on the map as a point, and each point contains meta-data with the original postal code and any other associated data linked to each postal code.

Looking beyond the base, examining the OBS and BCCR databases spatially involved a simple process of geocoding. Data was formatted in each of the datasets, and the geocoding operation in ArcGIS using the address locator was used. This process produces the spatial locations for both the OBS and the BCCR data as points on the map, which can now be presented in various ways according to the meta-data to supplement statistical analyses of these databases.

Chapter 6: Results

For ease of review, results are presented separately by database. A summary of the frequencies is first presented to give a simple overview of the cases, after which the results are presented for the comparison of ethnicity to other variables, by year. The results are then presented exclusively for South Asian cases, examining the association between different variables, presented by year. In the OBS database, results are also presented for the analyses of risk habit information and verrucous histopathology.

6.1 OBS Database

6.1.1 Frequencies

There were a total of 1,552 cases of oral cancer, dysplasia, and hyperplasia in 2007 and 2013 in the OBS that met this study's inclusion criteria. Table 6.1 outlines the frequency of these cases, both South Asian and the general population, categorized by year and by sex, age at diagnosis, histopathological diagnosis, and lesion site. These will be discussed in greater detail in the sections to follow. There were a total of 117 South Asian cases, with 35 of these cases in 2007 and 82 in 2013. There were generally more males than females, and slightly more cases under the age of sixty years. The most common diagnosis was hyperplasia, followed by mild dysplasia; SCC was generally more common than severe dysplasia, and occurred in similar frequency to moderate dysplasia. The most common lesion sites for both populations included the ventro-

lateral tongue, gingiva, and buccal mucosa, though the frequency of lesions of these sites varied between the South Asian population and the general population.

	All (N=1552)		2007 (n=681)		2013 (n=871)	
	SA (n=117) (%)	Other (n=1435) (%)	SA (n=35) (%)	Other (n=646) (%)	SA (n=82) (%)	Other (n=789) (%)
Sex						
Male	82 (70)	802 (55.9)	22 (62.9)	349 (54)	60 (73.2)	453 (57.4)
Female	35 (30)	633 (44.1)	13 (37.1)	297 (46)	22 (26.8)	336 (42.6)
Age						
< 60 years	71 (60)	736 (51.3)	21 (60)	357 (55.3)	50 (61)	379 (48)
≥ 60 years	46 (40)	699 (48.7)	14 (40)	289 (44.7)	32 (39)	410 (52)
Diagnosis						
SCC	10 (8.5)	105 (7.3)	2 (5.7)	42 (6.5)	8 (9.8)	63 (8)
C*IS*	0	23 (1.6)	0	11 (1.7)	0	12 (1.5)
D3	5 (4.2)	41 (2.9)	2 (5.7)	23 (3.6)	3 (3.7)	18 (2.3)
D2	8 (6.8)	131 (9.1)	2 (5.7)	68 (10.5)	6 (7.3)	63 (8)
D1	26 (22)	303 (21.1)	9 (25.7)	155 (24)	17 (20.7)	148 (18.7)
Hyperplasia	68 (58.5)	832 (58)	20 (57.2)	347 (53.7)	48 (58.5)	485 (61.5)
Lesion Site						
Gingiva	38 (32.5)	446 (31.1)	12 (34.3)	197 (30.5)	26 (31.7)	249 (31.6)
Buccal mucosa[+]	38 (32.5)	275 (19.2)	12 (34.3)	134 (20.7)	26 (31.7)	141 (17.9)
FOM	2 (1.7)	83 (5.8)	1 (2.9)	42 (6.5)	1 (1.2)	41 (5.2)
VL Tongue	29 (24.8)	397 (27.7)	8 (22.7)	171 (26.5)	21 (25.6)	226 (28.6)
D Tongue	4 (3.4)	30 (2.1)	1 (2.9)	9 (1.4)	3 (3.7)	21 (2.7)
Soft Palate	6 (5.1)	90 (6.3)	1 (2.9)	49 (7.6)	5 (6.1)	41 (5.2)
Hard Palate	0	75 (5.1)	0	27 (4.2)	0	48 (6.1)
Other	0	28 (2)	0	11 (1.7)	0	17 (2.2)
Not Spec.	0	11 (0.7)	0	6 (0.9)	0	5 (0.5)

Table 6.1 OBS frequencies summary
SA: South Asian
SCC: Squamous cell carcinoma
C*IS*: Carcinoma *in situ*
D3: Severe dysplasia
D2: Moderate dysplasia
D1: Mild dysplasia
FOM: Floor of mouth
VL Tongue: Ventro-lateral tongue
D Tongue: Dorsal tongue
Other: Lip, external lip
Not spec.: Not specified
[+] Includes buccal/labial and vestibular mucosa

The mean age at diagnosis in OBS in 2007 and 2013 was 58.4 years, with a standard deviation of 13.8 (Figure 6.1). In the general population, the mean was 58.7 years with a standard deviation of 13.9 (Figure 6.2) while the mean age of South Asian cases was 54.5 years with a standard deviation of 14.2 (Figure 6.3).

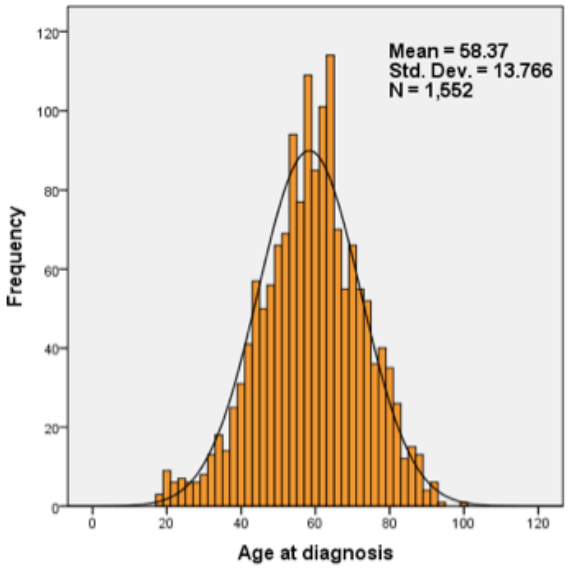

Figure 6.1 OBS mean age

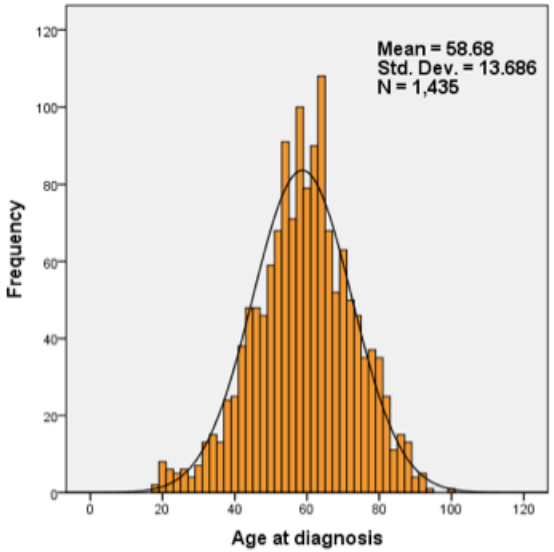

Figure 6.2 OBS mean age: general population

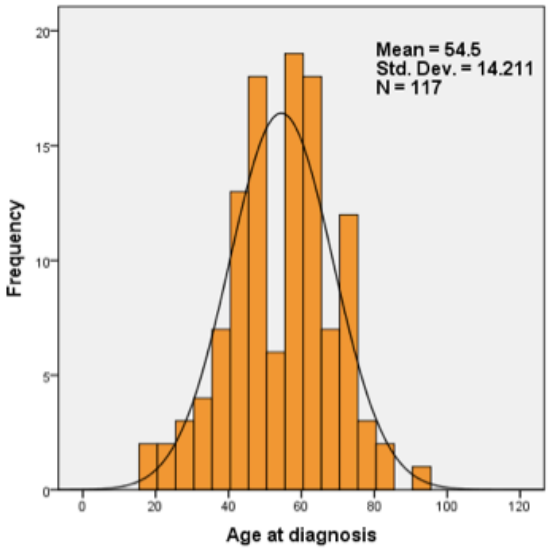

Figure 6.3 OBS mean age: South Asian population

6.1.2 Ethnicity

6.1.2.1 Ethnicity and Demographics

First, demographic data including sex and age at diagnosis were compared between South Asian cases and the general population for each year, and for both years together. Figures that describe this data can be found in Table 6.1.

6.1.2.1.1 Ethnicity and Sex

Gender distribution in the database varied by ethnicity; the distribution of these independent variables was examined. In 2007, the proportion of male and female cases was 54% and 46% respectively in the general population. In South Asian cases, 63% of cases were male, and 37% were female (Figure 6.4). This distribution indicates that a greater proportion of South Asian cases were male than in the general population. The inverse is true of females: there was a smaller proportion female cases in the South Asian population, compared to the general population.

Data from the OBS in 2013 also indicates gender differences between South Asians and the general population. The proportion of male and female cases was 59% and 41% respectively in the general population. Of South Asian cases, 73% were male, and 27% were female (Figure 6.5). A greater proprtion of cases were male in the South Asian population than in the general population.

When examining all cases in 2007 and 2013 (Figure 6.6), the South Asian popuation shows a greater variation in the proportion of male to female cases than in the general population. While the proportion of male to female cases was 57% and 43% respectively in the general population, over 70% of South Asian cases were male, with only 30% of cases female. This indicates an overall ratio of 2.3:1 males to females in the South Asian population, while this ratio in the general population was 1.3

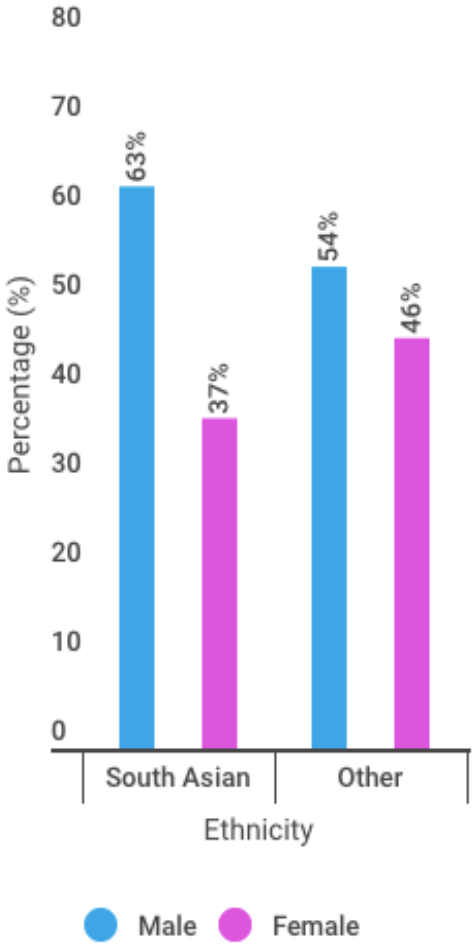

Figure 6.4 OBS 2007 ethnicity and sex

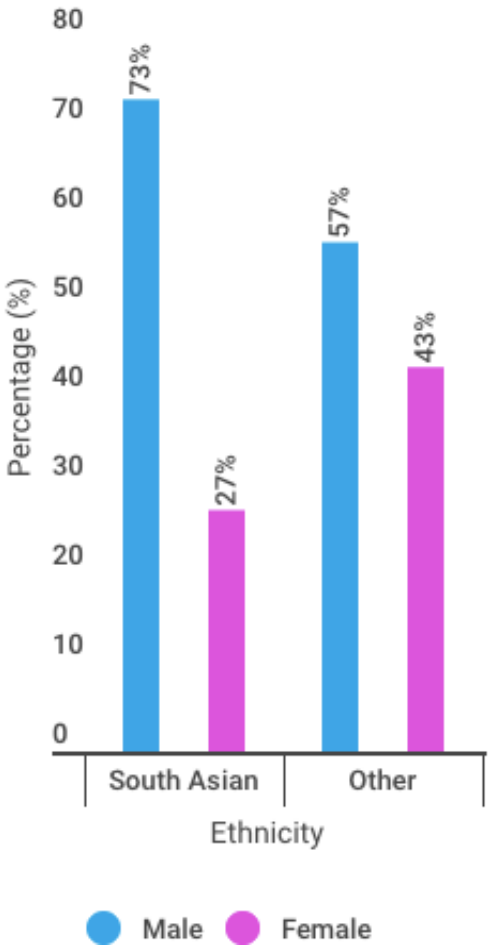

Figure 6.5 OBS 2013 ethnicity and sex

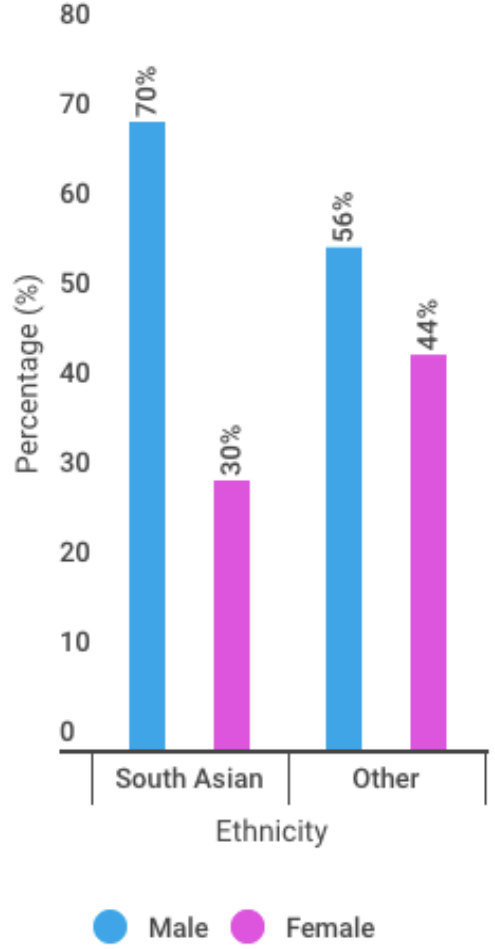

Figure 6.6 OBS 2007 & 2013 ethnicity and sex

6.1.2.1.2 Ethnicity and Age at Diagnosis

Age at diagnosis varied by ethnicity; the distribution of these independent variables was examined. In 2007, the proportion of cases below the age of sixty years, and sixty years and above was 55% and 45% respectively in the general poulation. However, in South Asian cases, 60% of cases were below the age of sixty years, while 40% were sixty years and above (Figure 6.7). There was a greater proportion of younger cases in the South Asian population than in the general population.

Similar trends were evident in the distribution of age at diagnosis in 2013. The proportion of cases below the age of sixty years, and sixty years and above was 48% and 52% respectively in the general population. Of South Asian cases, 61% were below the age of sixty years, while 39% were sixty years and above (Figure 6.8). This indicates that South Asian cases in this population were younger than in the general population.

Overall, age at diagnosis varied between the South Asian population and the general population. When considering all cases in 2007 and 2013 (Figure 6.9), while the proportion of cases below the age of sixty years and those sixty years and above was 51% and 49% respectively in the general population, over 60% of South Asian cases were below the age of sixty years, with only 40% of cases sixty years and above. This indicates that a greater proportion of cases occurred at a younger age in this South Asian population.

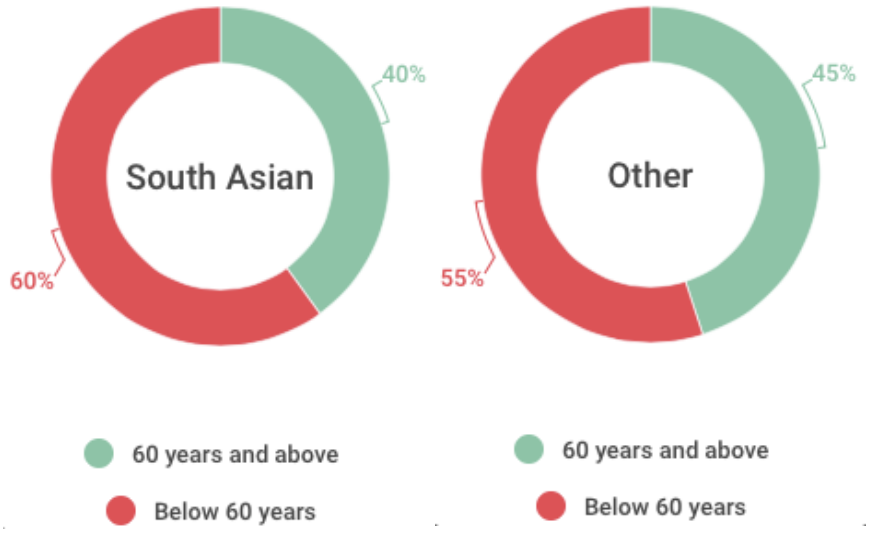

Figure 6.7 OBS 2007 ethnicity and age at diagnosis

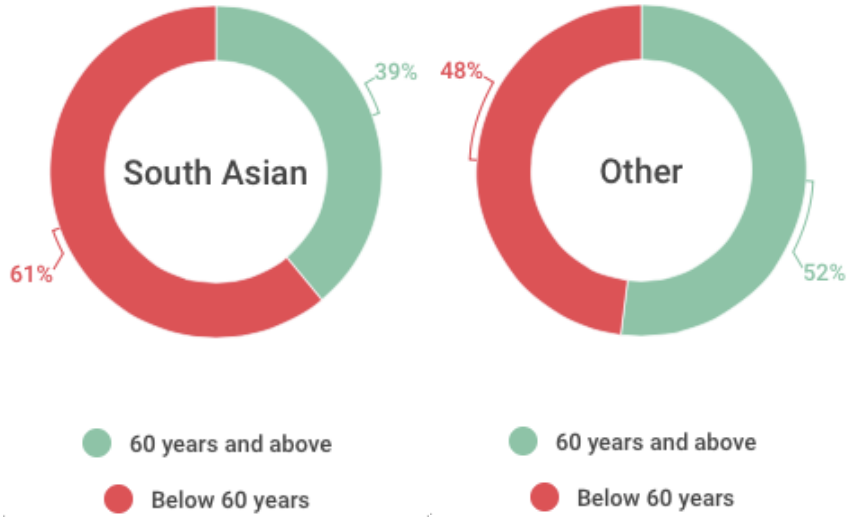

Figure 6.8 OBS 2013 ethnicity and age at diagnosis

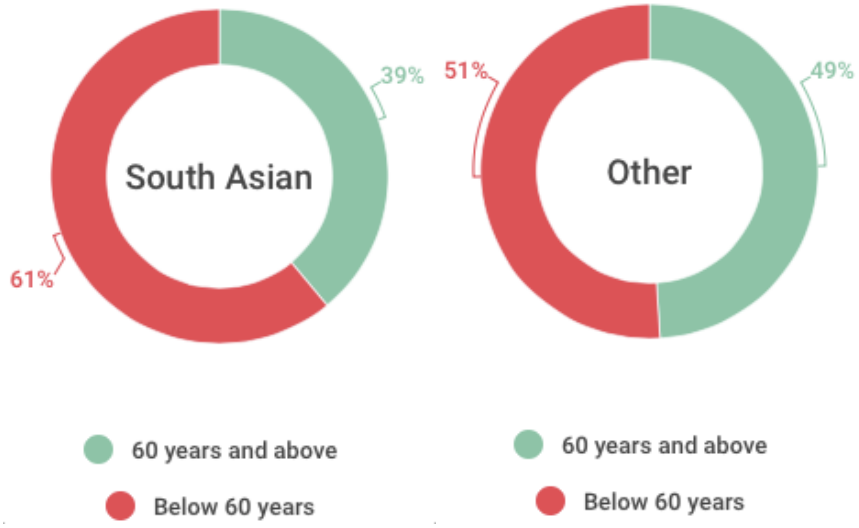

Figure 6.9 OBS 2007 & 2013 ethnicity and age at diagnosis

6.1.2.2 Ethnicity and Histopathological Diagnosis

Trends in histopathological diagnosis did not differ significantly between South Asian cases and the general population (Table 6.2). There were no significant differences in diagnoses between South Asian cases and the general population ($p>0.05$), and rates of cancer, dysplasia, and hyperplasia were similar in both populations across both years. Cancer diagnoses included SCC, C*IS*, and severe dysplasia. Data was recategorized to include only SCC and C*IS* in cancer diagnoses, and severe dysplasia categorized with mild and moderate dysplasias; this change had no significant effect on the results.

In 2007, diagnoses in the general population were most commonly hyperplasias (54%), followed by dysplasias (34%) and cancers (12%). Table 6.2 indicates that rates were similar in the South Asian population, with rates of 57%, 32%, and 11% respectively. Findings in 2013 were similar;

the majority of diagnoses in the general population were hyperplasias (61%), followed by dysplasias (27%) and cancers (12%). Table 6.2 shows that rates were similar in the South Asian poulation with rates of 59%, 28%, and 13% respectively. When considering all cases in 2007 and 2013 (Table 6.2), the most common diagnoses in the general population were hyperplasias (58%), followed by dysplasias (30%) and cancers (12%). Rates in the South Asian poulation were similar at 58%, 29%, and 13% respectively. Hyperplastic lesions were more common than dysplastic lesions, and that cancerous lesions were the least frequently diagnosed, at a rate of 12% in the general population and 11-13% in the South Asian population.

	All (%)	SA (%)	Other (%)	*p-value*	OR (95% CI)
2007	n=681	n=35	n=646		
Diagnosis					
Cancer[a]	80 (11.7)	4 (11.4)	76 (11.8)		0.91 (0.3-2.7)
Dysplasia	234 (34.4)	11 (31.4)	223 (34.5)	*0.919**	0.86 (0.4-1.8)
Hyperplasia	367 (53.9)	20 (57.2)	347 (53.7)		1
Diagnosis					
Cancer [b]	55 (8.1)	2 (5.7)	53 (8.2)		0.65 (0.1-2.9)
Dysplasia	259 (38)	13 (37.1)	246 (38.1)	*0.846**	0.92 (0.4-1.9)
Hyperplasia	367 (53.9)	20 (57.2)	347 (53.7)		1
2013	n=871	n=82	n=789		
Diagnosis					
Cancer[a]	104 (11.9)	11 (13.4)	93 (11.8)		1.2 (0.6-2.4)
Dysplasia	234 (26.9)	23 (28.1)	211 (26.7)	*0.854*	1.10 (0.6-1.9)
Hyperplasia	533 (61.2)	48 (58.5)	485 (61.5)		1
Diagnosis					
Cancer[b]	83 (9.5)	8 (9.8)	75 (9.5)		1.08 (0.4-2.3)
Dysplasia	255 (29.3)	26 (31.7)	229 (29)	*0.864*	1.15 (0.7-1.9)
Hyperplasia	533 (61.2)	48 (58.5)	485 (61.5)		1
2007 & 2013	n=1552	n=117	n=1435		
Diagnosis					
Cancer[a]	184 (11.8)	15 (12.8)	169 (11.8)		1.08 (0.6-1.9)
Dysplasia	468 (30.2)	34 (29.1)	434 (30.2)	*0.928*	0.96 (0.6-1.5)
Hyperplasia	900 (58)	68 (58.1)	832 (58)		1
Diagnosis					
Cancer[b]	138 (8.9)	10 (8.6)	128 (8.9)		0.96 (0.5-1.9)
Dysplasia	514 (33.1)	39 (33.3)	475 (33.1)	*0.991*	1.01 (0.6-1.5)
Hyperplasia	900 (58)	68 (58.1)	832 (58)		1

Table 6.2 OBS ethnicity and diagnosis

SA: South Asian

[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia

[b] Includes squamous cell carcinoma and carcinoma *in situ* only

*1 cell (16.7%) had an expected count less than 5; therefore a Fisher's Exact Test was used

6.1.2.3 Ethnicity and Lesion Site

To better understand differences in anatomical lesion sites between South Asian cases and the general population, differences in lesion sites between South Asian cases and the general population were examined (Tables 6.3).

South Asian cases were more likely to occur at sites considered high-risk in South Asian countries, compared to cases in the general population. In 2007, 51% of lesions in the general population occured at South Asian high-risk sites, including the gingiva and buccal mucosa, while 69% of South Asian cases occurred at these sites, showing a statistically significant difference (p=0.046) between these groups. Sites considered to be high-risk in Western countries, including the ventral and lateral surfaces of the tongue and the floor of the mouth, only saw about 33% of lesions in the general population, and 26% of lesions in the South Asian population. Similar findings were evident in 2013, with 49% of lesions in the general population occuring at South Asian high-risk sites, while 63% of South Asian cases occurred at these sites, again showing a statistically significant difference (p=0.016); these rates were slightly lower than those in 2007. Only 33% of lesions in the general population, and 27% of lesions in the South Asian population, occurred at sites considered high-risk in the West.

When considering all cases in 2007 and 2013, 50% of lesions in the general population occured at South Asian high-risk sites, while 65% of South Asian cases occurred at these sites, showing a statistically significant difference (p=0.002) between these populations. Only 33% of lesions in the general population occurred at sites considered high-risk in Western countries, and 27% of

lesions in the South Asian population. Ethnicity did not appear to have an impact on Western high-risk lesion sites; both the South Asian population and the general population have similar risk of having a lesion at Western high-risk sites. However, South Asian high-risk sites were found to vary between ethnic groups. South Asian patients are 1.84 times more likely to have lesions at sites that are considered high-risk in South Asian countries. While fewer cases in the general population occurred at these sites, these still accounted for over 50% of lesions in the general population, compared to only 32.9% at Western high-risk sites.

	All (%)	SA (%)	Other (%)	*p-value*	OR (95% CI)
2007	n=681	n=35	n=646		
Lesion Site					
Western HR[a]	222 (32.6)	9 (25.7)	213 (33)	*0.372*	0.70 (0.3-1.5)
Western Other	459 (67.4)	26 (74.3)	433 (67)		1
SA Risk					
SA HR[b]	355 (52.1)	24 (68.6)	331 (51.2)	***0.046***	2.08 (1.1-4.3)
SA Other	326 (47.9)	11 (31.4)	315 (48.8)		1
2013	n=871	n=82	n=789		
Western Risk					
Western HR[a]	289 (33.2)	22 (26.8)	267 (33.8)	*0.199*	0.72 (0.4-1.2)
Western Other	582 (66.8)	60 (73.2)	522 (66.2)		1
SA Risk					
SA HR[b]	442 (50.7)	52 (63.4)	390 (49.4)	***0.016***	1.77 (1.1-2.8)
SA Other	429 (49.3)	30 (36.6)	399 (50.6)		1
2007 & 2013	n=1552	n=117	n=1435		
Western Risk					
Western HR[a]	511 (32.9)	31 (26.5)	480 (33.4)	*0.124*	0.72 (0.5-1.1)
Western Other	1041 (67.1)	86 (73.5)	955 (66.6)		1
SA Risk					
SA HR[b]	797 (51.4)	76 (65)	721 (50.2)	***0.002***	1.84 (1.2-2.7)
SA Other	755 (48.6)	41 (35)	714 (49.8)		1

Table 6.3 OBS ethnicity and lesion site
HR: High risk
SA: South Asian
[a] Includes ventro-lateral tongue and floor of the mouth
[b] Includes gingiva, buccal/labial and vestibular mucosa

6.1.3 South Asian Cases

The following sections examine South Asian cases exclusively.

6.1.3.1 Age at Diagnosis and Histopathological Diagnosis

There were no significant differences between age at diagosis and histopathological diagnosis, in any year (Table 6.4). This indicates that age at diagnosis was not related to the cancer, dysplasia, or hyperplasia diagnoses in the South Asian population.

In 2007, there was a greater proportion of hyperplasias in South Asian cases below the age of sixty years (67%) than in cases sixty years and above (43%). The rate of dysplasia was also higher in younger cases, with more than twice the rate of those in older cases. There were no diagnoses of SCC or C*IS* in cases sixty years of age and above, while two cases of cancer were diagnosed in patients under the age of sixty. It should be noted that the counts are small, and hence the statistical analysis lacks power.

Rates of of hyperplasia were similar in both age groups in 2013, at 58% in those aged below the age of sixty, and 59% in those sixty years and above. Rates of dysplasia were also similar in both age groups. There was a slightly higher rate of cancer in those ages sixty years and above. It should be noted that the counts are small, and hence the statistical analysis lacks power.

When considering all South Asian cases in 2007 and 2013, there was a higher rate of dysplasia in those below sixty years of age (61%), compared to those aged sixty and above (54%). There were slightly higher rates of dysplasia and cancer in those aged sixty and over, at 37% and 15% respectively, compared to 31% and 8% in those below the age of sixty, although these findings were not statistically significant.

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007	n=21	n=14		
Diagnosis				
Cancer[a]	3 (14.3)	1 (7.1)	*0.152**	1.29 (0.1-15.0)
Dysplasia	4 (19)	7 (50)		0.24 (0.1-1.2)
Hyperplasia	14 (66.7)	6 (42.9)		1
Diagnosis				
Cancer[b]	2 (9.5)	0 (0)	*0.079*$^{+}$	N/A
Dyslasia	5 (23.8)	8 (57.1)		0.27 (0.1-1.2)
Hyperplasia	14 (66.7)	6 (42.9)		1
2013	n=50	n=32		
Diagnosis				
Cancer[a]	5 (10)	6 (18.8)	*0.400*	0.55 (0.1-2.0)
Dysplasia	16 (32)	7 (21.9)		1.49 (0.5-4.3)
Hyperplasia	29 (58)	19 (59.4)		1
Diagnosis				
Cancer[b]	4 (8)	4 (12.5)	*0.732*	0.66 (0.1-2.9)
Dyslasia	17 (34)	9 (28.1)		1.24 (0.5-3.3)
Hyperplasia	29 (58)	19 (59.4)		1
2007 & 2013	n=71	n=46		
Diagnosis				
Cancer[a]	8 (11.3)	7 (15.2)	*0.750*	0.66 (0.2-2.1)
Dysplasia	20 (28.2)	14 (30.4)		0.83 (0.4-1.9)
Hyperplasia	43 (60.6)	25 (54.3)		1

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007 & 2013	n=71	n=46		
Diagnosis[+]				
Cancer[b]	6 (8.5)	4 (8.7)	*0.784*	0.87 (0.2-3.4)
Dyslasia	22 (31)	17 (37)		0.75 (0.3-1.7)
Hyperplasia	43 (60.6)	25 (54.3)		1

Table 6.4 OBS age at diagnosis and histopathological diagnosis (South Asian cases)
[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia
[b] Includes squamous cell carcinoma and carcinoma *in situ* only
*3 cells (50%) have expected count less than 5; therefore a Fisher's Exact Test was used
[+] 2 cells (33.3%) have expected count less than 5; therefore a Fisher's Exact Test was used
N/A: The OR could not be produced as one of the cells was a zero

6.1.3.2 Age at Diagnosis and Lesion Site

There was no significant difference between age at diagnosis and lesion site in the South Asian population (Table 6.5). There were few cases at Western high-risk sites in 2007; the majority of cases presented at South Asian high-risk sites for both age groups. There were 71% of cases below the age of sixty years, and 64% of cases aged sixty years and above, presented at South Asian high-risk sites.

Data from 2013 showed similar trends, with few cases occuring at Western high-risk sites: 24% in ages below sixty years, and 31% in sixty years of age and above. The majority of cases presented at South Asian high-risk sites for both age groups, with 66% of cases below the age of 60 and 59% of cases aged sixty years and above.

There were generally few cases at Western high-risk sites in the OBS in both 2007 and 2013: 24% of cases occurred at these sites in patients under sixty years of age, and 30% in patients sixty years of age and above. The majority of cases presented with lesions at South Asian high-risk sites for both age groups, with 68% of cases below the age of sixty and 61% of cases aged sixty years and above occuring at these sites. Although these findings were not statistically significant, South Asian cases were more likely to occur at sites considered high-risk in South Asian countries, and were less likely to occur at sites considered high-risk in Western countries.

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007	n=21	n=14		
Western Risk				
Western HR[a]	5 (23.8)	4 (28.6)	*0.752**	0.78 (0.2-3.6)
Western Other	16 (76.2)	10 (71.4)		1
SA Risk				
SA HR[b]	15 (71.4)	9 (64.3)	*0.656**	1.39 (0.3-5.9)
SA Other	6 (28.6)	5 (35.7)		1
2013	n=50	n=32		
Western Risk				
Western HR[a]	12 (24)	10 (31.3)	*0.470*	0.69 (0.3-1.9)
Western Other	38 (76)	22 (68.8)		1
SA Risk				
SA HR[b]	33 (66)	19 (59.4)	*0.543*	1.33 (0.5-3.3)
SA Other	17 (34)	13 (40.6)		1
2007 & 2013	n=71	n=46		
Western Risk				
Western HR[a]	17 (23.9)	14 (30.4)	*0.437*	0.72 (0.3-1.7)
Western Other	54 (76.1)	32 (69.6)		1

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007 & 2013	n=71	n=46		
SA Risk				
SA HR[b]	48 (67.6)	28 (60.9)	*0.456*	1.34 (0.6-2.9)
SA Other	23 (32.4)	18 (39.1)		1

Table 6.5 OBS age at diagnosis and lesion site (South Asian cases)
HR: High risk
SA: South Asian
[a] Includes ventro-lateral tongue and floor of the mouth
[b] Includes gingiva, buccal/labial and vestibular mucosa
*1 cell (25%) had an expected count less than 5; therefore a Fisher's Exact Test was used

6.1.3.3 Sex and Histopathological Diagnosis

Sex and histopathological diagnosis were examined for each year, and for both years together (Tables 6.6). There was no significant difference between males and females in terms of diagnosis, indicating that although the majority of South Asian cases are male, the rates of cancer, dysplasia, and hyperplasia are similar in both males and females.

Although these findings were not statistically significant, data from 2007 shows that a slightly greater proportion of cancers were female (15%) compared to male (9%). Similarly, in 2013, a slightly greater proportion of SCC and C*IS* diagnoses were female (14%) compared to male (8%). Overall, the proportion of cancers and dysplasias was slightly higher in South Asian females than in males, while hyerplasias were slightly more common in males than females.

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007	n=22	n=13		
Diagnosis				
Cancer[a]	2 (9.1)	2 (15.4)		0.67 (0.1-5.7)
Dysplasia	8 (36.4)	3 (23.1)	*0.666**	1.78 (0.4-8.8)
Hyperplasia	12 (54.5)	8 (61.5)		1
Diagnosis				
Cancer[b]	1 (4.5)	1 (7.7)		0.67 (0.1-12.3)
Dysplasia	9 (40.9)	4 (30.8)	*0.803**	1.5 (0.3-6.6)
Hyperplasia	12 (54.5)	8 (61.5)		1
2013	n=60	n=22		
Diagnosis				
Cancer[a]	8 (13.3)	3 (13.6)		0.79 (0.2-3.5)
Dysplasia	15 (25)	8 (36.4)	*0.572*	0.56 (0.2-1.7)
Hyperplasia	37 (61.7)	11 (50)		1
Diagnosis				
Cancer[b]	5 (8.3)	3 (13.6)		0.49 (0.1-2.4)
Dysplasia	18 (30)	8 (36.4)	*0.593*	0.67 (0.2-1.9)
Hyperplasia	37 (61.7)	11 (50)		1
2007 & 2013	n=82	n=35		
Diagnosis				
Cancer[a]	10 (12.2)	5 (14.3)		0.78 (0.2-2.6)
Dysplasia	23 (28)	11 (31.4)	*0.858*	0.81 (0.3-1.9)
Hyperplasia	49 (59.8)	19 (54.3)		1
Diagnosis				
Cancer[b]	6 (7.3)	4 (11.4)		0.58 (0.1-2.3)
Dysplasia	27 (32.9)	12 (34.3)	*0.732*	0.87 (0.4-2.1)
Hyperplasia	49 (59.8)	19 (54.3)		1

Table 6.6 OBS sex and histopathological diagnosis (South Asian cases)

[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia

[b] Includes squamous cell carcinoma and carcinoma *in situ* only

*3 cells (50%) have expected count less than 5; therefore a Fisher's Exact Test was used

6.1.3.4 Sex and Lesion Site

There was no significant difference between males and females when examining lesion sites. Sex and lesion site were examined for each year, and for both years together (Table 6.7).

In 2007, 54% of South Asian female cases and 77% of male cases presented with lesions at South Asian high-risk sites, including the gingiva and buccal mucosa. More South Asian males (77%) had lesions at these sites than females (54%). Of interest, South Asian women (38.5%) were more prone to have lesions at Western high-risk sites than males (18.2%). Findings were similar in 2013, with 68% of South Asian female cases and 62% of male cases presenting at South Asian high-risk sites. Overall, while not statistically significant, the majority of South Asian cases occurred at South Asian high-risk sites for both males (66%) and females (63%), with few cases occuring at sites considered high-risk in Western countries.

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007	n=22	n=13		
Western Risk				
Western HR[a]	4 (18.2)	5 (38.5)	*0.185**	0.36 (0.1-1.7)
Western Other	18 (81.8)	8 (61.5)		1
SA Risk				
SA HR[b]	17 (77.3)	7 (53.8)	*0.078**	2.91 (0.7-12.8)
SA Other	5 (22.7)	6 (46.2)		1
2013	n=60	n=22		
Western Risk				
Western HR[a]	16 (26.7)	6 (27.3)	*0.956*	0.97 (0.3-2.9)
Western Other	44 (73.3)	16 (72.7)		1
SA Risk				
SA HR[b]	37 (61.7)	15 (68.2)	*0.587*	0.75 (0.3-2.1)
SA Other	23 (38.3)	7 (31.8)		1
2007 & 2013	n=82	n=35		
Western Risk				
Western HR[a]	20 (24.4)	11 (31.4)	*0.430*	0.70 (0.3-1.7)
Western Other	62 (75.6)	24 (68.6)		1

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007 & 2013	n=82	n=35		
SA Risk				
SA HR[b]	54 (65.9)	22 (62.9)	*0.756*	1.14 (0.5-2.6)
SA Other	28 (34.1)	13 (37.1)		1

Table 6.7 OBS sex and lesion site (South Asian cases)
HR: High risk
SA: South Asian
[a] Includes ventro-lateral tongue and floor of the mouth
[b] Includes gingiva, buccal/labial and vestibular mucosa
*1 cell (25%) had an expected count less than 5; therefore a Fisher's Exact Test was used

6.1.3.5 Histopathological Diagnosis and Lesion Site

Histopathological diagnosis and lesion site were examined for each year, and for both years together (Table 6.8). There was a statistically significant difference between lesion sites and histopathological diagnosis within the South Asian population in the OBS. South Asian high-risk sites were more likely to present with hyperplastic lesions, whereas other sites, including ventral and lateral surfaces of the tongue, were more likely to present with dysplasias and cancerous lesions (p=0.006). When looking at cases in both 2007 and 2013, only 6.6% of lesions in the South Asian population that occurred at the gingiva and buccal mucosa were cancerous, while 24.4% of lesions at other sites were cancerous. Of 15 cancer cases, only five (33.3%) occurred at gingiva and buccal mucosa, and ten (66.7%) occurred at other sites, including ventral and lateral tongue. This indicates that the majority of cancer cases in the South Asian population occur at sites other than those considered high-risk in the South Asian poulation. On the other hand, 71% of dysplasias and hyperplasias occurred at South Asian high-risk sites, while only

29% occurred at other sites. While these results are considered statistically significant, it is important to take note of the low counts, and the lack of power in this analysis.

	Western HR[c] (%)	Western Other (%)	*p-value*	OR (95% CI)	SA HR[d] (%)	SA Other (%)	*p-value*	OR (95% CI)
2007	n=9	n=26			n=24	n=11		
Diagnosis								
Cancer[a]	3 (33.3)	1 (3.8)		17 (1.3-223)	1 (4.2)	3 (27.3)		0.11 (0.1-1.3)
Dysplasia	3 (33.3)	8 (30.8)	***0.043***	2.1 (0.3-12.9)	8 (33.3)	3 (27.3)	*0.136*	0.89 (0.2-4.7)
Hyperplasia	3 (33.3)	17 (65.4)		1	15 (62.5)	5 (45.5)		1
Diagnosis								
Cancer[b]	1 (11.1)	1 (3.8)		5.7 (0.3-117)	1 (4.2)	1 (9.1)		0.33 (0.1-6.4)
Dysplasia	5 (55.6)	8 (30.8)	*0.232*	3.5 (0.7-18.6)	8 (33.3)	5 (45.5)	*0.606*	0.53 (0.1-2.4)
Hyperplasia	3 (33.3)	17 (65.4)		1	15 (62.5)	5 (45.5)		1
2013	n=22	n=60			n=52	n=30		
Diagnosis								
Cancer[a]	5 (22.7)	6 (10)		4.17 (1.1-17)	4 (7.7)	7 (23.3)		0.19 (0.1-0.8)
Dysplasia	9 (40.9)	14 (23.3)	***0.044***	3.21 (1.0-9.9)	12 (23.1)	11 (36.7)	***0.024***	0.36 (0.1-1.1)
Hyperplasia	8 (36.4)	40 (66.7)		1	36 (69.2)	12 (40)		1
Diagnosis								
Cancer[b]	3 (13.6)	5 (8.3)		3.0 (0.6-15.2)	4 (7.7)	4 (13.3)		0.33 (0.1-1.5)
Dysplasia	11 (50)	15 (25)	***0.046***	3.67 (1.2-11)	12 (23.1)	14 (46.7)	***0.034***	0.29 (0.1-0.8)
Hyperplasia	8 (36.4)	40 (66.7)		1	36 (69.2)	12 (40)		1
2007 & 2013	n=31	n=86			n=76	n=41		
Diagnosis								
Cancer[a]	8 (25.8)	7 (8.1)		5.92 (1.8-20)	5 (6.6)	10 (24.4)		0.17 (0.1-0.6)
Dysplasia	12 (38.7)	22 (25.6)	***0.005***	2.8 (1.1-7.3)	20 (26.3)	14 (34.1)	***0.006***	0.48 (0.2-1.1)
Hyperplasia	11 (35.5)	57 (66.3)		1	51 (67.1)	17 (41.5)		1

	Western HR[c] (%)	Western Other (%)	*p-value*	OR (95% CI)	SA HR[d] (%)	SA Other (%)	*p-value*	OR (95% CI)
Diagnosis								
Cancer[b]	4 (12.9)	6 (7)		3.5 (0.8-14.3)	5 (6.6)	5 (12.2)		0.33 (0.1-1.3)
Dysplasia	16 (51.6)	23 (26.7)	***0.012***	3.61 (1.5-8.9)	20 (26.3)	19 (46.3)	***0.027***	0.35 (0.2-0.8)
Hyperplasia	11 (35.5)	57 (66.3)		1	51 (67.1)	17 (41.5)		1

Table 6.8 OBS histopathological diagnosis and lesion site (South Asian cases)
HR: High risk
SA: South Asian
[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia
[b] Includes squamous cell carcinoma and carcinoma *in situ* only
[c] Includes ventro-lateral tongue and floor of the mouth
[d] Includes gingiva, buccal/labial and vestibular mucosa

6.1.4 Risk Habit Data Among South Asian Cases

Pathology reports of South Asian cases were reviewed to identify risk habit information. Risk habit information is a required field of the biopsy requisition forms that dentists and dental specialists utilize when submitting biopsies to the OBS.

6.1.4.1 Frequencies

The presence of risk habit information in pathology reports was limited. Only 28.2% of South Asian pathology reports contained information on risk habits (Table 6.9). Cases where risk habit information was known (n=33) were statisticlly analyzed to examine differences between risk habits and variable ssuch as sex, age at diagnosis, histopathological diagnosis and lesion site. Risk habit data was available for 7 of 35 South Asian cases (20%) in 2007, and 26 of 82 cases (32%) in 2013, which showed a slight incease in the inclusion of risk habit information. It should be noted that the counts are small, and hence the statistical analyses in the sections to follow lack power.

	OBS		
	All (n=117) (%)	2007 (n=35) (%)	2013 (n=82) (%)
Risk Habit			
Never smoking or chewing[+]	11 (9.4)	2 (5.7)	9 (11)
Smoking	6 (5.1)	2 (5.7)	4 (4.9)
Chewing[+]	8 (6.8)	1 (2.9%)	7 (8.5)
Smoking & chewing	0	0	0

	All (%)	2007 (%)	2013 (%)
Former smoking	4 (3.4)	2 (5.7)	2 (2.4)
Former chewing[+]	2 (1.7)	0	2 (2.4)
Former both	2 (1.7)	0	2 (2.4)
No data available	84 (71.8)	28 (80)	56 (68.3)

Table 6.9 OBS risk habit data frequencies summary

[+] Includes areca nut, betel quid with and without tobacco, and smokeless tobacco

6.1.4.2 Sex

Risk habit information was compared between males and females for each year, and for both years together (Table 6.10). Males were more likely to smoke (33.3%) or chew (41.7%), while females were more likely to have either no risk habits (66.7%), or both smoke and chew (11.1%). It should be noted that the sample size was very small, with only nine cases where risk habit was identified for females, resuting a low power and lack of generalizability of results. As a result, odds ratio for risk habit analyses were not calculated.

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007	n=5	n=2		
Risk Habit				
Neither	1 (20)	1 (50)	*0.646*	1
Smoking	3 (60)	1 (50)		3.0 (0.1-107-5)
Chewing[+]	1 (20)	0		N/A
Both	0	0		N/A
2013	n=19	n=7		
Risk Habit				
Neither	4 (21.2)	5 (71.4)	***0.048***	1
Smoking	5 (26.3)	1 (14.2)		6.25 (0.5-77.5)
Chewing[+]	9 (47.4)	0		N/A
Both	1 (5.3)	1 (14.3)		1.25 (0.1-26.9)

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007 & 2013	n=24	n=9		
Risk Habit				
Neither	5 (20.8)	6 (66.7)	***0.034***	1
Smoking	8 (33.3)	2 (22.2)		4.80 (0.7-33.8)
Chewing[+]	10 (41.7)	0		N/A
Both	1 (4.2)	1 (11.1)		1.2 (0.1-24.5)

Table 6.10 OBS sex and risk habit
[+] Includes areca nut, betel quid with and without tobacco, and smokeless tobacco
N/A: The OR could not be produced as one or more of the cells was a zero

6.1.4.3 Age at Diagnosis

Risk habit did not have impact on age at diagnosis. Age at diagnosis and risk habit information was examined for each year, and for both years together (Table 6.11). When examining cases from both 2007 and 2013, most cases with a known chewing habit (80%) were diagnosed under the age of sixty years. Overall, while the majority of cases with known risk habits (63.6%) were under the age of sixty, there was no statistical difference between age at diagnosis and risk habit.

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007	n=5	n=2		
Risk Habit				
Neither	1 (20)	1 (50)	*0.646*	1
Smoking	3 (60)	1 (50)		3.0 (0.1-107.5)
Chewing[+]	1 (20)	0		N/A
Both	0	0		N/A
2013	n=16	n=10		
Risk Habit				
Neither	5 (31.3)	4 (40)	*0.662*	1
Smoking	3 (18.8)	3 (30)		0.80 (0.1-6.3)
Chewing[+]	7 (43.8)	2 (20)		2.80 (0.4-21.7)
Both	1 (6.3)	1 (10)		0.80 (0.1-17.2)

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007 & 2013	n=21	n=12		
Risk Habit				
Neither	6 (28.6)	5 (41.7)	*0.622*	1
Smoking	6 (28.6)	4 (33.3)		1.25 (0.2-7.1)
Chewing[+]	8 (38.1)	2 (16.7)		3.33 (0.5-23.5)
Both	1 (4.8)	1 (8.3)		0.83 (0.1-16.9)

Table 6.11 OBS age at diagnosis and risk habit
[+] Includes areca nut, betel quid with and without tobacco, and smokeless tobacco
N/A: The OR was not calculated as most of the cells were zero

6.1.4.4 Histopathological Diagnosis

Risk habit did not have an impact on histopathological diagnosis. Histopathological diagnosis and risk habit information was examined for each year, and for both years together (Table 6.12). Of South Asian cancer cases with known risk habit information in 2007, both of these cases (100%) were smokers. However in 2013, cancer cases included risk habits such as chewing habits and both smoking and chewing, as well as no risk habits, but no cases linked with a smoking habit alone. Overall, the data could not conclude that risk habits had an impact on histopathological diagnosis.

	Cancer [a] (%)	Dysplasia (%)	Hyperplasia (%)	*p-value*
2007	n=2	n=1	n=4	
Risk Habit				
Neither	0	0	1 (25)	*0.358*
Smoking	2 (100)	0	2 (50)	
Chewing[+]	0	0	1 (25)	
Both	0	1 (100)	0	

	Cancer [a] (%)	Dysplasia (%)	Hyperplasia (%)	*p-value*
2013	n=3	n=12	n=11	
Risk Habit				
Neither	1 (33)	4 (33)	4 (36)	*0.484*
Smoking	0	4 (33)	2 (18)	
Chewing[+]	1 (33)	3 (25)	5 (46)	
Both	1 (33)	1 (8)	0	
2007 & 2013	n=5	n=13	n=15	
Risk Habit				
Neither	1 (20)	5 (38)	5 (33)	*0.673*
Smoking	2 (40)	4 (31)	4 (27)	
Chewing[+]	1 (20)	3 (23)	6 (40)	
Both	1 (20)	1 (8)	0	

Table 6.12 OBS histopathological diagnosis and risk habit
[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia
[b] Includes squamous cell carcinoma and carcinoma *in situ* only
The OR could not be produced as one or more of the cells was a zero

6.1.4.5 Lesion Site

Anatomical lesion sites varied based on known self-reported risk habits (Table 6.13). The number of cases in 2007 and 2013 alone were too small inferential statistics, however when examining data from both 2007 and 2013, there was a statistically significant difference between lesion sites based on risk habit (p=0.021). 100% of cases with current or former chewing habits (n=10) experienced lesions at South Asian high-risk sites, including the gingiva and buccal mucosa. In South Asian patients who smoked, 50% presented with lesions at Western high-risk sites including the ventro-lateral surfaces of the tongue and the floor of the mouth. All patients with chewing habits had lesions at South Asian high-risk sites, compared to patients with no known risk habits who more commonly presented with lesions at Western high-risk sites.

	Western HR[a] (%)	Western Other (%)	*p-value*	OR (95% CI)	SA HR[b] (%)	SA Other (%)	*p-value*	OR (95% CI)
2007	n=3	n=4			n=3	n=4		
Risk Habit								
Neither	1 (33.3)	1 (25)	*0.646*	1	0	2 (50)	*0.233*	N/A
Smoking	2 (66.7)	2 (50)		1.00 (0.1-29.8)	2 (66.7)	2 (50)		N/A
Chewing[+]	0	1 (25)		N/A	1 (33.3)	0		N/A
Both	0	0		N/A	0	0		N/A
2013	n=9	n=17			n=17	n=9		
Risk Habit								
Neither	5 (55.6)	4 (23.5)	*0.062*	1	4 (23.5)	5 (55.6)	*0.062*	1
Smoking	3 (33.3)	3 (17.6)		0.80 (0.1-6.3)	3 (17.6)	3 (33.3)		1.25 (0.2-9.9)
Chewing[+]	0	9 (52.9)		N/A	9 (52.9)	0		N/A
Both	1 (11.1)	1 (5.9)		0.80 (0.1-17.2)	1 (5.9)	1 (11.1)		1.25 (0.1-26.9)
2007 & 2013	n=12	n=21			n=20	n=13		
Risk Habit								
Neither	6 (50)	5 (23.8)	***0.041***	1	4 (20)	7 (53.8)	***0.021***	1
Smoking	5 (41.7)	5 (23.8)		0.83 (0.1-4.6)	5 (25)	5 (38.5)		1.75 (0.3-10.0)
Chewing[+]	0	10 (47.6)		N/A	10 (50)	0		N/A
Both	1 (8.3)	1 (4.8)		0.83 (0.1-16.9)	1 (5)	1 (7.7)		1.75 (0.1-36.3)

Table 6.13 OBS lesion site and risk habit

HR: High risk

SA: South Asian

[+] Includes areca nut, betel quid with and without tobacco, and smokeless tobacco

[a] Includes ventro-lateral tongue and floor of the mouth

[b] Includes gingiva, buccal/labial and vestibular mucosa

N/A: The OR was not calculated as most of the cells were a zero

6.1.5 Verrucous Histopathology and Ethnicity

The rates of verrucous diagnosis did not differ between South Asian cases and the general population. In 2007 and 2013, a total of 90 cases were diagnosed as having a verrucous configuration, representing 6% of the sample (Table 6.14). The prevalence of verrucous lesions in the general population was 5.9%, with a similar rate of 7% in the South Asian population. Demographic, histological, and risk habit information was reviewed for each of the eight cases. Due to a lack of data on risk habit information, it was not possible to identify trends or associations between risk habits such as betel quid use and lesions of verrucous configuration.

	All (n=1552) (%)	SA (n=117) (%)	Other (n=1435) (%)	*p-value*	OR (95% CI)
Histology					
Verrucous	92 (6)	8 (7)	84 (5.9)	*0.744*	1.18 (0.6-2.5)
Other	1458 (94)	109 (93)	1349 (94.1)		1

Table 6.14 Ethnicity and verrucous configuration

6.1.5.1 Verrucous Configuration in South Asian cases

A review of the histology of South Asian cases presenting with lesions of verrucous configuration was assessed along with sex, age, risk habit, and lesion site (Table 6.15). There were three cases in 2007, and five in 2013. All cases but one presented on gingiva and buccal mucosa, while the remaining case presented on the dorsal tongue. The small number of cases, as well as lack of information on risk habits, prevented further analysis of South Asian cases with verrucous diagnoses.

2007				
Sex	Age	Risk Habit	Lesion Site	Histology
M	55	N/A	Maxilla	Mild dysplasia, verruciform config.
F	67	N/A	Gingiva	Marked hyperkeratosis, slight verruciform surface
M	56	N/A	Buccal mucosa	Verruciform configuration
2013				
Sex	Age	Risk Habit	Lesion Site	Histology
F	84	N/A	Buccal mucosa	Verrucous carcinoma
M	61	N/A	Buccal mucosa	Verrucous carcinoma
M	34	N/A	Dorsal tongue	Verrucous hyperplasia
F	77	Never	Gingiva	Hyperorthokeratosis, verruciform conf.
M	50	N/A	Gingiva	Marked hyperorthokeratosis, focal verruciform conf.

Table 6.15 Histopathology of South Asian cases with verrucous configuration
M: Male
F: Female
N/A: Risk habit data not available

6.1.6 OCPL cases in the OBS database

When comparing cases in the OCPL to those in the OBS database, only a small proportion of OBS cases were recruited to the OCPL study (Table 6.20). In 2007, 60% of cancers (n=49) and 36% of dysplasias (n=85) were recruited to the OCPL, while those numbers decreased in 2013 to 11.5% of cancers (n=12) and 24% of dysplasias (n=24).

Similarly, only a small proportion of South Asian cases in the OBS were recruited to the OCPL study (Table 6.16). In 2007, 100% of South Asian cancer cases (n=4) and 65% of dysplasias (n=2) were recruited to the OCPL. The proportion of South Asian cancer cases recuited in 2013 decreased to 27% (n=3), and the proption of dysplasia cases recruited increased slightly to and 8.6% (n=6) (Table 6.17). It is of importance to note than not all patients diagnosed with cancers and dysplasias meet recruitement criteria.

	2007		2013	
	Cases	OCPL cases (%)	Cases	OCPL cases (%)
Total	315	134 (42.5)	338	69 (20)
Cancer[a]	81	49 (60)	104	12 (11.5)
Dysplasia	234	85 (36)	234	57 (24)

Table 6.16 OCPL cases

[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia

	2007		2013	
	Cases	OCPL cases (%)	Cases	OCPL cases (%)
Total	35	6 (17)	81	9 (11)
Cancer[a]	4	4 (100)	11	3 (27)
Dysplasia	31	2 (6.5)	70	6 (8.6)

Table 6.17 OCPL South Asian cases

[a] Includes squamous cell carcinoma, carcinoma *in situ*, and severe dysplasia

6.1.7 Dental Network Capacity in OBS

In order to assess the capacity of the dental network, the total number of biopsies from the OBS were obtained, as well as the number of dental profesionals performing biopsies (Table 6.18). This was compared against the total number of dental professionals in the province to determine the proportion of dentists that are performing biopsies.

Using Census data, the population in BC grew from approximately 4.1 million to 4.4 million from 2006 to 2011, an increase of 6.9%. [151] It is estimated from these figures that the population in BC between 2007 and 2013 grew to a similar extent. In 2007, there were 2,919 dentists and dental specialists in BC, giving the province a ratio of 1:1,409 dental practitioner to population. In 2013, there were 3,156 dentists and dental specialists with a ratio of 1:1,394, which remains similar to the ratio in 2007.

	2007	2013
BC population*	4,113,487	4,400,057
Total biopsies	4,484	6,114
Total dental professionals+ in B.C.	2,919	3,156
Dental professionals performing biopsies	138 (4.7%)	206 (6.5%)

Table 6.18 OBS dental network capacity
* Based on data from 2006 and 2011 Canadian Census [151]
+Dentists and dental specialists

The five LHAs with the greatest number of dentists include Vancouver city centre, Burnaby, Surrey, Richmond, and Coquitlam. Population totals, including South Asians, in these cities are outlined in Table 6.19.

The greatest number of dentists were found in Vancouver city centre, which includes downtown Vancouver and the broadway corridor. This area contains only 2.3% of the BC general population, and 0.7% of BC's South Asian population. In contrast, Surrey also has a large number of dentists, but contains 7.5% of BC's general population, as well as 29% of BC's South Asian population.

	Proportion of BC General Population	Proportion of BC South Asian Population	Proportion of BC Dential Practitioners
Vancouver	2.3%	0.7%	10.6%
Burnaby	4.5%	4.5%	8.3%
Surrey	7.5%	29.0%	8.0%
Richmond	3.9%	3.7%	6.6%
Coquitlam	4.4%	2.1%	6.6%

Table 6.19 BC local health areas with the most dental practitioners

6.1.7.1 Biopsy Activity

The biopsy activity of dental professionals in BC was analyzed (Table 6.18). The total number of biopsies, and dental practitioners performing biopsies, increased in the OBS from 2007 to 2013. In 2007, there were a total of 4,484 biopsies received through the OBS. There were a total of 2,919 dentists and dental specialists in the province, and 138 (4.7%) of these performed biopsies that were diagnosed as hyperplasias, dysplasias, or oral cancers through the OBS.

In 2013, there were 6,114 biopsies received through the OBS, an increase of 36% from 2007. There were a total of 3,156 dentists and dental specialists, 206 (6.5%) of which performed biopsies that were diagnosed as hyperplasias, dysplasias, or oral cancers through the OBS. While the number of dental practitioners performing biopsies represents only a small proportion of the total number of practitioners, there was a 48% increase in the number of dental practitioners who performed oral biopsies from 2007 to 2013. Considering population growth (approximately 6.9%) and growth within the profession (approximately 8%), this increase is a meaningful finding.

6.1.7.2 Spatial Analysis

An analysis of where the biopsies were performed was completed using GIS. The maps of the spatial analysis are presented on a base-map of South Asian population density. Surrey has the highest South Asian population (30%), followed by Abbotsford (19%), Delta (14%), South Vancouver (14%), and South Okanagan (6%). Overall, the majority of biopsies were clustered in

cities, where dental practitioners tend to be located. Point-density analysis was used to determine that Vancouver, Kelowna, and Prince George were the cities with the highest density of biopsies in the province.

In 2007 in the OBS database, the spatial analysis shows that while there are few biopsies coming from Northern parts of BC, there appear to be several dental practitioners in these areas (Figure 6.10).

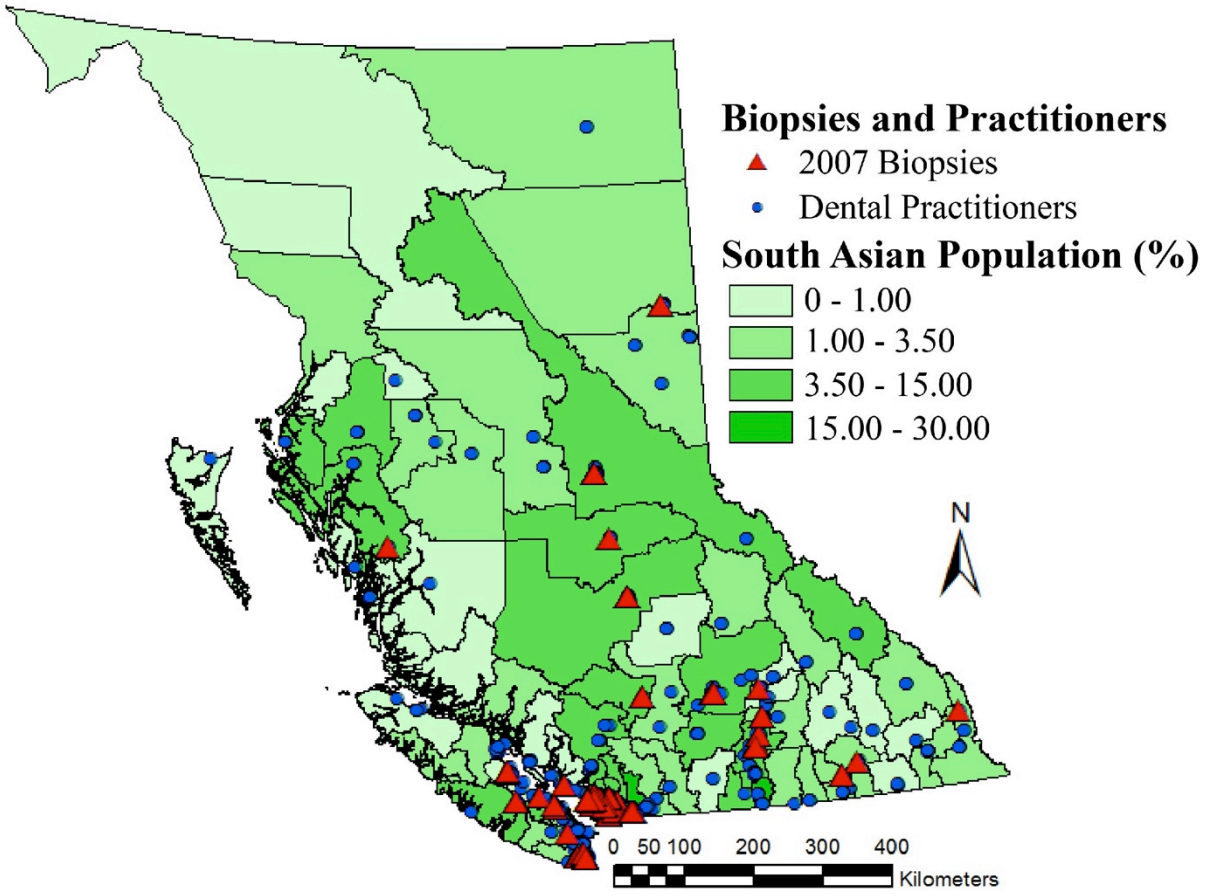

Figure 6.10 Map of OBS biopsies and dental practitioners in 2007

When examining the South Asian cases from the OBS database in 2007, findings show that biopsies come mostly from Greater Vancouver, with two biopsies in Victoria, and one biopsy each in Abbotsford, Williams Lake, and Prince George (Figure 6.11).

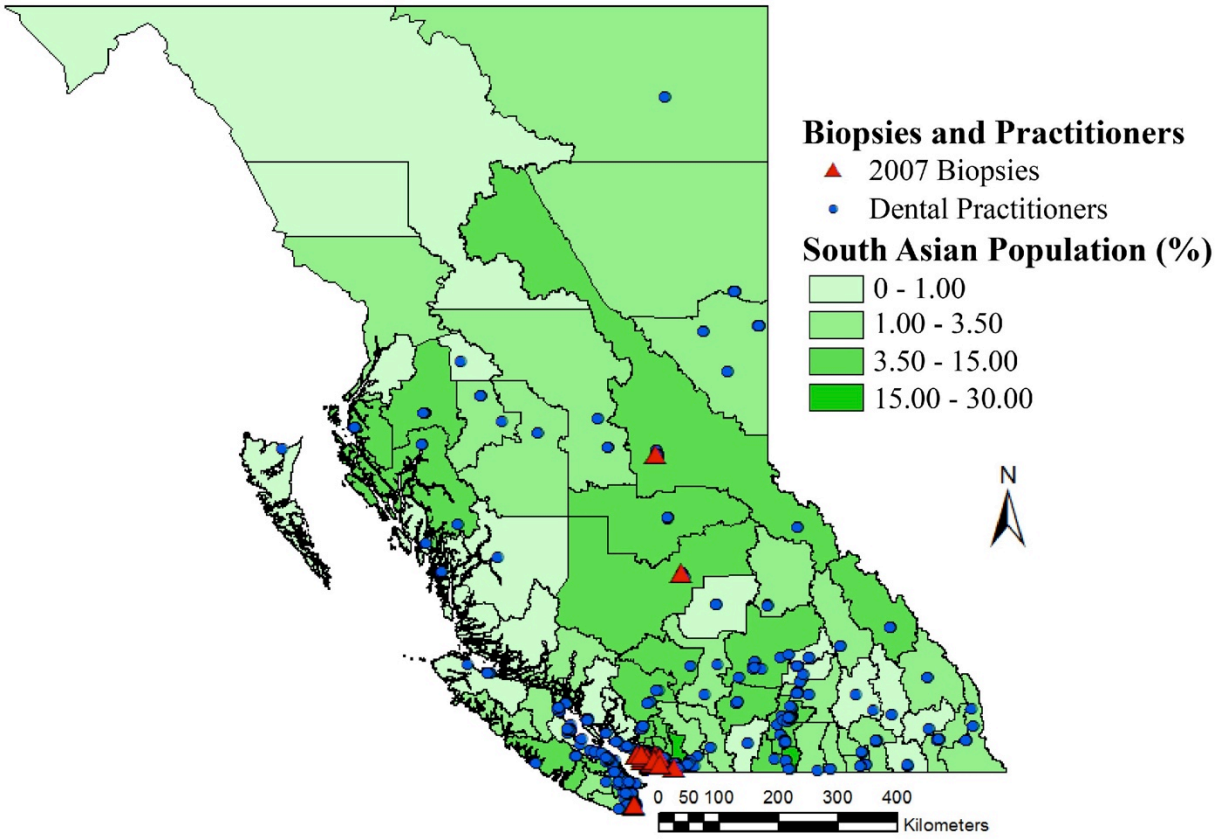

Figure 6.11 Map of OBS South Asian biopsies and dental practitioners in 2007

When examining the Metro Vancouver area (Figure 6.12), findings show that 15 biopsies were in Vancouver, eight biopsies were in Surrey, two in Burnaby, two in Langley, and one each in Richmond, Coquitlam, Maple Ridge.

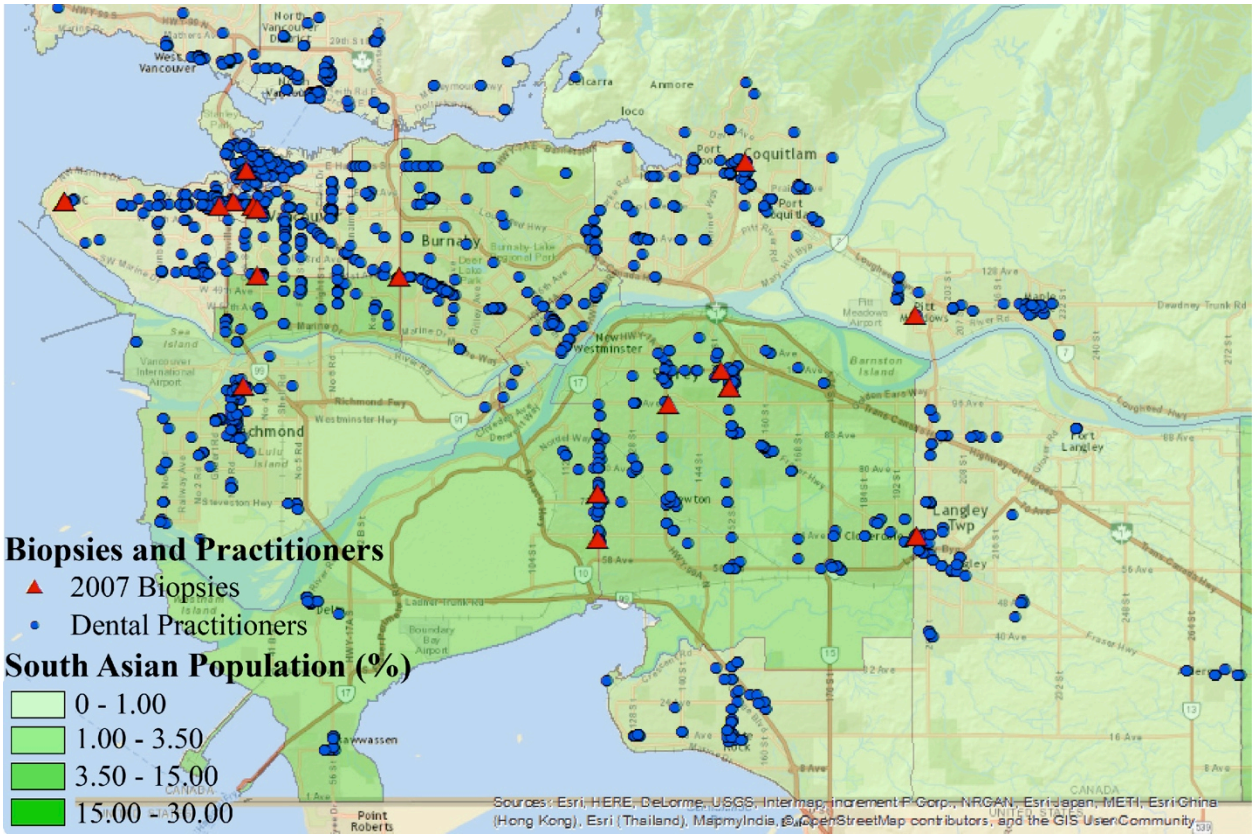

Figure 6.12 Map of OBS South Asian biopsies and dental practitioners in 2007 - Metro Vancouver

In 2013 in the OBS database, the spatial analysis shows that the number of dental practitioners in Northern BC is similar to the data from 2007, however in 2013 there were two additional biopsies coming from Northern areas such as Terrace and Gitanmaax (Figure 6.13).

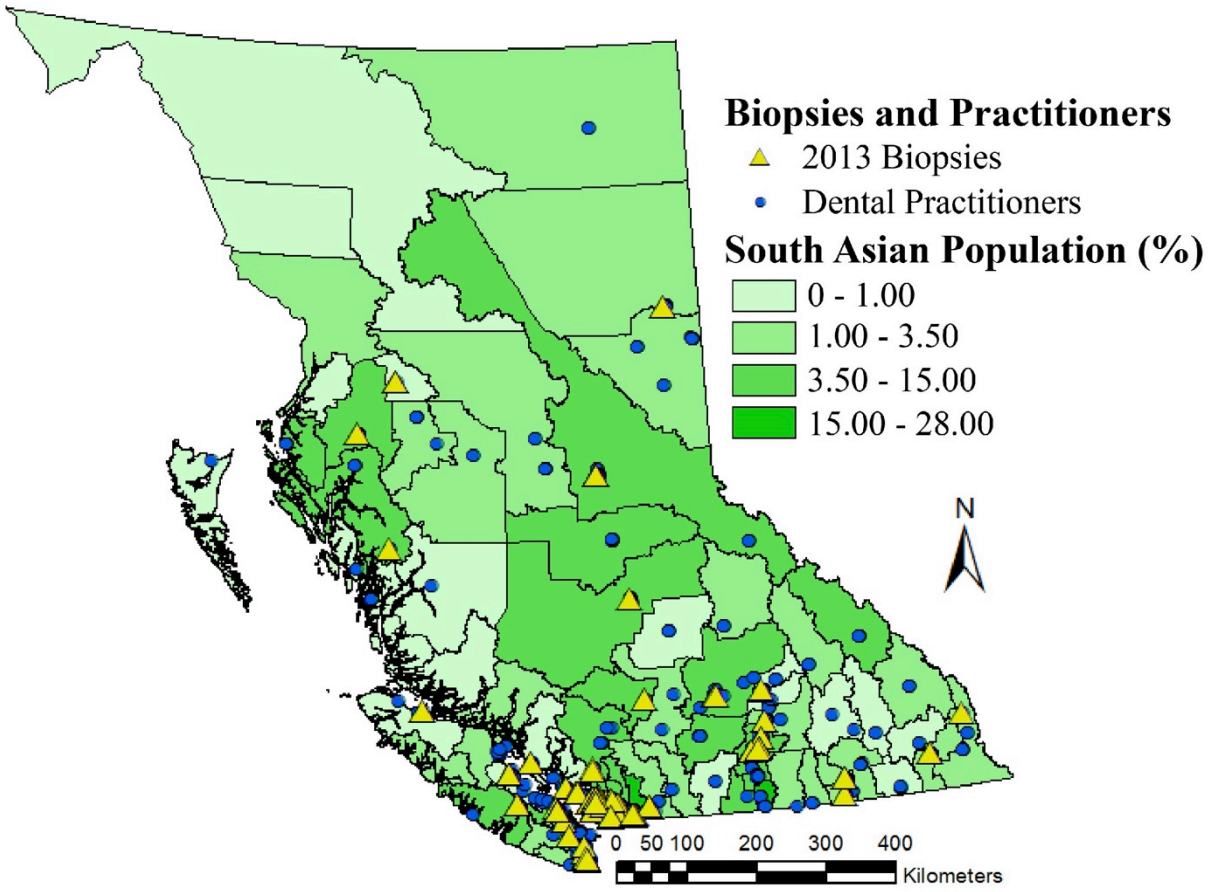

Figure 6.13 Map of OBS biopsies and dental practitioners in 2013

When examining the South Asian cases from the OBS database in 2013, findings show that the biopsies come mostly from Metro Vancouver, with two biopsies in Victoria, two biopsies in Nanaimo, two biopsies in Kamloops, and one biopsy each in Abbotsford, Lillooet, Williams Lake, and Prince George (Figure 6.14). The number of biopsies was greater, and there was greater variety in the cities where these biopsies were performed, than in 2007.

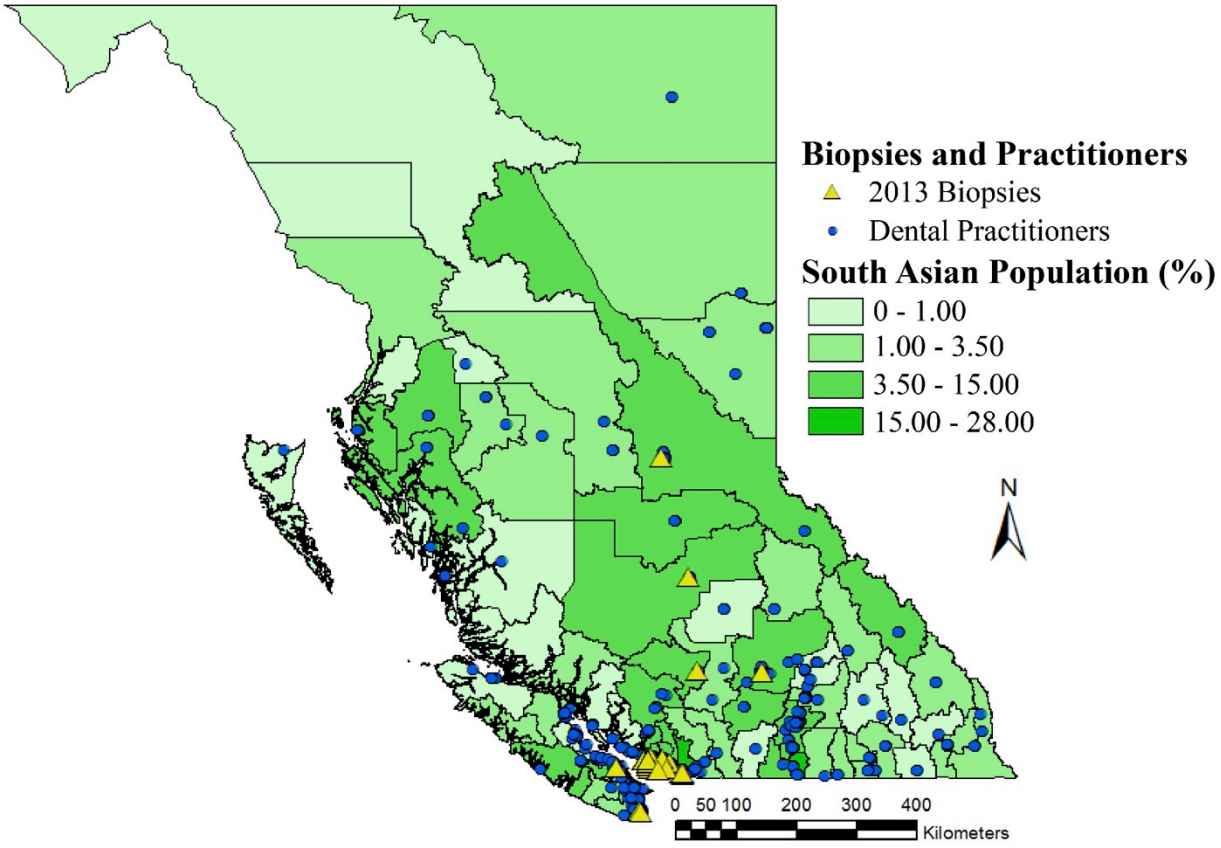

Figure 6.14 Map of OBS South Asian biopsies and dental practitioners in 2013

When examining the Metro Vancouver area (Figure 6.15), findings show that 35 biopsies were in Vancouver, 15 biopsies were in Surrey, five biopsies were in Burnaby, four biopsies were in North Vancouver, three biopsies were in each Richmond and Coquitlam, and one biopsy was in each Langley and Maple Ridge. There were no biopsies performed in North Vancouver in 2007 and four in 2013, as well as a general increase in the number of biopsies each of the other areas.

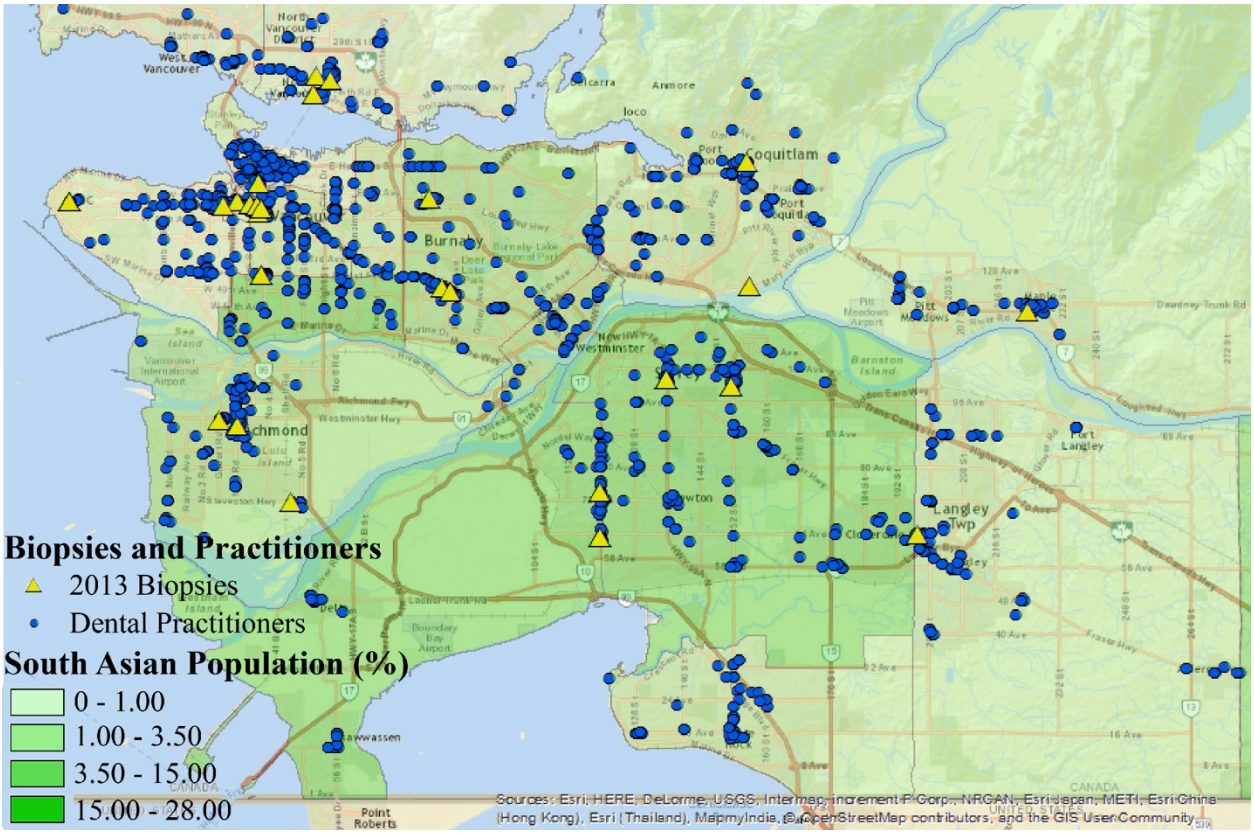

Figure 6.15 Map of OBS South Asian biopsies and dental practitioners in 2013 - Metro Vancouver

6.1.7.3 Changes Since the 2008 Biopsy Guidelines

Based on data from Census Canada, the population in BC increased by about 6.9% between 2007 and 2013. Within this same time frame, the number of dentists and dental specialists in BC increased from 2,919 to 3,156, a growth of 8%. The total number of biopsies received by the OBS increased by 36%, and the number of dental practitioners submitting biopsies to the OBS increased by 48%.

Since the introduction of the biopsy guidelines in 2008, the total number of biopsies performed has increased, and there is greater variety in the areas where biopsies are performed across the province. There has been a slight increase in biopsies performed in Northern BC, including areas such as Terrace and Gitanmaax.

6.2 BCCR Database

6.2.1 Frequencies

There were a total of 494 cases of oral cancer and severe dysplasia in 2007 and 2013 in the BCCR that met this study's inclusion criteria; Table 6.20 outlines the frequencies of these cases categorized by year and by sex, age at diagnosis, histopathological diagnosis, and lesion site. It should be noted that there were only eleven South Asian cases in the BCCR in 2007, and only five in 2013, resulting in a small sample size and consequent lack of power.

	All (N=494)		2007 (n=305)		2013 (n=189)	
	SA (n=16) (%)	Other (n=478) (%)	SA (n=11) (%)	Other (n=294) (%)	SA (n=5) (%)	Other (n=184) (%)
Sex						
Male	7 (43.8)	356 (74.5)	6 (54.5)	212 (72.1)	1 (20)	144 (78.3)
Female	9 (56.3)	122 (25.5)	5 (45.5)	82 (27.9)	4 (80)	40 (21.7)
Age						
< 60 years	8 (50)	196 (41)	6 (54.5)	113 (38.4)	2 (40)	83 (45.1)
≥ 60 years	8 (50)	282 (59)	5 (45.5)	181 (61.6)	3 (60)	101 (54.9)
Diagnosis						
SCC	16 (100)	454 (95)	11 (100)	280 (95.2)	5 (100)	175 (95.1)
C*IS*	0	21 (4.4)	0	14 (4.8)	0	7 (3.8)
D3	0	2 (0.4)	0	0	0	2 (1.1)

	All (N=494)		2007 (n=305)		2013 (n=189)	
	SA (n=16) (%)	Other (n=478) (%)	SA (n=11) (%)	Other (n=294) (%)	SA (n=5) (%)	Other (n=184) (%)
Lesion Site						
Gingiva	1 (6.3)	20 (4.2)	0	14 (4.8)	1 (20)	6 (3.3)
Buccal mucosa[+]	1 (6.3)	17 (3.6)	0	12 (4.1)	1 (20)	5 (2.7)
FOM	0	35 (7.3)	0	25 (8.5)	0	10 (5.4)
VL Tongue	8 (50)	69 (14.4)	6 (54.5)	51 (17.3)	2 (40)	18 (9.8)
D Tongue	0	3 (0.6)	0	3 (1)	0	0
Soft Palate	6 (37.4)	304 (63.6)	5 (45.5)	166 (56.5)	1 (20)	138 (75)
Hard Palate	0	7 (1.5)	0	5 (1.7)	0	2 (1.1)
Other	0	22 (4.6)	0	18 (6.1)	0	4 (2.2)
Not Spec.	0	1 (0.2)	0	0	0	1 (0.5)

Table 6.20 BCCR frequencies summary
SA: South Asian
D3: Severe dysplasia
FOM: Floor of mouth
VL Tongue: Ventro-lateral tongue
D Tongue: Dorsal tongue
Other: Lip, external lip
Not spec.: Not specified
[+] Includes buccal/labial and vestibular mucosa

The mean age at diagnosis in 2007 and 2013 was 63.4 years with a standard deviation of 12 (Figure 6.16). In the general population, the mean age was 63.5 years with a standard deviation of 11.9 (Figure 6.17) while the mean age of South Asian cases was 60.8 years with a standard deviation of 16.1 (Figure 6.18).

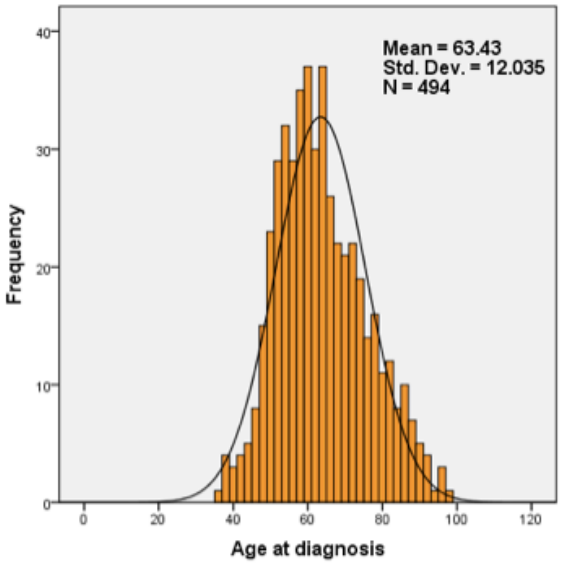

Figure 6.16 BCCR mean age

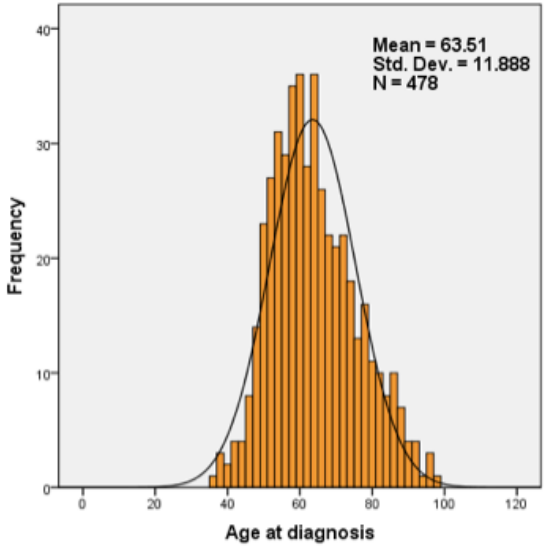

Figure 6.17 BCCR mean age: general population

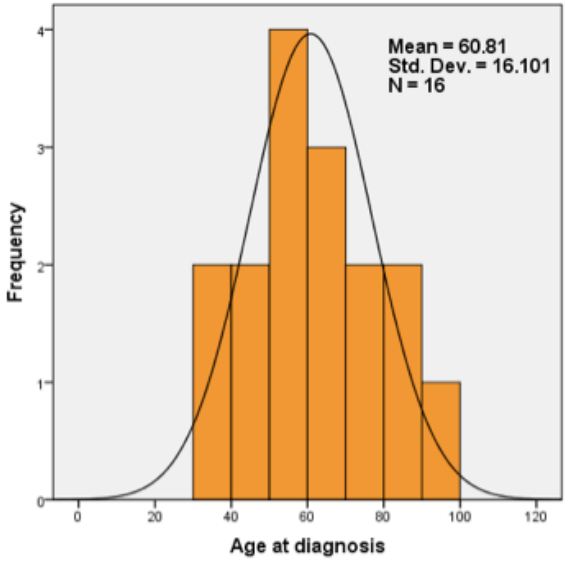

Figure 6.18 BCCR mean age: South Asian population

6.2.2 Ethnicity

6.2.2.1 Ethnicity and Demographics

Demographic data including sex and age at diagnosis was compared between South Asian cases and the general population within the BCCR database.

6.2.2.1.1 Ethnicity and Sex

There was a greater difference between the sexes within the general population; the vast majority of cases were male. In 2007 the distribution of male and female cases was 72% and 28% respectively in the general population. In South Asian cases, however, only 55% of cases were male and 45% were female (Figure 6.19).

The distribution of male and female cases in 2013 was 78% and 22% respectively in the general population. However, 20% of South Asian cases were male, while 80% were female (Figure 6.20).

When considering all BCCR cases in 2007 and 2013 (Figure 6.21), while the proportion of male to female cases was 75% and 25% respectively in the general population, only 44% of South Asian cases were male, with 56% of cases being female. This indicates a ratio of 3:1 male to female cases in BCCR in the general population, while this ratio in the South Asian population is 0.8:1, with a greater number of female South Asian case

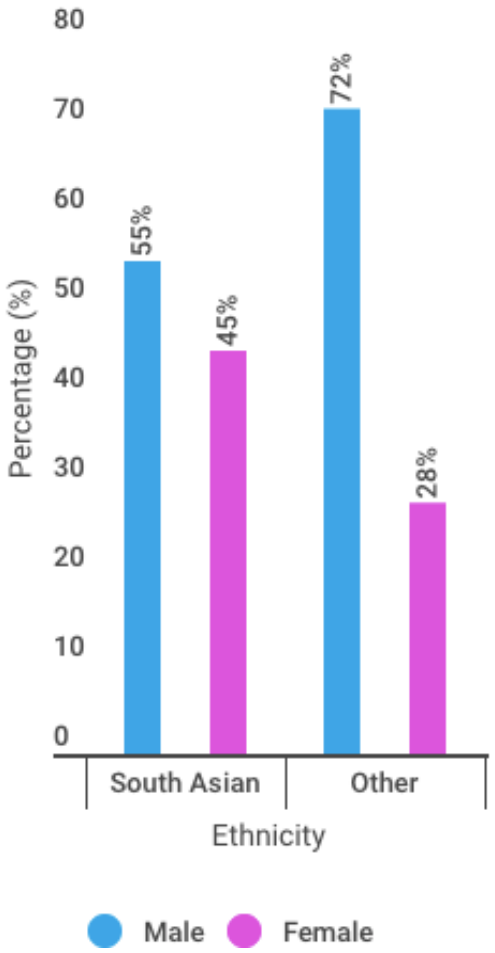

Figure 6.19 BCCR 2007 ethnicity and sex

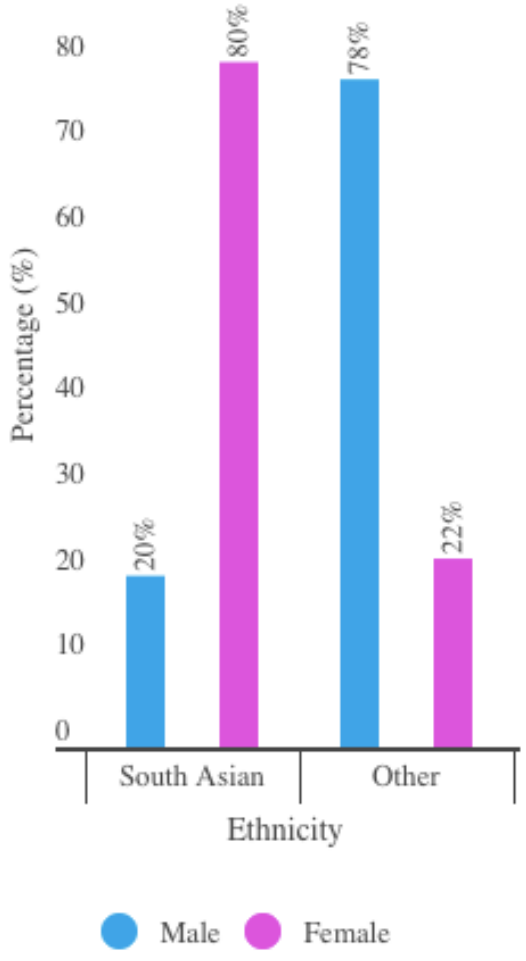

Figure 6.20 BCCR 2013 ethnicity and sex

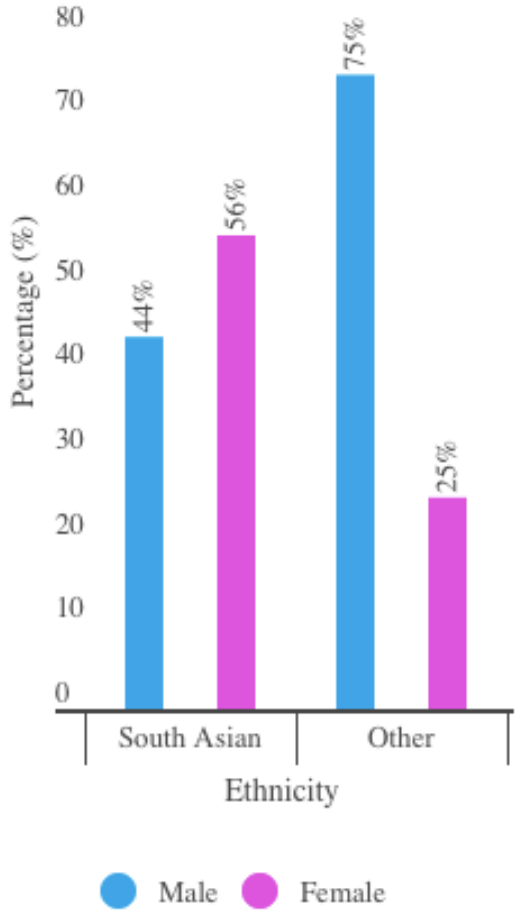

Figure 6.21 BCCR 2007 & 2013 ethnicity and sex

6.2.2.1.2 Ethnicity and Age at Diagnosis

Trends in age at diangosis varied within the BCCR. In 2007 the distribution of cases below the age of sixty years, and sixty years and above was 38% and 62% respectively in the general poulation. Of South Asian cases, 55% were below the age of sixty years, and only 45% were sixty years and above (Figure 6.22).

Trends in 2013 were more similar between the South Asian popuation and the general population. The distribution of cases below the age of sixty years, and sixty years and above was 45% and 55% respectively in the general population. Of South Asian cases, 40% were below the age of sixty years, and 60% were sixty years and above (Figure 6.23).

When considering all cases in 2007 and 2013 (Figure 6.24), while the proportion of cases below the age of sixty years and those sixty years and above is 41% and 59% respectively in the general population, half of South Asian cases were below the age of sixty years, with the other half of cases sixty years and above. This indicates that a greater proportion of cases occurred at sixty years and above in the general population, while cases in the general population were generally more evenly distributed.

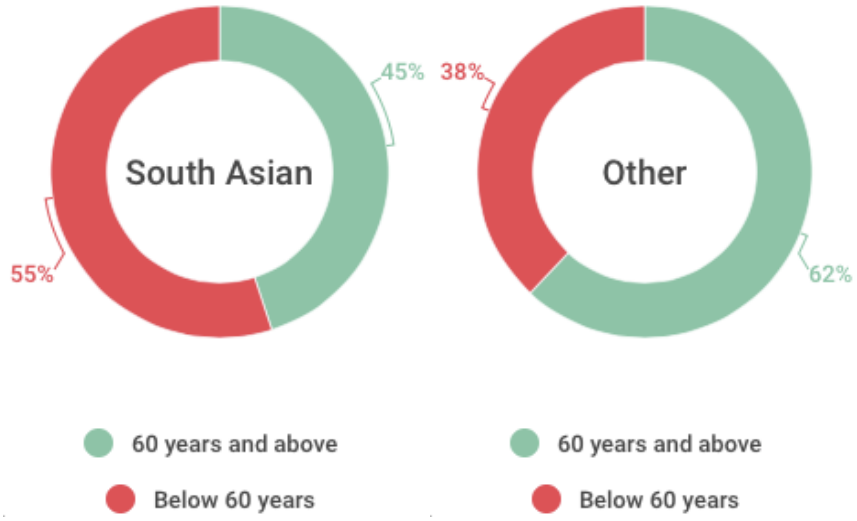

Figure 6.22 BCCR 2007 ethnicity and age at diagnosis

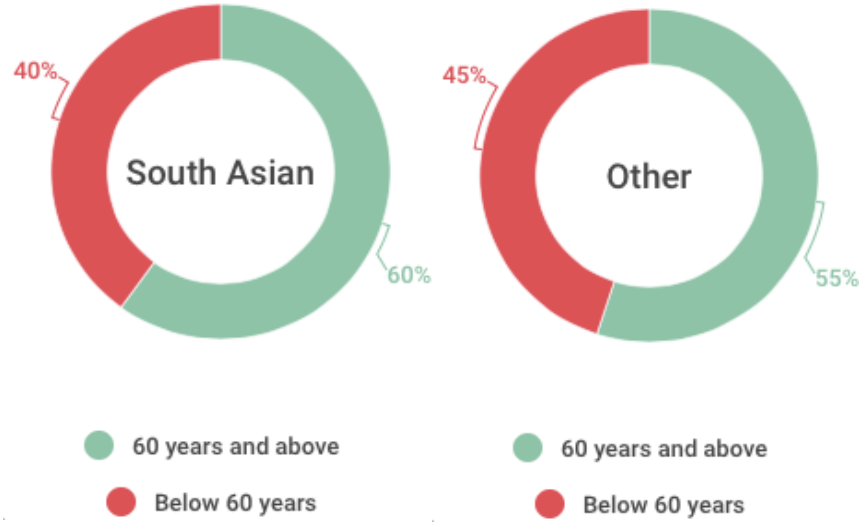

Figure 6.23 BCCR 2013 ethnicity and age at diagnosis

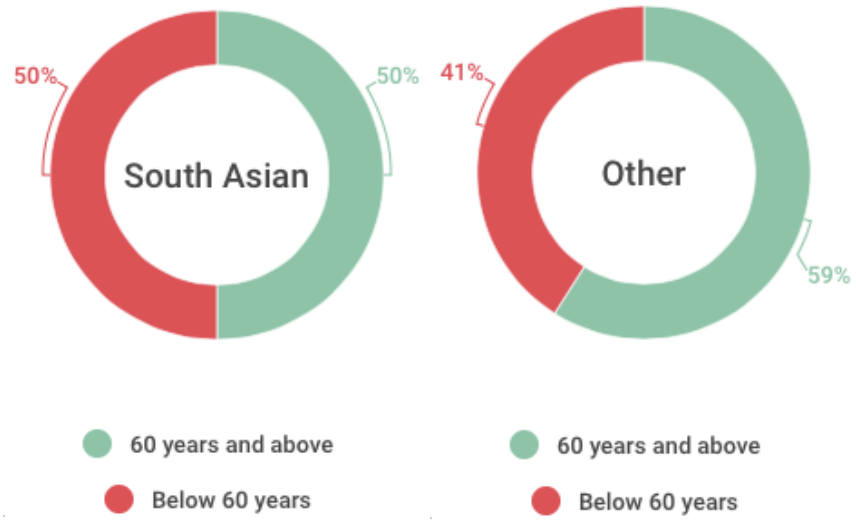

Figure 6.24 BCCR 2007 & 2013 ethnicity and age at diagnosis

6.2.2.2 Ethnicity and Histopathological Diagnosis

Statistical analyses were not performed to examine differences between ethnicity and diagnosis, as nearly all cases (95-100%) within the database were SCC.

6.2.2.3 Ethnicity and Lesion Site

There were statistically significant differences between lesion sites based on ethnicity (Table 6.21). In 2007 and 2013, there was a greater proportion of South Asian cases occurring at Western high-risk sites (50%) than cases in the general population occurring at these sites (21.8%). Less than one third of cases in the general population occurred at Western high-risk sites. Overall, very few cases occurred at South Asian high-risk sites; 7.7% of cases in the general population, and 12.5% of South Asian cases occurred at these sites.

	All (%)	SA (%)	Other (%)	*p-value*	OR (95% CI)
2007	n=304	n=11	n=294		
Western Risk					
Western HR[a]	82 (26.9)	6 (54.5)	76 (25.9)	***0.035***	3.44 (1.1-11.6)
Western Other	223 (73.1)	5 (45.5)	218 (74.1)		1
SA Risk					
SA HR[b]	26 (8.5)	0	26 (8.8)	*0.302*	N/A
SA Other	279 (91.5)	11 (100)	268 (91.2)		1
2013	n=189)	n=5	n=184		
Western Risk					
Western HR[a]	30 (15.9)	2 (40)	28 (15.2)	***0.043***	3.71 (0.6-23.2)
Western Other	159 (84.1)	3 (60)	156 (84.8)		1
SA Risk					
SA HR[b]	13 (6.9)	2 (40)	11 (6)	***0.014***	10.49 (1.6-69.4)
SA Other	176 (93.1)	3 (60)	173 (94)		1
2007 & 2013	n=494	n=16	n=478		
Western Risk					
Western HR[a]	112 (22.7)	8 (50)	104 (21.8)	***0.008***	3.6 (1.3-9.8)
Western Other	382 (77.3)	8 (50)	374 (78.2)		1
SA Risk					
SA HR[b]	39 (7.9)	2 (12.5)	37 (7.7)	*0.487*	1.70 (0.4-7.8)
SA Other	455 (92.1)	14 (87.5)	441 (92.3)		1

Table 6.21 BCCR ethnicity and lesion site

[a] Includes ventro-lateral tongue and floor of the mouth

[b] Includes gingiva, buccal/labial and vestibular mucosa

N/A: The OR could not be produced as one of the cells was a zero

6.2.3 South Asian Cases

The following sections examine South Asian cases exclusively.

6.2.3.1 Age at Diagnosis and Histopathological Diagnosis

Age at diagnosis and histopathological diagnosis were not examined, as nearly all cases (95-100%) within the database were SCC.

6.2.3.2 Age at Diagnosis and Lesion Site

Anatomical lesion sites did not differ significantly by age at diagnosis (Table 6.22). There were very few cases at South Asian high-risk sites.

	< 60 years (%)	≥ 60 years (%)	*p-value*	OR (95% CI)
2007	n=6	n=5		
Western Risk				
Western HR[a]	3 (50)	3 (60)	*0.740*	0.67 (0.1-7.4)
Western Other	3 (50)	2 (40)		1
SA Risk				
SA HR[b]	0	0	-	N/A
SA Other	6 (100)	5 (100)		1
2013	n=2	n=3		
Western Risk				
Western HR[a]	1 (50)	1 (33.3)	*0.709*	2.0 (0.1-78.3)
Western Other	1 (50)	2 (66.7)		1
SA Risk				
SA HR[b]	1 (50)	1 (33.3)	*0.709*	2.0 (0.1-78.3)
SA Other	1 (50)	2 (66.7)		1
2007 & 2013	n=8	n=8)		
Western Risk				
Western HR[a]	4 (50)	4 (50)	*1.000*	1.00 (0.1-7.1)
Western Other	4 (50)	4 (50)		1
SA Risk				
SA HR[b]	1 (12.5)	1 (12.5)	*1.000*	1.00 (0.1-19.4)
SA Other	7 (87.5)	7 (87.5)		1

Table 6.22 BCCR age at diagnosis and lesion site (South Asian cases)
HR: High risk
SA: South Asian
[a] Includes ventro-lateral tongue and floor of the mouth
[b] Includes gingiva, buccal/labial and vestibular mucosa
N/A: The OR could not be produced as one of the cells was a zero

6.2.3.3 Sex and Diagnosis

Sex and histopathological diagnosis were not examined, as nearly all cases (95-100%) within the database were SCC.

6.2.3.4 Sex and Lesion Site

Anatomical lesion sites did not differ significantly by sex (Tables 6.23). The number of cases identified at South Asian high- and low-risk sites were similar among both males and females. There was a higher proportion of female cases at Western high-risk sites, while male cases were found more commonly at Western low-risk sites.

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007	n=6	n=5		
Western Risk				
Western HR[a]	2 (33.3)	4 (80)	*0.122*	0.13 (0.1-1.9)
Western Other	4 (66.7)	1 (20)		1
SA Risk				
SA HR[b]	0	0	-	N/A
SA Other	6 (100)	5 (100)		1
2013	n=1	n=4		
Western Risk				
Western HR[a]	0	2 (50)	*0.361*	N/A
Western Other	1 (100)	2 (50)		1
SA Risk				
SA HR[b]	1 (25)	1 (100)	*0.171*	0.14 (0.1-5.9)
SA Other	3 (75)	0		1

	Male (%)	Female (%)	*p-value*	OR (95% CI)
2007 & 2013	n=7	n=9		
Western Risk				
Western HR[a]	2 (28.6)	6 (66.7)	*0.131*	0.20 (0.1-1.7)
Western Other	5 (71.4)	3 (33.3)		1
SA Risk				
SA HR[b]	1 (14.3)	1 (11.1)	*0.849*	1.33 (0.1-25.9)
SA Other	6 (85.7)	8 (88.9)		1

Table 6.23 BCCR sex and lesion site (South Asian cases)
HR: High risk
SA: South Asian
[a] Includes ventro-lateral tongue and floor of the mouth
[b] Includes gingiva, buccal/labial and vestibular mucosa
N/A: The OR could not be produced as one of the cells was a zero

6.2.4 Dental Network Capacity in BCCR

The total number of cancer diagnoses within the BCCR was assessed, and cases from the BCCR also found in the OBS database were confirmed (Table 6.24). This assessment identified that 61.9% to 69.1% of cancer diagnoses were diagnosed outside of the OBS, likely through other pathology services or through the medical system. The OBS received 30.9% to 38.1% of cancer biopsies found in the BCCR. Additionally, eight cancer cases in 2007, and ten cases in 2013, were diagnosed in the OBS but not located within the BCCR.

	2007 (%)	2013 (%)
Total diagnoses in BCCR*	189 (100)	305 (100)
Diagnoses also in OBS	72 (38.1)	94 (30.9)
Diagnoses not in OBS	117 (61.9)	211 (69.1)
Diagnoses in OBS not in BCCR	8	10

Table 6.24 OBS and BCCR dental network capacity
***** Total diagnoses that met inclusion criteria

6.2.4.1 Spatial Analysis

The BCCR database in 2007 shows a slightly more even distribution of dental practitioners and biopsies (Figure 6.25) compared to spatial analyses of biopsies in the OBS in 2007. This is an interesting finding, as the biopsies from the BCCR also come from medical practitioners.

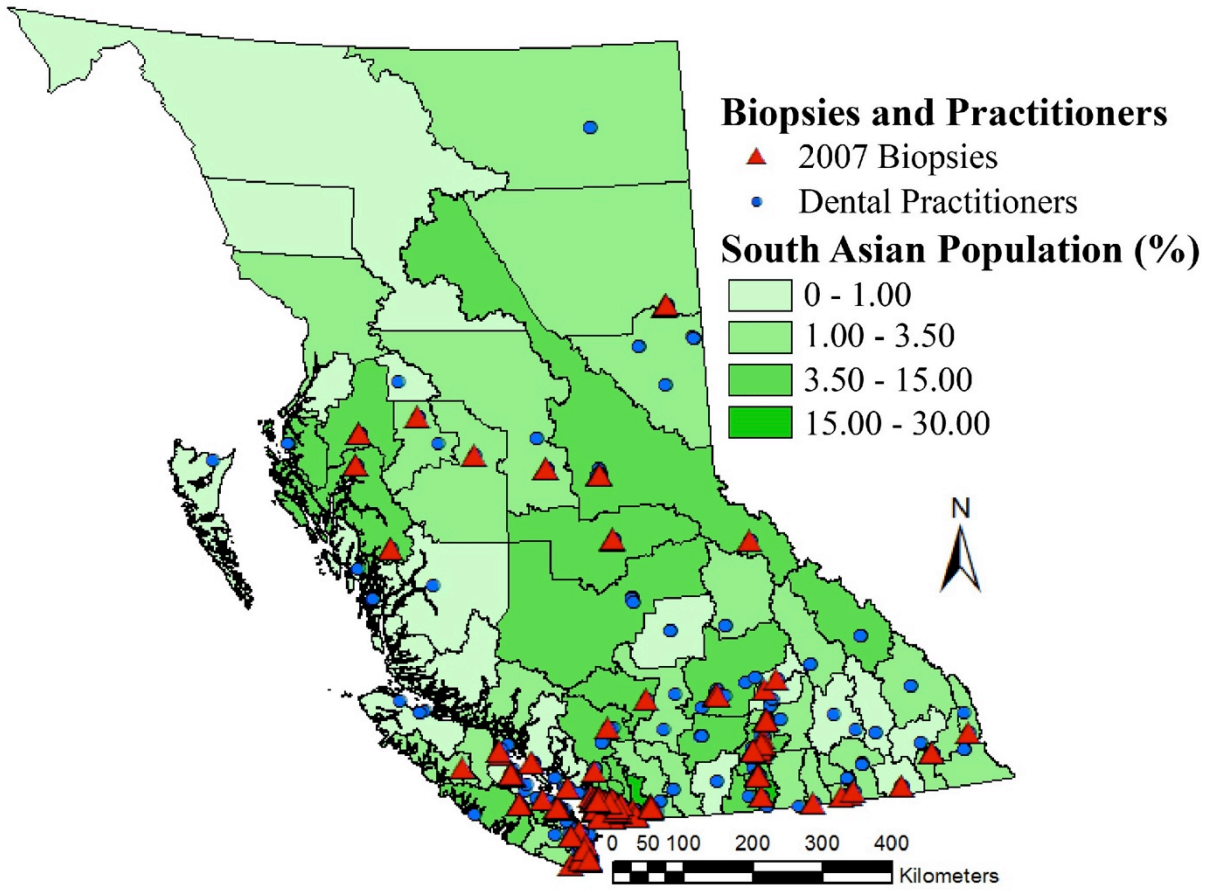

Figure 6.25 Map of BCCR biopsies and dental practitioners in 2007

When examining the South Asian cases from the BCCR database in 2007, findings show that the majority of biopsies came from Metro Vancouver, with one biopsy in Vernon and one in Victoria (Figure 6.26).

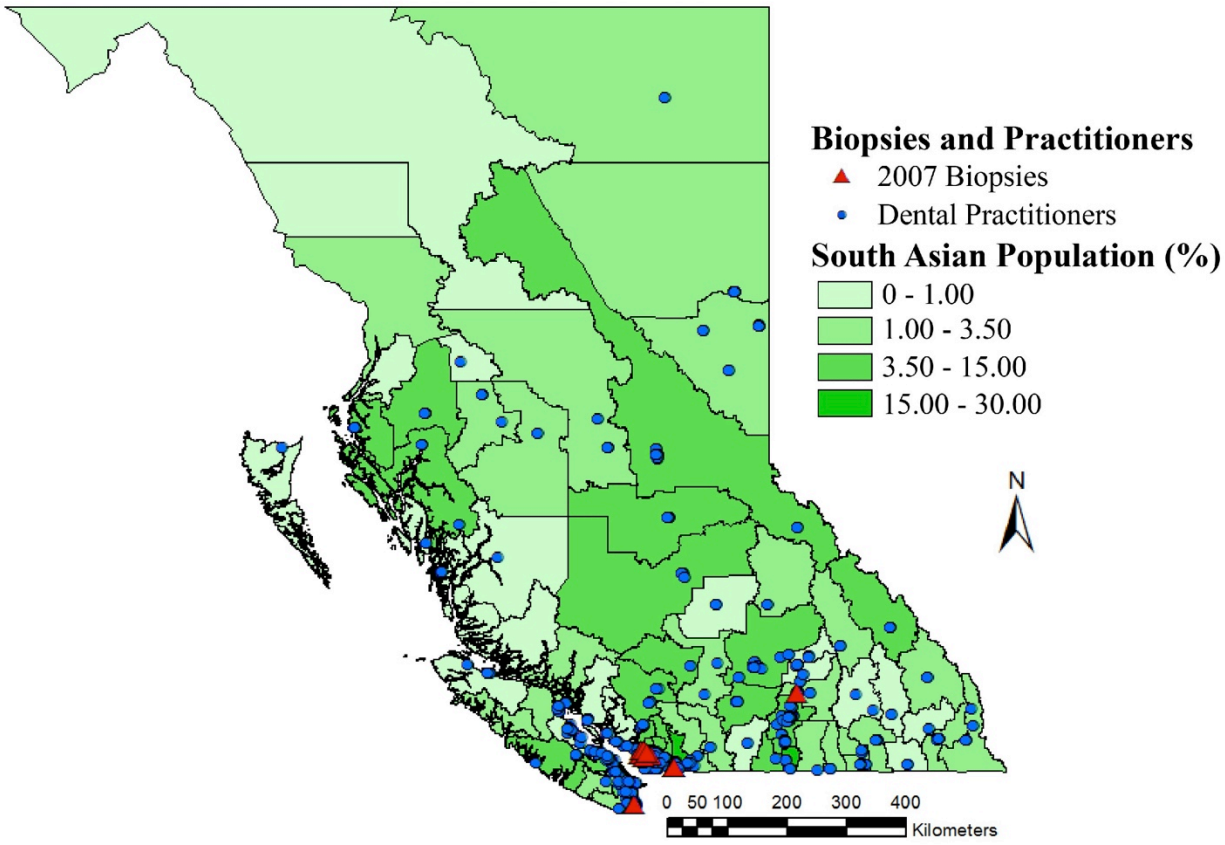

Figure 6.26 Map of BCCR South Asian biopsies and dental practitioners in 2007

When examining the South Asian cases in the Metro Vancouver area (Figure 6.27), findings show that there were three biopsies in Vancouver, two biopsies in Abbotsford, two biopsies in Burnaby, and one biopsy each in West Vancouver, North Vancouver, Vernon, and Victoria.

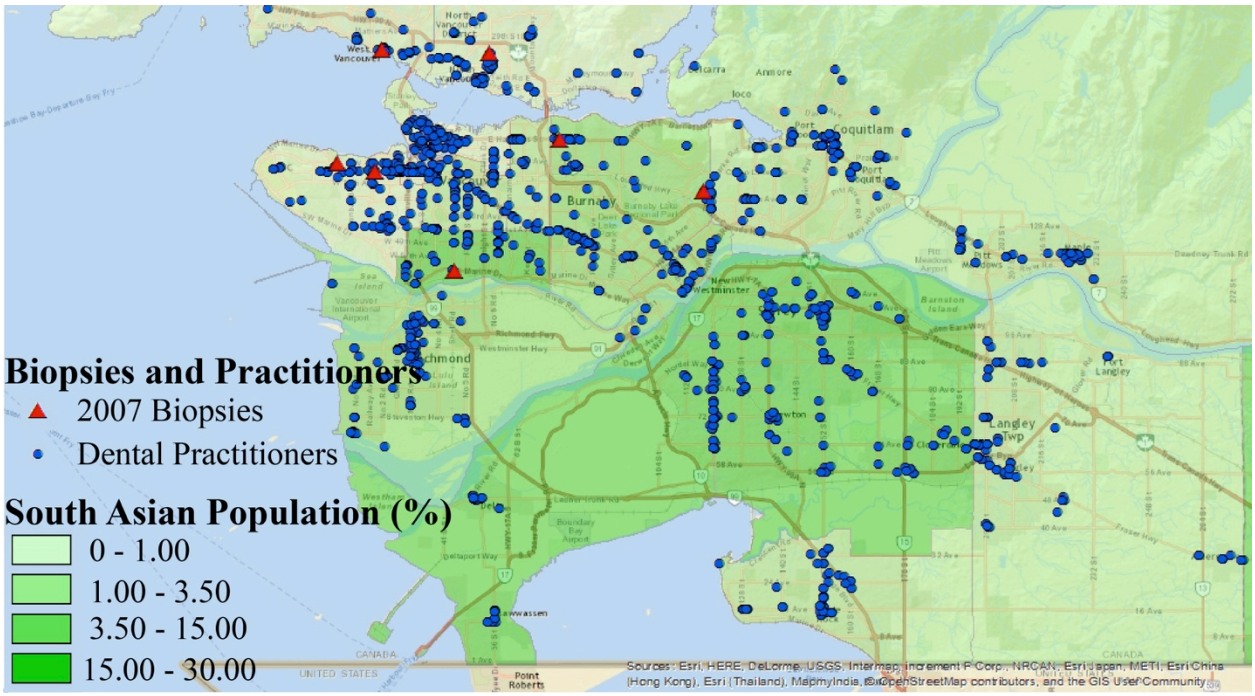

Figure 6.27 Map of BCCR South Asian biopsies and dental practitioners in 2007 - Metro Vancouver

The BCCR database in 2013 also shows a slightly more even distribution of dental practitioners and biopsies (Figure 6.28) compared to spatial analyses of biopsies in OBS in 2013.

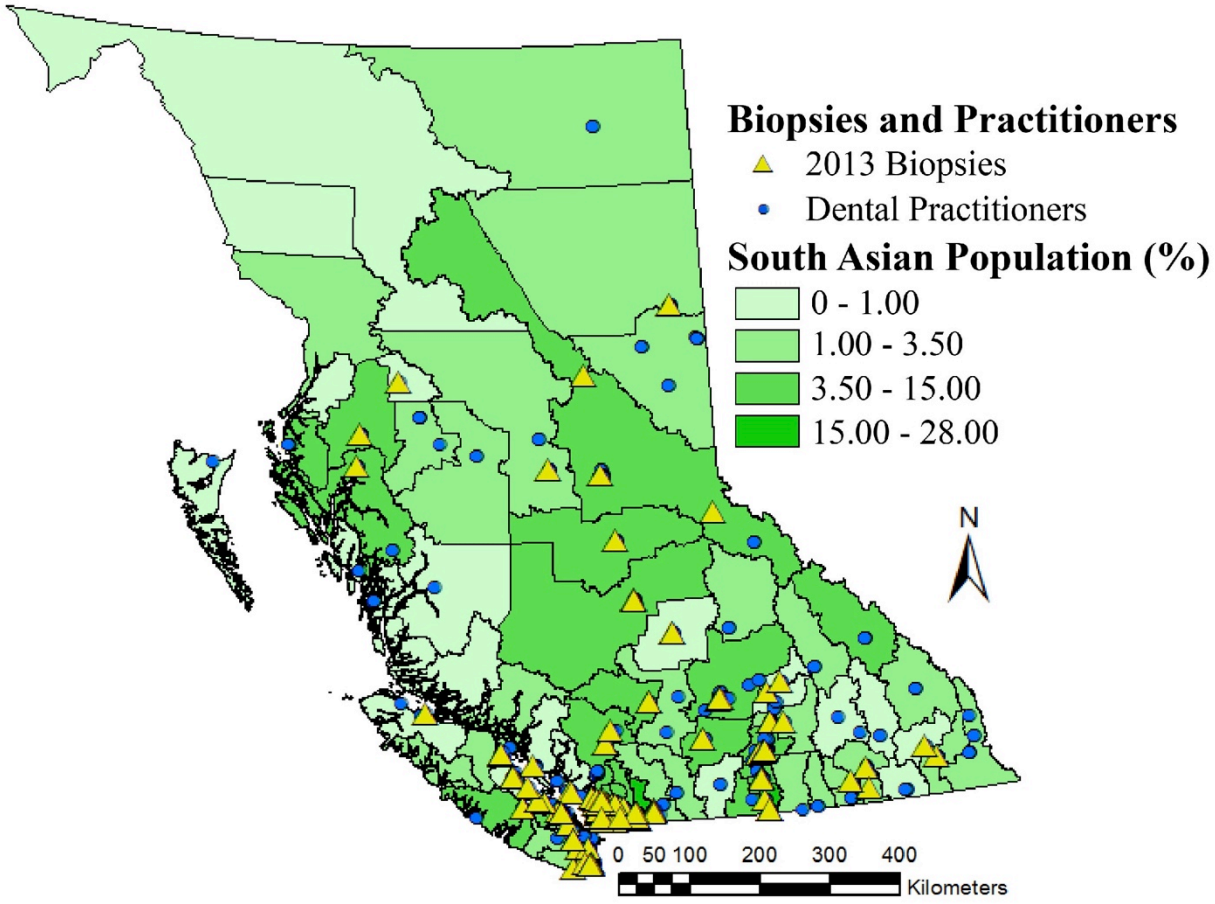

Figure 6.28 Map of BCCR biopsies and dental practitioners in 2013

When examining the South Asian cases from the BCCR database in 2013, findings show that all five biopsies again came from Metro Vancouver (Figure 6.29).

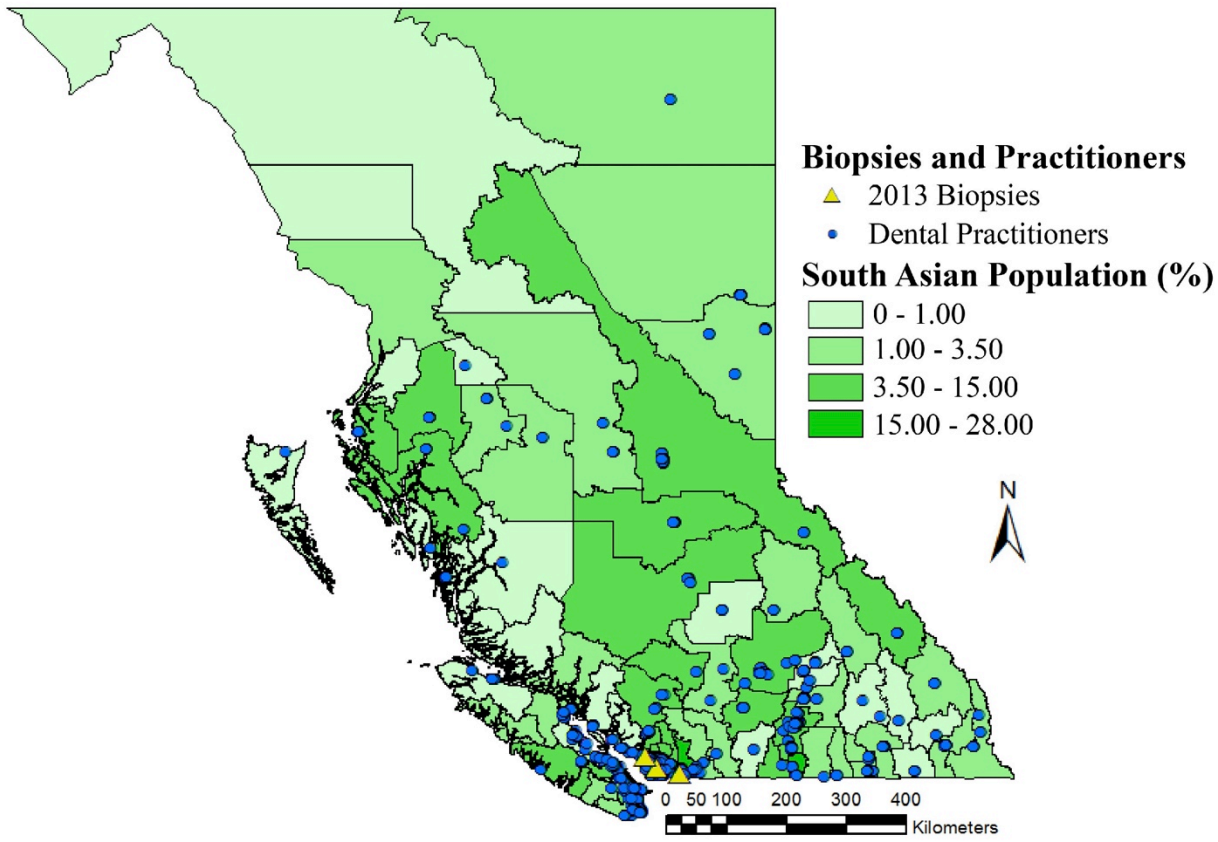

Figure 6.29 Map of BCCR South Asian biopsies and dental practitioners in 2013

When examining the South Asian cases in the Metro Vancouver area (Figure 6.30), findings show that 2 biopsies were in Surrey, 2 biopsies were in Abbotsford, and one biopsy in West Vancouver.

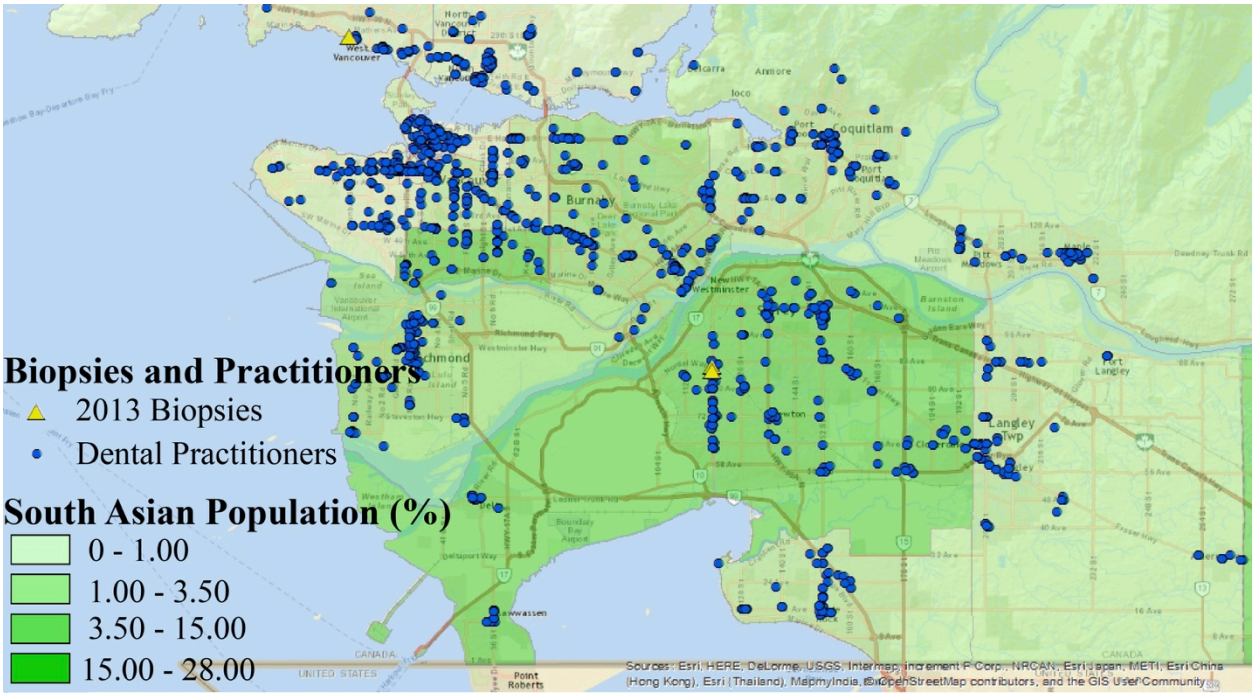

Figure 6.30 Map of BCCR South Asian biopsies and dental practitioners in 2013 - Metro Vancouver

Chapter 7: Discussion

7.1 Biology and Trends

7.1.1 Demographics

South Asian cases in the OBS database were predominantly male, with a rate of about 70%, compared to about 57% male cases in the general population. This finding suggest that males in the South Asian population are at an increased risk of oral cancer and dysplasia, which is corroborated by existing evidence in this population. [3,8,77] While the proportion of male to female cases remained generally stable in the general population from 2007 to 2013, there was an increase from 63% to 73% in the proportion of male cases in the South Asian population. This indicates that more men are being diagnosed, whether as a result of increased incidence of disease, or of increased access to care.

In the BCCR database, the vast majority of cases in the general population were male, accounting for approximately 75% of all cases. Differences between the sexes in South Asian cases were less drastic; approximately half of the cases were male and half were female. The high proportion of male cases in the general population is of interest, and may reflect increased incidence of cancer in males or early access to care in females, resulting in fewer cancer diagnoses within the BCCR in women. It is important to note that the number of South Asian cases in 2007 and 2013 were very small, with a total of only sixteen cases for both years combined. This poses limitations in terms of power and generalizability.

Over 60% of South Asian cases in the OBS were under sixty years of age, compared to 51% in the general population. The proportion of cases below sixty years of age, and those sixty years and above, remained steady within both populations from 2007 to 2013. This younger age at diagnosis within the South Asian population is consistent with existing research in this population.[3,8,77] Additionally, initiation of tobacco use, both smoked and smokeless, as well as the use of areca nut and betel quid, in South Asian countries is known occur at a young age[63], and may be reflected in the findings of this study. Other potential factors may include heavier use of tobacco and/or alcohol in South Asian individuals, resulting in a younger age at diagnosis. Detailed risk habit information would be needed to further explore such trends. The older age groups (sixty years of age and over) had more cases of cancer, which is expected due to the increased risk of cancer associated with increased age.[3,74] It is interesting to note, however, that hyperplasias were generally more prominent in the younger age groups (below the age of sixty years) than in the older age groups. It is unclear whether this may be due an increased risk of hyplerpastic lesions in the younger age group, or simply a higher risk of progression or cancers in the older age group, hence a decrease in hyperplasia diagnoses.

The BCCR database showed similar trends, with 50% of South Asian cases under sixty years of age, compared to 41% in the general population. However, it also showed an increase in the proportion of cases below the age of sixty years from 2007 to 2013 in the general population, from 38% to 45% respectively. Similar findings have been outlined by Laronde *et. al.* in 2008, discussing the increased incidence of cases in younger patients.[78] This may indicate a trend that SCC and C*IS* are being diagnosed at an increasingly younger age. It should again be noted that

the sample size of South Asian cases in 2007 and 2013 was very small, posing limitations in terms of power and generalizability of these findings.

7.1.2 Histopathological Diagnosis

Data from the OBS did not show a significant difference in histopathological diagnoses between the South Asian population and the general population. Rates of cancer, dysplasia and hyperplasia were similar between the South Asian population and the general population in 2007 and 2013.

Data from the BCCR indicated that the vast majority of cases within the registry were SCC, with only 21 cases (4.4%) of C*IS* and 2 cases (0.4%) of severe dysplasia in both years combined. Data from the OBS confirms that rates of C*IS* and severe dysplasia are generally low, though it also demonstrates that cases of severe dysplasia, while identified as requiring treatment with curative intent, are often not registered in the BCCR. It is of high importance to investigate these cases and determine why they were not followed in terms of recurrences, progression, types of treatments, and general surveillance.

Due to the small proportion of cases with information available on risk habits, this study did not have the ability to link verruciform lesions with the use of areca nut or chewed tobacco. Hazarey *et. al.* found that South Asians are more prone to verrucous lesions, due to an association identified with the use of betel quid and smokeless tobacco.[37] This study was not able to

corroborate these findings, potentially due to the small number of cases presenting with lesions of verrucous configuration.

7.1.3 Anatomical Lesion Site

In Western countries, the most common site for lesions is the tongue, whereas common lesion sites in South Asian countries include the gingiva and buccal mucosa. [76,77] In the OBS database, a high proportion of cases occurred at South Asian high-risk sites; 50% in the general population, and 65% in the South Asian population, while a much lower proportion of cases presented with lesions at sites considered high-risk in Western countries. Interestingly, these are anatomical lesions sites that dental profesionals are taught to associate with an increased risk for premalignant and malignant lesions. This finding highlights the importance of updating dental practitioners' knowledge regarding what constitutes high risk and common lesion sites associated with premalignant and malignant lesions.

In the OBS database, although the majority of lesions occurred at South Asian high-risk sites, findings showed that only a small proportion of lesions at these sites were cancerous (7%), compared to higher rates of cancer at other sites (20%). Of fifteen South Asian cancer cases, five (33%) occurred at South Asian high-risk sites, and ten occurred at other sites, eight (53%) of which were located at Western high-risk sites. In the BCCR, however, only 21.8% of cancer cases in the general population occurred at Western high-risk sites. This indicates two thirds of cancer cases in the general population in the BCCR occurred at sites not considered high-risk for this group, although it should be noted that the vast majority of lesions in the BCCR occur in the

oropharynx and soft palate. This is likely due to the medical nature of the biopsies and diagnoses within the BCCR, and the consideration that these sites are more difficult for dental practitioners to access and biopsy. These sites are often referred to medical doctors or otolaryngologists for biopsy. Of dysplasias and hyperplasias in South Asian cases, 71% occurred at South Asian high-risk sites, with only 22% occurring at Western high-risk sites. These findings highlight changes in trends regarding anatomical lesion sites.

More South Asian males (77%) had lesions at South Asian high-risk sites than females (54%). Of interest, South Asian women (38.5%) were more prone to have lesions at Western high-risk sites than males (18.2%). This may indicate the presence of unreported risk habits in South Asian women.

7.1.4 Risk Habits

Areca nut and betel quid are risk habits unqiue to South Asian popuations, and these are associated with lesions sites at the gingiva and buccal mucosa. [76,77] Based on self-reported risk habit information, it was found that 100% of the cases with current or former chewing habits (n=10) experienced lesions at gingiva and buccal mucosa, sites considered to be high-risk in South Asians. While this sample size is very small, and does not achieve statistical power, it is a worthwhile observation from this study.

Collection of risk habit information is challenging. Less than 30% of pathology reports for South Asian individuals contained information on risk habits. This trend highlights the need to

reinforce complete data collection when submitting biopsy requisition forms. It may also reflect a lack of willingness on the part of South Asian patients regarding disclosure of risk habits; individuals may be concerned about prejudices and a lack of understanding linked to such habits. For example, only one female reported a chewing habit, compared to 11 males. Evidence suggests that overall rates of use of areca nut and betel quid are similar among men and women [64], hence it is possible that females may not be reporting this habit as readily as males in this study. While the sample size of cases with risk habit information was rather small (n=33), it is also possible that the numbers are representative of risk habit trends in the South Asian population in BC, indicating that a greater proportion of males present with a chewing habit compared to females. Additionally, risk habit information obtained did not contain any information about alcohol consumption, which is another important risk factor for oral cancer.

7.2 Databases

7.2.1 Ethnicity Data

Ethnicity is not routinely collected in Canada. Cases in both the OBS and the BCCR did not contain information on ethnicity. The OCPL study, which gathers self-reported ethnicity data through the use of an initial questionnaire, was accessed and linked to cases in the OBS. In this study, only 17% of South Asian cases had self-reported ethnicity through the OCPL. The ethnicity of the remaining cases was determined through the use of name recognition software programs. While this approach has been shown to have a high accuracy, it is limited in its ability to determine ethnicity for many groups such as individuals of mixed ethnicity, those whose

names are not strongly linked to a particular ethnicity, and individuals who adopt a partner's name which is of a different ethnicity. As BC is an increasingly multi-cultural province, it is of increasing importance to actively collect self-reported ethnicity data in health care systems in order to reflect the most accurate findings.

While self-definition is considered the ideal method of determining ethnicity, it is important to consider that ethnicity identified by an individual can only be as detailed as the groupings available to them. For example, in this study, South Asian ethnicity was one group. This grouping includes Pakistani, Indian, Bangladeshi, Sri Lankan, and numerous ethnicities that individuals identify with. These various ethnicities have different habits and different cultural values and beliefs. By grouping these ethnicities together into such a broad category, within-group heterogeneity is lost, and the value of ethnic categorization as a guide to providing culturally appropriate health care is greatly diminished. The use of more detailed ethnic categories in research would be an asset in planning successful programs and services for ethnic populations.

7.2.2 Risk Habit Data

While most cases in this study did not have any data available regarding risk habits, response rates for South Asian males and females were similar, at 29% and 26% respectively. This could be either a result of a lack of information provided by the patient, or by a lack of information sought by the dental practitioner. There was a slight increase in risk habit information; 20% of South Asian pathology reports in 2007 had information on risk habits, and this number increased

to 32% in 2013. This may be linked to increased awareness of dental practitioners regarding biopsy recommendations, and may be related to the CDSBC's 2008 biopsy guidelines. Continuing to strive to increasing dental practitioners' awareness of the importance of collecting risk habit information at the time of biopsy requisition is an important step in addressing the lack of data being reported; dental practitioners should be encouraged to report whether a risk habit exists, or whether a patient has refused to disclose this information. Complete information on risk habits that would enable researchers to examine trends in risk habits linked to biopsies and diagnoses in BC.

7.2.3 OCPL Recruiting

Results of this study indicated a decrease in the proportion of cases being recruited to the OCPL study. Recruitment of cancers decreased from 60% to 11.5%, which is likely related to changes in recruitment criteria for the OCPL study. The recruitment of dysplasias saw a less drastic decrease, from 36% in 2007 to 24% in 2013. The OCPL acknowledges a decrease in active recruitment, for example the cessation of recruitment of cancers in approximately 2010, which may account for some of these changes. It is interesting, however, to observe that only 36% of dysplasias were recruited to the study even in times of active recruitment. This may be related to patients' geographical location, for example a lack of ability to attend clinics and follow-ups in Greater Vancouver to participate in the study, and changes to OCPL infrastructure.

Another interesting finding is that recruitment of South Asian cases was noticeably lower, over both time periods. In 2007, only 17% of South Asian cancer cases were recruited to the study,

which decreased to 11% in 2013. For cases of dysplasia, a mere 6.5% was recruited in 2007, which increased marginally to 8.6% of South Asian cases in 2013. This shows that recruitment of South Asian cases is particularly unsuccessful. It is important to investigate further into possible reasons why South Asian individuals might refuse to take part in this study. Some possible reasons include a potential lack of communication between OCPL staff and South Asian patients, language barriers, fear of discrimination, and personal preference. The OCPL has recently made efforts to increase ties with the South Asian community and has introduced a dysplasia clinic in a community with a high South Asian population.

7.2.4 OBS and BCCR databases

The BCCR database identified a large proportion of oral cancer cases (61%-69%) that were not present in the OBS database. This indicates that while the OBS is generally believed to receive the majority of oral biopsies in BC, it realistically receives approximately 31-38% of biopsies. This presents an important limitation to the generalizability of this study: while nearly all cases of oral cancer in BC in 2007 and 2013 were identified, data from the OBS is necessary to provide information regarding dysplasias and hyperplasias. It can estimated that the proportion of dysplasia and hyperplasia diagnoses received by the OBS is similar to the proportion of cancer biopsies received, which is less than half. However, there is no way of knowing what the true proportion of these biopsies is without collaboration with other pathology review services in the province; such collaboration is strongly recommended for future investigations. The OBS is recently introduced an online biopsy and referral system, which includes online requisition forms and the implementation of a new surveillance system, which will aim to monitor dental

practitioner activity within the screening network. This new system presents the opportunity to provide a more detailed account of the biopsies that come through the OBS pathology service, and will also provide an opportunity to network with other pathology services across the province.

On the other hand, the OBS database contained several oral cancer cases that were not found in the BCCR. Eight such cases were identified in 2007, and ten in 2013. This indicates that while these cases were diagnosed, they were not included within the cancer registry itself. It is possible that these cases did not receive care in BC, indicating that they either sought no care, or received care elsewhere, or that particular practitioners were potentially not aware of the referral pathway for cancer and hyperplasia diagnoses.

7.3 Access to Care

There were 4,484 biopsies received by the OBS in 2007, and 6,114 in 2013. This is an increase of 36% over the span of six years. This may be indicative of increased access to care, but also be attributable to increased awareness of the OBS itself. It is possible that, following the publication of the 2008 biopsy guidelines, more dental practitioners became aware of the OBS and opted to utilize this pathology service. An assessment of other pathology review services in BC would be necessary to determine if there were overall increases in the number of biopsies in the province, or simply a greater number of biopsies submitted to the OBS. The OBS received 35 South Asian cases in 2007, and 82 in 2013. This in an increase from 5.4% in 2007 to 9.5% in 2013. This

indicates that, whether for reasons of increased access to care or increased incidence, the proportion of South Asian biopsies in the OBS increased from 2007 to 2013.

The BCCR contained eleven South Asian cases in 2007, and decreased to five cases in 2013. This is a decrease from 3.6% in 2007 to 2.6% in 2013. This shows that, whether a result of decreased access to care or decreased incidence, the proportion of South Asian biopsies in the BCCR decreased slightly from 2007 to 2013.

Overall there was an increase in South Asian cases in the OBS, and a decrease of these cases in the BCCR. Possible reasons for this trend include that cases may be diagnosed earlier prior to cancer diagnosis, and hence resulting a decrease in case sin the BCCR. Since the OBS includes dysplasia and hyperplasias as well, it is possible that we may be seeing more of these cases, and decreasing cancer cases, which may indicate an increase in early detection.

The five LHAs with the largest number of dental practitioners in BC include Vancouver city centre, Burnaby, Surrey, Richmond, and Coquitlam. These areas had a steady proportion of dental practitioners (6.6% to 10.6%) and slightly lower proportion of South Asians compared to the general population, with the exception of Surrey. While 8% of dental practitioners are located in Surrey, and approximately 7.5% of the BC population reside there, nearly one third of all South Asians in the province are located here. It is interesting to note that so many South Asians reside in this area, representing good access to care for these South Asian individuals as Surrey is the region with the third highest concentration of dental practitioners in BC.

It would be important to identify South Asian dental practitioners and their locations in the province in order to better assess access to care for the South Asian population, as it is theorized that South Asian patients prefer to seek care from South Asian health care professionals.

7.3.1.1 Dental Network Capacity

While this study found that the total number of dental practitioners performing biopsies increased by nearly 50% from 2007 to 2013, the proportion of dentists and dental specialists in BC that performed biopsies remains small, at 4.7% in 2007 and 6.5% in 2013. General dentists may not feel comfortable performing biopsies due to a lack of expertise, and may prefer to refer to specialists with greater experience in this area. Dentists outside of Metro Vancouver and other major cities may benefit from continuing education regarding performing biopsies in order to better serve suburban and rural populations.

7.3.2 Biopsy Guideline Update

Lesions presenting at gingiva and buccal mucosa are considered low-risk in the general population, but considered high-risk in South Asian populations due to the possible presence of associated risk factors such as the use of areca nut and chewed tobacco. Results from this study indicate that approximately 50% of lesions in the general population occur at these sites, as well as approximately 65% of lesions in the South Asian population. The high rate of occurrence at sites considered low-risk in Western countries is a very interesting finding. Biopsy guidelines

introduced in 2008 by the CDSBC and the BCCA suggest "paying particular attention to the high-risk sites for the development of oral cancer including the lateral and ventral aspects of the tongue, floor of mouth and the soft palate complex." [108] Inclusion of gingiva and buccal mucosa as common sites for oral lesions is of high importance to reflect current findings.

These guidelines also identify tobacco and alcohol as major risk factors. While this is true for the general population in BC, it is important to bring awareness to additional risk factors for oral cancer which play a significant role in the South Asian immigrant population. An update on these biopsy guidelines that will reflect current information and cultural variety/competency is strongly encouraged.

7.3.3 South Asian Oral Cancer Prevention Programs

Fewer South Asian men were diagnosed with oral cancer in the BCCR. It would be beneficial to implement awareness and prevention initiatives targeting South Asian men, as well as initiatives focused on increase awareness of the link between the use of chewed substances and oral cancer. The use of questionnaires to gather data on risk habits would be of particular relevance to such programs. It is crucial to promote culturally competent care in order to encourage South Asian patients to feel comfortable disclosing information regarding risk habits to dental and medical professionals, and increase their participation in oral cancer prevention programs.

7.4 Limitations

This study accessed data from the OBS and the BCCR exclusively. A limitation of this approach is that there are other pathology review services within the province, which receive and process biopsies outside of the OBS. It would be important to investigate how these pathology services might be included in future analyses to provide increased accuracy regarding the number of types of biopsies in BC. This study is also subject to selection bias, in that only two databases were accessed, and we now know that the OBS only represents slightly over one third of all oral biopsies in the province. This gives the study a limited generalizability, and may not be accurately representative of the general population.

This study had a small number of cases, particularly South Asian cases in the BCCR, and therefore the study has limited generalizability. Pooling of data over a number of years would improve the sample size. It is also important to note that due to multiple statistical comparisons of the data, there is an increased probability that some of the results found to be significant were by chance.

There are also limitations related to the use of name recognition software programs. For example, name recognition software may not be able to distinguish individuals of mixed ethnicities, those with names who are not strongly associated with a certain ethnicity, or those who have adopted their partner's surname of a different ethnicity. Due to these considerations, ethnicity assigned through the use of name recognition software programs will never be

completely accurate. It is, however, an accurate method of obtaining data on ethnicity, particularly in the absence of such data.

7.5 Future Direction

Future investigations in this field could include other diagnoses, such as oral lichen planus and oral lichenoid lesions, which are believed to play a role in oral cancer progression [152,153] as well as OSF and verrucous configuration; obtaining a greater number of cases would facilitate these investigations. An increase in the number of cases would also allow for narrower, hence more detailed, grouping of data within the databases. For example, differentiating between Hindu and Sikh rather than categorizing both as South Asian would allow for the development of culturally-competent oral cancer prevention programs within various diverse South Asian communities. Similarly, a greater number of cases would allow researchers to distinguish between different risk habits, for example the use of betel quid with and without tobacco.

Future studies could, in partnership with other pathology services, investigate the number of oral biopsies that are seen outside of the OBS each year. Such research could provide definitive data regarding the total number of biopsies in BC, and would enrich data on dysplasias, as well as the ability to design prevention programs accordingly. The use of administrative data, such as population data, could also serve to locate biopsies completed by physicians, otolaryngologists, and other dental practitioners that may not be visible through OBS, giving more depth to the research.

Chapter 8: Conclusion

Oral cancer, dysplasia and hyperplasia trends vary between South Asians and the general population. Rates of cancer, dysplasia and hyperplasia are higher in South Asian males than males in the general population. South Asian cases are diagnosed at younger ages than in the general population, with the mean age at diagnosis below the age of sixty years of age. Lesion sites most common in South Asians include the gingiva and buccal mucosa. These lesion sites are common within the general population as well.

While access to care appears to have increased from 2007 to 2013 in terms of increased geographical diversity in the location of biopsies across BC, certain areas with high South Asian population densities have few dental practitioners and few to no biopsies being performed in these areas. This suggests that South Asian patients often travel to larger cities for biopsies, or seek care outside of the province. The total number of biopsies received by the OBS increased by 36% from 2007 to 2013, and the number of South Asian biopsies increased by 45%. The number of dental practitioners performing biopsies also increased, as well as the number of South Asian cases seen in the OBS. Risk habit and ethnicity information was not often collected in pathology reports and databases; dental practitioners should be educated regarding importance of this information in enriching the knowledge regarding oral cancer, particularly in immigrant populations. Some important considerations and next steps from this study include:

- Motivating dental practitioners to gather information on ethnicity and risk habits when collecting biopsies
- Setting standards regarding the inclusion of ethnicity data in BC and in Canada

- Consideration of variances in what constitutes ‘high-risk’ between different populations, and the impact of these considerations on screening and educating
- Increasing awareness regarding risk factors among various population
- Promoting cessation of risk habits across various populations
- Further investigation of spatial analyses
- Tailoring initiatives to reach areas at high-risk for oral cancer that may have poor access to care

In summary, South Asians present with different trends in oral precancerous and cancerous lesions, related to the presence of varied risk habits in this population; messages regarding oral cancer prevention should aim to be heard by high-risk populations. These trends and differences should inform the development of screening and health promotion programs, as well as continuing education of dental professionals.

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Appendices

Appendix A Sample OBS Pathology Report

Vancouver CoastalHealth
Promoting wellness. Ensuring care.

CoPath

Anatomical Pathology

Sun Set
Allogeneic Archive System

VANCOUVER COASTAL HEALTH
VANCOUVER GENERAL HOSPITAL
Department of Pathology and Laboratory Medicine
855 West 12th Avenue, Vancouver, BC, V5Z 1M9
Inquiry TEL 1-877-747-2522 FAX (604) 875-4797

Oral Pathology Consultation Report

Case Number: UD15- XXXX	**Patient's Name:**
Collect Date:	MRN:
Receive Date:	PHN:
Date Reported:	DOB/Gender:
	Ordering Physician:
	Copies To:

Final Diagnosis:
Tissue from left buccal mucosa: well-differentiated squamous cell carcinoma, the changes have involved the biopsy margins.

Electronically signed by Lewei Zhang, D.D.S.

Clinical History as Provided by Submitting Physician:
Differential diagnosis: Recurrent dysplasia
Incisional; 9 mm x 9 mm; left buccal mucosa; asymptomatic; red, nodular/granular, 3 months
This was not visible 6 months ago, tissue here was clear in WLN and AF July 2014 so I put 3 months for duration in as an estimation

Specimens Received:
A: 9mmx9mm left buccal mucosa

Gross Description:
Received is a single container labelled with the patient's name, demographics and LEFT BUCCAL MUCOSA. It contains a tan soft tissue fragment measuring 0.7 x 0.5 x 0.2 cm. The resection margin is inked blue. The specimen is bisected and submitted in toto in cassette A1.

VT/mo

Appendix B OBS Biopsy Requisition Form

Vancouver CoastalHealth
Promoting wellness. Ensuring care.

BC ORAL BIOPSY SERVICE
Vancouver General Hospital
Room 1400 JPPN1
910 West 10th Avenue,
Vancouver, BC, V5Z 1M9
Fax: 604-875-4797

For reports call 1-800-992-8801

Patient: _____ _____
(Last Name) (First)

Date of Birth: _____/ _____/ _____ **Sex:** M ☐ F ☐ **Ethnic Origin:** _____
Day Mon Yr

Care Card # _____ (MSP , RCMP, WCB please circle)

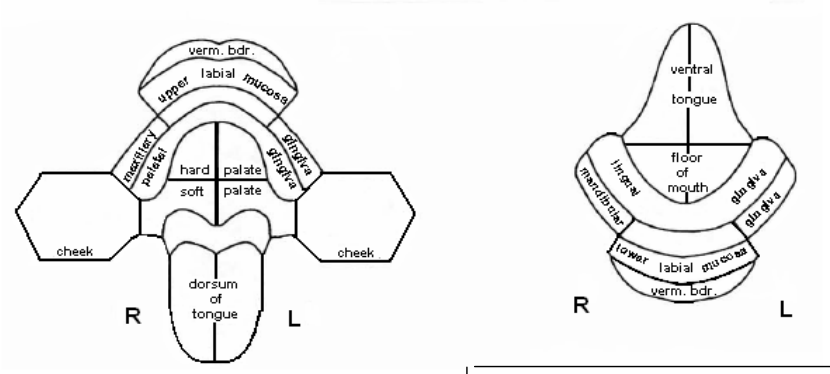
Date of Biopsy: _____/ _____/ _____ **X-ray Enclosed:** Y ☐ N ☐
Day Mon Yr

Clinical History

1. History of chief complaint. 2. Clinical/Operative findings. 3. Tobacco Use: Past ☐ Present ☐

Clinical Diagnosis _____

Indicate on the diagram below the exact site of the biopsy



8 7 6 5 4 3 2 1	1 2 3 4 5 6 7 8
8 7 6 5 4 3 2 1	1 2 3 4 5 6 7 8

Doctor: _____ **College #:** _____

Address: _____

Phone: _____ **Fax:** _____

Signature: _____

Appendix C OCPL Initial Questionnaire

BC Cancer Agency

INSERT PATIENT ID LABEL HERE

DATE FILLED: _____

Oral Study

(Confidential when completed)

This form asks a variety of questions about you and your environment, which may affect or be related to your health. The information you provide will help us better understand and prevent disease

Please complete each question as best you can even if you are not sure of your answer

Thank you for your time.

20020218- Q9 and Q10 removed

20010410- Q9 edit

ORAL STUDY QUESTIONNAIRE

1. In addition to being Canadian or a landed immigrant, what is your ethnic or cultural heritage?

   (Check one box only):
   - ☐ White
   - ☐ East or South-east Asian (eg. China, Japan, Indonesia, Philippines, Vietnam)
   - ☐ South Asian (eg. India Pakistan, Sri Lanka)
   - ☐ First Nations
   - ☐ Black
   - ☐ Other (Please Specify)_____

2. a) What is the highest grade (or year) of high school or elementary school that you have completed?
   Grade ___ Never attended school ____

   b) How many years of post-secondary school have you completed (college, university)?
   Years ___ None __

3. a) Have you ever used chewing tobacco?
   Yes ☐ No ☐

   b) Have you ever used betel nut?
   Yes ☐ No ☐

4. Have you ever regularly smoked cigarettes, cigars or pipes more than once per week for one year or longer? Yes ☐ No ☐

   If Yes, please specify:

   a) At what age did you begin smoking:
   Cigarettes? ____
   Cigars? ____
   Pipes? ____

   b) Do you currently smoke:
   Cigarettes? Yes ☐ No ☐
   Cigars? Yes ☐ No ☐
   Pipes? Yes ☐ No ☐

   c) If you have quit smoking, at what age did you permanently stop:
   Cigarettes? ____
   Cigars? ____
   Pipes? ____

d) Looking back over your entire life, on average, how many did you usually smoke *per day*?

	Before Age 20 years	In your 20's	In your 30's	In your 40's	In your 50's	60's & older
Cigarettes	_____	_____	_____	_____	_____	_____
Cigars	_____	_____	_____	_____	_____	_____
Pipes	_____	_____	_____	_____	_____	_____

5. Looking back over the last year, please think about your exposure to the smoke of others, either at home, at work, and in public places (such as restaurants, recreational facilities).

Are you regularly exposed to smoke of others:

At home?	Yes	☐	No	☐
At work?	Yes	☐	No	☐
In public places?	Yes	☐	No	☐

If Yes, to any of the above, please specify:

How often are you regularly exposed to smoke of others:

	Never	Less than once a month	More than once a month but less than once a week	At least once a week	Daily
At home?	☐	☐	☐	☐	☐
At work?	☐	☐	☐	☐	☐
In Public Places?	☐	☐	☐	☐	☐

6. Looking back over your entire life, please check the age periods in which you were daily exposed to the smoke of others.

Before Age 20 years	In your 20's	In your 30's	In your 40's	In your 50's	60's & older
☐	☐	☐	☐	☐	☐

7. Have you ever regularly consumed alcoholic beverages more than once per month for one year or longer? Yes ☐ No ☐

If Yes, please specify:

a) At what age did you begin drinking:

Beer?	____
Wine?	____
Spirits (liquor)?	____

b) Do you currently drink:

Beer?	Yes	☐	No	☐
Wine?	Yes	☐	No	☐
Spirits (liquor)?	Yes	☐	No	☐

c) If you have quit drinking, at what age did you permanently stop:

Beer?	____
Wine?	____
Spirits (liquor)?	____

d) On average, how much did you usually drink *per week*:

Beer	____	bottles
Wine	____	glasses
Spirits (liquor)	____	(shots – 1 oz.)

8. Have any of your immediate family members (parents, brothers/sisters, daughters/sons, grandparents, aunts/uncles related by birth not marriage) had cancer in the head and neck region (excluding skin cancer)? Yes ☐ No ☐

If Yes, please specify all who had head and neck cancer:

- ☐ Parents
- ☐ Brothers/sisters
- ☐ Daughters/sons
- ☐ Grandparents
- ☐ Aunts/uncles related by birth not marriage