# "Multi-National Analysis and Machine Learning-Base Prediction of Oral Cancer Trend and Incidence Globally, in South Asia and Bangladesh and Global"

By Name: Dawa Tshering ID: 21136005 Name: Sushila Limbu ID: 20236025 Name: Tshewang Palden ID: 20236024

A thesis submitted to the Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of Bachelor of Science in Biotechnology.

Department of Mathematics and Natural Sciences.

Brac University

August, 2024

©2024. Brac University

All rights reserved.

# Declaration

It is hereby declared that

- 1. The thesis submitted is my/our own original work while completing degree at Brac University.
- 2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
- 3. The thesis does not contain material which has been accepted, or submitted, for any other degreeor diploma at a university or other institution.
- 4. We have acknowledged all main sources of help.

# Student's Full Name & Signature:

Student Full Name: Dawa Tshering

Student ID: 21136005

Student Full Name: Sushila Limbu

Student ID: 20236025

Student Full Name: Tshewang Palden

Student ID: 20236024

# Approval

The thesis/project titled "Multi-National Analysis and Machine Learning-Base Prediction of Oral Cancer Trend and Incidence Globally, in South Asia and Bangladesh" submitted by

- 1. Dawa Tshering (21136005)
- 2. Sushila Limbu (20236025)
- 3. Tshewang Palden (20236024)

Of fall 2020 and Spring 2021 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Science in Biotechnology on August 27, 2024.

# **Examining Committee:**

1. Supervisor

Munima Haque, PhD

Associate Professor, Department of Mathematics and Natural Sciences

Brac University

2. Co-supervisor

Md. Akhtaruzzaman, PhD

Chief Medical Physicist, Evercare Hospital Chattogram

3. Program Director

Munima Haque, PhD

Associate Professor, Department of Mathematics and Natural Sciences

Brac University

4. Chairperson

Md. Firoze H. Haque, PhD

Chairperson, Department of Mathematics and Natural Sciences

Brac University

#### Abstract

This proposal includes a comprehensive examination of oral cancer frequency and patterns from a multi-national perspective, particularly regarding Bangladesh. This study will mainly involve the usage of secondary data review; comparative analysis; and predictive modeling to compare aspects such as incidence rates, screening practices, and healthcare systems across nations. Machine Learning algorithms can predict the future trends of oral cancer until 2030. A detailed analysis of 54 oral cancer patients in Bangladesh has revealed essential demographic, clinical, andtreatment factors. The majority of differences were observed in the aged of diagnosis, sex distribution, duration of treatment, frequency of screenings, incidence and survival rates. It was revealed thatBangladesh and Afghanistan recorded early diagnoses of cancer due the higher tobacco use whiledeveloped countries showed it is late due to the early detection techniques. In developed countries, early detection screening is common, unlike South Asian nations which practice symptomatic screening only. The rising death rates indicate inadequate medical facilities in South Asian countries like Afghanistan and Bangladesh. Predictive modeling indicates that by 2030 there will be a global rise in the incidence of oral cancer due to some risk factors like tobacco use, alcohol intake as well as human papillomavirus (HPV) exposure. Between the years 2023 and 2030, it is expected that the incidence in Bangladesh will increase by 4 percent. The leading public health programs should aim to increase the uptake of HPV vaccination, lowering betel nut consumption, and encourage exercise. These results call for an allinclusive public health policy toward the prevention, early detection, and efficient management of oral carcinoma.

#### **Keywords:**

- Oral Cancer
- Bangladesh
- Machine Learning
- Comparative Analysis
- Predictive Modelling
- Demographic Analysis
- Public Health policy
- Healthcare System

#### Acknowledgment

We would like to express our gratitude towards Dr. Md. Firoze H. Haque, Chairperson of the Department of Mathematics and Natural Sciences, BRAC University, whose initiation in the integration of the Research course into our curriculum has greatly enhanced our experience.

Secondly, we are thankful to our supervisor, Dr. Munima Haque, Associate Professor and Course Coordinator of the Biotechnology Program at the Department of Mathematics and NaturalSciences, BRAC University, for guiding, supporting, and sharing knowledge with us throughout this journey.

Next, we would like to express our heartfelt gratitude to our research collaborator, Dr. Md. Aktharuzzaman, Chief Medical Physicist of Evercare Hospital Chattogram who helped us collect primary data and believed in us. Similarly, we areextremely grateful to our research contributor, Dr. Rubama Karim, Department of Radiation Oncology, Ahsania Mission Cancer and General Hospital, Dhaka, who also provided us with primary data, and without that effort, our research wouldn't have been completed. We are indebted to your collective efforts and professionalism which was the cornerstone of our thesis experience.

Finally, we are grateful to all our friends and seniors whose encouragement and support helped usmove forward and ultimately to a successful completion of this thesis. Your advice and insights have always been invaluable, helping us to direct even through complicities.

Sincerely,

Dawa Tshering (21136005)

Sushila Limbu (20236025)

Tshewang Palden (20236024)

# **Table of Contents**

Sl.No	Section Title	Page. No
1	Declaration	i
2	Approval	ii
3	Abstract	iii
4	Acknowledgement	iv
5	Table of Contents	v-vii
6	List of Tables	viii
7	List of Figures	viii-x
8	List of Acronyms	xi
9	Chapter 1: Introduction	
	<ul> <li>1.1 Background and Significance of Oral Cancer</li> <li>1.2 Research Aims and Objectives</li> </ul>	1-3
	<ul><li>1.3 Scopes of the study</li><li>1.4 Research Questions and Hypothesis</li></ul>	
10	Chapter 2: Literature Review	
	2.1 Definition, incident and mortality	
	2.2 Types of Oral Cancer	4-27
	2.3 Risk Factors of Oral Cancer	
	2.4 Stages of Oral Cancer	
	2.5 Diagnosis and Screening methods of	

	Oral Cancer.	
	2.6 Treatment Options	
	2.7 Treatment available in different	
	countries	
	2.8 Screening methods used by different countries	
11	Chapter 3: Methodology	
	3.1 Research outline for Comparative Analysis, Predictions of Oral cancer	
	Incidence using Machine Learning, Oral	
	Cancer Death Rate Analysis and	
	Demographic, clinical and Treatment	
	Characteristics Analysis.	
	3.2 Materials and Methods for Dataset 1:	
	Secondary Data Analysis	
	3.3 Materials and Methods for Dataset 2:	28.20
	Oral Cancer Mortality Rate Analysis	28-39
	3.4 Materials and methods for Dataset 3:	
	Predictive Modeling of Oral Cancer	
	Incidence	
	3.5 Materials and Methods for Dataset 4:	
	Primary Data	
12	Chapter 4: Findings and Implications	
	4.1 Findings of Dataset 1: Secondary	
	Data Analysis	
	4.2 Findings of Dataset 2: Mortality Rates	
	Analysis of Oral Cancer.	

	<ul> <li>4.3 Findings of Dataset 3: Predictive</li> <li>Analysis of Oral Cancer in the world and</li> <li>Bangladesh</li> <li>4.4 Findings of Dataset 4: Primary Data</li> </ul>	40-74
13	Chapter 5: Summary and Limitations 5.1 Summary 5.2 Limitation	74-77
14	Chapter 6: Conclusion	78
15	Reference	78-90

# List of Tables

Name of the Table	Page Number
Table 1: Screening Methods by Country	26

# List of Figures

Name of the Figures	Page Number
Figure 01: Screening methods available by country	27
Figure 02: Comparative age of diagnosis of oral cancer across countries.	40
Figure 3: Gender distribution of oral cancer cases by country	42
Figure 4: Comparative analysis of oral cancer treatment duration by country.	43
Figure 5: Comparative analysis of oral cancer screening frequencies by country.	44
Figure 6: Comparative analysis of oral cancer survival rates by country.	45
Figure 7: Comparative analysis of oral cancer incidence rates by country.	46
Figure 8: Mortality rates of oral cancer in Afghanistan from 1990 – 2023.	48
Figure 9: Mortality rates of oral cancer in Bangladesh from 1990 - 2023.	49
Figure 10: Mortality rates of oral cancer in Bhutan from 1990 - 2023.	50

Figure 11: Mortality rates of oral cancer in India from 1990 - 2023.	51
Figure 12: Mortality rates of oral cancer in Maldives from 1990 - 2023.	52
Figure 13: Mortality rates of oral cancer in Nepal from 1990 - 2023.	53
Figure 14: Mortality rates of oral cancer in Sri Lanka from 1990 - 2023.	54
Figure 15: Mortality rates of oral cancer in USA from 1990 - 2023.	55
Figure 16: Mortality rates of oral cancer in Europe from 1990 - 2023.	56
Figure 17: Global oral cancer incidence from 1990 – 2023.	58
Figure 18: Predicted global oral cancer incidence from 2023 - 2030.	59
Figure 19: Oral cancer incidence of Bangladesh from 1990 - 2023.	60
Figure 20: Predicted oral cancer incidence of Bangladesh from 2023 – 2030.	61
Figure 21: Pie chart showing percentage of male and female participants.	63
Figure 22: Bar graph showing number of participants in each age group.	64
Figure 23: Pie chart showing dwelling of participants in form of percentage.	65
Figure 24: Pie chart showing history of any cancer in the family of participants in the form of percentage.	66
Figure 25: Pie chart showing history of oral cancer in the family of participants in the form of percentage	67

Figure 26: Bar graph showing smoking status of the participants.	68
Figure 27: Bar graph showing tobacco consumption status of the participants.	69
Figure 28: Bar graph showing alcohol drinking status of participants.	70
Figure 29: Bar graph showing betel quid chewing status of the participants	71
Figure 30: Bar graph showing HPV vaccination status of the participants.	72
Figure 31: Pie chart showing awareness status of participants in the form of percentage.	73

# List of Acronyms.

- 1. **OSC:** Squamous Cell Carcinomas.
- 2. VC: Verrucous Carcinoma.
- 3. SCSC: Sarcomatous Carcinomas.
- 4. **BSCC:** Basaloid Squamous Cell Carcinomas.
- 5. **PSCC:** Papillary Squamous Cell Carcinomas.
- 6. ASCC: Adenoid Squamous Cell Carcinomas.
- 7. ACC: Adenoid Cystic Carcinomas.
- 8. HPV: Human Papillomavirus.
- 9. SEER: Surveillance Epidemiology and End Result Program.
- 10. LINAC: Linear Accelerator Machine.
- 11. EGFR: Epidermal Growth Factor Receptor.
- 12. ICI: Immune Checkpoint Receptor.
- 13. PD-1 Inhibitor: Programmed Cell Death-1 inhibitor.
- 14. PDT: Photodynamic Therapy.
- 15. ECT: Electrochemotherapy.
- 16. AJCC: American Joint Committee on Cancer.
- 17. UICC: Union for International Cancer Control.
- 18. TNM System: Tumor size (T), Lymph Node Involvement (N) and Metastasis (M).
- 19. ENE: Extranodal Extension.
- 20. CIS: Carcinoma In-Situ.
- 21. OEC: Exfoliative Cytology
- 22. MRI: Magnetic Resonance Imaging
- 23. PET: Positron Emission Tomography
- 24. CT: Computed Tomography
- 25. FDG: Fluorodeoxyglucose
- 26. GBD: Global burden of Diseases
- 27. FNA: Fine Needle Aspiration
- 28. GHDx: Global Health Data Exchange.

# **Chapter 1: Introduction**

# 1.1 Background and Significance of Oral Cancer

Oral cancer is the 13th most common cancer in the world and it is linked to many risk factors. Among the risk factors, tobacco use, alcohol consumption, and Human Papillomavirus are the most common causes of this cancer. The primary sites for this cancer include lips, tongue, oral cavity, gingiva, and oropharynx. Despite the introduction and development of various treatment options for this cancer, developing countries and underdeveloped countries are still facing significant health concerns due to limited resources and facilities for diagnosis, screening, and treatment of this cancer (Aghiorghiesei et al., 2022; WHO, 2023; Cancer of the Oral Cavity and Pharynx - Cancer Stat Facts, n.d.). The nuanced understanding of its risk factors, epidemiology, screening methods, diagnosis, and treatment efficacies are vital for the development of targeted prevention and treatment options.

# **1.2 Research Aims and Objectives**

The Primary objective of this research is to thoroughly study and analyze oral cancerparticularly focusing on the Oral cancer scenario of Bangladesh. The objectives are;

- The thorough literature review to map and understand the current scenario of oral cancer research.
- The comparative studies and analysis of oral cancer across South Asian countries and developed countries like the USA and European countries to observe the global pattern of oralcancer and disparities.
- The use of machine learning applications to predict the future scenario of oral cancer in the world and Bangladesh and its comparative analysis.
- The in-depth examination and studies of oral cancer in Bangladesh, particularly focusing on challenges and epidemiological trends.

# **1.3 Scope of the study**

This study explores the oral cancer scenario across South Asian countries including Afghanistan,Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka, and developed countries like the USA and European countries but particularly focusing on Bangladesh. Through the analysis of data fromthose nations, the study aims to provide the global perspectives of oral cancer comprehensively. The wide categories of data including demographic information, clinical features, and epidemiology will be used to provide the detailed landscape of oral cancer.

# **1.4 Research Questions and Hypothesis**

# **1.4.1 Research Question**

- What are the prevailing global patterns in oral cancer indicated by data collected from diverse countries?
- What role do lifestyle behaviors, such as tobacco use, alcohol consumption, and dietary habits, play in shaping oral cancer incidence and progression in Bangladesh?
- How can collaborative efforts between healthcare professionals, policymakers, and communitystakeholders be leveraged to address the rising burden of oral cancer and reduce disparities inaccess to care and outcomes across diverse populations?
- To what extent does the oral cancer landscape in Bangladesh compare and contrast with that of other countries under investigation?
- How accurate and reliable are machine learning algorithms in forecasting future trends in oralcancer incidence on both a global scale and specifically in Bangladesh?

# 1.4.2 Hypothesis

- There are significant differences in oral cancer incidence and nature of oral cancer in Bangladesh and other countries that are under study.
- The trend of oral cancer in Bangladesh might be attributed to certain risk factors and demographic details which are more common in Bangladesh compared to other countries which are under study.
- ◆ The screening and treatment facilities are almost similar in South Asian countries.
- ◆ The mortality rates of oral cancer are increasing every year.
- Machine learning applications can give the estimated projections of oral cancer in the world and Bangladesh, helping in the healthcare planning for the future.

#### **Chapter 2: Literature Review**

#### 2.1 Definition, incident, and mortality

Oral Cancer, commonly known as cancer of mouth is a condition in which the cells in the mouth or lips grow uncontrollably. This can happen when a mutation in the cell's DNA leads to the limitlessreplicative potential of abnormal cells (cancerous cells), invading normal cells, and metastasis. Most oral cancer happens in squamous cells. Oral cancer can develop in different parts of the mouth such as the pharynx, tonsils, salivary glands, the surface of the tongue, lips, roof of the mouth, gums, and inner lining of the cheeks (Mayo Clinic, 2024). Oral cancer is a complex disease influenced by both genetic and environmental factors. According to an article by The Oral Care Foundation, a mutation in the p53 gene of chromosome number 17 plays a significant rolein oral cancer development. Normally, the p53 gene or TP53 gene acts as a tumor suppressor generegulating the cell's growth and division preventing the development of a tumor. However, when the p53 gene gets mutated, it loses its ability to actively prevent the cells from dividing thereby leading to tumor, gain-of-functions, invasion, lack of apoptosis, and metastasis. On the other hand, human papillomavirus (HPV) can promote the development of cancer by inserting pieces of its DNA into a person's cells. This can trick the human cells into making proteins such as E6 and E7which can turn normal cells into cancerous ones. Formation of these proteins can lead to the degradation of p53 genes promoting uncontrollable cell growth (The Oral Cancer Foundation, n.d). The environmental factors that influence the development of oral cancer include smoking, chewing tobacco, consumption of alcohol, use of betel quid, and risky lifestyles such as poor hygiene (Asian Pacific Journal of Environment and Cancer, 2024). There are various characteristics due to normal cells can be differentiated with cancerous cells. Normal cells respond to growth signals by stopping the growth when it's enough; however, cancer cells become autonomous in growth signals acquiring the ability to increase uncontrollably. The normal cells undergo programmed cell death after the cell matures or is damaged; however, cancer cells suppress genes and pathways that normally initiate the cells to die. The blood vessels in normal cells aid in the normal repair and growth of the cells; however, in cancer cells, tumor angiogenesis occurs where cancer cells have their own blood vessels and blood supply. The normal cell appears uniform under the microscope; however, cancerous cells vary in size and shape (Eldride, 2023).

According to the National Institute of Dental and Craniofacial Research (2023), the incident rate (2015-2019) for oral cancer shows 11.5 adults for every 100,000 individuals. The incidence rate depends on various factors such as age, race, and gender. There is a significantly higher rate of oral cancer occurrence for males than females. Also, the incident rate for White males is higher than for Black and Hispanic males which can be due to tobacco or alcohol consumption, genetic factors, access to health care, socioeconomic factors, and HPV vaccination. Furthermore, the oralcancer incidence rate is directly proportional to age; older people have more chances to develop oral cancer than younger age group people.

According to SEER (Surveillance, Epidemiology, and End Results Program), the mortality rate for oral cancer has decreased from 3.3 to 2.5 per 100,000 individuals from 1992 to 2020. It also shows that 5-year Relative survival (2013-2019) is about 68.5 % which means that 68.5% of peoplecan survive for 5 years after being diagnosed with oral cancer (National Cancer Institute, SEER, n.d). Also, if an individual has stage 1 or stage 2 oral cancer, the survival rate of 5 years is typically between 70 to 90 percent (healthline, 2020). Furthermore, the 5-year survival rate for localized cancer is 83 percent; for cancer that has spread to other parts of the body is 38 percent; and 64 percent for cancer that is spread to nearby lymph nodes (National Cancer Institute, n.d). According to the American Cancer Society (2024), it isestimated that America will have 58,450 new cases of oral cancer in 2024 with 13,230 deaths.

#### 2.2 Types of oral cancer

There are different types of oral cancer such as squamous cell carcinomas, lymphoma, minor salivary gland carcinoma, mucosal melanoma, and verrucous carcinoma.

# 2.2.1 Squamous Cell Carcinomas (SCC)

Squamous cell carcinomas (OSCC) are the most common types of skin cancer. It starts in squamous cells. Squamous cells are thin and flat cells found in the epithelial tissues in our mouth. The actual reason for this type of carcinoma is unknown however factors such as smoking, chewingtobacco, exposure to radiation, and genetic mutation also contribute to its formation. Generally, itis a slow-growing tumor affecting the hard and soft palate, gums, and cheek. In most cases, squamous cell carcinoma can be asymptomatic during its initial phase of development. It is characterized by white and red lesions with partly uneven surfaces and distinct borders (International Journal of Oral Science, 2023). The prognosis of this carcinoma depends on several factors such as the age of the patient, and the stageof the tumor; if the tumor stage is

low, the prognosis is good however, if it has undergone metastasis, the prognosis can be unpredictable, the health of the patient, whether the person is having tumor for the first time or is it recurring, etc (DoveMed, 2019). Patients who have OSCC can undergo varioustreatment options such as surgery, chemotherapy, and radiation therapy depending on size and stage of the tumor and health status of the patient. There are different types of OSCC such as verrucous carcinoma (VC), spindle cell/sarcomatous carcinoma (SCSC), basaloid SCC (BSCC), papillary SCC (PSCC), and adenoid SCC (ASCC) (National Library of Medicine, 2014).

#### 2.2.2 Oral Lymphomas

Oral Lymphoma can occur in the tonsil, soft tissues or jaw, salivary glands, and maxilla. Oral Lymphoma is a very rare type of cancer. There are two types of lymphoma such as Hodgkin's lymphoma and non-Hodgkin's lymphoma. Some of the treatment options for oral Lymphoma arechemotherapy, drug therapy, and radiation therapy. During the treatment, oral hygiene is considered very essential (National Library of Medicine, 2016).

#### 2.2.3 Minor Salivary Gland Carcinoma

Minor salivary gland carcinoma is a type of tumor that is formed from small glands. These small glands can be found on the roof of the mouth, inside the cheek, and under the lining of the tongue and lips. Generally, salivary gland carcinoma is categorized into 3 different histological grades based on cell differentiation, mitotic activity, and nuclear features grade 1, grade 2, and grade 3. Grade 1 are tumors that are well differentiated and closely resemble normal salivary glands. It hasslow growth and a good prognosis. Grade 2 is moderately differentiated and characterized by metastasis nature, infiltrating surrounding tissues. It has a poor prognosis compared to grade 1. Grade 3 salivary gland carcinoma is poorly differentiated and aggressive. It has rapid growth and a very poor prognosis (American Cancer Society, 2022). Some of the minor salivary gland carcinomas are adenoid cystic carcinoma. Some minor salivary gland carcinomas are more prevalent among women than men such as Polymorphous adenocarcinoma. Some of the treatment options for salivary gland carcinoma include surgery, chemotherapy, radiation therapy, immunotherapy, targeted therapy, and palliativecare (Mayo Clinic, 2024).

#### 2.2.4 Mucosal Melanoma

Mucosal Melanoma for oral is a very rare type of cancer. The initial stage of the cancer might show loss of pigmentation, or change of color in the area where the tumor is developing. It can develop rapidly with a poor prognosis. The actual reason for the cause of this type of cancer is unknown however factors such as drinking alcohol, chewing tobacco, malignant changes in a person's melanocytes, and genetic mutation can increase its cause. A person can appear asymptomatic until the later stage of the cancer development. A scoring system (A, B, C, D) is used to differentiate between malignant and benign oral melanoma. Radiotherapy and immunotherapy are the primary treatment options for mucosal melanoma (Medical News Today, 2023).

# 2.2.4 Verrucous Carcinoma

Verrucous Carcinoma is a type of oral cancer often seen in men. It is a very rare type of cancer formed due to atypical squamous cell lining. Like most of the rare types of oral cancer, this also does not show any symptoms at its initial stages however, as it develops, it is indicated by soreness, redness, or whitish patches inside your mouth. Like most oral cancers, factors such as drinking alcohol, chewing tobacco, genetic mutation, and smoking can increase the risk of verrucous carcinoma. This type of cancer has a very slow growth rate and it has a good prognosis. Some of the treatment options for verrucous carcinoma include radiation therapy, chemotherapy, immunotherapy, laser therapy, cryotherapy, and targeted therapy (Healthline, 2024).

## 2.3 Risk Factors of Oral Cancer

#### 2.3.1 Tobacco Use

Tobacco use is a strong risk factor for oral cancer. Several chemicals present in tobacco and smoking kill tissues in the lips and mouth area and provide the perfect environment for malignant transformation. Polycyclic aromatic hydrocarbons, nitrosamines, and heavy metal compounds in tobacco smoke cause cellular mutations that develop into tumors, and cohort studies showuniformly positive associations between smoking and an increase in oral cancer incidence (Jiang et al., 2019).

#### **2.3.2 Alcohol Consumption**

It is widely acknowledged that alcohol consumption is a well-established risk factor for oral cancerthat operates through multiple biological pathways. Ethanol and its metabolites cause oral tissue oxidative damage, DNA injury, and inflammation, initiating and promoting tumorigenesis within the tissue. The relationship between alcohol consumption and oral cancer risk is dose-dependent and has been consistently found in prospective epidemiological research, and heavy drinkers are at the highest risk (Rumgay et al., 2021).

#### 2.3.3 Human Papillomavirus (HPV) Infections

HPV infections are majorly responsible for oral cancer and occur through high-risk HPV strains which include HPV-16 and HPV-18. They commonly integrate into the oral epithelial cells' DNAleading to malignant transformation. Numerous epidemiological studies associate HPV infection with oral cancer; oropharyngeal cancer is primarily linked with unique clinical and molecular characteristics. The consensual presence of HPV DNA in oral cancer tissues supports a causal relationship. HPV infections have a great contribution to the multifactorial cases of oral cancer, especially among the young population with no history of traditional oral cancer risk factors (Haghshenas et al., 2022). HPV vaccine is thus an essential primary prevention measure against high-risk strains that could augment the occurrence of HPV-related oral cancers. Further, notwithstanding the unknown factors, targeted measures such as vaccination are still vital to alleviate the burden of HPV-related oral cancers.

#### 2.3.4 Age

Older age is a major risk factor for oral cancer, presenting as an incidence rate that rises with age. Age is thus indicative of a potential causal association, because of the direct link with an increasing lifetime exposure to risk factors and cellular changes that may support cancer initiation and progression. Indeed, older age is a major risk for oral cancer, with the great bulk of cases occurringin people aged 45 to 55 and older (Risk Factors: Age, 2021). Further, given the non-modifiable nature of age, regular screening should ideally help ensure that timely treatment and diagnosis are assured. An intricate relationship of additional factors in individual susceptibility and severity is evident to explain why not all older patients eventually develop oral cancer. It is critical that howage interacts with other risk factors is comprehensively explored to provide insights for developing effective preventive and intervention strategies for oral cancer in older age.

#### 2.3.5 Sun Exposure

Sun exposure has been identified as one of the leading causes of oral cancer, with most cases resulting from the sun's harmful ultraviolet radiation on oral tissues. Epidemiological studies havedemonstrated that oral cancer is more common in areas with high UV radiation from sun exposure(Agrawal et al., 2013). These relationships imply that there is a natural cause-effect relationship, and this assertion is also consistent with the biological mechanism of action.

#### 2.3.6 Poor Oral Hygiene

Poor oral hygiene is another risk factor for oral cancer and suboptimal dental care measures like regular brushing, flossing, and dental examination can prevent it. Epidemiological studies have consistently associated poor oral hygiene and oral cancer, demonstrating oral poor hygiene as a proven risk factor. Hence, poor oral hygiene exerts a causal factor in the oral cavity, predisposing to oral cavity cancer. Poor oral hygiene facilitates the accumulation of dental plaque, inflammatory gum disease, constant inflammation, and a conducive environment for cancer initiation and progression in the oral cavity (Mathur et al., 2018).

#### 2.3.7 Diet

Diet is another established risk factor for oral cancer, and some dietary practices are associated with increased oral cancer risk. Epidemiological evidence from multiple studies indicates an increased risk of oral cancer with the consumption of processed meats, red meats, and foods rich in sugars. This association has the capacity for causality, as supported by biological mechanisms (Rodríguez-Molinero et al., 2021). Dietary exposures cause an attributable fraction of oral cancercases, particularly in communities with large quantities of such foods consumed.

#### **2.3.8 Family History**

A family history of oral cancer is a well-recognized risk factor for oral cancer, possibly indicating a genetic predisposition to the condition. The observed relationship between oral cancer and a family history of the same disease meets critical appraisal criteria and allows causal inference. Although not all people having a family history develop these conditions, genetic consultation and predisposition testing are crucial for efficient identification and preventive surveillance measuresapplication (Radoï et al., 2013).

#### **2.3.9 Chronic Irritation**

One more established causal factor of oral cancer is chronic irritation due to long-lasting exposure of oral tissues to various irritants. These might include rough teeth surfaces, badly fitting dentures, or other mechanical, chemical, or physical stimuli. Continuous irritation might lead to chronic inflammation and tissue damage, followed by cellular changes in the oral mucosa that can be conducive to cancer development (Piemonte et al., 2018). In the majority of cases, chronic irritation is an avoidable cause of the condition.

#### 2.3.10 Weakened Immune System

The weakened immune system is one of the risk factors of oral. A weakened immune system exposes the oral cavity to the risk of cancer development as the body's ability to identify and eliminate abnormal cells is significantly weakened. Higher oral cancer incidences have been observed in persons with a weakened immune system, such as persons living with HIV/AIDS or under an immunosuppressive medication (Patini et al., 2023).

#### 2.3.11 Betel Quid Chewing

Chewing of betel quid is the most common habit of people in South Asian countries and has beenwidely regarded as the leading cause of oral cancer. The carcinogenic substances that damage theDNA and ultimately lead to oral cancer. This has also been supported by the epidemiological studies conducted which revealed that betel quid chewing increased the likelihood of oral cancer (Guha et al., 2014).

#### **2.3.12 Occupational Exposure**

One of the factors leading to oral cancer is occupational exposure. Occupational exposure occurswhen individuals are exposed to carcinogens in the working environments. Carcinogenic substances such as asbestos, formaldehyde, and wood dust result in the damage of DNA in the oralmucosa which causes inflammation causing oral cancer (Barul et al., 2017).

#### 2.3.13 Gastroesophageal Reflux Disease (GERD)

Gastroesophageal reflux disease (GERD) is an indigestion condition that occurs when the stomachacid goes back into the esophagus and causes heartburn and regurgitation. This GERD is one of the risk factors of oral cancer as Long-standing exposure of our oral tissues to gastric refluxate due GERD causes inflammation and electrophoretic changes. There are suspicions from epidemiological reports that GERD accounts for Oral cancer although it is not well illustrated howmuch risk GERD poses to oral carcinoma (Tran et al., 2023).

#### 2.4 Stages of Oral Cancer

The staging of oral cancer according to the American Joint Committee on Cancer (AJCC), the World Health Organization (WHO), and the Union for International Cancer Control (UICC) depends on the TNM staging system (Kato et al., 2020). The TNM system stands for Tumor size (T), lymph Node involvement (N), and Metastasis (M) respectively.

# **2.4.1 Tumor** (T)

The T in the TNM staging system of oral cancer refers to the tumor, which includes the details regarding the size of the tumor as well as its depth within the oral cavity. The T stage is classified from T1 to T4 with each section indicating different descriptions of the tumor. In the T1 stage, thetumor is located within the tissues of the mouth and the size is 2 cm or smaller in diameter with adepth of less than 5 millimeters (Oral and Oropharyngeal Cancer - Stages and Grades, 2023). Similarly, in the T2 stage, the size of tumors is either 2 centimeters or smaller but deeper than 5 millimeters, extending up to 10 millimeters, or larger than 2 centimeters but no larger than 4 centimeters with a depth of 10 millimeters or less. In the T3 stage, the cancer progresses much further to a size greater than 2 cm but no smaller than 4 centimeters and deeper than 10 mm. T4 issubdivided into T4a and T4b. T4a refers to the tumor that is extended beyond the mouth and invades surrounding regions like skin, bone, or cavities of facial hair. On the other hand, T4b signifies the spread of the tumor into adjacent areas like the base of the skull, space behind the jaw, or the region of the neck surrounding major arteries like the carotids

#### 2.4.2 Lymph Node Involvement (N)

The second stage in the TNM staging system is the lymph Node involvement and this staging mainly includes the condition of the lymph nodes, which are kidney-shaped structures of the immune system found at the meetings of major blood vessels in the neck, thorax, axilla, and abdomen. The key function of lymph nodes is filtering fluids from interstitial soft tissues and sending them back to the vascular vessels of the immune system (Bujoreanu & Gupta, 2023). In the context of oral cancer, the lymph nodes are assessed to find the presence of cancer, whether itcontains the size of the node affected and also the location of the node concerning the neck, and whether cancer has invaded surrounding tissue through a condition called extranodal extension(ENE). The N stage of oral cancer is further classified into N0, N1, N2, and N3.

No refers to the absence of tumor cells in the lymph nodes. N1 shows the tumor in one of the lymph nodes that is on the same location as the neck. The size of the cancer is smaller than 3 centimeters and the tumor has not invaded the surrounding tissue (Cancer Staging, 2022). N2 is further divided into three subcategories: N2a, N2b, and N2c. N2a shows a tumor that has a size of3 centimeters to 6 centimeters without extra nodal extension in one single lymph node that is located at the exact location of the primary site. N2b indicates tumors on multiple lymph nodes inthe same location as its primary site with their sizes all lower than 6 centimeters and without extra nodal extension. N2c also indicates cancer in lymph nodes with a size lower than 6 centimeters without spreading into the surrounding tissue. N3 is further divided into N3a and N3b. N3a refersto a condition in which one lymph node that has a size larger than 6 centimeters contains tumor cells without extra nodal extension. N3b signifies any number of lymph nodes with tumor cells, with the tumor invading the tissues surrounding the lymph nodes.

#### 2.4.3 Metastasis (M)

The third stage in the TNM staging system is Metastasis which indicates if the tumor has invaded and reached different tissues and organs of the body. The Metastasis stage is divided into stages namely M0 and M1. M0 shows that the tumor has not invaded and reached other parts of the body while M1 indicates the invasion of tumor cells' secondary sites such as tissues and organs other than its primary location such as the lungs, liver, bones, etc (Rosen & Sapra, 2023).

Doctors combine the information from the T, N, and M to find the stage of the cancer. For instance, in the case of oral cancer, it is classified into 5 stages starting from stage 0 to stage 4. The stages are shown in Roman numerals I, II, III, and IV.

#### 2.4.4 Stage 0 or Carcinoma in Situ (CIS)

Stage 0 cancer is also called carcinoma in situ (CIS) and it signifies the early stage of cancer due to this, doctors often call it pre-cancer. Abnormal cells are found at the linings of the lips and oralcavity. Such abnormal cells can lead to tumor cells and invade surrounding healthy tissue (Tis, N0, M0). If the pre-cancer is not treated on time, it will become invasive and cause metastasis (Cheung et al., 2019).

# 2.4.5 Stage I

At this stage, the cancer has been formed. The size of the tumor is 2 cm or less than 2 cm, and theinvasion depth is 5 mm or less than that. The tumor in this stage is not in the lymph nodes, tissues, and organs of the body ( $T_1$ ,  $N_0$ ,  $M_0$ ).

#### 2.4.6 Stage II

In this level, the scale of the tumor is two cm or less, even as the invasion depth lies between five and 10 mm. The tumor at this level also can be greater than 2 cm but much less than four cm withits intensity of invasion at 10 mm or less. The tumor has not reached lymph nodes or different tissues and organs of the body (T2, N0, M0) (Cheung et al., 2019).

#### 2.4.7 Stage III

In Stage III the tumor size is more than 4 cm, with an invasion intensity of more than 10 mm. Thetumor has now not reached lymph nodes or other components of the body (T3, N0, M0). Stage IIItumors also can exhibit another shape. A cancer in a single lymph node that is three cm or less than that without the presence of ENE and has not reached other body tissues and organs (T1 to T3, N1, M0).

#### 2.4.8 Stage IVa

At this level, the tumor consists of the encircling regions which include the mandible, muscle mass of the tongue, maxillary sinus, and skin or tumor. If the tumor has reached the lymph node, it willbe the only node in the same location as that of the primary site and the cancer in this stage will be3 cm or less than that without ENE. The tumor still has not invaded other body tissues and organs(T4a, N0 or N1, M0).

Stage IVa can also exhibit another form in which the tumor is small and has not invaded nearby regions. The tumor has reached 1 or more lymph nodes, but the sizes are less than 6 cm without ENE. Still, the cancer has not invaded other tissues and organs of the body (T1 to T4a, N2, M0).

#### 2.4.9 Stage IVb

The first form of Stage IVb is that the tumor can be of any size and the cancer is found in a lymph node and with its size larger than 6 cm with or without the presence of ENE. Cancer has still not reached other body parts (any T, N3, M0). Another form of this stage is that the tumor has reached the bones and muscles at the mouth or the base of the skull, the arteries present internally (carotidarteries). The tumor may involve the lymph nodes, but it has not invaded other body parts (T4b, any N, M0).

#### 2.4.10 Stage IVc

At this stage, the tumor has become invasive and caused metastasis reaching to other tissues and organs such as the lungs and bones (any T, any N, M1).

#### 2.5 Diagnosis and Screening Methods for Oral Cancer

#### 2.5.1 Diagnosis of Oral Cancer

Prompt and accurate diagnosis is essential for timely intervention and improved patient outcomes.Some of the vital diagnostic methods and techniques are described below:

#### **2.5.2 Physical Examination**

Physical examination is the primary assessment method for oral cancer. It mainly includes visual inspection and palpation in which lymph nodes, salivary glands, and other external structures are examined first and then followed by an internal assessment of the buccal cavity (Borse et al., 2020). In such internal and external examinations, the examiner will mainly focus on abnormalities like irregularities, swelling, and superficial anatomy changes, soreness, lumps and difficulties in jaw movement, swallowing, and chewing. The palpation method is mainly done externally as wellas internally on the parotid gland, a submandibular and sublingual gland.

#### 2.5.3 Histopathological Examination

Histopathological examination revealed that oral cell cells exhibit a range of characteristics extending from slow-growing tumors to highly aggressive ones with huge invading potential. From *histopathological perspective*, this ability of oral cancer cells to progress within the oral cavity, from initial dysplasia to advanced malignancy is crucial in identifying the growth of cells, maturation abnormalities, atypia, and alterations in structures of epithelial tissues (Talpoş et al., 2022). The identification of oral lesions are vital step in histological investigations due to the manifestations of histopathology in regions that seemed unaffected during physical examination.

#### 2.5.4 Vital staining Techniques

Tissue staining techniques can also be used in oral cancer diagnosis, in which tolonium chloride (toluidine blue) staining is commonly used for the identification of abnormalities in the oral cavity.Toluidine blue is a dye that stains tissue components that have acidic properties like RNA and DNA (Sudheendra et al., 2014). Since it is cheap and easy to access, this technique is very helpfulin areas that are limited in resources. Toluidine blue when blended with Lugol's iodine aids to the identification of inflamed lesions and the prediction of malignant lesions differentiation which makesit very important in the diagnosis of oral cancer.

# 2.5.5 Biopsy

The biopsy is the removal of tissues from a suspected area by surgical methods and treating it under microscopic examination to confirm the presence of oral cancer. Different types of biopsiesinclude brush biopsy, incisional biopsy, and exfoliative cytology.

#### 2.5.5.1 Brush Biopsy

Brush Biopsy includes the epithelial cells from oral lesions being scraped painlessly. This methodis not expensive and a very sensitive method with 90% sensitivity (Borse et al., 2020). This methodmainly targets suspicious lesions, along with colored oral lesions.

# 2.5.5.2 Exfoliative Cytology

Exfoliative cytology, on the other hand, is a non-invasive technique that heavily relies on epithelial physiology which involves the collection of exfoliated cells for microscopic examination for easydetection of oral cancer (Borse et al., 2020). However, exfoliative cytology lacks sensitivity and specificity.

# 2.5.5.3 Incisional Biopsy

In an incisional biopsy, a tissue sample is selectively chosen as representative for diagnosis upon indication of malignancy via exfoliative cytology (OEC). As compared to other techniques it is highly accurate as it targets specific regions of the lesion, making it extra useful when full lesion removal is not feasible like in lichen planus or when during the uncertainty of clinical diagnosis (Borse et al., 2020). Samples collected from biopsy are sent to laboratories for further examinationfollowed by experts using microscopic techniques and unique staining agents to classify various types of cancer cells based on their structural changes. Although biopsy is the standard method indiagnosis for cancers, its drawbacks include the invasive, painful, and surgical intervention of thistechnique.

# 2.5.6 Radiology and Imaging Techniques

Different advanced imaging techniques, including magnetic resonance imaging (MRI), positron emission tomography (PET), and computed tomography (CT) have been employed to diagnose oral cancer (Zhou et al., 2022).

# 2.5.6.1 Magnetic Resonance Imaging (MRI)

MRI offers imaging of structures of the oral cavity and adjacent areas in detail, providing valuable discrimination of soft tissues which is crucial in assessing the spread of tumor along with the depth of its invasion, and extent of lymphadenopathy (Borse et al., 2020). The multiplanar views and high-contrast resolution make MRI accurate in identifying the spread of oral cancer to nearby soft tissues. Moreover, MRI helps in the identification of the source of a lesion, its position, and margins which makes it a supportive method for biopsy for oral cancer screening.

#### **2.5.6.2** Positron Emission Tomography (PET)

PET scans are used in assessing the spread of cancer cells to lymph nodes and other tissues and organs. In this technique, radioactive dye is administered orally or intravenously and emitted gamma rays from the decay of positron are scanned. This method helps in lymph node staging, and even if some other metastasis is detected, the treatment technique remains the same if nodes are separate (Borse et al., 2020). PET scans use fluorodeoxyglucose (FDG) to find the state of lymph nodes, which shows the vitality of PET scanning in the early detection of oral cancer.

#### 2.5.6.3 Computed Tomography (ICT)

CT scans use radiation like X-rays and computer technology to produce body images, which facilitates the localization of malignant lesions and their assessment. Easily accessible and effective cost-effective, CT scans are a vital standard imaging tool for the detection of neck and head cancers (Pulumati et al., 2023). However, it cannot detect early-stage lesions properly in thebuccal cavity, unless enhanced with intravenous contrast medium.

#### 2.5.7 X-ray

X-rays, like panorex scan, help find cancer spread beyond the mouth and oropharynx, along with jawbones to show the presence of tumor cells in the form of images (Borse et al., 2020). On top ofthat, radiological methods like fluoroscopy also help in finding cancer along with its stages. Optical spectroscopy methods like laser-induced tissue autofluorescence are some of the novel oral cancer diagnosis methods.

#### 2.5.8 Biomarker Detection and Biosensors

Biomarkers expressed in saliva or serum can also help in oral cancer detection due to their overexpression during the onset of disease and correlate with alterations in metabolome, proteomeand transcriptome during initiation, promotion, and progression of the cancer. Vital biomarkers like TSG p16, and DNA ploidy are often expressed with oral malignancy progression, where p53protein expression is considered a primary indication (Umapathy et al., 2023). Salivary biomarkerslike circulating tumor DNA, extracellular vesicle, and miRNAs help in early oral cancer detection. Other advanced techniques such as Enzyme-Linked Immunosorbent Assay (ELISA), Polymerase Chain Reaction (PCR), Deoxyribonucleic Acid (DNA) arrays, immunohistochemistry, mass spectrometry, and Nuclear Magnetic Resonance (NMR) are employed in biomarker detection.

Nano-biosensor-based immunosensing has largely assisted in oral cancer diagnostics. Various biosensors such as electrochemical and paper-based types have been developed and electrochemical biosensors have been considered advanced and widely applicable owing to their quantitation ability and lower detection limits. Examples include electrochemical sensors like microRNA for oral cancer detection.

#### 2.6 Treatment Options

The treatment for oral cancer depends on various factors such as the size of the cancer, stage, location (if the cancer is a localized one or is spread to nearby lymph nodes and organs), age of the patient, and general health. Depending on the above information of an individual, the treatmentcan vary deciding whether to undergo surgery, radiotherapy, chemotherapy, or targeted medicineand immunotherapy. (National Health Service, 2023).

#### 2.6.1 Surgery

Surgery for oral cancer can be categorized as glossectomy, excision biopsy, mandibulectomy, maxillectomy, neck dissection, wide local excision, and dental implant. Glossectomy is the type of surgery that removes tongue cancer. This surgery depends on the size of the cancer, if it's small then a partial glossectomy is done however if the cancer is large, the larger part of the tongue maybe taken out. Excision biopsy is a type of surgery in which a part of the tissue is removed for examination to confirm whether that particular area has developed cancer or benign (The THANG Guide, 2022). Mandibulectomy is a type of surgery that removes part of the jawbone. This is done when the tumor has occurred very close or is connected to the jaw bone. This surgery is prevalent for oral cancer initiated at the lower gums or the floor of the mouth. There can be marginal or segmental mandibulectomy, marginal mandibulectomy includes the removal of the rim of the jawbone followed by allograft to cover the incision and segmental mandibulectomy includes the removal of the thick mandible followed by the rebuilding of the jawbone. Maxillectomy is a type of surgery to remove bones in the hard palate (roof of the mouth) Memorial Sloan Kettering Cancer Center (Mouth Cancer Surgery, n.d). Next, neck dissection is a type of surgery to remove lymph nodes on the neck to remove cancer or the possibility of spreading cancer to the sites. Wide local excision is a type of surgery that includes the removal of tumor tissues along with a margin of healthy tissues at the site of a tumor. The reason for the removal of the margin of healthy tissue is to ensure complete removal of the tumor cell. Reconstructive surgery is recommended to reconstruct the mouth, which helps regain the ability to eat and talk. It often uses allograft to reconstruct the mouth (Mayo Clinic, 2022).

#### 2.6.2 Chemotherapy

Chemotherapy is a type of therapy in which anticancer medicines destroy cancer cells. There are different types of medicines such as carboplatin, docetaxel, fluorouracil, cisplatin, and paclitaxel which can be used as adjuvant treatment, neoadjuvant treatment, chemoradiation or chemotherapy. Different drugs/ medicines are also used in combination with chemotherapy to treat oral cancer such as cisplatin and paclitaxel, carboplatin and paclitaxel, cisplatin and methotrexate, and cisplatin and 5-fluorouracil (Canadian Cancer Society). Drugs like carboplatin and cisplatin are alkylating agents used to treat damaged DNA to prevent cell proliferation (Cancer Research UK, 2022). Similarly, methotrexate and fluorouracil are antimetabolites that prevent RNA and DNA synthesis preventing cell proliferation. Also, docetaxel and paclitaxel are plant alkaloids that also interfere with cell proliferation. However, there are also several side effects when the healthy cells are affected while destroying the cancerous cells. Some of them are a weakened immune system, fatigue, diarrhea, loss of appetite, kidney and bladder issues, hair loss, heart problems, increased chance of infection, and low platelet count (Canadian Cancer Society, n.d).

# 2.6.3 Radiation Therapy

Radiation therapy includes the introduction of radiation particles in high doses or X-rays to destroycancer cells or delay their development. When this therapy is introduced, the division and the spread of the cancerous cells are hindered. According to the American Cancer Society (2021), radiation therapy can be used based on the stage of the oral cancer and in combination or alone. That is to say, radiation therapy itself can be used as a main treatment for people who cannot undergo other surgeries. It can also be used as an adjuvant therapy which is to kill any cancer cellsthat are left after certain surgery and cannot be seen with our naked eyes after performing certain surgery. Additionally, it can also be used as neoadjuvant therapy where large cancers usually shrink before performing other surgery. Also, it can be used as an alternative to chemotherapy while undergoing targeted drugs. Radiation therapy is sometimes used along with chemotherapy and is called concurrent chemoradiation therapy. Some oral cancers have a high risk of recurring after undergoing a particular surgery so, radiation therapy can be used in such cases. Tumors usually recur if it's very large, cancer that has spread to nerves (perineural invasion), two or more lymph nodes have cancers, cancer spread outside the lymph node capsules (extracapsular extension), or cancer larger than 3cm on the lymph node (Canadian Cancer Society, n.d). However, there are certain side effects of undergoing radiation therapy

which include dry mouth, damage of thyroid glands, osteoradionecrosis of the jaw, swelling of the head and neck, redness of skin in treated regions, and difficulty in swallowing (Medical News Today, 2023). Typically, there are two types of radiation therapy namely External beam radiation therapy (EBRT) and brachytherapy. In EBRT, before the treatment takes place, a patient is positioned on the treatment table and a CT scan is used to locate the exact location of the tumor; this is called the simulation process (NationalCancer Institute, 2018). During this simulation, the amount of radiation dose is determined. When the actual treatment occurs, EBRT makes use of a linear accelerator machine (LINAC) to deliver the beam of radiation precisely to the tumor location (Department of Radiation Oncology, n.d). The fractionation approach delivers a small dose of radiation for several weeks daily. When the X-rays are released, they interact with the atoms in the cells which release the electrons from the atoms resulting in the formation of free radicals. These radicals are highly reactive and can cause damage to the cells. The ionization radiation can also break the double standard DNA within the cell. When the cancerous cells undergo such damage, it cannot undergo repair as it lacks the repairing ability mechanism preventing the division and replication. The cancer cells then result in cell apoptosis eventually (National Cancer Institute, 2019). The nearby normal cells also getaffected by the radiation but recover over time.

#### 2.6.4 Targeted Drug Therapy

Targeted drug therapy uses specific drugs to target the molecules and the growth and proliferation of the cancer cells without affecting normal cells. These drugs can be used in combination with other therapies or can be used on their own. Some examples of targeted drug therapy are Cetuximab (Erbitux), Bevacizumab (Avastin), and Pembrolizumab (Keytruda). Targeted therapy is also called precision or personalized medicine (American Cancer Society, 2021). This therapy is classified into small molecular drugs and large molecular drugs: small molecular drugs are verytiny and can enter a cancer cell and block the cells by targeting it, and large molecular drugs workby weakening or destroying the enzyme or proteins on the surface of the cell (Targeted Cancer Therapy | Targeted Drug Therapy for Cancer, n.d.). Cetuximab (Erbitux) is a monoclonal antibody that targets Epidermal Growth Factor Receptor (EGFR) growth. EGFRs are proteins that are found on the surface of some cells and play an important rolein cell growth and division. When EGFR gets mutated, uncontrolled cell growth and division takeplace such as in oral cancer. When cetuximab is introduced through intravenous infusion, it inhibits the working of EGFR proteins and stops excessive growth of the cancerous cells. However, this treatment also has some side effects such as shortness of breath, itchiness, low blood pressure, heart

problems, sensitivity to the sun, tiredness, electrolyte abnormalities, muscle and joint pain, and nausea (Cancer Resources from Onocolink, Treatment, Research, Coping, Clinical Trials, Prevention, n.d.).

#### 2.6.5 Immunotherapy

Immunotherapy uses the immune system to fight oral cancer. Immune checkpoint inhibitor is a type of immunotherapy. Immune Checkpoint Inhibitors (ICI) are monoclonal antibodies that stimulate the immune system by blocking important regulatory systems known as checkpoints. It can be used in combination with other therapies such as radiotherapy and chemotherapy, and can also be used as a main therapy for various cancers. According to a medically reviewed paper by Pope (2023) on anti-PD-1 and anti-PD-L1 mAb, PD-1 receptor presents on the surface of T cells and PD-L1 present on different cells such as normal cells, immune cells, inflammatory cells, and tumor cells interacts acting as a checkpoint to prevent the immune system from initiating autoimmunity. The T cells also release cytokines (interferons) when they sense any threats such as the presence of tumor cells. However, the cancer cell takes advantage of this PD-1 and PD-L1interaction tricking and preventing the T cells from attacking the tumor cells. Also, when the T cells release interferons (IFN- $\gamma$ ), instead of acting as an immune response, it upregulates PD-L1 expression on tumor cells which sends inhibitory signals to T cells (Brahmer, et al, 2015). As a result, the tumor cells may proliferate and metastasis may occur. However, anti-PD-L1 (Avelumab, Durvalumab, and Atezolizumab) and anti-PD-1 (Nivolumab, Pembrolizumab, and Cemiplimab) block the interaction between PD-L1 and PD-1 enhancing the T cells activity against tumor cells. There are some side effects of ICIs which may include diarrhea, nausea, fatigue, vomiting, and itching reaction (National Cancer Institute, 2022).

# 2.6.6 Photodynamic Therapy

Photodynamic therapy (PDT) is a type of treatment that uses specific drugs named photosensitizers(such as porfimer sodium and aminolevulinic acid) followed by exposing the cancer area to a certain wavelength of light to kill the cancer cells. First, the photosensitizer is allowed to be absorbed by the cancer cells which is administered through the bloodstream or directly to the affected area. Then a laser or LED is introduced which activates the photosensitizer that produces a form of oxygen that destroys the cancer cells. Some of the limitations of PDT are that this treatment is feasible only in the areas where light can reach, patients with metastatic cancer cannotbe treated with this method, and it does not apply to people with certain blood diseases. After thetreatment by PDT, people are often sensitive to bright

lights and sunlight, so they should stay indoors (PDT | What is PDT? | Photodynamic Therapy, n.d.).

# 2.6.7 Electrochemotherapy (ECT)

Electrochemotherapy is a treatment for oral cancer in which chemotherapeutic drugs such as cisplatin or bleomycin are delivered into tumor cells followed by exposing it to high-voltage electric pulses that permeabilize the tumor cells' membrane. These drugs are used in a minimum inhibitory concentration reducing the side effects and making it tolerable for the patients. This method of treatment doesn't affect the healthy cells surrounding the cancer cells. Some limitations of ECT are it is effective for the small size of tumors, and the electric field distribution determines the efficiency of ECT (Morozas et al., 2024).

# 2.6.8 Hyperthermia therapy

Hyperthermia Therapy is a type of treatment that utilizes heat to kill cancer cells. Ultrasonic hyperthermia is a type of hyperthermia that is very common for treating oral cancer. It can be used in combination with other treatments such as chemotherapy and radiotherapy (What is Hyperthermia? | Hyperthermia to Treat Cancer, n.d.).

# 2.6.9 Cryotherapy

Cryotherapy is a type of oral cancer treatment that uses substances like Agron gas, liquid nitrogen, or liquid nitrous oxide creating an extremely cold condition to kill abnormal tissues. (31). It is usedfor the treatment of oral cancer such as oral squamous cell carcinoma and oral verrucous carcinomaand precancers such as oral verrucous hyperplasia and oral leukoplakia (30). This method can be used to treat both internal and external tissues. If the abnormal tissue or tumor is located inside themouth, an instrument named cryoprobe is through small cuts and if the tumor is located at an external location, a swab or other devices are used to apply the freezing substance. Limitations of cryosurgery can be bleeding, loss of feeling, swelling, or skin infections however, it's also considered minimally invasive treatment (Professional, 2024).

#### 2.6.10 Laser therapy

Laser therapy makes use of high-energy wavelengths which are very precise with narrow beams to shrink or activate chemicals to kill tumor cells. Three different types of lasers are used such as carbon dioxide, Neodymium: yttrium aluminum garnet, and Argon. Limitations of laser are someof these treatments may not last long so, they might be repeated and it is very costly (Laser Treatment for Cancer, n.d.).

#### 2.6.11 Palliative care

Palliative care is also one of the treatments for oral cancer patients to improve the quality of life by taking into account not just science-based treatment but also the spiritual, social, and psychological well-being of patients. It also aims to help them deal with nausea, pain, discomfort, and shortness of breath. Supportive care for oral cancer focuses on encouraging spiritual, emotional, physical, and mental well-being. After the treatment, people can face a loss of hope andmixed emotions so, to cope with such emotions supportive care is considered important. Nutritional support means helping patients diagnosed with oral cancer to look into their dietary habits to make sure that they don't eat food that hampers the treatment process and improves theirquality of life.

#### 2.6 Treatment Available in Different Countries

#### 2.6.1 Afghanistan

The oral cancer treatment available in Afghanistan includes surgery and palliative care. Access to good healthcare infrastructure and advanced treatment options is limited and it poses a significant challenge. In addition, the limited qualified surgeon also poses a limitation to treatment for oral cancer as a limited number of surgeries will be performed in a year (Abdullah et al., 2020). The emphasis on improving healthcare infrastructure is still unclear.

#### 2.6.2 Bangladesh

Treatment for oral cancer in Bangladesh comprises surgery, radiation therapy, and chemotherapy. The lack of access to advanced treatments in the country forces the system to stress early diagnosisand surgical intervention. In other words, the system aims at diagnosing cancer at earlier stages toaddress the issue through surgery that is still relatively effective in cases of timely intervention that is facilitated by awareness of the scarcity of advanced treatment (Sultana & Malik, 2014).

#### 2.6.3 Bhutan

The treatments available for oral cancer in Bhutan are surgery and palliative care. Access to advanced treatments and good healthcare infrastructure pose significant challenges for the treatment of oral cancer. However, efforts are going on to establish a good healthcare system withadvanced treatment options for the public residing in both rural and urban (Ministry of Health, 2017).

#### 2.6.4 India

Oral cancer treatment facilities in India include surgery, radiation, chemotherapy, immunotherapy, and palliative care. Many advanced treatments are emerging and available in urban centers, but rural areas continue to face multiple challenges as these health facilities are limited. The general public health system is structured towards affordability and accessibility, allowing a large population to benefit from these services, although uptake is lower in rural areas compared to urbanareas (Best Oral Cancer Treatment in India | American Oncology Institute, n.d.).

#### 2.6.5 Maldives

The treatment for oral cancer in the Maldives includes surgery, chemotherapy, radiotherapy, and palliative care. Access to advanced treatment options for oral cancer is limited and the country relies on neighboring countries and developed countries for specialized oral cancer treatment. Thecountry is emphasizing the development of a better healthcare infrastructure with advanced treatment options for everyone (Cancer Maldives 2020 Country Profile, n.d.).

# 2.6.6 Nepal

Oral cancer treatment in Nepal consists of surgery, radiation therapy, chemotherapy, and palliativecare. The country has limited access to cutting-edge treatment and the country is facing providing citizens with proper healthcare. The country's health care system is focusing on increased coverageof the population in the outlying regions to drastically improve the number and quality of oral cancer care available in all regions. The urban areas have better healthcare infrastructure and access to available treatment but some of the rural areas still face significant challenges in havingaccess to available treatment for oral cancer (Gyawali et al., 2020).

#### 2.6.7 Pakistan

The treatment for oral in Pakistan includes surgery, radiation therapy, chemotherapy, and palliativecare. Access to the most cutting-edge oral cancer therapies is limited and the country relies heavilyon first-line treatment approaches. The infrastructure and resource restrictions in Pakistan possesscritical barriers that restrict the availability and quality of patient care. However, numerous social, political, and local efforts have been and continue to be made to address this issue and improve the overall health provision (Khokhar et al., 2021).

#### 2.6.8 Sri Lanka

The treatment for oral cancer in Sri Lanka includes or encompasses surgery, radiotherapy, chemotherapy, and palliative care. The healthcare system is becoming more accessible to advancedand effective treatments in industrialized cities, whereas rural healthcare still struggles with significant issues and obstacles. The priority of the healthcare system is the affordability and development of public healthcare infrastructure for patients with oral cancer to have access to better treatment facilities in every part of the country (Kosgallana et al., 2023).

# 2.6.9 United States of America

Oral Cancer Treatment in the United States of America encompasses several advanced modalities ssuch as surgery, radiation and chemotherapy, targeted therapy, immunotherapy, and supportive care. In every case, the patients have an opportunity to undergo advanced treatment due to the useof cutting-edge technology in the treatment method. That is in line with the commitment of the medical sector of the USA to a multidisciplinary approach, as well as personalized medicine. Thiskind of approach helps develop an individual treatment program consisting of the recommendations and treatment-related actions provided by the expert in each medical area (Treating Oral (Mouth) and Oropharyngeal (Throat) Cancer | Mouth & Throat Cancer Treatment,n.d.)

## 2.6.10 Europe

Oral cancer treatment in Europe comprises a broad spectrum of modalities, which consist of surgery, radiotherapy, systemic therapy including chemotherapy, and targeted therapy and immunotherapy. A common factor in all European countries is the rigorous treatment guidelines, which underpin the high standards of care available to cancer patients across the continent. These guidelines are evidence-based and are created in collaboration with cancer physicians and clinicalresearchers nationwide. There is a provision that patients receive the most recent and effective medical treatments, which are updated regularly based on the latest research and studies (EuropeanParliment, n.d).

## 2.7 Screening Methods Available in Different Countries.

Country	Primary Screening Method	Secondary Screening Method
USA	Visual Inspection, Oral brush biopsy, and Tissue fluorescence visualization	Biopsy, Imaging techniques, and Fine needle aspiration (FNA)
Europe	Visual Inspection, Oral brush biopsy, and Tissue fluorescence visualization	Biopsy, Imaging techniques, and Fine needle aspiration (FNA)
South Asian Countries	Visual Inspection	Biopsy

Table 2.7.1. Screening Methods used by country

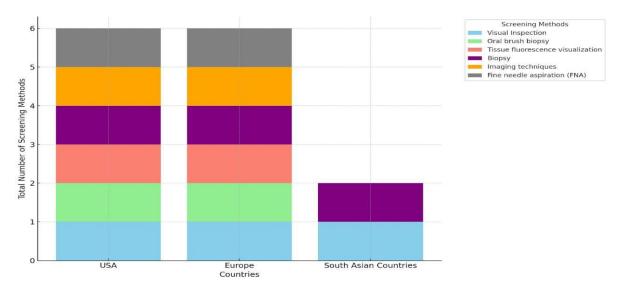


Figure 2.7.1: Screening methods available by country

The figure 2.7.1 revealed a detailed outline of screening methods including the primary and secondaryused for oral cancer across the south Asian countries and Europe as well as the USA. The representation in each country is divided into segments corresponding to the distinct screening techniques applied including Visual Inspection, Oral Brush Biopsy, Tissue Fluorescence Visualization, Biopsy, Imaging Techniques, and Fine Needle Aspiration (FNA). This format highlights the range and wide variety of methods employed in each region, showcasing a clear comparative view of the methods taken in oral cancer screening globally

## **Chapter 3: Methodology**

This chapter outlines the methodology that was employed to address and discuss the objectives and goals of the research. This provides the overview of the approach used to collect, analyze and interpret the data, ensuring transparency and reproducibility of the research process.

# **3.1. Research Outline for Comparative Analysis and Predictions of oral Cancer Incidence using Machine Learning.**

The comprehensive outline for this research is designed mainly for the analysis and interpretation of oral cancer data that is collected from south Asian countries namely Afghanistan, Bangladesh,Bhutan, India, Nepal, Pakistan, and Sri Lanka along with Europe and the USA with a particular emphasis on Bangladesh. The framework is mainly designed around five datasets each providing key role in future prediction of oral cancer incidence and mortality rates.

#### 3.1.1 Secondary Data Analysis:

For the secondary data analysis, the data from the south Asian countries and the Europe and the US are used followed by the Python-based analysis to draw a comparison on the incidence rate oforal cancer, various screening methods, and healthcare services. This will help to identify the patterns of oral cancer incidence globally.

#### 3.1.2 Oral Cancer Death Rate Analysis:

The oral cancer mortality data are compiled and the examination of mortality rate and its trends over the years are analyzed using Python-based comparative analysis. The effectiveness of various oral cancer screening methods and treatment techniques are also evaluated.

## 3.1.3 Future Predictions Using Machine Learning:

The linear regression model is used for the prediction of future incidence of oral cancer up to 2030 globally as well as in Bangladesh. Following this, the accuracy of this model is assessed with thehelp of historical data which will ultimately aid in the planning of healthcare services and resource allocation.

## 3.1.4 Demographic, Clinical, and Treatment Characteristics Analysis:

The data of oral cancer recorded from Bangladesh are analyzed in detail. Along with that, the demographic trends, clinical presentation, and treatment outcomes are explored. Finally, Python-based statistical methods are used to find correlations and important factors affecting the prognosis of oral cancer.

This detailed framework will ensure that the dataset will provide a comprehensive status of oralcancer and its future trends with a focus on enhancing the medical facilities and techniques in treating oral cancer.

## 3.2. Materials and Method for Data set 1: Secondary Data Analysis

#### 3.2.1. Data Collection

## 3.2.1.1. Data Source:

The process of collecting data was precisely designed to align with the research objectives and questions and build a strong basis for the further comparison of the oral cancer data retrieved fromvarious countries. The sources used to collect data include several secondary resources such as scientific research from online databases, other library sources, and the official health statistics from countries that are used for analysis in this study. The criteria for selecting the sources were quite straightforward as the information which were directly related to the research such as treatment evaluation, survival rates, and mechanisms of detection was included. The analysis included the many different countries such as SAARC nations: Afghanistan, Bangladesh, Bhutan,India, Maldives, Nepal, Sri Lanka, Pakistan, USA, and Europe which have variations in terms of geographical locations and economic growth. This analysis will give a comprehensive global picture of oral cancer.

## **3.2.1.2 Data Acquisition:**

Detail on the appropriate datasets from national cancer registries and international databases was requested following formal communication. Furthermore, a systematic literature review was performed to obtain additional data from proper foundations of peer-reviewed studies. Data extraction techniques depended on automated methods when available. Collection was done manually in contexts in which sources were not digitized. This exhaustive process was used to ensure the collection of adequate diverse and reliable data to analyze and assess patterns in the epidemiology of oral cancer and disparities in oral cancer care.

# 3.2.3. Data Variables

The comparisons for research were done based on the following variables;

- Age at diagnosis (Mean)
- Gender distribution
- Treatment durations (Longest treatment duration in months)
- Screening frequency (annual, biannual, etc.)
- Survival rates
- Incidence rates of oral cancer

## 3.2.4 Data Processing and Analysis

## 3.2.4.1 Data Coverage:

The secondary covers a wide range of factors that will align with our research objectives and questions. The factors that the research will cover are Age at diagnosis, gender distribution, treatment durations, Screening frequency, survival rates, and Incidence rates of oral cancer.

## **3.2.4.2**. Analytical Approach:

For achieving a comprehensive comparative study, the Python programming language was used. The analysis was performed with the help of powerful libraries, including Pandas to facilitate efficient data manipulations and Matplotlib to generate informative visual materials. Those tools played an important role in enabling the standardization of the data to ensure that it was possible to conduct a comparative analysis across diverse datasets.

## 3.2.4.3 Methodological Framework:

- 1. Data Extraction: The required data were extracted from the collection of the data set whichwas maintained by each country and then it was organized in such a way that detailed analysis can be easily carried out.
- 2. Data Cleansing: The data that was extracted was extensively cleaned to avoid discrepancies and maintain the data integrity for subsequent data analysis. The solutions were taken to resolve the issues of missing data, outliers, and biases.
- 3. Data Standardization: The standardization of data was carried out for comparing across thevarious datasets and maintaining consistency in variables and measurement units.
- 4. Data Analysis: Statistical methods were employed to carry out the comparative analysis among different countries through the data of various variables. The statistical methods which were used are regression analysis and survival analysis. In addition, sensitivity analyses were carried out to test the robustness of the findings.

## **3.2.4.4 Validation and Quality Assurance**

Throughout the thesis and process of analysis, the quality and reliability of the data were ensured through various measures. The measures that were taken for the aforementioned purposes are validation checks, sensitivity analysis, and detailed documentation of the steps of data processing. Moreover, any limitations of the data or any biases of the data were acknowledged.

## 3.3. Materials and Methods for Dataset 2: Oral Cancer Death Rate Analysis

## 3.3.1. Objective

The key objective of this study was to examine and draw an analysis regarding the oral cancer mortality patterns across different south Asian countries namely Afghanistan, Bangladesh, Bhutan, India, Nepal, Pakistan, and Sri Lanka along with Europe and the USA. The review will focus on the territorial variations and worldly examples in death rates caused by oral cancer, subsequently outfitting a near focal point through which the worldwide effect of the illness could be surveyed.

## 3.3.2. Data Source

The dataset required for this research was extracted mainly from the Global Burden of Disease (GBD) which is a comprehensive regional and global research program of disease burden that mainly aims to provide a detailed picture of deaths and disability in different countries including the time and age. The oral cancer numbers from 1990 to 2021 were extracted from the GBD. GDB is a reliable source with more than 607 billion comprehensive estimations from more than 204 countries with data from the local level to the regional to the national level and 12000 collaborators from over 160 countries contributing GDB data.

The data for 2022 and 2023 were extracted from the Cancer Today subsite of the Global Cancer Observatory. Global Cancer Observatory is a reliable data visualization tool globally that provides details about national estimates of the mortality of 27 types of cancer in 184 countries, which mainly relies on the GLOBOCAN database.

## 3.3.3 Data Analysis Tools and Techniques

## 3.3.3.1 Python

The examination was built using the programming biological system called Python, which is known for its high-level adequacy in information examination and significant indentation. Python'svast library environment, Pandas in specific for information dealing and Matplotlib for perception, the foundational basis of this scientific approach.

#### 3.3.3.2 Pandas

For its consistency in ingestion, cleansing, and change of the dataset, Pandas offers structures and operations in refining notable data and the manipulation of numerical tables and time series.

#### 3.3.3.3 Matplotlib

This Python programming language library was useful in the arrangement of quantitative information into charts, typifying the directions of oral cancer mortality over the specified countries.

#### 3.3.4. Methodology:

## 3.3.4.1. Data Preparation:

The beginning engagement with the dataset covers an exhaustive observation tounderstand its construction and constituents. Unwanted qualities were removed, sharpening the focus on relevant factors such as the nation, year, and oral cancer mortality rates.

#### 3.3.4.2. Country-Specific Analysis

Specific charts were accurately obtained for each country, portraying the worldly hub and mortality rates, in this way showing accurate numbers and trends of mortality rates over time in detail.

#### **3.3.4.3.** Comparative Analysis

To produce a comprehensive understanding of the information, an integrator chart was designed which will compare the oral cancer mortality directions of all the countries used against the collective scenery of Europe. This comparative design was vital in perceiving the relative death oforal cancer over changed geographic and socio-economic strata. This deliberate approach, throughaccurate information planning and vital utilization of Python's information examination capabilities, guaranteed that the investigated questions were tended to with expository meticulousness, giving a substantive comparative understanding of oral cancer's mortality patternsuniversally.

#### 3.4. Materials and Method for Data set 3: Predictive Modeling of Oral Cancer Incidence

This chapter delineates the methodological framework and analytical methods used to study the temporal trend of oral cancer incidence globally and specifically in Bangladesh. The main objective of this study was to forecast the trajectory of the oral cancer incidence of the year 2030 for the population of the world and Bangladesh using observational data. Predicting the oral cancerincidence in the year 2030 was accomplished through the use of qualitative machine-learning techniques that assist in developing a formal model. The factors that are affecting the trend of oralcancer in the world and within Bangladesh were understood through the utilization of both retrospective and predictive analysis. Owing to that, the comparative analysis was possible and enabled to explain the regional disparities and facilitate making changes in the public health interventions and policy formulations.

#### 3.4.1. Data Sources

The study used two different types of data to draw its analysis:

#### **3.4.1.1.** Historical Data

A comprehensive repository of authentic information chronicling oral cancer incidence globally and in Bangladesh from 1990 to 2023 served as the observational foundation of this investigation. For the data extraction of oral cancer incidence in the world and Bangladesh from 1990 to 2021, we used the latest version of the GBD 2021 and the Global Health Data Exchange (GHDx) online data source query tool. The data extraction was according to GBD's operation guide and set the disease type, incidence, and year options without any inclusion/exclusion criteria. For the years 2022and 2023, we extracted the data from authentic secondary resources.

#### **3.4.1.2. Predictive Data**

The predictive data targets the study's prognosis, which mainly involves machine-learning models and a series of linear regressions predicting the number of cases from 2024 to 2030 globally including Bangladesh. The reliance on historical data and its trends serves as a reference in predicting future trends which will ultimately assist in outlining the reasonable trajectory of oral cancer incidences in Bangladesh and the world.

# 3.4.2. Data Preparation and Cleaning

A meticulous curation of data was carried out to ensure analytical veracity:

# 3.4.2.1. Verification of Data Integrity

The consistency of the data was ensured through a comprehensive review and any inconsistency was rectified for accuracy.

# 3.4.2.2. Standardization

The homogenizations of the datasets were carried out to facilitate the analysis of the datasets andto carry out the comparison.

# 3.4.2.3. Normalization

When interventions are required due to the discrepancy in the data, the normalization protocols were utilized to harmonize the data value ranges, ensuring statistical equity and integrity within the methodology section of the research.

# **3.4.3. Analytical Methods**

The analytical approach unfolded in multiple phases that included both analysis of historical trends and predictive modeling by machine learning models.

# 3.4.3.1. Historical Trend Analysis

In the first phase, the graphical illustrations that depict the incidence of oral cancer in the world and within Bangladesh from 1990 to 2023 were carried out.

## **3.4.3.2.** Predictive Modeling:

- **Model Selection:** The linear regression was selected owing to their analytical clarity and proficiency in discerning the longitudinal trends.
- Model Implementation: The analytical instruments were actualized using sophisticated data processing tools, where 'Year' served as the predictor, and 'Oral Cancer Cases' as the outcomevariable.
- Model Training and Validation: The models were trained using historical data, validated through cross-validation techniques, and were used to test on another testing dataset. The Retrieved incidence of oral cancer was used to forecast the incidence of oral cancer from 2024to 2030 for the global and Bangladesh population.
- Sensitivity Analysis: The sensitivity analysis was carried out to observe and understand how changes in the input variables affect the prediction of the model.
- Uncertainty Quantification: To quantify the uncertainty of the predictions of the model, the prediction intervals were utilized.

## 3.4.4. Visualization

Data that was retrieved was in the numerical data and it is challenging to make comprehensible insights. Owing to that, visualization of the data plays a crucial role as good comprehensible insights can be made.

## 3.4.4.1. Historical Trend Graphs

The predictive analysis, both globally and in Bangladesh, was placed on the established visualization chart of the historical continuum of incidence of oral cancer as the backdrop.

# 3.4.4.2. Predictive Trend Graphs

These charts have projected variability of oral cancer incidence in the long term, overlaying genuine statistics to provide a viewpoint on historical variations with specific prospects throughout the future from a global standpoint and specifically focusing on the future trend of oral cancer in Bangladesh.

## 3.4.5. Interpretation and Discussion

The comparative predictive analysis of Global and Bangladesh conveys the following findings.

## **3.4.5.1.** Disparities in Trends

The disparities in oral cancer incidence in the world and within Bangladesh were highlighted.

## **3.4.5.2. Driving Factors**

The possible causes of differences in the expected burden of oral cancer in the world and within Bangladesh have been reviewed. Some of the factors the two areas may differ in include demographics, health care, economics, and social factors.

## **3.4.5.3. Implications for Policy**

Analyzed the implications of the identified disparities for public health policies and interventions address the oral cancer burden in the world and within the Bangladesh context.

## 3.4.6. Implications and Recommendations

In light of the findings uncovered, the study suggested interventions with a focus on the identified disparities in oral cancer incidence trends between global and Bangladesh datasets:

# 3.4.7. Public Health Strategies

Recommended specific public health strategies and interventions tailored to the unique needs andchallenges in each region. This could be based on the healthcare infrastructure, access and utilization of screening and treatment facilities, and socioeconomic conditions.

## 3.4.7.1. Ongoing Surveillance

Raised the importance of continuous surveillance and monitoring of oral cancer to track the oral cancer trend and to evaluate the impacts of any implemented interventions.

# 3.4.7.2. Community Awareness

Emphasized community-based awareness programs to enlighten the public about oral cancer's risk factors, early detection, and prevention.

# 3.5. Materials and Method for Data Set 4: Primary Data

# 3.5.1. Research Design

This research follows a cross-sectional study design where quantitative and qualitative data were collected from the participants through survey and past data collection.

# 3.5.2. Sampling strategy

A purposive sampling strategy was used to collect data from 54 oral cancer patients through surveyquestions which we have designed.

# **3.5.3. Data collection methods:**

There were 12 survey questions designed to collect both qualitative and quantitative data. Both types of data were collected through closed-ended questions with predetermined response options. There were four sections in the survey questions:

- Demographic information: This section had questions about participants' gender, age, place ofresidence (rural/urban), number of children, family history of cancer in general, family historyof oral cancer in particular
- 2. Knowledge of oral cancer: This section collected information about participants' awareness oforal cancer
- 3. Health Behavior: This section collected information about participants' daily habits such as smoking, drinking, or chewing tobacco, their HPV vaccination record, and on what basis they expose themselves to the sun.
- 4. Symptoms of oral cancer: This section collected information about which area of the mouth they developed oral cancer.

#### 3.5.4 Data collection procedure

All the data were obtained from an oral cancer patient. Before collecting any information, we consulted our supervisors and relevant authorities like doctors to maintain the integrity, confidentiality, and accuracy of the research process. In the initial stage, we sought guidance and assistance from our supervisor to help us connect to the authorities in charge so that we could obtain accurate information in the field of oral cancer. With their experts and collective efforts, information was collected from those patients who came seeking treatment in the hospitals. During the survey, information related to demographics, health habits, awareness of oral cancer, and symptoms was asked. However, participants were also ensured that they had oral cancer developedor undergoing oral cancer treatment. This research was conducted from June 2023 until July 2024.

## 3.5.5 Data Analysis

The collected data will be statistically analyzed using SPSS. We will be using descriptive statistics to summarize, compare, and visualize the data. Next, we will be using regression analysis to understand the future trends and patterns of oral cancer in Bangladesh based on the data we collected.

#### **3.5.6 Ethical considerations**

Before the survey, all potential participants gave a verbal agreement to be part of the survey. They were also briefed about the purpose and background of the study. Participant's personal information and identity were maintained confidential and none of the information collected was used for purposes other than for the agreed reason (s).

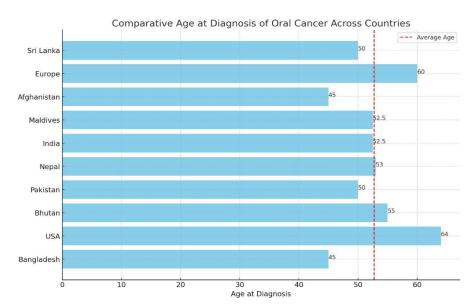
## 3.5.7 Validity and Reliability

To ensure the validity of the survey questions, our supervisor's assistant was sought. To ensure the reliability of the survey, all the participants were asked the same questions in the same order to maintain consistency and unbiasedness.

#### **Chapter 4: Findings and Implications**

This significant chapter will mainly drive into the results of an extensive investigation focusing ondifferent vital aspects of oral cancer in various countries. The information presented in this sectionhas been derived from the comparative studies elucidated in previous sections. The dataset backingthese findings is a result of data sourced from different countries including Afghanistan, Bhutan, European countries, India, Nepal, Pakistan, Sri Lanka, and the USA. This study specifically collects data regarding age at diagnosis, distribution of gender, screening frequencies, treatment duration, rate of survival, and incidence rate recorded within the healthcare systems of the nationsincluded above.

#### 4.1. Data set 1 Findings



#### 4.1.1. Age at diagnosis

Figure 4.1.1: Comparative age of diagnosis of oral cancer across countries

The comparative study showed significant variations in the age at diagnosis of oral cancer in the countries selected for investigation. For instance, the age at diagnosis of oral cancer ranges from as young as 45 years old in Afghanistan and Bangladesh to as old as 64 years in the USA. Similarly, in South Asian countries like Afghanistan, Bangladesh, India, Nepal, Pakistan, and Sri Lanka, theage of diagnosis ranges from 45 to 50 years which falls under the lower section in the age of diagnosis. The reasons for such lower age at diagnosis in South Asian countries could be due to the use of tobacco products and betel quid. Along with that, another possible reason could be due to the huge population and limited access to the screening program. In contrast, European countries and the USA revealed much higher age for the diagnosis which ranges from 65 to 70

years. This result could be attributed to the advanced healthcare system, effective and frequent cancer screening programs, and other lifestyle factors. The availability of advanced medical systems and screening centers aids in the early detection of cancer and prevents it from progressing to further stages, thus delaying the age at diagnosis. In addition, lifestyle factors in European countries and the USA may also lead to the reduction of the prevalence of risk factors of oral cancer as compared to South Asian nations. Countries like Bhutan and Maldives on the other hand, have a mid-range age at diagnosis of oral cancer which is between the age of 50 to 64 years. This trend could have been due to the moderate access to healthcare facilities which caused diagnoses at mid-age. Another reason could be due to the variations in exposure to risk factors as compared to those countries with higher and lower age at diagnosis. The variations in the age of diagnosis of oral cancer across the countries put an emphasis on the importance of region-specific public health strategies. These improvements in health infrastructure, education and screening programs could ultimately benefit those South Asian countries which showed younger diagnosis age. Conversely, the higher-income countries should continue with their effective screening process and even focuson improving the current facilities and programs. In addition, the current lifestyle which has a lower risk of leading to oral cancer should be addressed to further minimize the risk. Furthermore, the research should be carried out to identify the local risk factors in each country that lead to the variation in the age at diagnosis and for introducing more effective tailored public health interventions.

## 4.1.2. Gender Distribution

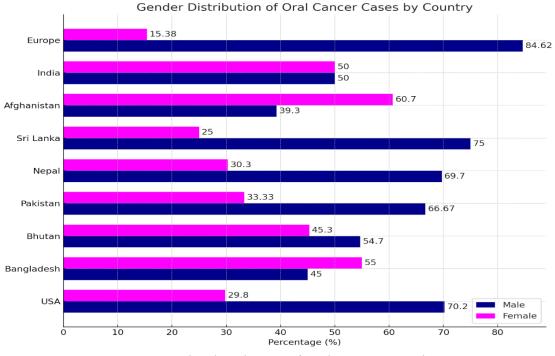
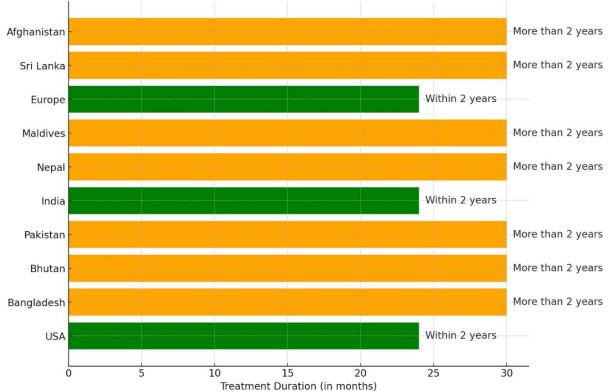


Figure 4.1.2. Gender distribution of oral cancer cases by country

There are stark differences in the gender distribution of oral cancer. Countries such as the USA, Bhutan, Bangladesh, Maldives, Pakistan, Nepal and Sri Lanka, and countries in Europe show that males are more prone to oral cancer compared to females. This might be due to the male consumingmore tobacco-related products. In addition, Afghanistan shows contrasting results where females are more prone to oral cancer compared to males. Furthermore, India exhibits that prevalence of oral cancer is equal in both males and females. This is due to the introduction of new betel quid items in the market which are consumed by females too. Cultural practices and lifestyle factors also influence the gender distribution of oral cancer cases. For instance, in South Asian countrieslike India and Sri Lanka, chewing betel quid is their tradition, and due to that, the distribution of gender is almost the same with India having 50% male and 50% Female. In addition, the countrieslike the USA, Bhutan, and countries in Europe males consumed more alcohol products and tobacco-related products leading to oral cancer.

## 4.1.3. Treatment Duration



Comparative Analysis of Longest Oral Cancer Treatment Durations by Country

Figure 4.1.3: Comparative analysis of oral cancer treatment durations by country

The comparative analysis across various countries exhibits the huge disparities in the treatment durations. These disparities in the treatment durations might be attributed to the differences in thehealthcare system, accessibility, and treatment methods available. Developed countries like the USA and countries in Europe show shorter treatment durations which is 2 years compared to SouthAsian Countries which takes more than 2 years. The shorter treatment durations in the USA and European countries might be due to the advanced medical technologies and more aggressive treatment protocols that will assist in the detection of cancer at an early stage and avoid becoming more complex form of tumor that cannot be treated easily. In addition, India also exhibits a treatment duration of 2 years and the plausible reason for this could be the development of urban healthcare facilities equipped with advanced medical technologies.

On the other hand, countries like Bangladesh, Bhutan, Pakistan, Nepal, Maldives, Sri Lanka, and Afghanistan exhibit treatment durations extending beyond 2 years. The plausible reasons for this longer treatment duration might be attributed to limited access to advanced treatment options and technologies, late diagnosis of the tumor when it has already reached the complex form and economic barriers that delay continuous and effective treatment. This trend exhibits the

disparities in the healthcare infrastructure and impacts of socio-economic on the outcome of treatment. Understanding these variations is vital for addressing the gaps in the cancer care and improving the overall treatment timelines and success rates regardless of the healthcare landscape.

#### **4.1.4. Screening Frequencies**

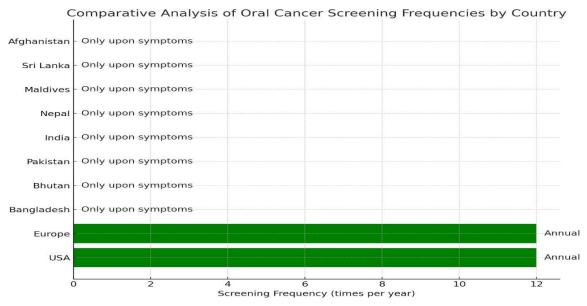
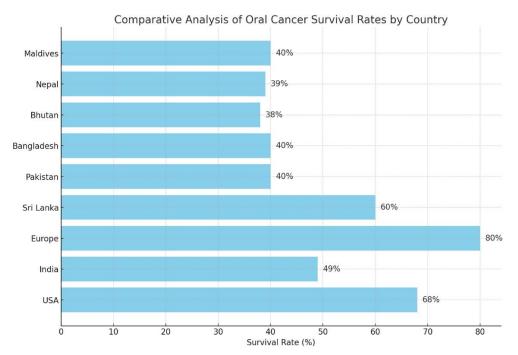


Figure 4.1.4: Comparative analysis of oral cancer screening frequencies by country

The countries in Europe and the USA follow a preventive approach to oral cancer screening and owing to that early detection and less invasive treatment will be possible which ultimately leads to better prognosis. As shown in the graph, these aforementioned countries have screening programs once a year. Owing to the regular screening programs, oral cancer can be diagnosed when it is in the pre-cancerous stage which will be less costly and easier to treat compared to the late stage where treating it will be costly and difficult. In contrast, South Asian countries follow a reactive approach where they screen for oral cancer only when patients with the symptoms of oral cancer visit the hospital. As shown in the graph, only upon symptoms, the screening will be carriedout. These differences in the screening frequencies highlight the scenario of the healthcare policies and differences in better and they also prioritize public health by investing large amounts of resources in better healthcare infrastructure and advanced medical technology. On the other hand, the countries in South Asia that carry out screening only upon symptoms might have limited resources for developing the healthcare infrastructure. In addition, differences in the healthcare policies and prioritization of public health might be the plausible

reason for lower screening frequencies. Furthermore, it might be due to the limited or lack of awareness programs about the importance of regular screening. These disparities highlight the importance of integrating regularscreening programs in the national healthcare strategy which will lead to early detection of oral cancer when it is in the pre-cancerous stage and treatment accordingly before it becomes complex.



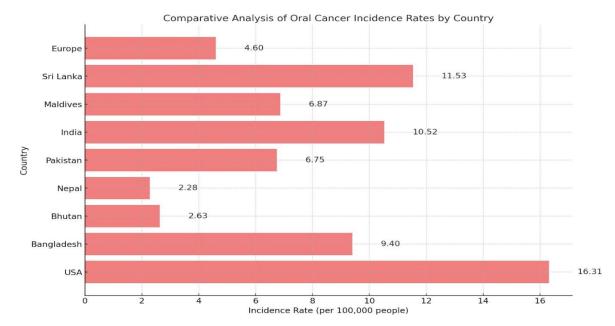
#### 4.1.5. Survival rates

Figure 4.1.5: Comparative analysis of oral cancer survival rates by country

The comparative analysis of survival rates for the surveyed countries shows a clear picture of differences in the healthcare infrastructure, access to effective medical care, and early detection practices. Europe showed an 80% survival rate which is the highest followed by the USA with a 68% survival rate. These higher survival rates compared to countries in South Asia might be attributed to better healthcare infrastructures, better healthcare policies, and access to advanced medical technologies. Moreover, proactive screening programs might be another reason for highersurvival rates as proactive screening programs lead to early detection of oral cancer and enable timely treatment.

On the other end of the spectrum, countries like Bangladesh, Bhutan, Nepal, Maldives, and Pakistan exhibit survival rates of 40%, 38%,39%, 40%, and 40% respectively. These survival rates are considered to be much lower survival rates compared to the global survival rate of oral cancerwhich is 68%. This might be owing to the limited access to quality healthcare facilities,

limited resources for cancer treatment, and diagnosis of cancer at the later stage which is difficult to treat. In addition, the reactive approach of screening programs for oral cancer might be another reason for these lower survival rates. India and Sri Lanka exhibit survival rates of 49% and 60% respectively and these survival rates are considered to be in the middle range. Though their survival rates are lower compared to global survival rates, these two countries might be doing better in terms of providing access to effective healthcare facilities and they might have some advanced medical technologies compared to neighboring countries with lower survival rates. This comparative analysis of oral cancer survival rates across the countries highlights the role of healthcare policies and resource allocation for public health programs for improving oral cancer survival rates across the globe.



## 4.1.6. Incidence rates

Figure 4.1.6: Comparative analysis of oral cancer incidence rates by country

There is a significant variation in the incidence rates of oral cancer among the country which are surveyed. The incidence rate is calculated for every 100,000 people in each country. India had anoral cancer incidence rate of 10.52 and this reflects the burden on the public health. These high incidence rates might be attributed to the use of tobacco, use of betel quid products, and the lack of awareness about the prevention of oral cancer. The USA and Sri Lanka showed higher incidencerates of 16.31 and 11.53 respectively. The lifestyle factors such as smoking, and alcohol consumption might be the plausible reasons for the higher incidence rates. In addition, it might bedue to the robust healthcare infrastructures that assist in diagnosing every possible case of oral cancer.

Conversely, countries like Bhutan and Nepal had an incidence rate of 2.63 and 2.28 respectively. These lower rates can be attributed to the limited access to quality healthcare facilities which leads to fewer diagnoses being carried out and recorded. In addition, Europe with incidence rates of 4.6can be attributed to better lifestyle choices and effective public health campaigns.

The countries like Bangladesh, Pakistan, and Maldives showed a intermediate incidence rate ranging between 6.75 and 9.4. These intermediate incidence rates can be attributed to the moderate healthcare facilities, variable reporting standards, and the consumption of related tobacco-relatedproducts and betel quid chewing which are the risk factors of oral cancer. Overall, the comparative analysis highlights the need for tailored public health interventions, access to quality healthcare facilities, and increased awareness of the prevention of oral cancer to address the variations in the incidence rates across the surveyed countries. In addition, countries with higher incidence rates of oral cancer might be targeted for health campaigns in the future.

#### 4.1.7. Conclusion of Findings.

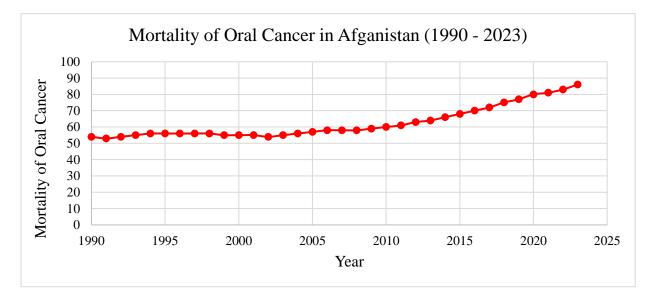
Significant disparities can be observed in various countries in terms of oral cancer factors like ageat diagnosis, gender distribution, duration of treatment, screening frequencies, survival rates, and incidence rates. These disparities are due to the differences in the healthcare systems, lifestyle factors, and cultural practices. Countries like Bangladesh and Afghanistan diagnose oral cancer ata younger age due to the prevalent use of tobacco and betel quid chewing. Conversely, developedcountries like the USA and countries in Europe get diagnosed with oral cancer at an older age due to lifestyle factors and the detection and treatment of oral cancer at an early age before it becomesto tumor. In addition, proactive screening methods are carried out in the USA and European countries whereas, South Asian countries are only screening for oral cancer when patients visit the clinics due to symptoms of oral cancer. Gender-wise, oral cancer is predominantly diagnosed in males compared to females in most of the regions except Afghanistan and India. In India, cases oforal cancer are almost same in the females and males due to the introduction of synthesized tobaccoproducts in the market which are consumed by both genders.

The differences in the treatment duration can be observed in developed countries like the USA and European countries, and South Asian countries. These differences are owing to the availability of advanced treatment options in those countries and differences in the healthcare facilities and priorities. In addition, South Asian countries follow reactive screening methods whereas, the USA and European countries follow proactive screening methods. In the case of

survival rates, minor differences can be observed among the South Asian countries and the USA and European countriesshow higher survival rates. There are minor differences in the incidence rates of oral cancer across the countries which are under study. In a nutshell, these disparities in diverse factors of oral cancer highlight the need for global collaborations and improvement in healthcare facilities, public healthservices, and awareness campaigns regarding oral cancer.

#### 4.2. Findings of Data set 2: Analyses of Mortality rates of Oral cancer

The following charts unveil the pattern of oral cancer mortality rates in South Asian countries mainly, Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Sri Lanka, the United States of America, and Europe using the data from 1990 to 2023. The population in each of the countries is obtained from the Data Catalog of the World Bank. The following interpretations reveal how multifaceted factors such as healthcare frameworks, socio-economic factors, and social impacts can change the mortality rate of oral cancer in different countries of South Asia as well as Europeand the USA.



#### 4.2.1 Afghanistan

Figure 4.2.1: Mortality rates of oral cancer in Afghanistan from 1990 – 2023

The figure 8 describes the mortality rate of oral cancer in Afghanistan from 1990 to 2023. The population in Afghanistan as of 2022 was 41.13 million and the mortality rate from 1990 to 2023 speaks volumes about the country's fight against oral cancer. Initially, the mortality of oral cancer in Afghanistan showed a stable rate with around 60 deaths per year. However, the rate increased steadily each year around 2008 and the death rate per year increased to almost 85 by the year 2023.

This increase in the rate of oral cancer mortality and the upward trend demands public health attention and the rise could be attributed to the lack of medical facilities and political instability inAfghanistan. This persistent rise in the mortality of oral cancer demands attention in the field of medical services like screening and testing, public awareness through advocacy, and improved treatments

#### 4.2.2. Bangladesh

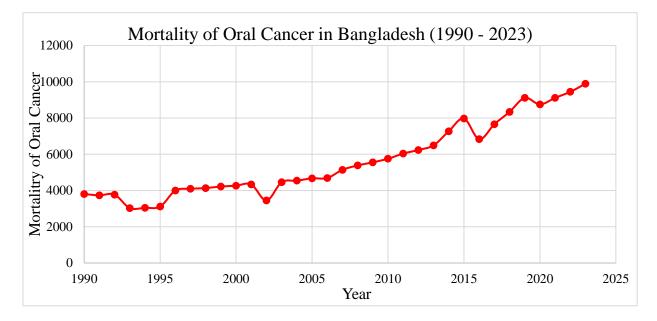


Figure 4.4.2: Mortality rates of oral cancer in Bangladesh from 1990 – 2023

The total population in Bangladesh counts at 171.2 million in 2022 and oral cancer mortality from 1990 to 2023 reveals an upward trend indicating the rise of deaths caused by oral cancer. The rateof oral cancer mortality in Bangladesh showed a stable trend until the early 2000s with a slight dipin 2002. However, after 2002 the graph showed an increase and steady rise in oral cancer deaths till 2015 and again a slight fall in 2016 followed by a steady rise. This overall upward trend could be due to smoking, tobacco use, chewing betel nuts late screening, and delayed medical access. Therefore, immediate medical intervention is required such as improved medical facilities like screening and testing, public awareness campaigns in rural areas, and improved treatment.

## 4.2.3. Bhutan

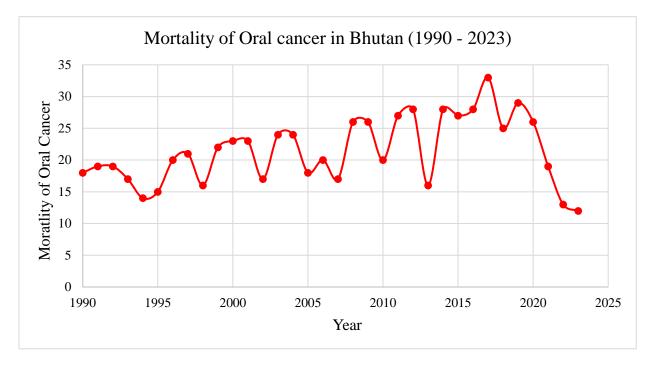


Figure 4.2.3. Mortality rates of oral cancer in Bhutan from 1990 – 2023

The total population of Bhutan counts at 782,455 as of 2022 and the rate of oral cancer mortality from 1990 to 2023 demonstrates the fight against oral cancer. The chart 4.2.3 shows. small changes in the rate of death caused by oral cancer over the years with a slight increase in rate in the late 1990sand mid-2010s. This slight increase may be due to the lack of medical facilities like screening andtesting centers, consumption of alcohol and chewing betel nuts as well as lack of awareness sinceBhutan was exposed to the outside world and lacks technological advancement. However, after 2017 the chart showed a downward trend indicating a decrease in death rate possibly due to the improved healthcare services and effective screening and testing machines along with improved awareness through education and advocacy and effective treatment with free healthcare services by the government.

## 4.2.4. India

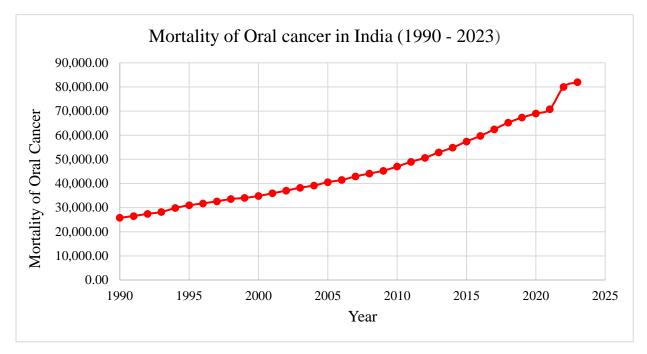


Figure 4.2.4: Mortality rates of oral cancer in India from 1990 – 2023

The population of India was counted at 1.417 billion as of 2022 and the mortality rate of oral cancer in India illustrates an upward trend with an approximate death of 30,000 in 1990 to nearly 80,000 in 2023. This continuous increase in the death rate due to oral cancer in India could be attributed to several factors such as the high consumption rate of tobacco, chewing betel nuts, alcohol consumption, and a high number of illiterate rural people. This steady rise in mortality ratedue to oral cancer suggests the need for improved healthcare facilities in both the ruler and urban areas with fervent screening and testing, advocacy, and initiating public awareness programs andimproved treatment facilities.

#### 4.2.5. Maldives

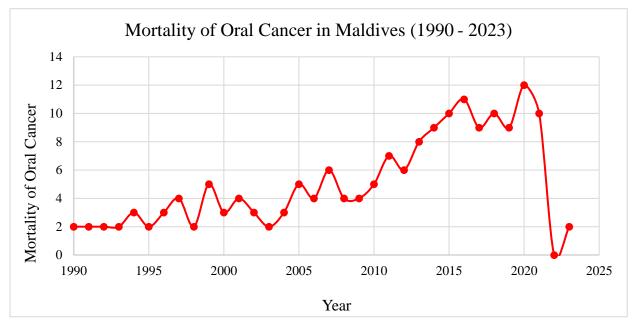


Figure 4.2.5: Mortality rates of oral cancer in Maldives from 1990 – 2023.

With a total population of around 523,787, the mortality rate of oral cancer in Maldives from 1990to 2023 shows the fluctuations of oral cancer death trend in Maldives. Initially, the death rate started at only 2 in 1990 with constant changes over the years. However, 2020 observed a dramaticrise in deaths which caused 12 people deaths and also 0 deaths in 2022 showing the fluctuations of rate of oral cancer death in Maldives. These dramatic changes in the death rate in less than 2 years are mainly due to the inconsistencies in the healthcare system of the country and the variation the health services offered by the government like screening and treatment services

#### 4.2.6. Nepal

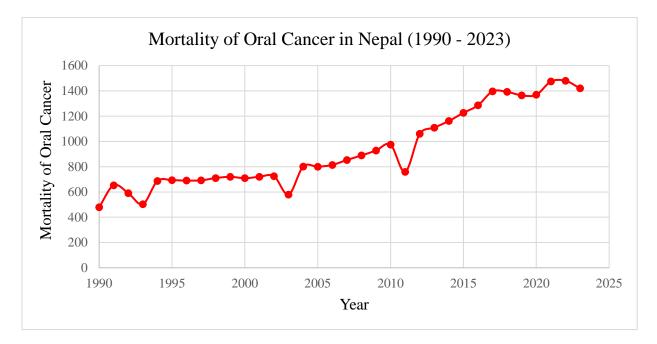


Figure 4.2.6: Mortality rates of oral cancer in Nepal from 1990 – 2023

With a population of nearly 30.55 million, the death rate due to oral cancer in Nepal fluctuated from 1990 to 2023. Oral cancer caused 500 deaths in 1990 and since then the rate increased over the years reaching around 1400 by 2023. In this course of trend from 1990 to 2023, it was observed that there was a small decrease in the overall death rate which was followed by an increase in number in the following years. This overall increase in the mortality rate of oral cancer in Nepal may be linked to a number of factors including, high consumption rate of tobacco, chewing betel nuts, alcohol consumption, and lack of public awareness. This rise of mortality rate could be prevented with improving healthcare facilities in both the ruler and urban areas with fervent screening and testing, advocacy and initiating public awareness programs and improved treatmentfacilities

# 4.2.7. Sri Lanka

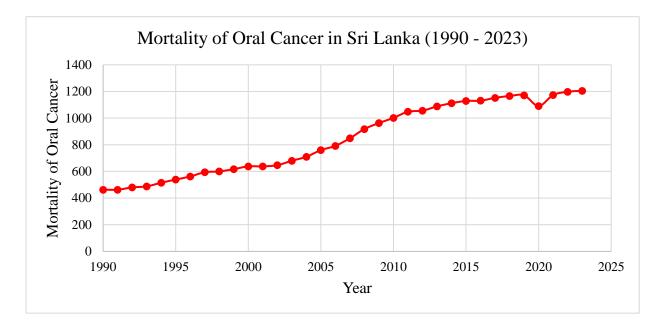


Figure 4.2.7: Mortality rates of oral cancer in Sri Lanka from 1990 – 2023

The total population in Sri Lanka was 22.18 million as of 2022 and the mortality of oral cancer in Sri Lanka showed an upward. This continuous increase in the death rate due to oral cancer in Indiacould be attributed to several factors such as the high consumption rate of tobacco, chewing betelnuts, alcohol consumption, and a high number of illiterate rural people. This steady rise in mortalityrate due to oral cancer suggests the need for improved healthcare facilities in both the ruler and urban areas with fervent screening and testing, advocacy, and initiating public awareness programs improved treatment facilities.

#### 4.2.8. USA

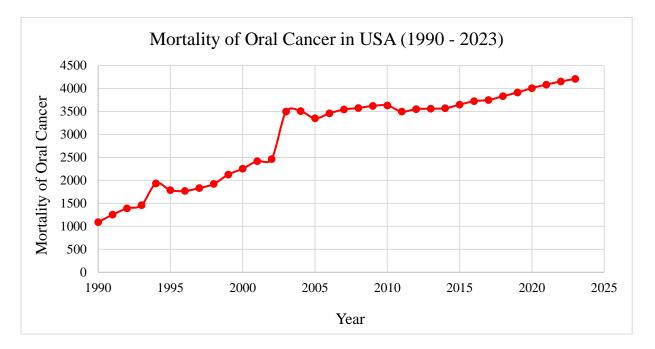


Figure 4.2.8: Mortality rates of oral cancer in the USA from 1990 – 2023

With a total population of 333.3 million in 2022, the mortality rate of oral cancer in the USA showsan upward trend from 1990 to 2023, with a sharp increase from around 2003. There is a constant rise in mortality rates from 1990 to 2003, followed by a period of stabilization with small fluctuations. There was a slight increase again in recent years, which shows that while there havebeen periods of control, the overall trend is upward. This pattern underscores the need for sustained and superior healthcare interventions, public awareness, and powerful screening programs to copewith the growing mortality rates of oral cancer in the USA.

## 4.2.9. Europe

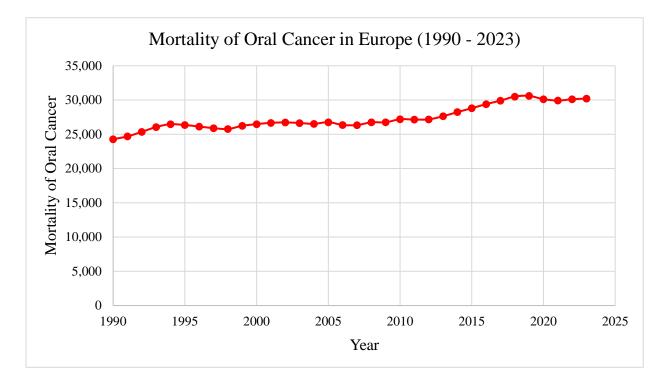


Figure 4.2.9: Mortality rates of oral cancer in Europe from 1990 – 2023

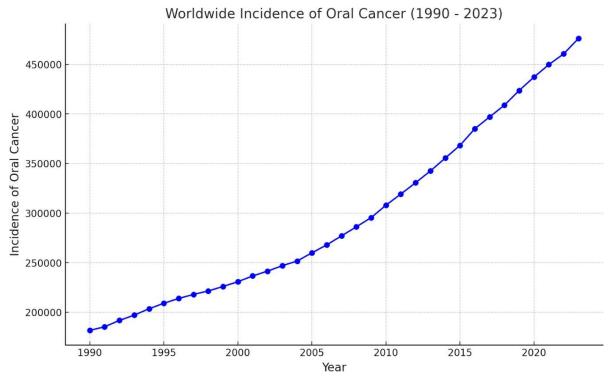
The 44 countries in Europe according to the United Nations make a total European population of about 741,716,264 in 2024. The mortality rate due to oral cancer in these 44 countries describes how the continent is dealing with oral cancer and the direction of the fight. The chart reveals the stable rate of oral cancer deaths from 1990 to 2023. It shows a small increase from the early 2000suntil 2018 and 2019 which recorded much higher death numbers. The stable trend implies that preceding actions against oral cancer were not really effective and thus demand improvement in healthcare services, awareness programs, and most importantly increased screening and treatmentoptions to lower the rate further.

#### 4.2.10. Comparative Analysis

The comparative analysis of oral cancer rates from 1990 to 2023 in the South Asian countries Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Sri Lanka, the USA, and European countries as well as Europe and the USA shows variation in the rate and the factors contributing to this trend. The mortality rate has been increasing in Afghanistan and Bangladesh mainly due to the lack of advanced medical infrastructure and services. Bhutan on the other hand, observed a slight rise in the 1990s and 2010s but the country showed drastic change after 2017 due to the improved healthcare services. Similar to Afghanistan and Bangladesh, India's mortality rate revealed an upward trend from 1990 to 2023 attributed to factors such as high smoking rate, tobacco consumption, and chewing betel nuts. The oral cancer death rate in Maldives revealed fluctuation and inconsistent patterns. Nepal also observed the variations and fluctuations in its death rate but an overall increase in rate as compared to 1990. The United States of America Also showed an increasing trend but with a state of stabilization, while Europe observed a constant ratewith a small increase. In the countries analyzed for this study, the most common factorscontributing to oral cancer include chewing betel nuts and consumption of tobacco, high smokingrate, inadequate healthcare infrastructure, and lack of public awareness.

#### 4.3. Findings of Data Set 3: Predictive Analysis of Oral Cancer in World and Bangladesh

This part will provide the findings that describe the trend of oral cancer incidence in the world and Bangladesh, and how it is changing over time. Primarily, the trend of the oral cancer incidence spanning from the year 1990 to 2023 is described in this part. In addition, the incidence of oral cancer in the year 2023 will be predicted based on historical data that includes oral cancer incidence spanning from 1990 to 2023. For readers who may straightforwardly explore this part, this chapter is fastidiously developed to stand alone, offering a clear, comprehensive view of the findings from the past to the future.



4.3.1. Global Oral Cancer Incidence (1990 – 2023)

*Figure4.3.1: Global oral cancer incidence from 1990 – 2023.* 

This analysis and graph are based on the historical data of oral cancer incidence in the world from the year 1990 to 2023. The graphs clearly show how oral cancer incidence had increased within 33 years and became one of the most common diseases in the world. The increase in oral cancer incidence exhibits and gives us insights into the kind of healthcare facilities had in the past. In addition, it provides information about limitations in access to oral cancer treatment facilities and societal shifts. Owing to those factors, there has been an increase in oral cancer incidence in the world.

## 4.3.2. Predicted Global Oral Cancer Incidence.

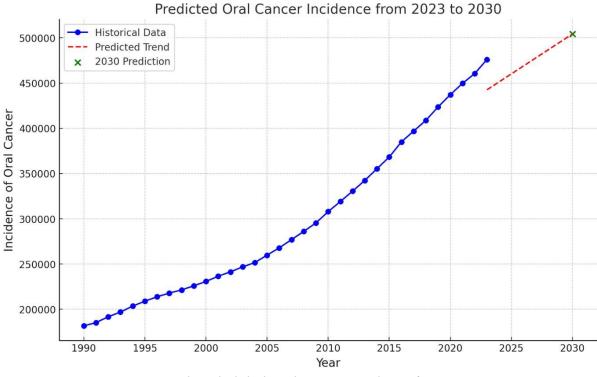


Figure 4.3.2: Predicted global oral cancer incidence from 2023 - 2030.

This graph predicts the incidence of oral cancer in the world in the year 2030. The prediction is carried out using the linear regression model based on the oral cancer incidence of the past 33 years. The model chosen uses the year to predict the incidence of oral cancer which resulted in projections that extend past trends into the future. If the changes in oral cancer incidence follow the trend of the past three decades without any changes in the healthcare facilities, treatment, andrisk factors then it is predicted that the oral cancer incidence in the world will be around 500,000 in the year 2030. This predicted incidence of oral cancer provides information to the policymakers to come up with policies that prioritize public health and introduce better diagnostic methods andtreatment facilities and also increases public awareness about oral cancer so that the future incidence of oral cancer can be reduced in the world.

## 4.3.3. Oral Cancer Incidence in Bangladesh (1990 – 2023)

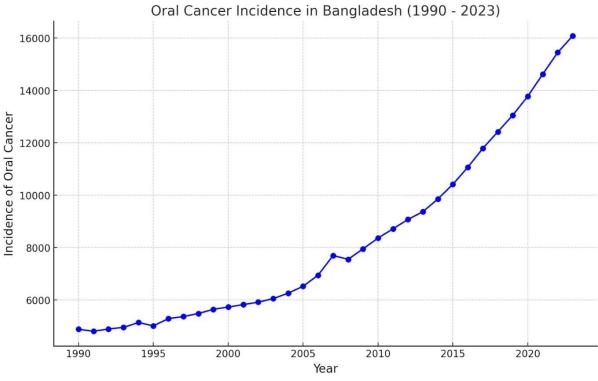


Figure 4.3.3. Oral Cancer Incidence of Bangladesh from 1990 - 2023.

This study and graph examine the changes in oral cancer incidence in Bangladesh from 1990 to 2023. It can be observed in the graph that, oral cancer incidence in Bangladesh has increased overthe years and has become one of the most common diseases in Bangladesh. These changes in oralcancer incidence provide information about the healthcare facilities available in the past for the diagnosis and treatment of oral cancer in Bangladesh. In addition, the increase in oral cancer incidence in Bangladesh provides information about the risk factors of oral cancer present in the country and also provides information about the evolving landscape of healthcare facilities and their ability to diagnose and treat oral cancer.

# 4.3.4. Predicted Oral Cancer Incidence of Bangladesh

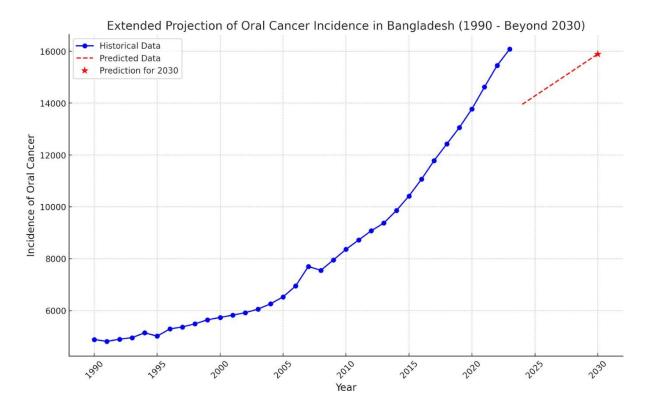


Figure 4.3.4: Predicted Oral cancer incidence of Bangladesh from 2023 - 2030

This graph predicts the oral cancer incidence in Bangladesh in the year 2030. The prediction is carried out using the linear regression model based on the oral cancer incidence of the past 33 years. The model chosen uses the year to predict the incidence of oral cancer which resulted in projections that extend past trends into the future. If the changes in oral cancer incidence follow the trend of the past three decades without any changes in the healthcare facilities, treatment, andrisk factors then it is predicted that the oral cancer incidence in Bangladesh will be around 17000 in the year 2030. This predicted incidence of oral cancer provides information to the policymakers to come up with policies that prioritize public health and introduce better diagnostic methods andtreatment facilities and also increases public awareness about oral cancer so that the future incidence of oral cancer can be reduced in Bangladesh.

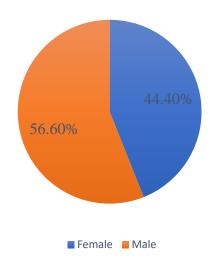
# 4.3.5. Findings and Comparative Analysis of predicted incidence of oral cancer in the world andBangladesh for the year 2030.

Significant differences can be observed in the predicted oral cancer incidence of the world and Bangladesh. The predicted oral cancer incidence in the world in the year 2030 is almost 8% higher than that of oral cancer incidence in the world in the year 2023. This increase is attributed to the universal risk factors of oral cancer like consumption of tobacco, use of alcohol, and exposure to HPV. Conversely, the predicted oral cancer incidence in Bangladesh for the year 2030 exhibits anincrease in oral cancer incidence by almost 4% from the incidence of 2023. The plausible reasonsfor the increase in incidence are the use of tobacco and betel quid chewing. Similar to every country in the world, the rise in oral cancer incidence over the years can be reduced by introducing proactive diagnosis and treatment methods. In addition, awareness about oral cancer can also assistin reducing oral cancer incidence in the future. The predicted incidence of oral cancer in the world my Bangladesh urges for the needs of global health initiatives to provide every country in the world with improved proactive screening programs and treatment facilities. Furthermore, it also urges policymakers to prioritize public health and come up with new policies and awareness campaigns about oral cancer.

# 4.4. Findings of Data Set 4: Primary Data

The information collected from 54 patients is used for a detailed examine of dataset 4, providing crucial demographic and clinical features related to oral cancer in Bangladesh. This analysis is very important for readers wishing to gain an understanding of the scope and specifics of oral cancer cases as well as their responses to screening within the framework of Bangladeshi context. The results are presented systematically, with visual aids that would help to understand them better, particularly emphasizing its relations with age as a demographic variable.

# 4.4.1. Gender



*Figure 4.4.1: Pie chart showing percentage of male and female participants.* 

The dataset utilized in our research on oral cancer unveils that amongst the oral cancer patients, 55.6% were male and 44.4% were female. It is evident from this distribution that there is a significant gender difference with regard to oral cancer occurrences within our patient community, as oral cancer is more prevalent among males than females. This variation is also illustrated in thepie chart, which indicates that preventive measures and therapeutic approaches towards the diseaseshould factor in issues unique to each gender. Further investigations into the origin of such gendervariations may give rise to important lessons which can be helpful in formulating improved healthcare programs.

# 4.4.2. Age group

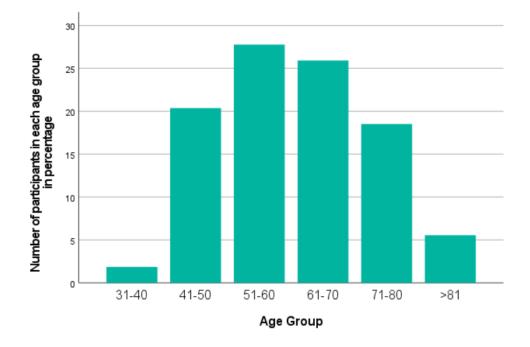


Figure 4.4.2: Bar graph showing number of participants in each age group.

Figure 4.4.2 demonstrates the extent to which different age groups are affected by oral cancer. In accordance with the data, the highest percentage of patients falls within the age range of 51-60years old, followed in close succession by those ageing from 61-70 years. Thus, these two categories account for significant portions of involved individuals while others like the 41-50 and71-80 years have their own substantial representation, though less than that exhibited by the formerones. It is worth observing that there are minimal amounts of this disease among the youngest category (31-40 years) along with its oldest counterpart (>81). This suggests that oral cancer is more prevalent in middle-aged adults within a given population although possible drops in incidence could happen for both young and old generations. Therefore, such a situation means thattargeted screening and preventive measures should be considered for people in the most affected age brackets.

# 4.4.3. Dwelling

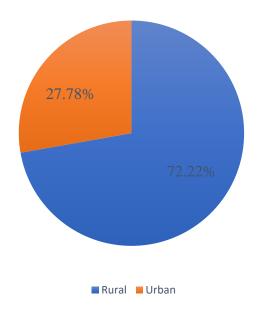
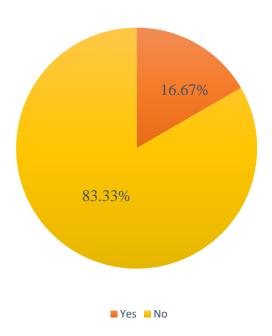


Figure 4.4.3: Pie chart showing dwelling of participants in the form of percentage.

Figure 4.4.3 display that among all patients suffering from oral cancer, 27.78% were living in urban areas while the remaining 72.22% lived in countryside regions. This kind of distribution appears to show that high numbers of oral cancer patients come from rural places. One possible factor putting this trend forward could be differences between urban and rural hygiene standards. Rural areas may be linked with poor access to clean water supplies, good sanitation systems as well as dental care services which can have an impact on oral health. For instance, where there are not good dental hygiene practices or lack preventive and diagnostic services this may put more peoplewho live in the villages at risk of contracting the disease. According to this data there is a need forpublic health initiatives that focus on improving both sanitation measures and provision of healthcare services in order to adequately prevent and treat oral cancers among rural populations.

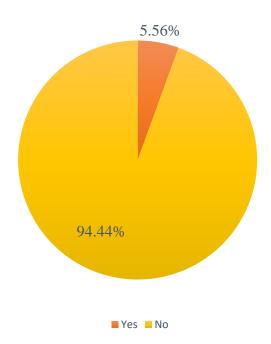
# 4.4.4. Do you have family history of any cancer?



*Figure 4.4.4: Pie chart showing history of any cancer in the family of participants in the form of percentage.* 

Figure 4.4.4 show that 16.67% of people with oral cancer have a family history of other cancers, while 83.33% do not have any such family history. This implies that there are probably many people who have oral cancer because they might have inherited it from their family members. Butmost patients do not share their family history with any other type of cancer so this indicates that even those who lack a genetic susceptibility may still be afflicted by oral cancer. Hence these results emphasize the need to take into account genetic as well as environmental factors towards understanding oral cancer risk in addition to calling for more comprehensive preventive measures aimed at addressing multiple potential risk factors beyond just family history.

## 4.4.5. Does anyone from your family has or had oral cancer?



*Figure 4.4.5: Pie chart showing history of oral cancer in the family of participants in the form of percentage.* 

It is estimated that only 5.56% of people suffering from oral cancer have any previous record of that disease in their families while the remaining 94.44% do not. Such low genetic factors concerning oral cancer in patients indicates how small is the number of those suffering from an inherited predisposition to it. Most patients with no family history suggest a possibility that their development can be attributed to others like lifestyle, environment, and personal health habits. This emphasizes the need for an integrated approach in terms of public health policies towards oralcarcinoma prevention and treatment which incorporates both genetic as well as non-genetic risk factors.

#### 4.4.6. Do you smoke?

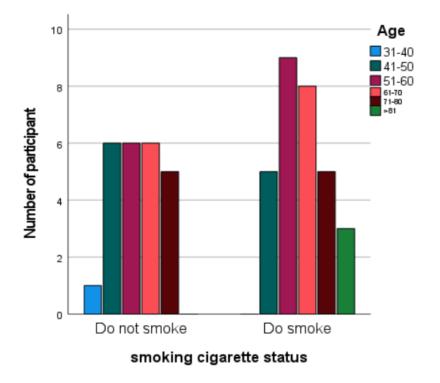


Figure 4.4.6: Bar showing smoking status of the participants.

The smoking status of oral cancer patients is shown in the bar chart by their group. There are more cigarette smokers in the age groups of 51-60 and 61-70 than there are in any other age group. Unlike smokers, the distribution of non-smokers among different age categories is more even withsignificant occurrences of non-smokers in the ranges of 41-50 and 51-60 years. In the young (31-40) and old (>81) age categories, however, fewer patients from both categories are found. This implies that there exists a link between tobacco use and occurrence of oral malignancies particularly among middle-aged adults to the elderly. Moreover, 51–70-year-olds had a higher proportion of people who were smokers thus emphasizing on need for focused cessation interventions so as to minimize chances for occurrence of oral carcinoma among this community.

## 4.4.7. Do you chew tobacco?

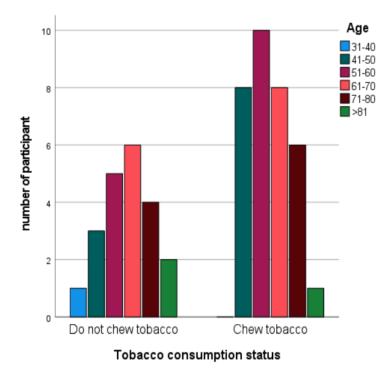
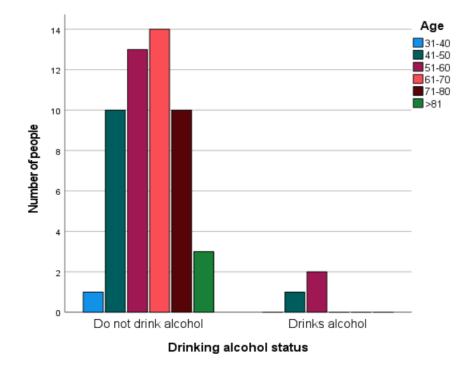


Figure 4.4.7: Bar graph showing tobacco consumption status of the participants.

Patients with oral cancer have been evaluated depending on how much tobacco they consume by age groups, as illustrated by the figure 4.4.7. Tobacco chewing was most prevalent among these patients and was particularly common among those aged between 51 and 60 and 61 to 70 years; out of which the highest number belongs to the one aged between 51-60 years. On the contrary, patients who do not use any form of tobacco were evenly distributed across ages 41-50, 51-60 and61-70 although their population is still lower as compared to chewing groups especially in the range of ages 51-60. The representation of younger (31-40) or older age groups (>81) in both categories is very low. Therefore, this distribution shows a significant relation between chewing tobacco and development of oral cancer mostly found in old age persons. From these findings it can be advocated that there is a need for public health programs to reduce chewing habits for mostvulnerable age categories which will help prevent oral cancers from occurring and spreading.

## 4.4.8. Do you drink alcohol?



*Figure 4.4.8: Bar graph showing alcohol drinking status of the participants.* 

Figure 4.4.8 displaying consumption of alcohol among people suffering from oral cancer indicates an impressive tendency for everyone in their various age brackets to avoid alcohol beverages entirely, with greatest concentration observed in persons 51 years old and above. However, it is mentioned that there are some youths who consume alcoholic drinks in small amounts such as individuals between the ages of thirty-one (31) and fifty (50). This pattern indicates that even though alcohol is often regarded as a cause of oral cancer, a greater contributioncould come from other factors in this set of people, revealing the necessity for strategic public health measures and awareness programs focused primarily at younger age groups which will effectively address and reduce these perils.

### 4.4.9. Do you chew betel quid?

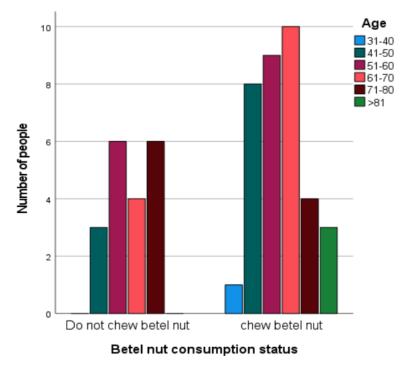


Figure 4.4.9: Bar graph showing betel nut consumption status of the participants

The figure 4.4.9 shows how betel nut was consumed among oral cancer patients depending on their age. From the graph, it can be deduced that there has been a very high percentage of betelnut consumers among various age sets with the highest amount being seen in individuals who are between 41 and 60 years old. Other age groups do not show significant consumption levels as expected from younger and older cohorts where the numbers significantly go down. This is alarming because there is evidence that betelnut consumption increases the chances of someone getting oral cancer at some point in life. Therefore, this compelling situation calls for urgent public health campaigns intending to craze down on it within populations likely to be hit hardest by this issue. It serves as an indicator of the necessary need for such campaigns that would endeavor to reduce the intake of betel nut among people at risk, as well as educate them about the health complication of using betel nuts constantly because there are also other preventions and health promotion programs designed to reduce oral cancer which must be put into account too.

#### 4.4.10. Did you get HPV vaccine?

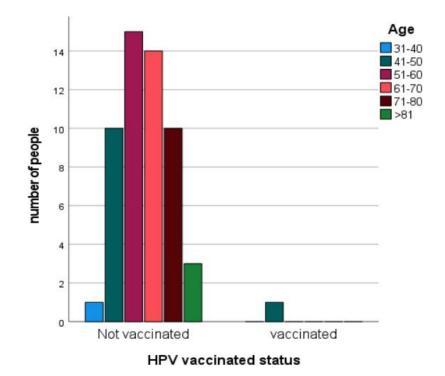
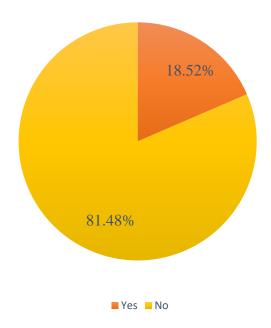


Figure 4.4.10. bar graph showing HPV vaccination status of the participants

The figure 4.4.10 presents an in-depth analysis of the HPV vaccination status among oral cancer patients from different age brackets. It is clear from the graph that a high number of patients in every age group are unvaccinated against HPV, with highest unvaccinated categories existing within ranges of ages 31-40, 41-50 and 51-60 years. On the other hand, all other age categories have low numbers of vaccinated individuals at their disposal. There is little uptake indicating gravest gaps in preventive health services aimed at combating HPV which has been shown to predispose people to certain forms of cancers affecting the mouth. This would herald a call for greater public health measures aimed at enhancing vaccination rates for those not covered or takingit; decreasingly would otherwise see a rise in cancers within that region hence still vice versa. Thereport highlights how important is the aspect of addressing HPV vaccination amongst wider cancerprevention plans.

### 4.4.11. Did you come across any campaign of oral cancer?



*Figure 4.4.11: Pie chart showing whether participants are aware of oral cancer in form of percentage.* 

The figure 4.4.11 indicate that only 18.52% of patients suffering from oral cancer have been exposed to awareness programs through campaigns, television and other mediums. On the other hand, a significant 81.48 % of them have never come across any awareness programs. This highlights thehuge gap in the access and effectiveness of oral cancer awareness initiatives. The low exposure to these awareness programs shows that many people may not be aware about oral cancer prevention, early detection and treatment options. Therefore, it is essential to increase the visibility and availability of such programs as they could help in reducing incidences and improving outcomes of oral cancer by educating more people about the disease.

#### 4.4.12. Conclusion of Findings of Primary Data.

Our research on oral cancer presents a thorough evaluation, pointing out an evident gender gap with men accounting for 55.6% of instances therefore suggesting that oral cancer influences genderunique risk factors. Data shows that in fact there are most cases among older adults; moreover, rural regions have higher prevalence rates this implies that lifestyle consists of determinant aspects in the spread of the illness. This indicates that further investigations on environmental and biological factors predisposing individuals to oral cancer are necessary. Besides, only few patientsclaimed to have relatives suffering from any form of cancer including oral cancer itself hence implying genetics may not be key; however, tobacco and alcohol usage as lifestyle-related risks is highly significant especially tobacco itself which has close relationships with the disease.

There are certain areas where public health can intervene to reduce the incidence of oral cancer such as vaccination rates against HPV are low and, in some cases, non-existent, while many older people consume betel nuts. Moreover, lack of knowledge and preventive action points out that there is an urgent need for better public health efforts. Public health programs aimed at awareness creation on risk factors like tobacco use or chewing betel nut should be promoted with the aim ofpromoting access to healthcare in rural areas. In addition, the fact that patients do very little exercise suggests a possible relationship between being inactive physically or exercising less frequently; therefore, promoting physical activity should be included as part of a holistic approachtowards the prevention of oral cancers. Therefore, these findings argue for the necessity of a comprehensive and integrated strategy in public health policy in order to tackle prevention, early diagnosis and treatment of oral cancer effectively.

#### **Chapter 5: Summary, Limitation and Future Perspectives.**

This chapter of thesis will serve as an overview of the research carried out on oral cancer in relation to incidence, prevalence and demographic and clinical features. This chapter is considered to be the end product of thorough investigative process using various data sources on trends in oral cancer, comparing them and projecting future cases along with an evaluation of patient records from Bangladesh. The section will assist readers through key steps in our research journey including objectives for the research to the research questions that motivated our studies followed by the literature review which places our work within the larger academic discourse regarding these issues. In line withthat this chapter will also present such findings and offers conclusions based on evidences gathered during our studies. The analysis will provide reflections that are made regarding differences or similarities between previous studies. The last part summarizes its thesis by emphasizing relevance of this study to ongoing efforts aimed at fighting against oral cancer.

## 5.1. Summary

This thesis has presented an all-inclusive study of oral cancer which is considered one of the pressinghealth problems with global ramifications. The aim of this research was to conduct a cross-country comparison and utilize machine learning methods in forecasting the occurrence rate of oral cancer in various countries with focus on Bangladesh. Therefore, this research examines datasets to find globaltrends we well as particular local challenges and also predict future occurrence rates.

The groundwork for this study includes a thorough literature review addressing the epidemiological profile of oral cancer along with its etiological factors and the current status of screening and prevention methods. The review also illustrated some new machine learning which increases the predictive analytics in healthcare. The research questions were addressed systematically using a carefully designed methodology. Global trends were identified by collecting and analyzingsecondary data from different countries. A machine learning model was then used to predict futureoccurrences of oral cancer in Bangladesh up to 2023, as well as worldwide trends. Furthermore, all the demographic, clinical and treatment features for 54 patients of oral cancer in Bangladesh were comprehensively analyzed using Python-based data analysis tools.

The findings showed significant variations in oral cancer occurrence, death rates and examination methods among different countries. According to the predictive model, Bangladesh was predicted to have a rise in oral cancer cases which highlights the pressing healthcare problems to be tackled. Basedon meticulous patient data analysis in Bangladesh, fundamental information on demographic and clinical features were derived indicating a call for specialized healthcare expert services. Collectively, these findings enhance our nuanced understanding of oral cancer and suggest future trends that will influence healthcare policies and practices in resource-constrained areas such as Bangladesh. A rise in oral cancer cases is expected and it demands an urgent need for proactive and targeted measures to deal with this increasing health concern.

# 5.2. Limitations

Despite a well-researched and thorough approach, this study has its own limitations. Firstly, the data was gathered mainly from the individual patients at hospitals located in Dhaka thus, findings might notreflect what other hospitals are like in other areas across the country. Moreover, since the geographic scope of this study was small and only few hospitals were consulted, it means that various health care providers situated outside of Dhaka have been ignored thereby generalizing these results to rest of Bangladesh would be difficult. Furthermore, based on just 54 individuals sampled as subjects in this study we conclude that such limited number cannot fully represent all possible kinds of treatment facilities available in Bangladesh with such wide geographical and healthcare differences from one state to other.

Besides, secondary information was taken mainly from authentic official websites which may consistof few errors or inaccuracies irrespective of their credibility. In addition to that, it is also possible thatthe countries compared in this research might have improved since the time the data was taken hence affecting veracity and pertinence of the comparative analysis made. Lastly, the findings and the information presented in this study might consist of few errors and might not be accurate or updated representation of current state of healthcare facilities; therefore, such aspects would impact the interpretations and conclusions made based on this data. Such limitations emphasis the need of cautionagainst generalizing the results while stressing upon more extensive future surveys with larger numbers frespondents.

# 5.3. Future Perspectives

It is crucial to increase public awareness about risk factors associated with the use of tobacco and alcohol consumption, as well as the significance of early detection through regular screenings in prevention and treatment of oral cancer. Broader access to affordable effective screening programs particularly in high-risk populations could drastically reduce incidence and mortality rates associated with the oral cancer. On top of, emphasis should be placed on merging advanced diagnostic technologies with personalized treatment strategies aimed at improving patient outcomes. Collaborative research initiatives focused on the genetic, environmental, and lifestyle factors that contribute to oral cancer will help inform evidence-based policies and target interventions; while also educational campaigns should address social-cultural barriers to early diagnosis and adherence to care.

# **Chapter 6: Conclusion**

In conclusion, this thesis has impacted awareness about the prominent challenges and disparities in oral cancer management globally. This research emphasizes the potentials of utilizing data science and predictive modeling as essential tools in fighting oral cancer. However, despite these improvements, there exist elements that need to be constantly considered with equal efforts from all stakeholders. Therecommendations as well as observations made in this article shall act as a reference point to guide future efforts in preventing or controlling oral cancer. It is through innovation promotion, building partnerships and remaining focused on enhancing public health that we can lessen the burden of oral cancer.

# Reference

Abdullah, M., Niazi, N., & Pakteen, M. (2020). Palliative care: the care that is rarely practiced in health system of Afghanistan. In *Springer eBooks* (pp. 447–454).

https://doi.org/10.1007/978-3-030-54526-0\_39

Admin. (2018, June 5). What's new in oral cancer research - Oral Cancer Foundation / Information and Resources about Oral Head. Oral Cancer Foundation | Information and Resources About Oral Head and Neck Cancer.

https://oralcancerfoundation.org/facts/whats-new-oral-cancer-research/

- Agarwal, V. K., Sharma, R., Gahlot, G., & Arnav, A. (2020). Clinical and Histopathological Correlation of p16 and p53 Expression in Oral Cancer. *Indian Journal of Surgical Oncology*, *12*(S1), 164–168. <u>https://doi.org/10.1007/s13193-020-01145-z</u>
- Agrawal, A., Shindell, E., Jordan, F., Baeva, L., Pfefer, J., & Godar, D. E. (2013). UV radiation increases carcinogenic risks for oral tissues compared to skin. *Photochemistry and Photobiology*, 89(5), 1193–1198. <u>https://doi.org/10.1111/php.12140</u>
- Anwar, N., Pervez, S., Chundriger, Q., Awan, S., Moatter, T., & Ali, T. S. (2020). Oral cancer:
  Clinicopathological features and associated risk factors in a high risk population
  presenting to a major tertiary care center in Pakistan. *PLoS ONE*, *15*(8), e0236359.
  https://doi.org/10.1371/journal.pone.0236359

Barul, C., Fayossé, A., Carton, M., Pilorget, C., Woronoff, A., Stücker, I., & Luce, D. (2017).
Occupational exposure to chlorinated solvents and risk of head and neck cancer in men: a population-based case-control study in France. *Environmental Health*, *16*(1).

https://doi.org/10.1186/s12940-017-0286-5

Best oral cancer treatment in India / American Oncology Institute. (n.d.).

https://www.americanoncology.com/cancer-we-treat/treatment/oral-cancer

Bhowmik, S. (2023, February 24). Radiation therapy for oral cancer.

https://www.medicalnewstoday.com/articles/radiation-therapy-for-oral-

cancer#summary

Brahmer, J. R., Hammers, H., & Lipson, E. J. (2015). Nivolumab: targeting PD-1 to bolster antitumor immunity. *Future Oncology*, *11*(9), 1307–1326.

https://doi.org/10.2217/fon.15.52

Cancer Maldives 2020 country profile. (n.d.). https://who.int/publications/m/item/cancer-mdv-

# 2020

Cancer of the oral cavity and pharynx - Cancer Stat Facts. (n.d.). SEER.

https://seer.cancer.gov/statfacts/html/oralcav.html

Cancer Research UK. (n.d.). Number stages and grades of mouth cancer. CANCER

RESEARCH UK. https://www.cancerresearchuk.org/about-cancer/mouth-

cancer/stages-types-grades/number-

stages#:~:text=Stage%200%20or%20carcinoma%20in%20situ%20(CIS)&text=Some

%20doctors%20prefer%20to%20call,develop%20into%20an%20invasive%20cancer

Cancer Resources from OncoLink, Treatment, Research, Coping, Clinical Trials, Prevention. (n.d.). *Cetuximab (Erbitux*®) / *OncoLink*. University of Pennsylvania - OncoLink. https://www.oncolink.org/cancer-treatment/oncolink-rx/cetuximab-erbitux-r

Du Cancer, C. C. S. /. S. C. (n.d.-a). *Chemotherapy for oral cancer*. Canadian Cancer Society. https://cancer.ca/en/cancer-information/cancer-types/oral/treatment/chemotherapy

Du Cancer, C. C. S. /. S. C. (n.d.-b). *Radiation therapy for oral cancer*. Canadian Cancer Society. <u>https://cancer.ca/en/cancer-information/cancer-types/oral/treatment/radiation-therapy</u>

Eldridge, L., MD. (2023, April 21). *Cancer Cells vs. Normal Cells: How Are They Different?* Verywell Health. <u>https://www.verywellhealth.com/cancer-cells-vs-normal-cells-</u> 2248794

Ellonen, R., Suominen, A., Kelppe, J., Willberg, J., Rautava, J., & Laine, H. (2023).
Histopathological findings of oral epithelial dysplasias and their relation to malignant transformation. *Cancer Treatment and Research Communications*, *34*, 100664.
https://doi.org/10.1016/j.ctarc.2022.100664

European Parliament. (n.d.). Background Note on Access to Cancer Treatment. In *European Parliament*.

https://www.europarl.europa.eu/cmsdata/224890/20210128\_Background\_note\_hearing \_\_access\_cancer\_treatment.pdf External beam radiation therapy (EBRT) - UCSF Department of Radiation Oncology. (2020, December 31). UCSF Department of Radiation Oncology.

https://radonc.ucsf.edu/conditions-treatments/types-of-treatment/external-beam-

radiation-therapy-ebrt/

External beam radiation therapy for cancer. (2018, May 1). Cancer.gov.

https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam

Guha, N., Warnakulasuriya, S., Vlaanderen, J., & Straif, K. (2014). Betel quid chewing and the risk of oral and oropharyngeal cancers: A meta-analysis with implications for cancer control. *International Journal of Cancer*, *135*(6), 1433–1443.

https://doi.org/10.1002/ijc.28643

- Gyawali, B., Sharma, S., Shilpakar, R., Dulal, S., Pariyar, J., Booth, C. M., & Poudyal, B. S. (2020). Overview of delivery of cancer care in Nepal: current status and future priorities. *JCO Global Oncology*, 6, 1211–1217. <u>https://doi.org/10.1200/go.20.00287</u>
- Haghshenas, M. R., Moosazadeh, M., Taghiloo, S., Sattari, S., Valadan, R., & Mousavi, T.
  (2022). Association between Human Papillomavirus and Oral Cancer in Iranian
  Clinical Samples: A Meta-Analysis Review. *Iranian Journal of Public Health*.
  https://doi.org/10.18502/ijph.v51i12.11459
- *Immune checkpoint inhibitors*. (2022, April 7). Cancer.gov. <u>https://www.cancer.gov/about-</u> <u>cancer/treatment/types/immunotherapy/checkpoint-inhibitors</u>

Jiang, X., Wu, J., Wang, J., & Huang, R. (2019). Tobacco and oral squamous cell carcinoma: A review of carcinogenic pathways. *Tobacco Induced Diseases*, 17(April).

https://doi.org/10.18332/tid/105844

Johnson, S. (2020, September 1). Oral cancers. Healthline.

https://www.healthline.com/health/oral-cancer

- Kasthuri, M., Babu, N., Masthan, K. M. K., & Sankari, S. (2015). Toludine Blue Staining in The Diagnosis of Oral Precancer and Cancer :Stains, Technique and its Uses - A Review. *Biomedical & Pharmacology Journal*, 8(october Spl Edition), 519–522.
  https://doi.org/10.13005/bpj/737
- Khokhar, M. A., Niaz, M. O., Aslam, A., Khan, H. A., Loya, A., Speight, P. M., & Khurram,
  S. A. (2021). Pakistan Oral Cancer Collaborative: analyzing barriers and obstacles to
  oral cancer diagnosis, treatment, and prevention in Pakistan. *Oral Surgery Oral Medicine Oral Pathology and Oral Radiology*, 132(3), 312–319.

https://doi.org/10.1016/j.0000.2021.04.058

Kosgallana, S., Jayasekara, P., Abeysinghe, P., & Lalloo, R. (2023). Oral health related quality of life of oral cancer patients treated with radiotherapy alone or with chemotherapy in a tertiary referral centre in Sri Lanka. *BMC Oral Health*, *23*(1).

https://doi.org/10.1186/s12903-023-02854-x

Laser treatment for cancer. (n.d.). American Cancer Society.

https://www.cancer.org/cancer/managing-cancer/treatment-types/lasers-in-cancer-

treatment.html

- Lin, S., DDS. (2021, July 19). *Causes and risk factors of oral cancer*. Verywell Health. https://www.verywellhealth.com/oral-cancer-causes-risk-factors-4017576
- List of Anti-PD-1 and PD-L1 monoclonal antibodies (immune checkpoint inhibitors) (antiprogrammed cell death-1 (PD-1) monoclonal antibodies). (n.d.). Drugs.com. https://www.drugs.com/drug-class/anti-pd-1-monoclonal-antibodies.html
- Mathur, R., Singhavi, H. R., Malik, A., Nair, S., & Chaturvedi, P. (2018). Role of poor oral hygiene in causation of oral cancer—A review of literature. *Indian Journal of Surgical Oncology*, *10*(1), 184–195. <u>https://doi.org/10.1007/s13193-018-0836-5</u>
- Ministry of Health. (2017). Bhutan Cancer Control Stragety. In *Ministry of Health*. <u>https://www.moh.gov.bt/wp-content/uploads/ict-files/2021/02/Bhutan-Cancer-Control-Strategy.pdf</u>
- Morozas, A., Malyško-Ptašinskė, V., Kulbacka, J., Ivaška, J., Ivaškienė, T., & Novickij, V. (2024). Electrochemotherapy for head and neck cancers: possibilities and limitations. *Frontiers in Oncology*, *14*. <u>https://doi.org/10.3389/fonc.2024.1353800</u>
- Mouth cancer Diagnosis and treatment Mayo Clinic. (2024, April 30).

https://www.mayoclinic.org/diseases-conditions/mouth-cancer/diagnosis-

treatment/drc-20351002

Mouth cancer surgery. (n.d.). Memorial Sloan Kettering Cancer Center.

https://www.mskcc.org/cancer-care/types/mouth/mouth-cancer-treatment/mouth-

cancer-surgery

Mph, Z. S. (2023, February 16). What to know about oral melanoma.

https://www.medicalnewstoday.com/articles/oral-melanoma#treatment

Oral Cancer 5-Year Survival Rates by Race, gender, and Stage of diagnosis. (n.d.). National

Institute of Dental and Craniofacial Research. https://www.nidcr.nih.gov/research/data-

statistics/oral-cancer/survival-rates

*Oral Cancer Incidence (New Cases) by age, race, and gender*. (n.d.). National Institute of Dental and Craniofacial Research. <u>https://www.nidcr.nih.gov/research/data-</u>

statistics/oral-cancer/incidence

- Oral Cavity & Oropharyngeal Cancer Key Statistics 2021. (n.d.). American Cancer Society. https://www.cancer.org/cancer/types/oral-cavity-and-oropharyngeal-cancer/about/keystatistics.html
- Pathak, J., Swain, N., Patel, S., & Poonja, L. (2014). Histopathological variants of oral squamous cell carcinoma-institutional case reports. *Journal of Oral and Maxillofacial Pathology*, 18(1), 143. <u>https://doi.org/10.4103/0973-029x.131945</u>
- Patini, R., Cordaro, M., Marchesini, D., Scilla, F., Gioco, G., Rupe, C., Lajolo, C., &
  D'Agostino, M. (2023). Is systemic immunosuppression a risk factor for oral Cancer?
  A Systematic Review and Meta-Analysis. *Cancers*, 15(12), 3077.
  https://doi.org/10.3390/cancers15123077

PDT / What is PDT? / Photodynamic Therapy. (n.d.). American Cancer Society.

https://www.cancer.org/cancer/managing-

cancer/treatmenttypes/radiation/photodynamic-

therapy.html#:~:text=Photodynamic%20therapy%20%28PDT%29%20is%20a%20trea tment%20that%20uses,also%20be%20called%20photoradiation%20therapy%2C%20p hototherapy%2C%20or%20photochemotherapy.

Professional, C. C. M. (n.d.). Cryotherapy. Cleveland Clinic.

https://my.clevelandclinic.org/health/treatments/21099-cryotherapy

Pulumati, A., Pulumati, A., Dwarakanath, B. S., Verma, A., & Papineni, R. V. L. (2023).

Technological advancements in cancer diagnostics: Improvements and limitations.

Cancer Reports, 6(2). https://doi.org/10.1002/cnr2.1764

*Radiation therapy for cancer.* (2019, January 8). Cancer.gov. <u>https://www.cancer.gov/about-</u>

cancer/treatment/types/radiation-therapy

Radiation therapy for oral cavity and oropharyngeal cancer. (n.d.). American Cancer Society. <u>https://www.cancer.org/cancer/types/oral-cavity-and-oropharyngeal-</u> cancer/treating/radiation-therapy.html

Radoï, L., Paget-Bailly, S., Guida, F., Cyr, D., Menvielle, G., Schmaus, A., Carton, M., Cénée, S., Sanchez, M., Guizard, A., Trétarre, B., Stücker, I., & Luce, D. (2013). Family history of cancer, personal history of medical conditions and risk of oral cavity cancer in France: the ICARE study. *BMC Cancer*, *13*(1). <u>https://doi.org/10.1186/1471-2407-</u>

<u>13-560</u>

Rodríguez-Molinero, J., Del Carmen Migueláñez-Medrán, B., Puente-Gutiérrez, C., Delgado-Somolinos, E., Carreras-Presas, C. M., Fernández-Farhall, J., & López-Sánchez, A. F. (2021). Association between Oral Cancer and Diet: An Update. *Nutrients*, *13*(4), 1299.
 <a href="https://doi.org/10.3390/nu13041299">https://doi.org/10.3390/nu13041299</a>

Rumgay, H., Murphy, N., Ferrari, P., & Soerjomataram, I. (2021). Alcohol and Cancer:

Epidemiology and Biological mechanisms. *Nutrients*, 13(9), 3173.

https://doi.org/10.3390/nu13093173

Salivary gland tumors - Diagnosis and treatment - Mayo Clinic. (2024, June 21).

https://www.mayoclinic.org/diseases-conditions/salivary-gland-cancer/diagnosis-

treatment/drc-20354155

Sankaranarayanan, R., Ramadas, K., Amarasinghe, H., Subramanian, S., & Johnson, N. (n.d.). Table 5.3, Clinical Staging of oral cancer, treatment modalities, and prognosis, by clinical Stage - Cancer - NCBI Bookshelf.

https://www.ncbi.nlm.nih.gov/books/NBK343649/table/part2.ch5.sec8.table3/

Squamous cell carcinoma of oral cavity - DoveMed. (n.d.). DoveMed.

https://www.dovemed.com/diseases-conditions/squamous-cell-carcinoma-oral-cavity

Srakocic, S. (2024, March 15). What does oral verrucous carcinoma look like? Healthline.

https://www.healthline.com/health/cancer/oral-verrucous-carcinoma#treatments

Sultana, N., & Malik, M. (2014). The overview of oral cancer and risk factors in Bangladesh. International Journal of Dental Sciences and Research, 2(5A), 8–10.

https://doi.org/10.12691/ijdsr-2-5a-3

Survival rates for oral cavity and oropharyngeal cancer. (n.d.). American Cancer Society.

https://www.cancer.org/cancer/types/oral-cavity-and-oropharyngeal-cancer/detectiondiagnosis-staging/survival-rates.html

Tan, Y., Wang, Z., Xu, M., Li, B., Huang, Z., Qin, S., Nice, E. C., Tang, J., & Huang, C. (2023). Oral squamous cell carcinomas: state of the field and emerging directions. *International Journal of Oral Science*, *15*(1). <u>https://doi.org/10.1038/s41368-023-00249-w</u>

*Targeted Cancer Therapy / Targeted Drug therapy for cancer*. (n.d.). American Cancer Society. <u>https://www.cancer.org/cancer/managing-cancer/treatment-types/targeted-</u> <u>therapy/what-</u>

is.html#:~:text=The%20action%20of%20targeted%20drugs%20can%20work%20to% 3A,cells%20to%20kill%20them%2C%20but%20not%20normal%20cells

The THANC Guide. (2022, July 20). Oral Biopsy · Diagnosis · Cancer Basics · THANC

Guide. THANC Guide ► Knowledge. Hope. Support. <u>https://thancguide.org/cancer-</u> basics/diagnosis/biopsy/oral/#:~:text=Excisional%20Biopsy%20In%20this%20techniq ue%2C%20the%20whole%20area,small%20and%20an%20excisional%20biopsy%20 will%20be%20performed. Tran, C. L., Han, M., Kim, B., Park, E. Y., Kim, Y. I., & Oh, J. (2023). Gastroesophageal reflux disease and risk of cancer: Findings from the Korean National Health Screening Cohort. *Cancer Medicine*, 12(18), 19163–19173. https://doi.org/10.1002/cam4.6500

Treating oral (Mouth) and oropharyngeal (Throat) cancer / Mouth & Throat Cancer

*Treatment*. (n.d.). American Cancer Society. <u>https://www.cancer.org/cancer/types/oral-</u> cavity-and-oropharyngeal-cancer/treating.html

Website, N. (2024, January 11). Treatment for mouth cancer. nhs.uk.

https://www.nhs.uk/conditions/mouth-cancer/treatment/

What is hyperthermia? / Hyperthermia to treat cancer. (n.d.). American Cancer Society.

https://www.cancer.org/cancer/managing-cancer/treatment-types/hyperthermia.html

What is salivary gland cancer? / Types of salivary gland cancer. (n.d.). American Cancer

Society. https://www.cancer.org/cancer/types/salivary-gland-cancer/about/what-is-

salivary-gland-cancer.html

What is the Oral Cancer Survival Rate? (2021, November 22). WebDental, LLC.

https://webdental.com/blogs/what-is-the-oral-cancer-survival-rate

Yang, G., Wei, L., Thong, B. K. S., Fu, Y., Cheong, I. H., Kozlakidis, Z., Li, X., Wang, H., & Li, X. (2022). A systematic review of oral biopsies, sample types, and detection techniques applied in relation to oral cancer detection. *BioTech*, 11(1), 5. <u>https://doi.org/10.3390/biotech11010005</u> Yu, C., Lin, H., Cheng, S., Sun, A., & Chen, H. (2014). Cryotherapy for oral precancers and cancers. *Journal of the Formosan Medical Association*, *113*(5), 272–277.

https://doi.org/10.1016/j.jfma.2014.01.014