

**EPIDEMIOLOGY OF ORAL CANCER IN INDIA
– A LIFE COURSE STUDY**

by

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'Knowing is not enough; we must apply.

Willing is not enough; we must do.'

-Johann Wolfgang von Goethe

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Abstract

Background: Oral cancer is a malignant disease contributing to one third of the total cancer burden in India. There is a worldwide social disparity in oral cancer incidence and survival. Life course epidemiology has shown that early-life socioeconomic conditions (SEC) could influence adult health through various pathways. Thus, the socioeconomic disparities in the occurrence of oral cancer underscore the importance of understanding the ‘life course processes’ operating between SEC at different stages in life and oral cancer. In addition to understanding socioeconomic disparities, practical solutions are required to reduce the burden of the disease. Early diagnosis and prompt treatment could reduce morbidity and mortality. Though visual screening helps in early diagnosis, it requires training and calibration of the screeners. Developing a simple screening model that can be utilized by untrained health care workers will be helpful in triaging asymptomatic adults with oral cancer.

Therefore a study was designed with the following hypotheses.

Research hypotheses

1. Accumulation of socioeconomic disadvantage over the life course is associated with oral cancer in the Indian population.
2. Early-life socioeconomic disadvantage has a lasting effect on the oral cancer outcome in adulthood in the Indian population.
3. An oral cancer screening model developed for the Indian population, to screen high-risk people from rural/remote areas, has good predictive ability.

Methods: A multicentre hospital based case-control study was conducted between July 2011 and August 2012 in Karnataka, India. Cases were newly diagnosed oral and oropharyngeal cancer patients and controls were patient-visitors or patients seeking care for other reasons. Data were collected through direct interviews, oral examination and record abstraction. Cases were ascertained from hospital records. A semi-structured questionnaire was designed to collect life course information on SEC, family structure, housing conditions, parental habits of tobacco, quid and alcohol use, parental education, family history of malignancy, participants’ own diet, tobacco, quid, alcohol use and oral hygiene behaviour. A life-grid was used to improve recall accuracy. All consenting participants underwent an oral examination following an interview by a trained examiner. Oral soft and hard tissues were examined for the presence of any oral mucosal lesions, teeth present and oral hygiene status.

Data were analysed using SAS v 9.2. Conventional logistic regression models were used to determine the associations between life course SEC and oral cancer. Marginal structural model (MSM) was built to estimate the controlled direct effect of childhood SEC on oral cancer in adulthood. The validity of effect measures was checked with sensitivity analysis. A multivariable logistic regression model was used to develop a screening model for identifying individuals at high-risk for developing oral cancer. The development of the model involved deriving risk scores for the predictors of oral cancer. The predictive ability of the screening model was examined with *c* statistics, sensitivity, specificity and predictive values.

Results: A total of 180 incident cases and 272 controls participated in the study. Of them, 163 cases and 264 controls had complete information on SEC at all three stages. Nearly two-thirds (65%) of participants were stable in low SEC across all stages. Low SEC at all the three stages (childhood, early adulthood and later adulthood) was associated with oral cancer after adjusting for age and sex. The association was strongest for those who remained in the low SEC at all the three stages. Odds ratios (OR) for oral cancer in socially mobile groups were intermediate to that of the stable groups. The largest differences in OR for oral cancer were observed between the stable groups.

The total effect model showed that the risk was 63% [Risk ratio (RR) = 1.63 (95% CI = 1.38–1.92)] higher for those who lived in low SEC in childhood than for those in high SEC. From the MSM, the estimated risk for developing oral cancer for those in low SEC during early-life was 48% [RR = 1.48 (95% CI = 1.43–1.53)], 24% [RR = 1.24 (95% CI = 0.88–1.74)] and 94% [RR = 1.94 (95% CI = 1.66–2.27)] greater than those in the high SEC after controlling for smoking, chewing and alcohol respectively. However, the adjusted effect of low SEC on oral cancer was null when analysed using conventional regression.

A screening model was developed using statistical methods that involved smoking, chewing quid and/or tobacco, alcohol, family history of upper aero-digestive tract (UADT) cancer, diet and oral hygiene behaviour as predictors. Total risk score that was derived from odds ratio ranged from 0 to 28. Area under the curve of the Receiver Operating Characteristic (ROC) curve for risk scores was 0.866. The sensitivity (0.928) and negative predictive value (0.927) were higher while specificity (0.603) and positive predictive value (0.607) were lower for risk scores cut-off of 6.

Conclusions: Low SEC in childhood and early adulthood are important in determining oral cancer in later adulthood. Early-life socioeconomic disadvantage increases the risk for oral

cancer that is not mediated by later life risk factors when MSM was used. The developed screening model using risk scores had satisfactory predictive ability in the study population. However, validation of the model in other settings is necessary before it can be recommended to identify subgroups of the people to be referred for further clinical evaluation.

Notes

References

References in this thesis follow a generic style that provides author-date citations where the author(s) and date of publication is listed in the parentheses. In the text, to differentiate work by same authors in the same year, a letter after the year is included. In this Harvard author-date referencing system, where there are three or more authors, the first author is listed followed by “et al.” in the text. All authors are listed in the bibliography.

List of Abbreviations

ASIR	Age-standardised Incidence Rate
AUC	Area Under Curve
NSAOH	Australian National Survey on Adult Oral Health
ARCPOH	Australian Research Centre for Population Oral Health
BMI	Body Mass Index
CI-S	Calculus Index – Simplified
CVD	Cardiovascular Diseases
CCI	Commission on Chronic Illness
CDE	Controlled Direct Effect
DI-S	Debris Index – Simplified
DM	Diabetes Mellitus
DAG	Directed Acyclic Graphs
EBV	Epstein Barr Virus
FN	False Negative
FP	False Positive
HH	Head of Household
HCGSC	HealthCare Global Speciality Centre
HCG-BIO	HealthCare Global-Bangalore Institute of Oncology
HPV	Human Papillomavirus
HSV-1	Human Simplex Virus-1
ICD	International Classification of Diseases
IPW	Inverse Probability Weight
KMIO	Kidwai Memorial Institute of Oncology
MSM	Marginal Structural Model

MSW	Medical Social Worker
NIDCR	National Institute of Dental and Craniofacial Research
NIDR	National Institute of Dental Research
NSAOH	National Survey of Adult Oral Health
NPV	Negative Predictive Value
OR	Odds Ratio
OHI-S	Oral Hygiene Index-Simplified
OPMD	Oral Potentially Malignant Disorders
PNG	Papua New Guinea
PAH	Polycyclic Aromatic Hydrocarbons
PPV	Positive Predictive Value
RCT	Randomised Controlled Trial
RERI	Relative Excess Risk due to Interaction
RR	Risk Ratio
ROC	Receiver Operating Characteristic
SSSBCH	Shri Shirdi Sai Baba Cancer Hospital
SLT	Smokeless Tobacco
SEC	Socioeconomic Conditions
SEP	Socioeconomic Position
SCC	Squamous Cell Carcinoma
SW	Stabilised Inverse Probability Weight
SEER	Surveillance, Epidemiology, and End Results
US	United States
USPSTF	United States Preventive Services Task Force
UADT	Upper Aerodigestive Tract
WHO	World Health Organization

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide.

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Signed _____

Sree Vidya Krishna Rao

_____/_____/_____

Date

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Chapter 1: Introduction

1 Introduction

‘No man, even under torture can say what a tumour is’

-Rudolf Virchow

Oral cancer is a disease of antiquity. *Sushruta Samhita*, a Sanskrit treatise of surgery, written in the Indian context gives a description of oral cancer. Its aggressiveness to spread locally involving surrounding structures causes disfigurement, affects function, and leads to physical and psychological discomfort ultimately affecting quality of life.

This chronic disease is a public health problem both in developing as well as developed countries. Around the world about 274,300 new cases of oral cancer occur each year, of which almost two-thirds are from developing countries (Petersen, 2005). Oral cancer is one among the four most common cancers in India (Ferlay et al., 2010b). It contributes to one-third of the total cancer burden in India, and continues to increase in epidemic proportions (Parkin et al., 2005; Johnson et al., 2011b; Gupta et al., 2012).

In India, where approximately two thirds of the population live in rural areas where lower educational attainment co-exists with a higher prevalence of tobacco and alcohol, a lack of knowledge about the potential harmful effects of tobacco, quid, and alcohol – all of which complicate the scenario. Oral cancer is mainly related to tobacco and alcohol use, and largely preventable. Since the introduction of pan masala and gutkha (blends of tobacco, areca nut, lime and catechu) in the 1970s in India, the epidemic of oral cancer has increased (Nair et al., 2004; Gupta et al., 2012). Furthermore, it is of note that socio-demographic correlates exist for oral cancer and its risk factors. Globally, socioeconomic inequalities in the incidence and mortality from oral cancer exist (Johnson et al., 2011b), and this is no exception in India

(Rajamanickam et al., 2007; Madani et al., 2010a). People at a higher risk of developing oral cancer are those living in low socioeconomic conditions (SEC) (Conway et al., 2008). Health behaviour is socially patterned (Kuh and Ben-Shlomo, 2004). Oral cancer and its main risk factors, such as tobacco and alcohol use, have social determinants (Neufeld et al., 2005; Rooban et al., 2010; Palipudi et al., 2012). People living in low SEC are more likely to develop behavioural risk factors for chronic diseases at an early age (Lynch et al., 1997).

Research on the socioeconomic inequalities in the occurrence of oral cancer has focused on the SEC in adulthood. Although this approach helps in assessing the association between SEC and oral cancer, it does not take into account the temporality of the relationship. The prolonged empirical induction period (Rothman, 1981) for oral cancer (i.e. the duration between exposure to causative factors and diagnosis of disease) signifies that the exposure to risk factors could have occurred earlier in life. Thus, it is imperative to consider the timing, duration, and later modification of exposure to risk factors. There is no empirical evidence to demonstrate whether SEC during early or later years of life determine the development of oral cancer in adulthood. Recent developments in life course epidemiology have shown that early-life SEC are determinants of health in adulthood (Power et al., 2005). Early-life SEC could influence adult health through various pathways. Thus, the socioeconomic disparities in the occurrence of oral cancer underscore the importance of understanding the 'life course processes' operating between SEC at different stages in life and oral cancer.

Despite the technological advances in diagnostic techniques and treatment, the survival rate in India is around 50% (Warnakulasuriya, 2009a). The disease is also still a cause of high morbidity and mortality in other countries. In a country like India, many of the cases reported are from rural areas where access to health care is less than in urban areas. Lack of knowledge about oral cancer in rural people, and financial difficulty in affording for health care services in urban areas may lead to further delay in the presentation of cases. As a result of the delay,

the disease would have progressed to advanced stages that would then have a poor prognosis. Screening programs to find oral cancer cases in the early stages could reduce morbidity and mortality. Identifying high-risk individuals could help in controlling oral cancer by creating awareness of oral cancer and its risk factors. A simple screening model would be helpful in screening high-risk individuals.

1.1 Rationale

India is a developing country. It is the second most populous country in the world, with the majority of people living in rural areas. Vast changes have been witnessed in the social structure of India since independence in 1947 (Mishra and Nayak, 2006). India, which was and is still largely a rural and agrarian country, has undergone industrialisation and globalisation post-independence (Jodhka). Associated with the changes in the socioeconomic structure has been growth in the urban population with migration of people from the rural areas in search of better opportunities for education and employment (Jodhka; Mishra and Nayak, 2006). Consequential to the socioeconomic development has been an improvement in health and educational facilities (Mishra and Nayak, 2006; Tharakan, 2008). However, there is a wide disparity in health and access to health care services in India. While well-equipped hospitals are present in urban areas, the health care services in rural areas are accessed through primary health centres (Amrith, 2009). Many national health programmes have been introduced to tackle both infectious and non-infectious diseases. The National Cancer Control Programme is one among them, and it depends heavily on primary health care workers (GOI). India is experiencing an increasing burden of oral cancer because of the growing incidence of the disease (ICMR, 2010). It is well known that detrimental health behaviours such as the use of tobacco, quid and alcohol are risk factors for oral cancer. However, there are still the socioeconomic determinants, the 'causes of causes' (Marmot, 2005), which need to be

investigated. The increasing incidence and moreover, frequent occurrence of oral cancer among the disadvantaged population demands investigation to discover whether the socioeconomic disadvantage has a causal implication in the development of oral cancer.

The mortality from oral cancer is higher in India than many developed countries and is caused by various factors such as poor nutritional status, advanced stages when diagnosed, inadequate access to health care and lack of timely treatment. The paradox is that the mouth is the most accessible area for visual examination, but oral cancer is still being diagnosed in its later stages. Researchers have conducted a randomised controlled trial (RCT) to examine the reduction in mortality due to the diagnosis occurring at early stages of oral cancer through visual screening by primary health care workers (Sankaranarayanan et al., 2013). However, employing visual screening requires training and periodic assessment of the screeners, and this questions whether the program is sustainable. Moreover, when primary health care workers are also involved in other national health programmes, their rigorous training and periodic assessment may limit their use in visual screening programmes. In such a situation, untrained personnel could be employed to triage asymptomatic individuals at high-risk for oral cancer when no screening programs exist in settings with restricted resources. Thus, there is need for a simple and easy screening model that could be used by untrained personnel to identify high-risk individuals in rural and remote areas.

Therefore, it will be very timely, and appropriate, to examine the association of SEC at different stages over the life-course with the development of oral cancer in adulthood, and to develop a screening model to identify high-risk individuals. A study was designed with the following research hypotheses, aims and conceptual framework:

1.2 Research hypotheses

1. Accumulation of socioeconomic disadvantage over the life-course is associated with oral cancer in the Indian population.
2. Early-life socioeconomic disadvantage has a lasting effect on the oral cancer outcome in adulthood in the Indian population.
3. An oral cancer screening model developed for the Indian population, to screen high-risk people from rural/remote areas, has good predictive ability.

1.3 Aims

1. To explore the critical period, social mobility, and accumulation models operating between socioeconomic conditions at different stages in life with oral cancer, in the Indian population.
2. To estimate the controlled direct effect of childhood socioeconomic conditions on oral cancer in adulthood, in the Indian population.
3. To develop and validate a screening model for oral cancer using risk scores in the Indian population.

1.4 Conceptual frameworks

Conceptual frameworks were developed to address specific aims.

1. Aim1: The first aim was to explore socioeconomic disparities in oral cancer using the three life-course models (critical, accumulation, and social mobility). The exploratory model was used to examine how SEC in childhood (6-10 years), early adulthood (20-25 years), and later adulthood (at the time of interview) is associated with the oral cancer. The critical period model gives information on the irreversibility of the effect, while the accumulation and social mobility models give an indication of accumulation

of the effect over the life-course and modification by later-life exposure, respectively.

The framework included confounders of exposure-outcome relation to obtaining unconfounded estimates, but it did not include the mediators (behavioural risk factors), in order to avoid collider bias.

2. Aim 2: The second aim was to examine the causal association between the child SEC and oral cancer in adulthood. For the causal approach, a conceptual framework was developed employing a directed acyclic graph (DAG). The exposure, intermediates, and covariates were considered in the temporal sequence following the order of occurrence of each factor in the life-course of individuals. A DAG helps in visualising the direction of relations between the variables and in identifying mediators and confounders. The direct and indirect pathways through the mediators, from the exposure to the outcome, were identified with the DAG. Marginal structural model (MSM) was employed to infer causal association between childhood socioeconomic disadvantage and oral cancer.
3. Aim 3: For the third aim, various factors (such as paternal and maternal education, childhood SEC, tobacco, quid, alcohol, diet, body mass index (BMI), family history of upper aerodigestive tract (UADT) cancer, and oral hygiene practices) were examined for their association with oral cancer. A prediction model for oral cancer was developed with strongly associated predictors. The developed model was validated for its prediction accuracy on a bootstrap sample.

1.5 Thesis structure

This thesis has been structured in publication format. Papers published/submitted for publication have been included in different chapters. One paper is a narrative review and three others are original research articles. However, additional chapters such as introduction, review of the literature, methods and discussion are presented to provide a clear description of the

research work. The three original research articles utilise exploratory, causal and prediction models that are commonly used in epidemiology to address the aims. An overview of thesis structure is as follows.

Chapter 1 sets the background for the life-course research on oral cancer.

Chapter 2 focuses on a review of the literature on oral cancer related to descriptive epidemiology, diagnosis, screening, risk factors, socioeconomic correlates of the disease and its risk factors, life-course models and life-grid in interviewing. The narrative review published in the *Asian Pacific Journal of Cancer Prevention* is a part of this chapter.

Chapter 3 describes the methods adopted in data collection for the life-course study in detail.

Chapter 4 explores different life-course models determining an association of SEC at different stages with oral cancer. This chapter is prepared in publication format and submitted for publication in the journal *Advances in Life Course Research*.

Chapter 5 examines the effect of early-life SEC on oral cancer adopting causal modelling approach. This chapter is prepared in publication format and submitted for publication in *Epidemiology*.

Chapter 6 reports on using life-course risk predictors to develop a screening model for oral cancer. This chapter gives a detailed description of developing a model with a Prediction Modelling approach. It also reports on the internal validation and predictive ability of the model in the study population. This chapter is prepared in publication format and submitted for publication in the journal *Community Dentistry and Oral Epidemiology*.

Chapter 7 presents a discussion of the research findings, strengths, limitations, implications and conclusions of the research.

Chapter 2: Review of the Literature

2 Review of the literature

This chapter presents a detailed literature review of descriptive epidemiology, models in life-course epidemiology, SEC and risk factors in the context of oral cancer.

2.1 Cancer of the oral cavity and oropharynx

Cancer is a malignant neoplastic disease where unlimited and uncoordinated growth of a population of cells occurs within a tissue and invades the surrounding tissues, causing destruction, and has the potential to spread to other parts of the body. Malignant neoplasms of the oral cavity or oropharynx predominately originate from epithelial tissue, although mesenchymal neoplasms can occur from, for example, bone, fibrous tissue and endothelial cells. Epithelial-derived neoplasms are classified as carcinomas and can arise from the epithelium of the oral cavity, oropharynx and salivary glands, as well as, less commonly, residual odontogenic epithelium within the jaw. Among them, squamous cell carcinoma (SCC) is the most common type.

By definition, SCC is ‘an invasive epithelial neoplasm with varying degrees of squamous differentiation and a propensity to early and extensive lymph node metastases occurring predominantly in alcohol- and tobacco-using adults in the fifth and sixth decades of life’ (Steinherz et al., 1986).

2.2 Clinical aspects

In this thesis, ‘Oral cancer’ is used as a collective term for oral cavity and oropharyngeal cancers. Clinical examination is the first step in the diagnosis of oral cancer. The oral cavity is easily accessible for inspection and palpation; these are conventional and basic methods in

oral cancer screening. Further details about the cancerous lesions/conditions are obtained with advanced diagnostic procedures that include histopathological examination and various imaging techniques.

2.2.1 Clinical features

Oral cancer is a silent disease in the initial stages, when the symptoms are either absent or very vague, and very minimal clinical findings are obvious from physical examination. Oral cancer may sometimes develop subsequent to other conditions in the mouth, referred to as oral potentially malignant disorders (OPMD). In many cases, the oral cancer lesion would be in advanced stages at the time of presentation to health care professionals. The signs and symptoms include a rapidly growing tumour mass with or without ulceration, a chronic non-healing ulcer, difficulty in speaking, trismus, dysphagia, bad breath and mobile teeth (Johnson et al., 2005). There may be pain when the lesion is infected or when there is secondary involvement of nerves, and occasionally spontaneous bleeding (Johnson et al., 2005).

2.2.2 Diagnosis

Advanced diagnostic tools used for diagnosis of oral cancer are magnetic resonance imaging, computed tomography, in and intra-oral radiographs and orthopantomographs. The gold standard test for diagnostic confirmation is histopathology. In some cases, when the presentation is only a neck swelling, fine needle aspiration cytology is performed (Johnson et al., 2005).

2.2.3 Histopathological types

Considering cancers of epithelial origin in the oral cavity and oropharynx, SCC is the most common type, comprising nearly 90% of diagnosis (Mashberg, 2000; Johnson, 2001; Sargeran et al., 2008). Other types, such as verrucous carcinoma, adenosquamous carcinoma,

mucoepidermoid cancer, adenoid squamous cell carcinoma cuniculatum and others, comprise the rest (Johnson et al., 2005).

2.2.4 Staging and prognosis

Staging of oral cancer is essential for treatment planning and also to estimate the prognosis (Baker, 1983). Staging is done mainly pre-operatively, but the stage may change due to additional findings intra-operatively (Asthana et al., 2003). Imaging techniques are employed to describe the morphology of the tumour, based on which Tumour Nodal Metastasis (TNM) staging (AJCC, 2012) is performed. The stage advances as the tumour grows in size and invades surrounding structures like cortical bone, muscles of the tongue, floor of the mouth, sinuses and facial skin and with regional metastasis to lymph nodes. There could be distant metastasis but this is rare. As the stage advances, the prognosis worsens, resulting in poor survival rates following cancer therapy. In addition to the cancer itself, other factors (such as the presence of co-morbidity, poor nutritional status, age, tobacco and alcohol use) affect the rate of survival (Ebrahimi et al., Online first April1, 2014).

2.3 Screening for oral cancer

Oral cancer is a disease that is suitable for screening because it satisfies some of the criteria of conditions for which screening can be implemented (Wilson and Jungner, 1968). Diagnosis differs from screening, depending on whom the tests are performed. Diagnostic tests are performed when a person presents with signs and symptoms, whereas screening is done for a person with no such signs and symptoms of the disease (Weiss, 2011). Screening can be employed to triage asymptomatic people with oral cancer for referral to further undergo diagnosis and treatment after diagnostic confirmation.

Screening is defined by the United States (US) multi-sponsored Commission on Chronic Illness (CCI) as ‘the presumptive identification of unrecognised disease or defect by the application of tests, examinations or other procedures that can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive screening result must be referred to their physicians for diagnosis and necessary treatment’ (CCI, 1957).

The above definition clearly distinguishes diagnosis and screening. In community settings, *mass screening* is performed when the whole population is targeted. An example of this is a RCT of a visual screening program for oral cancer detection conducted in Kerala, India (Sankaranarayanan et al., 2013). The trial was carried out over a period of 13 years in which, on average, 22,205 people were screened four times at 3-year intervals. However, *selective screening* could be done for high-risk patients to reduce the number of negative persons identified for referral (Wilson and Jungner, 1968). Nevertheless, dental visits provide occasions for *opportunistic screening* by dentists (Lim et al., 2003).

2.3.1 Principles of screening

Wilson and Jungner (1968) have discussed 10 general principles of screening for early detection of diseases. In this section, the principles of screening have been reviewed with regard to oral cancer in India.

1. The condition sought should be an important public health problem

Oral cancer is a public health problem in India with high incidence and mortality rates.

The consequences are serious being physically, psychologically and financially demanding for oral cancer patients if not treated in its early stages.

2. There should be accepted treatment for patients with recognised disease

Accepted treatment modalities such as surgery, chemotherapy or radiotherapy are provided in various cancer hospitals in India for early stages of oral cancer or OPMD. As the TNM stage at diagnosis advances, the five-year survival reduces (Garzino-Demo et al., 2006). Early detection and prompt treatment improves survival and reduces the negative impact on quality of life of the affected patients.

3. Facilities for diagnosis and treatment should be available

Following screening, those with positive result should be provided with facilities to undergo confirmatory diagnosis and treatment if the diagnosis is confirmed. There are government cancer hospitals and registries in different regions of India. In addition, there are private hospitals, mostly located in urban areas that provide diagnostic and therapeutic services to cancer patients.

4. There should be a recognisable latent or early symptomatic stage

Oral cancer is a chronic disease with a long latent period. In its pre-cancer/early stages, oral cancer remains asymptomatic but could be identified using visual screening.

5. There should be a suitable test or examination

Oral visual examination is usually performed to detect oral cancer. However, screeners require intensive training to perform visual screening to increase the sensitivity and specificity of detection. New approaches may be devised, so that less trained personnel may be used for mass screening programs.

6. The test should be acceptable to the population

Techniques such as mouth self-examination (Elango et al., 2011), oral visual examination (Kumar et al., 2011) and toluidine blue application (Feaver et al., 1999) have been found to be highly acceptable methods used to screen for oral cancer (Paudyal et al., 2014).

The other principles which follow have yet to be researched with regard to oral cancer and include:

7. The natural history of the condition, including development from latent to declared disease should be adequately understood.
8. There should be an agreed policy on whom to treat as patients
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to the possible expenditure on medical care as whole
10. Case-finding should be a continuing process and not a “once and for all” project

2.3.2 Screening techniques and their predictive ability

Easy access to physically examine the oral cavity makes visual examination a useful technique to screen for cancer of the oral cavity. The primary/standard screening test for oral cancer has been systematic visual examination. The World Health Organization (WHO) provides a detailed guide to performing examination of the oral mucosa (Kramer et al., 1980). Additional diagnostic aids include oral cytology, toluidine blue use to stain the malignant lesions, and advanced light-based tests (Lingen et al., 2008). One of the requisites for implementing a screening test is to identify the disease at the latent stage or while it is yet symptom-free or early in the symptomatic stage (Wilson and Jungner, 1968). Therefore, a screening test should be able to identify OPMD cases that have the potential to undergo malignant transformation.

A systematic review of 36 reports published between 1966 and 2002 found insufficient evidence to support the effectiveness of community-based visual screening to enhance early detection of oral cancer (Patton, 2003). It suggested screening of high-risk individuals to augment the effectiveness of such programs. Recently, in 2014, the United States Preventive

Services Task Force (USPSTF) reviewed seven studies, many of which were conducted in countries such as India and Taiwan that have a high incidence rate for oral cancer. It estimated the predictive ability of visual screening for oral cancer and OPMD, as shown in Table 2.1. The sensitivity and positive predictive value varied widely. The specificity ranged between 54% and 99.9%. The negative predictive value of the visual screening was high (73.3–99.3%).

Table 2.1 Predictive ability of visual screening as reported in 36 studies

Parameters	Range (%)
Sensitivity	18.0–94.3
Specificity	54.0–99.9
Positive predictive value	17.0–86.6
Negative predictive value	73.0–99.3

Adapted from USPSTF (Moyer and Force, 2014)

According to the USPSTF review, the evidence was inadequate to support either the benefits or harm of identifying oral cancer with visual screening. It also concluded that screening for oral cancer and treatment of such screened oral cancer cases could improve five-year survival, but the data were from only one RCT on visual screening (Sankaranarayanan et al., 2013). However, these recommendations were directed towards primary health care workers as screeners, and not specialists such as dentists or physicians (Moyer and Force, 2014).

Nevertheless, the randomised controlled oral cancer screening trial conducted in India was able to show that screening improved the early detection of oral cancer cases in the intervention group relative to the control group (Ramadas et al., 2003; Sankaranarayanan et al., 2013). Thus, the mortality rate was lower because of screening. It could be more cost

effective if the program was directed towards high-risk populations (Subramanian et al., 2009). In addition, there were some drawbacks with the screening program such as problems with logistics and non-compliance of those people identified as requiring further diagnosis and treatment.

Many target groups have been utilised in the past as screeners. They can be broadly grouped into specialists (trained dentists, physicians, otolaryngologists, surgeons, physicians) and trained health care workers (primary health care workers and college graduate students) (Patton, 2003). Systematic review and meta-analysis of seven studies demonstrated that the discriminatory ability of primary health care workers and trained dentists was not different (Moles et al., 2002; Downer et al., 2004). However, the primary health care workers had received substantial training to perform the screening.

The advantages of screening include early diagnosis and reduction in morbidity and mortality. The reduction in morbidity can further have an impact on the quality of life of the cases screened and diagnosed with oral cancer. There are potential drawbacks of false-positives from screening such as cost of confirmatory tests, travel costs, and also the anxiety created among those identified for follow-up. The over-treatment of the precursor lesions (OPMD in the form of surgery) that would have regressed adds to the cost (Moyer and Force, 2014). Another drawback is the sustainability problem related to logistics and difficulty in training the personnel in primary health care.

2.3.3 What more could be done?

In countries with a low incidence of oral cancer, opportunistic screening is better suited for screening as it would be cost-effective (Warnakulasuriya and Cain, 2011). However, in countries with high incidence, selective screening could be more cost-effective. For example, there are untrained primary health care personnel who could be utilised to screen high-risk

individuals in India. If a simple algorithm is developed using common risk factors of the target population, it could be used by the untrained personnel to identify high-risk individuals, it would be one step further towards controlling oral cancer and its adverse consequences.

2.4 Global epidemiology of oral cancer

2.4.1 Incidence

Oral cancer is a problem in many parts of the world. Oral cavity cancer along with oropharyngeal cancer stands sixth in the position of the commonest cancers. In the European Union, it is the eighth most common malignancy (Ferlay et al., 2010a). The incidence varies widely across countries. South and Southeast Asian countries, France, Hungary, Brazil and Papua New Guinea (PNG) are some of the countries with high incidence rates (Warnakulasuriya, 2009a; Ferlay et al., 2013). The estimated age-standardised incidence rate (ASIR) for the world is four per 100,000, including both men and women. The incidence in men (ASIR = 5.5 per 100,000) is greater than in women (ASIR = 2.5 per 100,000). This gender difference in the incidence is observed in both more developed and less developed countries. The lowest incidence rates (ASIR = < 1.0 per 100,000) are seen in females in some parts of Africa, Eastern Asia and some Pacific islands, while the highest incidence rate (ASIR = 34.8 per 100,000) is observed in men from Melanesia (Ferlay et al., 2013).

Table 2.2 Countries with highest and lowest age-standardised incidence rates of oral cancer in both sexes according to GLOBOCAN 2012 (Ferlay et al., 2013)

Continent	Country with highest incidence	ASIR (Per 100,000)	Country with lowest incidence	ASIR (Per 100,000)
Africa	France, La Reunion	12.0	Cape Verde	0.3
America	France, Guadeloupe	10.4	Nicaragua	1.2
Asia	Bangladesh	18.3	Kuwait	1.5
Europe	Hungary	16.7	Cyprus	1.9
Oceania	PNG	27.2	Samoa	1.2

2.4.2 Trend

Globally, there has been a slight decline in the incidence rates of oral cavity and other pharyngeal cancers among men and women over the past decade (2002–2012) (Ferlay et al., 2010b; Ferlay et al., 2013). The incidence among men reduced from 6.3 to 5.5 for oral cavity and 3.8 to 3.2 for other pharyngeal sites per 100,000 men. For women, the estimates declined from 3.2 to 2.5 for oral sites and 0.8 to 0.7 per 100,000 for other pharyngeal sites. In the past, the incidence increased in France until 1980 and declined between 1980 and 2000. In the USA, incidence increased from 1995 to 2004 and has fallen since then (Warnakulasuriya, 2009a). The incidence rate of oral cancer in Australia is similar to other western countries below the global rate, and showed a decreasing trend from 1982-2008 (Ariyawardana and Johnson, 2013). In New Zealand, incidence rates for oral cavity cancers increased for both men and women during 1957-1991 (Cox et al., 1995). Later studies showed that oral cavity cancer incidence rate remained stable for both men and women in New Zealand between 2001 and 2010 (Elwood et al., 2014). Overall, there seems to be a fall in the incidence of oral cancer.

2.4.3 Prevalence

The prevalence of oral cancer cases following diagnosis is low because of high mortality rates except for lip cancer, for which the five-year survival rate since diagnosis is more than 90%. The prevalence is lower with a greater number of years since diagnosis. The prevalence is high in South Asian countries (India, Bangladesh, Sri Lanka, and Pakistan), some countries of West Asia (Yemen), and Melanesia (PNG) (Bray et al., 2013).

The prevalence to incidence ratio (P:I) is 3.0 for oral sites and 2.8 for other pharyngeal sites that includes the oropharynx for both men and women. The P:I is similar for men and women (Bray et al., 2013).

2.4.4 Mortality and survival

The mortality rates are estimated for people diagnosed with oral cancer. According to GLOBOCAN 2012 (Ferlay et al., 2013), mortality for both sexes was 3.6 per 100,000 due to oral cancer. The age-standardised mortality was greater for men (4.9/100,000) than women (2.6/100,000). In European countries, mortality specific to oral cancer increased between 1950 and 1980 (La Vecchia et al., 2004) and declined thereafter. The five-year survival rates observed from Surveillance, Epidemiology, and End Results (SEER) Program data showed that the survival rate increased from 53.3% in 1970-77 to 62.7% during 1999-2006 in the U.S. (Altekruse et al., 2010). Age-standardised mortality in women has increased in some European countries such as Hungary, Belgium, Denmark and Slovakia (Johnson et al., 2011a). In Brazil, the mortality from oral cancer has remained stable for both genders between 1979 and 2002 (Boing et al., 2006).

2.4.5 Socioeconomic inequalities in oral cancer

A social gradient exists for health. Social inequalities in various health outcomes have been observed in both developed and developing countries. There are differences in the incidence, mortality and survival specific to oral cancer (Johnson et al., 2011b). People of low SEC have higher mortality and lower five-year survival post-therapy than their counterparts (Merletti et al., 2011). This difference could be related to a delay in presentation, an individual's characteristics (such as nutrition, diet, awareness about the disease), as well as the uptake of screening programs that have a socioeconomic component (Kumar et al., 2001; Ramadas et al., 2008). Oral cancer is more frequently seen among those from the low socioeconomic strata and those living in deprived areas. Low income, low levels of education and occupation (Greenberg et al., 1991; Madani et al., 2010a; Boing et al., 2011) are linked to oral cancer in developing and developed countries. It has also been found that regular tobacco and alcohol

consumption have social determinants – where the regular use of tobacco and alcohol is higher in the low SEC group (Neufeld et al., 2005; Rooban et al., 2010; Noonan and Duffy, 2014). It is believed that the social inequality in oral cancer may be explained by the risk factors. Still, there is some extent of risk among people of low SEC that is not explained by their behaviour (Greenberg et al., 1991; Boing et al., 2011). A recent report states that SEC are risk factors for oral cancer independent of health behaviours (Conway et al., 2008). Some studies done to understand the relationship between SEC and oral cancer have been reviewed below.

2.4.5.1 Studies conducted using individual-based measures

Elwood et al (1984) found from a Canadian case-control study that unskilled workers had a higher adjusted odds ratio (OR = 1.6, 95% CI = 1.0-2.5) than skilled workers/professionals for developing cancers of oral cavity, pharynx and larynx.

A hospital-based case-control study conducted in Italy showed that oral cavity cancers were more common among farmers and manual labourers than clerical/professional workers (Franceschi et al., 1990).

Ferraroni et al (1989) observed a strong inverse association of social class and education with mouth and pharyngeal cancer in Italy.

Greenberg et al. (1991) in their U.S. study, investigated relation between individual socioeconomic measures and oropharyngeal cancer among male cases and controls.

Education and occupational status were not associated with oropharyngeal cancer. However, marker of social insecurity, low (<82.6) and medium (82.6-92.6) percentage of years worked were independently positively associated with oropharyngeal cancer.

Choi and colleagues (1991) in 1986-89, studied the distribution of oral, pharyngeal and laryngeal cancer cases, and controls by education and occupation in Korea. Cases were found to be more commonly less educated (no schooling/primary school) and agricultural workers or unemployed than controls.

A population-based case-control study (Dikshit and Kanhere, 2000) conducted in India between 1986 and 1992 showed that no education (never versus ever) was associated with oral cavity (OR = 2.4, 95% CI = 1.5-3.7) and oropharyngeal (OR = 1.7, 95% CI 1.2-2.4) cancers, when adjusted for age. The association disappeared when adjusted for age, smoking and quid chewing.

A multi-centre case-control study in Turkey showed that low education was associated with oral cancer (Guner et al., 2005). Cases were more commonly less educated and farmers than controls. There was no relation between income and oral cancer.

In Brazil, a case-control study was conducted to examine the relation between occupational status and oral/oro-pharyngeal cancer in males. The authors found that those who worked in vehicle maintenance shops had higher odds (OR = 2.45, 95% CI = 1.14-5.27) for oral/oropharyngeal cancer than other occupational groups after adjusting for age, alcohol and smoking (Andreotti et al., 2006).

2.4.5.2 Studies conducted using area-based measures

The association between 2 year overall survival of oral cancer patients with neighbourhood socioeconomic measures was studied in Taiwan (Lee et al., 2012). There was no difference in survival by neighbourhood socioeconomic condition measured by neighbourhood income. However, patients with low individual SEC living in disadvantaged neighbourhood had

higher hazard ratio (1.46-1.64) than oral cancer patients with high individual SEC living in advantaged neighbourhood.

Sharpe et al (2012) investigated socioeconomic inequalities in UADT cancers using area-based deprivation measure - the Carstairs Index in Scotland. People living in most deprived areas (Carstairs index 10) had higher relative risk than those living in least deprived areas (Carstairs index 1).

2.4.6 Global epidemiology of risk factors for oral cancer

2.4.6.1 Tobacco and alcohol

Tobacco and alcohol use are the most preventable causes of oral cancer. About 75% of all oral cancers can be attributed to tobacco in either smoking or smokeless forms (Radoi et al., 2013a; Kamangar et al., 2009). Smokeless tobacco (SLT) use is reported by both men and women, in developed and developing countries. Furthermore, SLTs are also used more commonly by children and young adults (Pednekar et al., 2009; Edvardsson et al., 2012; Agaku et al., 2013). It is available as finely chopped tobacco leaves, powder, and also commercially packed flavoured tobacco in Southeast Asian countries; however, in developed nations like the United States of America, Sweden and the United Kingdom, SLT is available as dry and moist snuff (soluble or insoluble). The health implications of SLT in the American and European populations may be far more extensive than previously believed. Although some of the meta-analytical studies have concluded that the risk of oral cancer from SLT is minor or moderate in European and American populations (Rodu and Jansson, 2004; Weitkunat et al., 2007), its effect may have been masked by smoking (Conway, 2008). Nevertheless, SLT has been established as a carcinogen (IARC, 2007). Moreover, the SLT in America and Europe may be different from that of Asian countries. Asians and some of the Asian migrants in America and Europe use SLT along with areca nut, lime and betel leaves

that are more carcinogenic (Guha et al., Online first May 14, 2014). The tobacco-specific nitrosamines content of Asian SLT products is greater than that of the American and European products (Stepanov et al., 2005).

Tobacco smoking in various forms, such as cigars, cigarettes, bidis and pipes, is prevalent across the world. There is considerable evidence that smoking plays an aetiological role in oral cancer. Smoking has an independent effect (Talamini et al., 1990) and interacts with SLT and alcohol (Ferreira Antunes et al., 2013; Petti et al., 2013b) to exert a joint effect which increases the risk for oral cancer. Differences in the prevalence of smoking and alcohol habits in men and women explain the gender differences in risk for oral cancer (Muscat et al., 1996).

There is evidence that alcohol is independently associated with oral cancer (Talamini et al., 1998) contributing to 7-30% of the oral cancer (Boffetta et al., 2006; Radoi et al., 2013a). Alcohol's independent effect is less (Petti et al., 2013a; Radoi et al., 2013a) but it has a synergistic effect on the carcinogenic potential of tobacco (Rajamanickam et al., 2007; Yen et al., 2008b).

2.4.6.2 Diet

Diet has been investigated for risk enhancement and risk reduction for oral cancer. Dietary intake of animal protein and fat is independently associated with oral cancer (Bravi et al., 2013). Consumption of processed meat increases the risk of oral cancer more than the total intake of red/white meat (Xu et al., 2014). Processed meat is frequently contaminated with nitroso compounds, which are known carcinogens (Tricker and Preussmann, 1991). In contrast, regular consumption of fish and dairy products reduces the risk (Levi et al., 1998). Dietary consumption of legumes, vegetables and fruits is found to be protective against oral cancer (Levi et al., 1998; De Stefani et al., 1999). In Brazil, reduced intake of fruits and vegetables increased the risk for oral cancer, whereas rice and beans conferred protection

against oral cancer (Marchioni et al., 2007). In some research, the protective effect of garlic and onion intake against oral cancer has been studied. Among the Southern European population, such 'allium' vegetables were associated with lower risk (Galeone et al., 2006). Curcumin, a chief polyphenol compound present in turmeric, has been proposed to be anti-carcinogenic, with support for the anti-cancer property of curcumin mostly from laboratory studies (Sharma et al., 2006). However, the debate regarding the anti-carcinogenic property of dietary items is still unresolved.

2.4.6.3 Poor oral health/hygiene

Poor oral hygiene has been associated with cancer, and increased mortality from cancer, as a result of oral infection (Söder et al., 2012). Tooth loss and poor oral hygiene reflecting poor oral health have been examined for an association with oral cancer (Talamini et al., 2000; Balaram et al., 2002). An Italian study showed that oral hygiene and general oral condition were marginally worse among cases than controls (Talamini et al., 2000). Zheng et al (1990) found that people with missing teeth and those reporting not brushing their teeth higher odds for oral cancer. The suggested pathways linking poor oral health and oral cancer are through human papillomavirus (HPV) infection promoted by the presence of inflammatory sites in the mouth (Tezal et al., 2012; Bui et al., 2013; Virtanen et al., 2013). The association is stronger for sites in the oropharynx than the oral cavity (Tezal et al., 2012). Besides HPV infection, other hypothesized explanation could be that oral cancer diagnosis is associated with irregular dental visits (Langevin et al., 2012), which is also associated with missing teeth (Renvert et al., 2011). The genetic studies support an interaction between alcohol and poor oral hygiene. Among those with slow alcohol-metabolising genotype (ADH1B), salivary ethanol concentration remains higher and for a longer duration which could be metabolised by enormous micro-organisms in those with poor oral hygiene, thus increasing the risk of oral

cancer (Tsai et al., 2014). Further evidence is required to understand the link between poor oral health and oral cancer.

2.4.6.4 Body mass index

Body mass index has been linked to oral and pharyngeal cancers. Lean body mass has been shown to enhance the smoking- and drinking-related odds ratio (OR) for oral/pharyngeal cancer (Lubin et al., 2010), but no association was observed with oral/pharyngeal cancer among never drinkers and never smokers (Nieto et al., 2003). On the contrary, overweight and obesity was associated with a lower risk for oral cancer (Radoi et al., 2013b). The relation between body mass and oral cancer is further supported by the data from a study in France showing lower risk with a gain in body mass between the age of 30 years and two years before the interview (Radoi et al., 2013b). There could be a potential bias from residual confounding or reverse causation. However, the underlying mechanism is yet unclear.

2.4.6.5 Human Papillomavirus

Recently, in many countries, it has been noted that the incidence of cancers in sites such as base of the tongue, tonsils and oropharynx (that are related to HPV infection) is increasing (Näsman et al., 2009; Auluck et al., 2010; Ariyawardana and Johnson, 2013), but not in other oral cavity sites. HPV infection of the oral cavity has gained importance as an emerging risk factor for oral cancer, being associated with a 3-5 fold higher risk. HPV subtypes 16 and 18 are found in 22% and 14% of oropharyngeal tumours respectively (Miller and White, 1996; Sugerman and Shillitoe, 1997; Gillison and Shah, 2001; Lindel et al., 2001; Mork et al., 2001). HPV infection is associated with poor oral health, sexual history, and improvement in disease-free survival following the treatment of oral cancer (Furniss et al., 2007; Tezal et al., 2012). However, the improved overall survival and disease-free survival for HPV-positive

oral cancer patients was confined to oropharyngeal sites and not the sites in the oral cavity (Ragin and Taioli, 2007).

2.5 Epidemiology of oral cancer in Asia

Title: Epidemiology of oral cancer in Asia in the past decade- An update (2000-2012)

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2.5.1 Statement of Authorship

Statement of Authorship

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2.6 Conclusion

This part of the review has drawn data from published articles that differ in study design, to narrate the scenario of epidemiology of oral cancer in Asian countries between 2000 and 2012. Comparison of estimates of oral cancer outcomes is limited because of the varying data collection methods used in the studies. The surveillance methods differ from country to country. While high quality data are available for incidence rates from cancer registries in India, the incidence rates are estimated from regional data or frequency data in countries such as Pakistan, Sri Lanka and Bangladesh. There are dissimilarities in the incidence rates of oral cancer across different countries in Asia. While there are some common factors like the use of tobacco, alcohol and quid chewing, there are some differences in the prevalence of habits, in addition to some still unknown or unexplained factors, other than social and economic factors in these Asian countries. High incidence is particularly observed in Asian countries with a cultural practice of chewing quid. Recently available quid sachets like gutkha and pan masala are used by children, men and women alike, and may increase oral cancer incidence. Tobacco chewing along with smoking and alcohol are the main reasons for the increasing incidence of oral cancer. Low SEC and diet low in nutritional value, i.e. lacking vegetables and fruits, contributes towards the risk. In addition, viral infections, such as HPV and oral hygiene, are other important risk factors.

(N.B. The paper on epidemiology of oral cancer in India concludes here)

2.7 Causality in cancer epidemiology

2.7.1 Causality, causal inference and cancer

In cancer research, carcinogenicity of exogenous environmental factors is usually established by the International Agency for Research on Cancer (IARC) and published in Monographs on various toxins, chemicals, occupational and environmental factors. The evidence comes from animal experiments, epidemiological studies and mechanistic considerations (Lagiou et al., 2005). Many epidemiological studies have examined the association between the exposures of interest and the disease/health outcomes. Exposure may be behaviour, a characteristic, or an intervention. In cancer epidemiology causality, of an exposure is based on findings from many observational studies that show an association between the exposure and outcome.

“Association” signifies a statistical dependence, which may be causal or non-causal.

Causation is different from association. Association can be in either direction while causation is directed (Glymour and Greenland, 2011). Association between two variables in a sample population is based on the relationship with the observed outcomes. Interpretation of an association as causal or non-causal has been generally based upon Hill’s criteria, which include strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experimental evidence and analogy (Hill, 1965). Of the nine Hill criteria temporality is of high importance in inferring causality. Nevertheless, the other eight criteria are not considered as evidence for causality and may even hamper causal inference (Lanes and Poole, 1984; Rothman and Greenland, 2005).

Causal inference is the central idea of epidemiology. Causation is thought of in counterfactual terms – ‘what if not...’ (i.e., counterfactual of the exposed is the unexposed and vice versa).

Therefore, an effect measure of an exposure on the outcome is defined counterfactually (Rothman et al., 2011b). The judgement of causality is inductive (Rothman et al., 2011b). The

counterfactual outcome is not observed, and is hence theoretical. Therefore, the individual causal effect cannot be estimated because of missing data, whereas a population causal effect can be sometimes estimated consistently, although indirectly (Hernan, 2004).

A cause is an exposure that increases the probability of occurrence of an outcome when all other conditions are fixed (Kundi, 2006). There is a temporal relation between exposure and outcome for causality. It is difficult to define a cause because most diseases are multifactorial. Therefore, causal inference is a carefully drawn judgement based on the pre-condition that confounding, potential biases and population equivalence have been thoroughly examined (Kundi, 2006).

2.7.2 Study designs for causal inference

When the goal is causal inference, the estimates of the effect of exposure on the outcome must be unconditionally unbiased or marginally unbiased (Rothman et al., 2011b).

Randomised controlled trials have been considered as the gold standard for inferring causality. There is exchangeability and identifiability because all of the confounders are considered to be randomly distributed (Greenland and Robins, 1986). The exchangeability refers to comparability of the effect of treatment as causal because the study and control groups are similar in all aspects except for the treatment. The identifiability refers to the outcome that is only due to treatment. The changes in the outcome are observed following intervention. However, it is not always possible or ethical to conduct RCTs to establish causality (West et al., 2008). Therefore, it is essential to draw causal inference from observational studies. For an exposure to be causative, 'temporality' is the main criterion, in accordance with the natural history of the disease (Kundi, 2006). Data obtained from observational studies employing cohort and case-control designs are compatible with the

requirements of temporality. Nevertheless, appropriate causal analysis depends on an understanding of the data collected and the design of the study (Robins, 2001).

2.7.3 Conceptual model for causal analysis

To tackle the problems of multifactorial causation, confounding, direct and indirect effects, a conceptual model needs to be considered (Rothman et al., 2011b). In recent years, causal diagrams or causal graphs have been developed to model causal pathways in epidemiology (Greenland et al., 1999). These are called ‘Directed Acyclic Graphs’ (DAG). These graphical methods help epidemiologists to intuitively understand confounding, selection bias, direct and indirect effects when the aim is causal analysis (Rothman et al., 2011b).

2.8 The life course approach for oral cancer

2.8.1 Relevance of the life course approach

Life-course epidemiology, since 1990s, has gained popularity in chronic disease research because of its approach to identify biological, behavioural and psychosocial processes that operate across the life span of an individual or a population (Blane et al., 2007). Life-course epidemiology is defined as ‘the study of long-term effects on chronic disease risk of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life’ (Kuh and Ben-Shlomo, 2004). The motive is to understand how the risks for a disease develop with the time and timing of exposures (Kuh and Ben-Shlomo, 2004).

Oral cancer (like other chronic diseases) has a long latent period and induction time. The time between the exposure and disease initiation, and its detection, is long. The prolonged empirical induction period (Rothman, 1981) indicates that exposure could have occurred early in life. There could be emergence of later risks (mediators) as a result of exposure to prior risk factors (distal) with the progression of time. Further, the duration and timing of exposure to

risk factors are also vital in determining their effects (Kuh and Ben-Shlomo, 2004). Life-course studies are appropriate to investigate chronic disease when there is a need for addition of a developmental dimension, to know whether there is a chain of risk that accumulates or modifies earlier exposure (Pickles et al., 2007). Life course epidemiology places an emphasis on temporality of an individual/population's experience of social and environmental factors within, as well as across, generations. Oral cancer is multifactorial; socioeconomic, behavioural (tobacco, quid and alcohol) and biological (genetic) factors are involved. Understanding the causal links among the socioeconomic, behavioural and biological factors can be assisted by adopting a life-course approach.

2.8.2 Life course models

There are mainly two basic models in life-course epidemiology: the critical period and accumulation models (Lynch and Smith, 2005). The pathway model can be considered as a variant of the accumulation model (Blane et al., 2007). Each of these is described below.

2.8.2.1 The critical period model

This model is based on the latency concept. Exposure(s) during specific window periods, which are sensitive/critical periods of development, have independent and long-term effects on health. This may or may not be modified by later life risk/protective factors (Kuh et al., 2003; Lynch and Smith, 2005).

2.8.2.2 The accumulation model

Risk from exposure at different critical periods or even in the absence of a critical period, risk over the life-course may accumulate to influence health outcomes (Lynch and Smith, 2005). The accumulation model is widely argued to be a social process and is supported by general

health and oral health studies (Thomson et al., 2004; Blane et al., 2007; Peres et al., 2011a). Accumulation of risk can be a co-occurrence of multiple exposures; for example, children from poor SEC may have a poor diet, and health risk behaviours (Lynch et al., 1997). This model focuses on the duration and the order in which exposure occurs. Accumulation may be due to the cumulative effects of independent and uncorrelated exposures or correlated exposure as in a chain of risk (Lynch and Smith, 2005).

2.8.2.3 The pathway model

The pathway model is based on the concept of a chain of risk factors, where one exposure leads to another exposure. The pathway model is considered as an alternative version of the accumulation model. For example, socioeconomic circumstances may influence oral hygiene, or health behaviour may affect oral/general health (Kuh and Ben-Shlomo, 2004).

2.9 Social epidemiology of oral cancer

A question arises: ‘what is the need for social epidemiology in oral cancer research?’

Graham and Schneiderman in 1972 highlighted that cancer prevention should be directed towards addressing sociological factors (Graham and Schneiderman, 1972). They stated that social epidemiology helps in understanding ‘how the behaviour might lead to disease and how modifying behaviour might prevent it’ (Graham and Schneiderman, 1972). This is true as far as the risk factors/health behaviours are concerned. Going beyond health behaviour, the aim of social epidemiology is to address social factors that determine behaviour as well as the disease. A disease of interest that has occurred in adulthood has been found to be consistently associated with poor SEC in childhood (Kuh and Ben-Shlomo, 2004). Those living in poor SEC in childhood attained lower levels of education and occupation subsequently in their life-course. Low SEC in early life may influence negative behaviour that later leads to disease

(Lynch et al., 1997). Considering inequality in oral cancer outcomes, as explained in previous sections (2.4.5 and 2.5.10), there is a need to investigate how the SEC at different stages in the life-course of an individual is associated with oral cancer. That means identifying the stage in life at which SEC is more crucial in determining oral cancer and the causal effect of early-life SEC on oral cancer that is not explained by the later-life risk factors.

Such an understanding is essential before undertaking any work to achieve a reduction in the socioeconomic inequalities of oral cancer.

2.10 Socioeconomic measures in life course research

A requisite for quantification of social inequalities in health is to have a comprehensive measure of socioeconomic status. The terms socioeconomic status and socioeconomic position (SEP), have been explained by various researchers based on the interpretation of terms. Socioeconomic status classification is based on the positions individuals occupy in the society and the prestige associated with it. Socioeconomic position is ‘an aggregate concept that includes both resource-based and prestige-based measures as linked to both childhood and adult social class position’ (Krieger et al., 1997). It includes occupational prestige, wealth and educational level. SEP may be measured at individual, household or neighbourhood levels (Krieger et al., 1997). The level at which SEP is measured represents access to resources. Social class can be at different levels over the life-course from infancy to adulthood or current position (Shavers, 2007). Two main approaches have been proposed by Kaplan (1999) for life-course measurement of SEP from infancy to adulthood or current position in health research. They are compositional (refers to individual characteristics) and contextual (refers to environmental characteristics of an individual) methods.

2.10.1 Individual-level measures

Three main measures, such as occupation, education and income, are used at an individual or household level.

2.10.1.1 Occupation

Occupation provides the linkage between education and income. It connotes access to resources, social standing, social networks, working conditions and behavioural risk (smoking and alcohol) (Galobardes et al., 2006a; Shavers, 2007). It may also relate to occupational exposures to stress, and physical and environmental hazards (Galobardes et al., 2006a).

Furthermore, employment status and health may be related to each other in either direction.

According to social causation theory, employment status determines health outcomes, and, according to the health selection theory, healthy people get work and remain employed for a longer time (Ross and Mirowsky, 1995). This dilemma may be sorted out to some extent by measuring SEP at different stages in life and by including details of the occupational role (Krieger et al., 1997).

One of the limitations of basing SEP on occupation is the difficulty in SEP assignment for dependants including children, spouses, unemployed, retirees, students, and those working in unpaid or informal jobs (Shavers, 2007). However, for the currently retired or unemployed, a previous occupation may be assigned (Grundy and Holt, 2001). For dependants, the head of household may be used. The advantages are that it can capture change from parental to one's own SEP. It can also be collected with less recall bias.

In India, where joint family structure exists with many dependants, women are frequently engaged in household roles (Bollen et al., 2001) and there are a large number of people

working in informal/unorganised jobs, due consideration has to be given to the use of occupation in measuring SEP.

2.10.1.2 Education

Education is a more commonly used socioeconomic indicator in epidemiological studies. It influences both occupation and income (Shavers, 2007). It generally reflects the intellect of a person. The better the education, the better are the job opportunities and the resources for adopting health promoting behaviour (Shavers, 2007). Since education is usually completed by early adulthood and is mostly stable thereafter, it limits the measurement of SEP thereafter. Education is measured as the number of years of education completed, or as the highest level of education attained. However, it can be used to measure changes from parental SEP to one's own SEP. It may be easier to measure, has a high response rate, and may be appropriate for people of wide age ranges and of different occupations (Krieger et al., 1997; Galobardes et al., 2006a). However it can differ in its relevance from cohort to cohort.

In the Indian context, to measure changes in SEP depending on education, many factors need to be considered. With globalisation and revolutionary changes in the educational system post-independence, there have been improvements in educational opportunities, including those for women.

2.10.1.3 Income

Income is a direct measure of materialistic status and can change within a short period. Thus, the dynamic aspect of income has to be taken into account in epidemiological studies (Krieger et al., 1997). Family or household income does not consider the number of dependants, but may be useful when measuring the income of non-earning members of the household. Equivalised income considers the number of people in the family and associated costs

(Galobardes et al., 2006a). It denotes the affordability to health care, nutrition, housing and schooling (Adler and Newman, 2002). The response rate to questions about income is often low, and recall bias is high.

In India, the difficulty in collecting information on income over the life-course can be more biased for childhood and for women. Some of the occupations are unpaid, seasonal and may be paid in material goods. For example, agricultural labourers may receive a part of the yield from the fields as payment for their labour.

In the measurement of life-course SEP, careful consideration has to be given to the population being studied, time, geographical location and dynamic changes with time. Each indicator of SEP has a different meaning (Kaplan, 1999) and may explain different pathways to health (Chittleborough et al., 2006).

2.10.2 Area-level measures

Area-level measures are contextual factors. At area-level SEP measures are used to examine the influence of neighbourhood socioeconomic circumstances on health. The area-level SEP may also be used as a proxy when individual-level SEP measures are not available (Galobardes et al., 2006b). Measures are aggregated from units of small areas demarcated by census tract or Zip codes, in which population is relatively homogenous.

Different area-based measures are used in different countries. Some of census-based SEP measures used in the U.S. include proportion of working class, proportion of employed persons in working-class occupation, proportion of people below poverty line, proportion of households owning home, proportions of persons living in households with ≥ 1 person/room and persons/square mile (Krieger et al., 1997).

In UK census-based indices have been used to measure deprivation. Some of the indices include Townsend index (Townsend et al., 1988), Breadline index (Gordon, 1995), Carstairs deprivation index (Carstairs and Morris, 1989), and Jarman or underprivileged area score (Jarman, 1983).

In a developing country such as India, it is difficult to collect life course data on socioeconomic circumstances at an area-level. Therefore, individual-level socioeconomic measures were used in this study.

Notes: In this thesis, education and occupation have been used as socioeconomic measures depending on the conceptual framework used to address each aim. The term ‘Socioeconomic condition’ has been used throughout the thesis.

2.11 Conclusion

From the literature review, it can be understood that social, diet, behavioural and biological factors accrue throughout life resulting in different health outcomes in terms of oral cancer. This could be further investigated by adopting a dynamic, life-course framework which enables the determination of the temporality of exposure (risk factors) and outcome (oral cancer) to some extent.

Chapter 3: Methodology

This chapter describes in detail the methodology followed to collect data for a larger study titled “Oral cancer- A life-course approach”. However, the data collection methods are explained briefly in the papers submitted for publication, which are retained in the respective Chapters (4, 5 and 6). In addition, each chapter describes the methods employed for data management and statistical analyses performed to address particular aims of each paper.

3 Methodology

3.1 Study design

A multicentre hospital-based case-control design was followed. Oral cancer is a relatively uncommon chronic disease with long induction and latency periods. Although a cohort design is more appropriate for life-course epidemiology of chronic diseases, a case-control approach is a more practical, inexpensive and efficient design for a rare disease such as oral cancer (Nicolau et al., 2007; Rothman et al., 2011b).

3.2 Study setting

The study was conducted in Karnataka state, India, between July 2011 and August 2012. The location, description and source populations of the selected cancer hospitals have been described below.

3.2.1 Cancer hospitals selected for the study

For data collection, six cancer hospitals in Karnataka state were approached. These hospitals provided treatment exclusively for cancer patients. Five were in Bangalore and one was in Manipal. Of the six hospitals approached, four major cancer centres granted permission to collect data. They were:

1. Shri Shirdi Sai Baba Cancer Hospital (SSSBCH)
2. Kidwai Memorial Institute of Oncology (KMIO)
3. HealthCare Global Speciality Centre (HCGSC)¹
4. HealthCare Global-Bangalore Institute of Oncology (HCG-BIO)¹

3.2.1.1 Location of the cancer hospitals

The cancer hospital (SSSBCH) at Manipal is situated in the coastal district of the Karnataka state. KMIO, HCGSC and HCG-BIO are situated in Bangalore, the capital city of Karnataka. The distance between Bangalore and Manipal is around 450 kilometers. The Figure below shows where the hospitals are situated in India.

Figure 3.1 Places where the selected cancer hospitals are located in India



3.2.1.2 Description of the cancer hospitals

1. SSSBCH is a constituent hospital of Kasturba Medical College, Manipal University.

Comprehensive cancer care is provided at this hospital.

2. KMIO is a public hospital that provides tertiary care for cancer patients.

¹ Constituent hospitals of HCG group

3. HCGSC is a tertiary care hospital providing services to cancer patients using advanced cutting-edge technology.
4. HCG-BIO is a constituent hospital of the HCG group providing tertiary care to cancer patients.

3.2.1.3 Source population for the cancer hospitals

The source population for the selected cancer hospitals is mainly the people of Karnataka state, although people from neighbouring states (e.g., Goa, Kerala, Tamil Nadu, Andhra Pradesh), and from the rest of country visit these hospitals for treatment. People from coastal areas, some of the inner districts and adjacent states seek care at SSSBCH. People from inner districts of Karnataka and other states of India seek care at KMIO, HCGSC and HCG-BIO.

3.3 Selection criteria

3.3.1 Selection criteria for cases

3.3.1.1 Case definition

A case was a person diagnosed with oral cancer, both clinically and histopathologically, who attended the selected cancer hospitals in Karnataka during the study period (July 2011-August 2012). The anatomical sites for oral cancer included C00-C10 according to the International Classification of Diseases, Oncology, 3rd edition, which correspond to:

Table 3.1 ICD-10 codes and corresponding oral and oropharyngeal sites

ICD 10 codes	Sites of malignant neoplasm
C00	Lip
C01	Base of tongue
C02	Other and unspecified parts of tongue
C03	Gum
C04	Floor of mouth
C05	Palate
C06	Other and unspecified parts of mouth
C07	Parotid gland
C08	Other and unspecified major salivary glands
C09	Tonsil
C10	Oropharynx

Oral cancer patients² satisfying the criteria defined below were invited to participate in the study. The criteria employed for selection of cases were as follows:

3.3.1.2 Inclusion criteria

1. Patients newly diagnosed with oral cancer attending selected cancer hospitals during the period- July 2011 to August 2012.
2. Males or females aged 18 years or more.
3. Patients providing consent to participate.
4. Patients with no cognitive problems.

3.3.1.3 Exclusion criteria

1. Patients with benign tumours.
2. Patients diagnosed with only premalignant disorder(s) and not malignancy.
3. Patients not providing consent.

² Both prevalent and incident cases were included. In this study, only incident cases were included for analysis to avoid prevalence-incidence bias.

4. Patients with secondaries, sarcomas and skin cancers of lips (because of pre-existing comorbidity and different etiopathology).

3.3.2 Selection criteria for controls

3.3.2.1 Principles of control selection

The control selection was mainly based on two basic principles:

1. The first principle was that the cases and controls should come from the same base population (Wacholder et al., 1992a). If the selected controls were to be affected by oral cancer, they would be diagnosed and treated at the same cancer hospital. In such settings, the controls could be selected from the patient group or patient visitors/caregivers to have the same secondary base population (secondary to case selection) (Armenian et al., 1988; Wacholder et al., 1992a). It is more appropriate if the control series is also from the same hospitals/referral centres (Wacholder et al., 1992a; Wacholder et al., 1992b; Rothman et al., 2011a).
2. The second principle was that the controls should be selected independent of their exposure to the risk factors that were being investigated (Wacholder et al., 1992a). The controls should be comparable to the cases in respect of the potential exposure to the risk factors but be free of the disease being studied. In hospital-based control series selection, those individuals seeking care for health problems that would be positively or negatively associated with exposure should be excluded (Rothman et al., 2011a). To minimise bias due to over-representation of any one diagnostic group, controls should be selected from different diagnostic groups coming from the same base population.

Hence, control series were chosen from different sources:

1. Relatives or friends or neighbours who visited or were carers of cancer patients attending selected cancer hospitals.

2. Relatives or friends or neighbours accompanying people seeking health care from health or referral centres associated with the cancer hospital.
3. People seeking health care from health or referral centres associated with the cancer hospital.

Another aspect considered was to avoid over-matching, i.e., by matching on a factor associated with exposure that could reduce the statistical efficiency (Rothman et al., 2011b).

Considering the above principles, the following criteria were proposed for control selection:

3.3.2.2 Inclusion criteria

1. Males or females aged 18 years or more.
2. Relatives, friends or neighbours who visited or were carers of cancer patients or hospital patients with medical conditions not related to tobacco or alcohol use.
3. Individuals providing consent.
4. No cognitive problems.
5. A control, if found to have an OPMD on examination, should still be included as a control.

The controls if confirmed with OPMD were still included as controls because the OPMD are causal intermediates between exposure to risk factors and oral cancer that have still not undergone malignant transformation and, by definition, ‘the outcome’ was ‘the malignant lesion’. The controls with OPMD represent the ‘at risk’ individuals in the population, and excluding them could introduce bias in the control selection (Poole, 1999). However, if diagnosed with oral cancer, they would be included as both cases and controls.

3.3.2.3 Exclusion criteria

1. Those diagnosed with malignant disease.

2. Relatives or friends or neighbours who visited or were carers of cancer patients suffering from UADT, lung and liver cancers, to avoid overmatching on socioeconomic factors, tobacco and alcohol.
3. Those not providing consent.

3.4 Sampling

3.4.1 Cases

Oral cancer cases were selected consecutively until the maximum time allocated for data collection or the estimated sample size was reached, whichever was earlier. The stipulated concluding date for data collection was August 2012, at which time case recruitment was stopped. Incident cases included patients diagnosed with oral cancer between July 2011 and August 2012. Cases were selected after they were diagnosed with oral cancer. However, some patients who had visited the hospital for diagnosis but who did not return to the same hospital for further consultation or treatment could not be included.

3.4.2 Controls

Controls were selected from the main cancer hospitals and health/referral centres, which were constituent centres of the main hospital. The referral centres provided care to the same population as the main cancer hospital. Controls were selected and recruited simultaneously with case recruitment (density method) (Rothman et al., 2011a). Controls were selected throughout the same period as cases.

They were not age- or sex-matched to cases because both of these parameters were measurable and could be controlled during data analysis. Furthermore, selecting matched controls based on confounders would result in increased study duration and reduced sample size by having to lose some cases if appropriate controls were not found.

3.5 Estimated sample size

The sample size calculation was based on the main objective of the study focusing on life-course SEC in relation to oral cancer.

A total of 126 incident cases and 251 controls were required to attain power of 0.80, considering the estimated OR of association between childhood SEC and oral cancer to be 2.0, proportion of controls with exposure to low SEC to be 60% and a case-control ratio of 1:2.

Of the life-course SEC, social mobility required a greater sample because the mobile groups would be small. The required sample size was estimated on the basis of an OR of 0.6 for oral cancer related to upward social mobility (considering many aspects related to SEC rather than social prestige that is used in a study on social mobility and UADT cancers (Schmeisser et al., 2010), because upwardly mobile group was anticipated to be the smallest group with a lower OR requiring a larger sample size. The power was set to 0.8 and assuming the proportion of exposure in controls to be 20%, a sample size of 364 cases and 727 controls was estimated considering a case:control ratio of 1:2.

The calculations were rounded up to the closest integer. The sample size was calculated using the Fleiss method with continuity correction factor – [statistical methods for rates and proportions formulae 3.18 and 3.19] with OpenEpi (Dean et al., 2011).

3.6 Study participant recruitment

3.6.1 Identification of oral cancer cases and controls

Patients with oral cancer were identified and enumerated from various registers maintained at the in-patient units, outpatient departments/clinics, registration counter, treatment planning, and surgery.

Potential controls were identified at the same places, from among visitors or carers of cancer patients, and at health/referral centres from among people seeking care or people who were patient companions.

3.6.2 Contacting participants and obtaining informed consent

The identified cases and controls were initially contacted by nurses and medical social workers (MSW), to determine whether they were eligible, and to ascertain whether they wished to participate in the study. Controls at health/referral centres were contacted by MSWs or other hospital staff and sometimes by the researcher, to ascertain their willingness to participate in the study. Each potential study participant was provided with an information sheet and a consent form. The researcher explained the purpose of the study, procedures, the risks and benefits of participating in the study, confidentiality, information about withdrawing from the study at any time, and the time taken to complete the interview and oral examination for each potential participant in the local language (Please see Appendix no. 2 for information sheet and consent form). The researcher discussed and clarified participants' questions/doubts regarding the research. If the potential participants agreed to participate in the study, informed consent was sought. A majority of them provided written informed consent. However, some of them gave only verbal informed consent (possibly because of limited literacy), but they were willing to participate, so they were still included in the study. Following consent, time

was scheduled for an interview and oral examination according to the participant's convenience.

3.7 Data collection

3.7.1 Data collection instruments and methods

Standard epidemiological methods were followed for data collection. Data for this life-course project were collected by interviewing, conducting oral examination, and abstracting details from medical records.

3.7.2 Preparing and pilot testing the questionnaire

A semi-structured questionnaire was designed to collect life-course information on SEC, family structure, housing conditions, parental education, parental and participants' own habits of tobacco, quid and alcohol use, family history of malignancy, dietary habits and oral hygiene behaviour. A life-grid was used to assist in improving recall. External events, for example, year of Indian independence, famine in Karnataka, and participant's own life events could help in recalling other experiences by relating to such events.

The questionnaire was first prepared in English at the Australian Research Centre for Population Oral Health (ARCPOH). Expert researchers at ARCPOH reviewed the initial draft of the questionnaire. Some minor changes were made for easy understanding by the participants, and for consideration of the researchers' comments. The questionnaire was translated to Kannada and then translated back to English to verify if the meaning remained the same. Translation was carried out by two translators who were proficient in both languages. The questionnaire was later tested, as a pilot run, by administering it to the first fifteen cases and controls in India. It was decided that only the questions requiring change

would be excluded from the analysis. However, there were no changes required, and hence all variables could be considered for analysis. (Please see Appendix no. 3 for questionnaire)

3.7.3 Conducting direct interviews

Direct interviews were conducted by the researcher (PhD Candidate), who is a community dentist, with previous experience in conducting interviews in epidemiological studies.

Information was collected retrospectively on the various risk factors such as tobacco, quid and alcohol use, living conditions, SEC, parental history, area of residence, family structure, diet, oral hygiene practices throughout the life-course. All participants were interviewed in the hospitals or referral centres to reduce differential recall. The interviews took place within one week of recruitment, in the regional language (Kannada) or English (when participants could speak English) and were completed in about an hour. Some assistance was sought from siblings/spouse/children/parents to complete a questionnaire for those respondents who had difficulty in speaking because of the cancer. The patient carers provided assistance by explaining when the speech was not clear, or elaborating on events the patient wanted to describe. The patient-companion provided information in the presence of the patient so that any confusion regarding the details of information could be clarified by the patient. Accuracy of information collected from cases and controls should be comparable. Therefore, information collected on risk factors was restricted to before the development of signs and symptoms or diagnosis of oral cancer for cases (to avoid accruing of exposure after disease development) and at the time of selection for controls (Wacholder et al., 1992a).

3.7.4 Use of the life grid

The life grid method was developed by Blane (1996) and validated by Berney and Blane (1997). The life grid is very useful in collecting life-course data by cross-referencing recalled information with personal life events or historical events. Such events act as triggers in

temporal referencing and assist in improving the accuracy of recall. In the present study, there were 12 columns in the life grid chart, arranged from left to right in order: year, external events, age, life events, area of residence, occupation, income, diet, smoking, SLT, quid and alcohol use. Cross-referencing each of the aspects along the columns with the participant's own life events (marriage, birth of a child, death of a family member) and major external events during their lifetime (for example political events, a natural disaster) was used as triggers to improve the accuracy in recall (Blane, 1996; Berney and Blane, 2003). Initially, changes in residential areas, occupational, dietary and behavioural histories were recorded with a life-grid that was later utilised as a guide throughout the structured part of the interview to keep a track of the timeline (Please see the questionnaire, Appendix no. 3 for life grid).

3.7.5 Training the examiner

The examiner in this present project (PhD Candidate) is a dentist who has previous experience in diagnosing oral mucosal lesions. The gold standard examiner (Professor KRT) trained the examiner at ARCPOH before the commencement of data collection. Since it was difficult to gather a range of oral mucosal lesions, the examiner was trained with clinical photographs as suggested by WHO (Kramer et al., 1980). Pictures of a variety of oral mucosal lesions provided by the US National Institute of Dental Research (NIDR), now the National Institute of Dental and Craniofacial Research (NIDCR), were used for training. When there were doubts, the trainer and the trainee discussed the clinical features until a consensus was reached.

3.7.6 Oral examination

The consenting participants underwent an oral examination, following the interview, by a trained examiner (PhD Candidate). Oral soft and hard tissues were examined for the presence

of any abnormal oral mucosal lesions, dentition and oral hygiene status. The clinical oral findings were recorded on an oral examination form (Please see Appendix no. 4).

3.7.6.1 Infection control protocol

Sterile equipment was used. After the examination instruments were cleaned and sterilised before the next use. The infection control protocol conformed to that specified by the hospitals as well as the ‘Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting’ amended 19 September 2002 (accessible at http://www.health.gov.au/pubhlth/strateg/communic/review/icg_pdf/icg_guide.pdf). Standard precautions (such as the use of gloves and a mouth mask, skin disinfectants, and hand-washing before and after contact with patients) were followed.

3.7.6.2 Oral examination equipment

Oral examination instruments included a mouth mirror, a PCP2 probe (HuFriedy, USA) to record OHI-S, tweezers and gauze.

3.7.6.3 Oral examination procedure

Oral examinations were performed in the hospital and took about 15 minutes for each participant. The participants were examined while seated on a chair with their back supported and under artificial illumination by a powerful headlamp.

3.7.6.3.1 Oral mucosal lesions/conditions

Examination for oral mucosal diseases and conditions was done as per the criteria put forth by the WHO (Kramer et al., 1980). The guidelines for oral epidemiological examination protocol

were similar to the Australian National Survey on Adult Oral Health (NSAOH) (2004-06) and Papua New Guinea National Oral Health survey (2007), with some modifications.

The oral examination began with the soft tissues, checking for the presence of oral mucosal lesions such as oral cancer, leukoplakia, erythroplakia, lichen planus, submucous fibrosis, candidiasis, oral hairy leukoplakia, necrotising gingivitis, necrotising periodontitis, ulcers (herpetic/aphthous/traumatic), cancrum oris, viral warts or any other lesions. Any lesion present was recorded along with the site of occurrence. For oral cancer lesions, details such as the site, size and morphological features (ulcerative/proliferative/ulcero-proliferative) were also recorded.

3.7.6.3.2 Dentition status

Teeth present during the examination were also recorded. Tooth/teeth were considered missing if they had been extracted due to caries/periodontitis or for cancer therapy. No radiographs were taken.

3.7.6.3.3 Edentulism

Edentulism was marked for upper and lower arches separately if the participant had no natural teeth or if they were all indicated for extraction.

3.7.6.3.4 Dentures

Denture wearing on the upper and lower arches was noted if the participant wore fixed/partial/complete dentures on a daily basis.

3.7.6.3.5 Oral hygiene status

Oral Hygiene Index-Simplified (OHI-S) (Greene and Vermillion, 1964) was recorded to measure oral hygiene status. The OHI-S is a simple and non-time consuming method to

objectively measure the oral hygiene status of a person. The index is calculated by summing up the Debris Index – Simplified (DI-S) and Calculus Index – Simplified (CI-S). DI-S and CI-S are recorded for the index tooth or its replacement tooth (16/17, 11, 26/27, 36/37, 31, 46/47) in each sextant. If both the index and replacement teeth are missing then that sextant is considered to be missing and is not given scores. The DI-S and CI-S range from zero to three while OHI-S range between 0-6 for an individual.

Interpretation of OHI-S scores:

Table 3.2 Interpretation of OHI-S scores

Score	Oral hygiene status
0	Excellent
0.1–1.2	Good
1.3–3.0	Fair
3.1–6.0	Poor

3.7.7 Record abstraction

The records of consenting patients diagnosed with oral cancer (cases) were accessed at the hospital wards or from the medical records department, where the patient files were stored and maintained. The medical records were scrutinised to record patients’ age, gender, address, date of initial diagnosis, tumour grading, staging, presence of comorbidities, treatment planned/received. A note was made if the patients had undergone oral prophylaxis before conducting an oral exam as part of this study, and if so oral hygiene status (Good/Fair/Poor) as recorded in the file was noted (Please see Appendix no.4 for the record abstraction form). Some information such as presence of co-morbidities were not recorded for controls because, the controls were selected from care-takers of patients many of whom did not have hospital records.

3.7.8 Referral

The oral findings requiring care were communicated to the participants and those requiring urgent care were advised to seek care immediately. Control participants who were found with any OPMD or suspicious oral cancer lesions were referred for further evaluation by specialists.

3.7.9 Quality assurance of data collected

To ensure the data quality, a protocol was followed. The protocol was based on NSAOH guidelines and the PNG survey (Please see Appendix no. 5 for Manual). Immediately after completion of data collection from each participant, the questionnaire, oral examination forms and data abstraction forms were checked for any missing information. The reasons for missing data were recorded so that the missing data could be then be re-coded during data entry, and therefore would be helpful during analysis. The researcher (PhD Candidate) periodically appraised regarding the data collection procedures to her supervisors through emails and during weekly Skype meetings. The principal supervisor (Professor KRT) visited India to monitor the data collection process.

3.7.10 Confidentiality

The questionnaire, oral examination, and record abstraction forms carried unique ID numbers which were used to link each to the other. Other documents with identification details were stored separately to maintain confidentiality.

3.10 Data entry and cleaning

Data recorded on the paper forms were entered into a computer using MS Access 2007. The database was set up in MS Access to minimise the errors during entry. Data were then imported into SAS[®] software (SAS Institute Inc., Cary, NC, USA) version [9.2] to carry out

cleaning and analysis. Data was cleaned by running frequency checks, missing values, discrepancies and outliers, before performing the analysis.

Data management and analyses to address each aim have been described in the published papers presented as chapters. Data that was sufficient to address the aims were analysed.

3.8 Ethics clearance

Ethics approval for the study was obtained from the Human Research Ethics Committee, the University of Adelaide, in April 2011 (H-064-2011). Later, additional ethics approval was obtained from the ethics committees of the hospitals where the project was carried out. They were Institutional Ethics Committees of Kasturba Medical College, Manipal and Central Ethics Committee, HealthCare Global, Bangalore (Please see Appendix no.1 for ethics approval letters).

Although permission was initially granted to collect data from one of the cancer hospitals in Karnataka, it was later withdrawn due to some administrative difficulties within the institution.

Chapter 4

4 The life course models: Exploring associations between socioeconomic conditions at three stages in life and oral cancer

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4.1 Statement of Authorship

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Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for the publication to be included in the candidate's thesis.

Name of Principal Author (Candidate)	Sree Vidya Krishna Rao		
Contribution to the Paper	Conceptualised the study, collected data, analysed and interpreted data, wrote manuscript, acted as corresponding author		
Signature		Date	29/05/2014

Name of Co-Author	Gloria Mejia		
Contribution to the Paper	Helped in conceptualising the study, supervised the development of work, helped in interpreting data, critically evaluated and edited the manuscript		
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Name of Principal Author (Candidate)	Sree Vidya Krishna Rao		
Contribution to the Paper	Conceptualised the study, collected data, analysed and interpreted data, wrote manuscript, acted as corresponding author		
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4.2 Abstract

Background: A life course approach is suitable in understanding the social and biological processes of chronic diseases. The aim was to examine three life course models to determine the association between SEC at three stages in life and oral cancer.

Methods: A hospital-based case-control study was conducted in India. This study formed part of a larger life course study on oral cancer. Life course information on the occupation of the head of household (HH) at different stages in life of the participants was recalled. SEC in childhood, early adulthood and later adulthood were considered. SEC was dichotomized as 'low' and 'high' based on the regular occupation of the HH. Analyses included participants for whom information on SEC was available for all three stages to assess for the critical period, social mobility and accumulation models. The association between SEC and oral cancer was assessed using unconditional logistic regression analysis.

Results: Of 180 incident cases and 272 controls, complete information on SEC at all three stages was available for 163 cases and 264 controls. Nearly two-thirds (65%) of participants were stable in low SEC across all stages. Low SEC at all the three stages was positively associated with oral cancer after adjusting for age and sex. The association was strongest for those who remained in low SEC at all three stages. A gradient was seen for intra-generational High-high, High-low, Low-high and Low-low groups with increasing odds ratios of 1.00 (ref), 1.27 (0.81–1.97), 1.93 (1.59–2.36) and 2.78 (1.61–4.79) respectively.

Conclusion: Low SEC in childhood and early adulthood is important in determining oral cancer in later adulthood.

4.3 Introduction

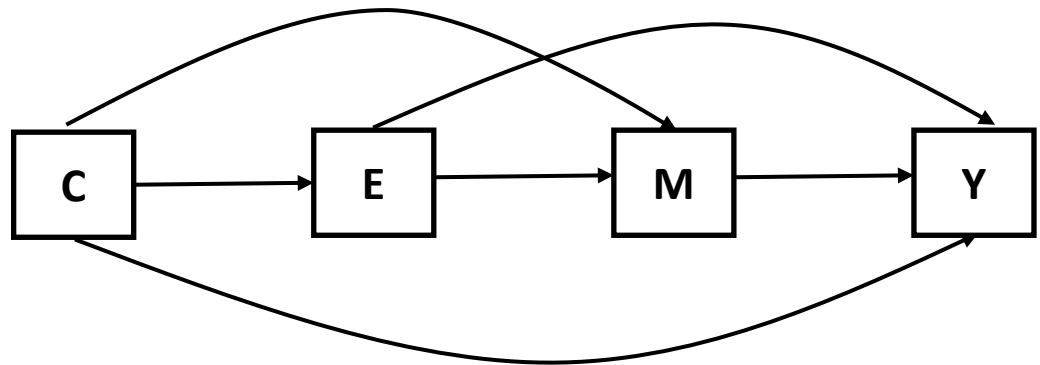
Oral cancer is a frequently fatal disease that adversely affects the quality of life of survivors. More than 273,000 people are affected by cancer of the oral cavity around the world every year (Ferlay et al., 2004), of which nearly two thirds live in developing countries (Warnakulasuriya, 2009a). In the Indian subcontinent, oral cancer is one of the six leading cancers because of its high incidence rate (Ferlay et al., 2004). Oral cancer is a public health problem contributing to one third of the total cancer burden in India (Parkin et al., 2005; Petersen, 2005).

Worldwide, socioeconomic inequalities exist for oral cancer (Greenberg et al., 1991; Conway et al., 2008; Johnson et al., 2011b). In the Indian population, oral cancer is more frequent among people of low SEC (determined by occupations such as farming, industrial or manual work) than among those of high SEC, such as those in white-collared/professionals jobs and businesses (Dhar et al., 2000; Balaram et al., 2002; Muwonge et al., 2008). Evidence suggests that general and oral health have social determinants (Thomson, 2012). Social and biological processes are interrelated, which underscores the importance of undertaking a social approach in cancer epidemiology (Graham and Schneiderman, 1972; Power and Hertzman, 1997; Krieger, 2005). While the social gradient in health is well recognized, the social epidemiology of cancer is still emerging (Kaufman, 1999).

For a chronic disease such as oral cancer, the exposure to risk factors occurs long before the development of the disease. Therefore, a life course perspective would be appropriate in understanding the social and biological processes. Moreover, the influence of SEC on health could be mediated through lifestyle and psychological factors (Adler and Newman, 2002; Harper et al., 2002; Matthews and Gallo, 2011).

There are three generally considered models in life course epidemiology. These are the critical period, social mobility and accumulation models (Kuh et al., 2003; Kuh and Ben-Shlomo, 2004). The critical period model implies that the exposure during a sensitive period in life has long-term effects. However, the risk may accumulate with multiple exposures throughout life. Accumulation has been argued to be the most fundamental of the three models (Power and Hertzman, 1997; Blane et al., 2007). Childhood SEC and accumulation of socioeconomic disadvantage over the life course have been shown to be associated with dental caries (Thomson et al., 2004; Peres et al., 2011a). Intra-generational and inter-generational social mobility is another model linked to outcomes. A case-control study found associations between intra-generational social mobility and UADT cancer (Schmeisser et al., 2010). The three life course processes (critical/social mobility/accumulation) may act individually or in combination. Empirically separating the inter-meshed life course processes is difficult (Hallqvist et al., 2004). However, to our knowledge, there are no studies that have investigated the association of life course SEC and oral cancer. This study was conducted with the aim to examine the three life course models to determine the association between SEC at three stages in life and oral cancer. In this paper, the authors seek to explore the critical, social mobility and accumulation of socioeconomic disadvantage models in relation to oral cancer.

Figure 4.1 Conceptual model



E- Exposure includes SEC at three stages in life or no. of occasions of low SEC or social mobility depending on the life course model

M-Risk factors such as tobacco, quid, alcohol and diet

Y-Oral cancer

C-Confounders include age and gender

4.4 Methods

4.4.1 Study design

This study formed part of a larger life course study on oral cancer conducted in India between July 2011 and August 2012, and employing a case-control design. The total study sample consisted of 180 cases and 272 controls. The sample for the present analysis included participants who were 25 years or older and for whom details on SEC were available at three time points.

The participants gave direct interviews in the hospitals to complete a semi-structured questionnaire followed by an oral examination and medical record abstraction. Potential participants providing informed consent were included. The study protocol was approved (H-064-2011) by the Human Research Ethics Committee, The University of Adelaide and the selected cancer hospitals.

4.4.2 Selection of cases and controls

Cases were recruited from four major cancer hospitals in Karnataka, India. During the study period, patients who were 18 years or older attending the chosen cancer hospitals with newly diagnosed oral and/or oropharyngeal cancer [International Classification of Diseases (ICD)-10: C00–C10] with histopathological confirmation attending the chosen cancer hospitals were selected and approached. Histopathological diagnosis of cases was obtained from the medical records.

Controls came from the same cancer hospitals and their medical health/referral centres. The health/referral centres catered to the same population as that of the main cancer hospitals to be reflective of the source population in their exposure pattern (Wacholder et al., 1992a).

Controls were selected and recruited throughout the study period similar to that of cases. This method of control selection is also known as density sampling (Rothman et al., 2011a). The selection criteria for controls were ≥ 18 years, not diagnosed with cancer, carers/visitors of cancer patients (not including UADT, lung and liver cancers to avoid overmatching on SEC) or those seeking medical care for medical conditions not related to tobacco and/or alcohol and not having cognitive problems. An oral examination was done to exclude the possibility of undiagnosed oral cancer.

4.4.3 Data collection

Life course information on the occupation of the head of household (HH) at different life stages of participants, parental and participants' highest educational level were recalled. The HH was usually the eldest male member of the family who financially controls and supports the other members of household. In childhood (6-10 years), the head was usually the participant's father in nuclear family and sometimes uncle/grandfather in joint families. Occupation in early adulthood (20-25 years) and later adulthood (at the time of interview)

recorded were of the participants if male and of husband/father if female. A life grid assisted in improving the recall by drawing references to personal life-events and external events (Blane, 1996; Berney and Blane, 2003).

Oral examination was done to record hard and soft tissue lesions/conditions and thus rule out oral cancer in controls. Oral cancer cases were confirmed with histopathological details from patients' records.

4.4.4 Measures

The dependent variable was a diagnosis of oral cancer according to the case definition described above. Independent variables were age, sex and SEC at three stages in life. SEC was dichotomized as 'low' and 'high' based on the regular occupation of the HH. The low SEC group included the unemployed, petty traders, and agricultural, industrial and manual workers. The high SEC group included those doing clerical jobs, teachers, professionals and businessmen. The categorization according to occupation correlated with their education. In India, completion of at least secondary school education is required to obtain jobs included under high SEC (Karnataka, 2005). People of low SEC are more likely to have not completed their schooling. Agricultural labourers/fishing people in rural/semi-urban areas with their lower level of education may eventually move to urban areas and undertake manual occupations such as labouring, construction work or start small petty (pan (betel quid) or tea and coffee vending) shops (Jodhka; Uma et al., 2013).

4.4.5 Statistical analyses

Analyses included participants for whom the information on SEC was available for childhood, early adulthood and later adulthood, to assess for the critical period, social mobility and accumulation models. This led to the exclusion of seven cases and eight controls

from analysis. Among the participants excluded from analysis, six controls were below the age of 25 years. Since missing data was for about 3% of the sample, complete case analysis was performed assuming that the data was missing at random.

SEC at three stages was considered individually as critical periods. Social mobility was movement in SEC from childhood to early adulthood, childhood to later adulthood and early-adulthood to later adulthood. The socially mobile groups were high-high (H-H), high-low (H-L), low-high (L-H) and low-low (L-L). Accumulation was the total number of stages in life that a participant was in a lower SEC. The score for each person could range from nil to three.

Association between SEC and oral cancer was assessed with crude and adjusted ORs with 95% confidence interval (CI) from unconditional logistic regression analysis. Including the lifestyle and behavioural factors that are intermediate factors (mediators) will introduce collider stratification bias (Robins and Greenland, 1992; Hernan et al., 2004). Therefore, ORs were adjusted only for confounders. Based on the conceptual model, age and sex were identified as the confounders of the SEC–oral cancer relation. ORs were considered to be statistically significant if the 95% CI did not include unity. Clustering was accounted for by averaging the ORs over clusters (cancer centres). The reference group was being in high SEC for all the models. SAS 9.2 was used for the analysis.

4.5 Results

Of 180 incident cases and 272 controls, complete information on SEC at all three stages was available for 173 cases and 264 controls. Median and maximum ages of participants included in the analyses were 54 and 88 years respectively. Among the participants, 158 (36.2%) were women. A sociodemographic description of cases and controls is presented in **Table 4.1**.

Table 4.1 Distribution of cases and controls according to sociodemographic characteristics

	Cases n (%)	Controls n (%)
Age (years)		
≤55	90 (52.0)	149 (56.4)
>55	83 (48.0)	115 (43.6)
Sex		
Male	136 (78.6)	143 (54.2)
Female	37 (21.4)	121 (45.8)
Critical period		
Childhood SEC		
Low	153 (88.4)	210 (79.6)
High	20 (11.6)	54 (20.4)
Early adulthood SEC		
Low	146 (84.4)	185 (70.1)
High	27 (15.6)	79 (29.9)
Later adulthood SEC		
Low	138 (79.8)	177 (67.1)
High	35 (20.2)	87 (32.9)
Accumulation		
No. of occasions in low SEC		
0	12 (6.9)	36 (13.6)
1	12 (6.9)	39 (14.8)
2	22 (12.7)	34 (12.9)
3	127 (73.5)	155 (58.7)
Social mobility		
Childhood to early adulthood		
High-high	14 (8.1)	41 (15.5)
High-low	6 (3.5)	13 (4.9)
Low-high	13 (7.5)	38 (14.4)
Low-low	140 (80.9)	172 (65.2)
Childhood to later adulthood		
High-high	12 (6.9)	39 (14.8)
High-low	8 (4.6)	15 (5.7)
Low-high	23 (13.3)	48 (18.2)
Low-low	130 (75.2)	162 (61.3)
Early adulthood to later adulthood		
High-high	22 (12.7)	67 (25.4)
High-low	5 (2.9)	12 (4.5)
Low-high	13 (7.5)	20 (7.6)
Low-low	133 (76.9)	165 (62.5)
Total	173 (39.6)	264 (60.4)

Table 4.2 presents the distribution of cases and controls according to eight possible trajectories in three stages. The majority (65%) were stable in low SEC at all stages. Socioeconomic mobility was observed in a quarter of the participants. Being upwardly mobile from childhood to early adulthood or between childhood and later adulthood were the common trajectories and downward mobility between early and later adulthood was uncommon.

Table 4.2 Distribution of socioeconomic trajectories among oral cancer cases and controls

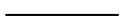
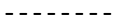
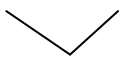
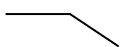
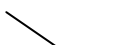
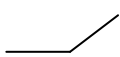
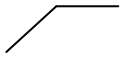
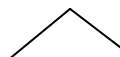
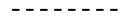

Trajectories		Cases n (%)	Controls n (%)	Total n (%)
	H-H-H	12 (6.9)	36 (13.6)	48 (10.9)
				
	H-L-H	0 (0)	3 (1.1)	3 (0.7)
	H-H-L	2 (1.2)	5 (1.9)	7 (1.6)
	H-L-L	6 (3.5)	10 (3.8)	16 (3.7)
	L-L-H	13 (7.5)	17 (6.5)	30 (6.9)
	L-H-H	10 (5.8)	31 (11.7)	41 (9.4)
	L-H-L	3 (1.7)	7 (2.7)	10 (2.3)
	L-L-L	127 (73.4)	155 (58.7)	282 (64.5)
				

Table 4.3 shows that low SEC at all the three stages was associated with oral cancer after adjusting for age and sex. Early adulthood low SEC was more strongly associated with the outcome when adjusted for SEC in the other two occasions.

Table 4.3 Unadjusted and adjusted odds ratio for socioeconomic conditions at various critical periods

Periods		Crude OR (95% CI)	OR ^a (95% CI)	OR ^b (95% CI)
Childhood	Low	2.04 (1.20–3.46)	1.90 (1.10–3.28)	1.14 (0.52–2.51)
	High	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Early adulthood	Low	2.43 (1.73–3.42)	2.57 (1.71–3.85)	1.93 (1.48–2.52)
	High	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Later adulthood	Low	2.06 (1.27–3.36)	2.17 (1.36–3.45)	1.37 (0.83–2.26)
	High	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)

^aAdjusted for age and sex; ^b Adjusted for age, sex and socioeconomic position at other periods

Living in low SEC in two or three stages in life was associated with oral cancer (**Table 4.4**).

The association was strongest for those who remained in the low SEC at all three stages.

Experiencing low SEC on one occasion had similar OR as that of stable at high SEC, whereas experiencing low SEC on two occasions had intermediate odds for oral cancer compared to high-high and low-low groups.

Table 4.4 Unadjusted and adjusted odds ratio of oral cancer for accumulation of number of occasions being in the low socioeconomic condition

No. of occasions in low SEC	Crude OR (95% CI)	OR ^a (95% CI)
0	1.00 (Ref)	1.00 (Ref)
1	0.98 (0.40–2.39)	0.84 (0.34–2.09)
2	2.10 (1.35–3.27)	1.88 (1.16–3.06)
3	2.71 (1.47–5.03)	2.60 (1.35–5.03)

^aAdjusted for age and sex

Table 4.5 presents the results for the social mobility models. Downward mobility from childhood to early adulthood showed higher odds for developing oral cancer. However, 95% CI included unity. Downwardly and upwardly mobile groups had similar OR for oral cancer. While downward social mobility from child to later adult stage was associated with oral cancer, the upward mobility was not associated. A gradient was seen for H-H, H-L, L-H and L-L groups with increasing OR of 1.00, 1.27, 1.93 and 2.78 respectively when analysed for social mobility from early adulthood to later adulthood. Being stable in low SEC across all periods was strongly associated with oral cancer.

Table 4.5 Association of social mobility with oral cancer

Social mobility	Crude OR (95% CI)	OR^a (95% CI)
Childhood to early adulthood		
High-high	1.00 (Ref)	1.00 (Ref)
High-low	1.46 (0.86–2.50)	1.47 (0.75–2.89)
Low-high	1.04 (0.45–2.41)	0.86 (0.35–2.04)
Low-low	2.56 (1.52–4.30)	2.45 (1.38–4.34)
Childhood to later adulthood		
High-high	1.00	1.00
High-low	1.95 (1.04–3.65)	2.00 (1.05–3.80)
Low-high	1.65 (0.73–3.76)	1.42 (0.63–3.23)
Low-low	2.89 (1.60–5.22)	2.76 (1.48–5.17)
Early adulthood to later adulthood		
High-high	1.00 (Ref)	1.00 (Ref)
High-low	1.38 (0.73–2.61)	1.27 (0.81–1.97)
Low-high	2.03 (1.63–2.52)	1.93 (1.59–2.36)
Low-low	2.64 (1.57–4.46)	2.78 (1.61–4.79)

^aAdjusted for age and sex

4.6 Discussion

This paper aimed to analyse the three life course models associating SEC across three different stages in life with oral cancer. This study examined SEC at three stages in life rather than just considering SEC at two stages. Due to lack of power authors could not further separate the trajectories.

4.6.1 Critical period

Low SEC in childhood, early adulthood and later adulthood were associated with oral cancer. Among three stages, the early adulthood was strongly associated with oral cancer.

4.6.2 Social mobility

Those moving away from the SEC between childhood and early adulthood had OR intermediate to stable groups (H-H and L-L). While the OR for oral cancer was higher with downward mobility (H-L) from childhood to current stage, there was no association with upwardly mobile (L-H) group. The findings were contrary for social mobility from early adulthood to current stage; the downwardly mobile (H-L) group showed no association and the upwardly mobile group (L-H) was associated with the outcome. Though this seems to support the idea that early adulthood is an important period, the effects of SEC at three stages are still mixed, because many of them who were in low SEC at early adult stage were also in low SEC at childhood. Thus there could be influence of childhood SEC, but is difficult tease it out.

4.6.3 Accumulation

Those remaining in low SEC across all three stages had the highest odds for oral cancer in later adulthood. There was a gradient in the increasing OR for oral cancer with wide disparity between the stable at low and stable at high groups. These findings support the argument put forth by other researchers that socioeconomic disadvantage accumulates over the life course (Blane et al., 2007).

It has been demonstrated empirically by Hallqvist et al. (2004) that mutual confounding between critical period, social mobility and accumulation mechanisms cannot be mitigated.

All three models are inter-meshed and they complement each other in explaining the observed socioeconomic difference in the occurrence of oral cancer.

Since this is the first study reporting on life course models for oral cancer, the ability for comparison is limited. Other studies on mortality, cardiovascular diseases and oral diseases have also found that accumulation is the most important of all the models (Thomson et al., 2004; Turrell et al., 2007; Peres et al., 2011a; van Rein et al., 2014). Despite the challenges in comparing the reports from developed and developing countries, the results have demonstrated that the effects of SEC on oral health are similar in the broader context (Peres et al., 2011b).

On one hand, to investigate chronic diseases with a long induction period, the life course approach is most suitable. On the other hand, there are difficulties in statistical methodologies for this approach (De Stavola et al., 2006). As the time interval between the exposure and the outcome is prolonged, the emergence of many mediators makes the statistical analysis a complex task. Conditioning on the mediators as in conventional regression procedures introduces selection bias (Hernan et al., 2004). Therefore, the analysis was restricted to assessing the association between SEC and oral cancer by adjusting for confounding by age and sex. Further studies should be undertaken using appropriate statistical procedures to understand the pathways linking life course SEC and oral cancer. There could be potential bias because analysis included participants for whom the data on SEC was available for all three stages. However, the proportion of missing data was very low.

Cohort designs are well-suited for life course studies. But for a rare disease (prevalence less than 10%) it would take a very long time to recruit required number of cases and be also more expensive. Hence the case-control design is a more feasible option for oral cancer, a relatively rare disease (Nicolau et al., 2007). Furthermore, the case-control design has been considered

as an “efficient cohort” design when controls are selected appropriately (Rothman et al., 2011a). A case-control design has been used previously to investigate early-life influences on stomach cancer, stroke and myocardial infarction (Maheshwaran et al., 2002; Hallqvist et al., 2004). There are a few limitations of the study. There is doubt regarding the validity of recall of exposure over the life course. A life grid was used to improve recall accuracy (Blane, 1996; Berney and Blane, 2003). Controls include more females than cases due to selection criteria. However, sex was considered as confounder and adjusted in the analysis. Moreover, matching on gender would reduce the study size. Some strengths of the study are- it was a multicentre study conducted to address the study objective. SEC was considered at three stages to examine the socioeconomic trajectories.

4.7 Conclusion

Low SEC in childhood, early adulthood and later adulthood are associated with oral cancer occurring in later adulthood. SEC in early adulthood is more strongly associated with oral cancer than SEC at other two stages. It is essential to improve the SEC of children from low socioeconomic strata by providing them better education to reduce the disparities in oral cancer occurrence. It is necessary to address socioeconomic disparities in addition to ongoing engagement of various organizations towards preventing and controlling the alcohol, quid and tobacco (known causes of oral cancer) use that are patterned by SEC.

Chapter 5

5 Estimating the effect of childhood socioeconomic disadvantage on oral cancer in India using marginal structural model

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5.1 Statement of Authorship

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Name of Principal Author (Candidate)	Sree Vidya Krishna Rao		
Contribution to the Paper	Conceptualised the study, collected data, analysed and interpreted data, wrote manuscript, acted as corresponding author		
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Signature		Date	

5.2 Abstract

Background: Early-life socioeconomic disadvantage could affect adult health directly or indirectly. There are no studies on the direct effect of early-life socioeconomic conditions on oral cancer occurrence in adult life.

Methods: A multicentre hospital-based case-control study was conducted in India. Life-course data were collected on SEC, risk factors and parental behavior through interview employing a life-grid. Oral cancer cases were ascertained from hospital records. Controls included hospital visitors not diagnosed with any cancer from the same hospitals. The early-life SEC measure was determined by occupation of the head of household (HH) in childhood (usually the participant's father). Adult socioeconomic measures included participant's education and current occupation of HH. A marginal structural model (MSM) with stabilized inverse probability weights was used to estimate the direct effect of early-life SEC on oral cancer. In this study, three mediators (smoking, chewing quid/tobacco and alcohol) were analyzed with three separate models.

Results: The total effect model showed that those in the low SEC in the early years of childhood had 63% [RR= 1.63 (95% CI = 1.38–1.92)] greater risk of oral cancer. From the MSMs, the estimated risk for developing oral cancer among those in low early-life SEC was 48% [RR = 1.48 (95% CI = 1.43–1.53)], 24% [RR = 1.24 (95% CI = 0.88–1.74)] and 94% [RR= 1.94 (95% CI = 1.66–2.27)] greater than those in the high SEC after controlling for smoking, chewing and alcohol respectively.

Conclusion: Early-life low SEC is shown to have a lasting effect on oral cancer not mediated by later life risk factors when MSM was used.

5.3 Introduction

A child grows up embodying surrounding physical and social circumstances (Krieger, 2005). Development of health initiates *in utero* and continues throughout one's life course (Gluckman et al., 2005). In life course epidemiology, critical periods, pathways and accumulation are the three models that operate exclusively or as a combination of two or more models (Kuh and Ben-Shlomo, 2004). Research has shown that early-life SEC affect adult health directly and indirectly (Kuh and Ben-Shlomo, 2004; Lynch and Smith, 2005; Cohen et al., 2010). The direct effect of early-life SEC is long-lasting and independent of adult SEC and risk factors of diseases, while the indirect effects are mediated through adult SEC and risk factors that develop later in life (Kuh and Ben-Shlomo, 2004; Lynch and Smith, 2005; Cohen et al., 2010). Currently, evidence for direct and mediated influences of early-life SEC on various health outcomes is available mainly from research conducted in high-income countries (Blane et al., 2007). A recent study among US adults has demonstrated that childhood socioeconomic disadvantage has direct effects on chronic health outcomes such as heart disease, diabetes and stroke (Nandi et al., 2012).

Oral cancer is a chronic disease with a high mortality rate (Dikshit et al., 2012). High incidence rates of oral cancer are observed in South and Southeast Asia (Warnakulasuriya, 2009a), and continue to rise in epidemic proportions, posing a public health problem in India (Gupta et al., 2012). A higher proportion of oral cancer cases in India is seen among farmers, fishermen and laborers, who are socioeconomically disadvantaged (Dhar et al., 2000; Rajkumar et al., 2003; Rajamanickam et al., 2007). Cancers have a long empirical induction period (Rothman, 1981). This long time gap between exposure to causative factors and disease detection indicates the possibility of exposure being in early life. However, it is not known whether early-life SEC has any influence on oral cancer. Causal roles of socially patterned behaviors like tobacco, quid and alcohol in the development of oral cancer have

been identified (Adler and Newman, 2002; Gilman, 2002; IARC, 2004b; IARC, 2004a; IARC, 2007; IARC, 2010). Further, to understand social disparities in oral cancer, it is essential to know whether the causal implication of the early-life SEC is critical or has a pathway through more proximate risk factors such as tobacco, quid and alcohol.

A hypothesis was proposed (based on the critical period model) that childhood socioeconomic disadvantage has a direct effect on oral cancer in adulthood. A conceptual framework was developed using a directed acyclic graph (DAG), as seen in fig.1 to identify the direct and indirect pathways for causal analysis. According to the DAG (fig 1), analyzing by conventional regression methods that condition on mediators will create a collider bias (Robins and Greenland, 1992). Additional bias could occur when endogenous confounders, which are descendants of childhood SEC, exist (Robins and Greenland, 1992). Robins and colleagues have shown that unbiased estimates can be obtained using a marginal structural model (MSM) under a counterfactual framework for causal inference (Robins, 1999; Hernan et al., 2000; Robins et al., 2000). A MSM allows accounting for time-dependent confounders by including them as inverse probability weights (IPW) to estimate the direct effect (Robins et al., 2000; Petersen et al., 2006). IPWs appropriately adjust for confounders thereby balancing exposure groups, similar to randomization in observational studies (Hernan et al., 2000; Robins et al., 2000). The aim of this study was to estimate the controlled direct effect (CDE) of child SEC on oral cancer that was not mediated by individual risk factors occurring in later life.

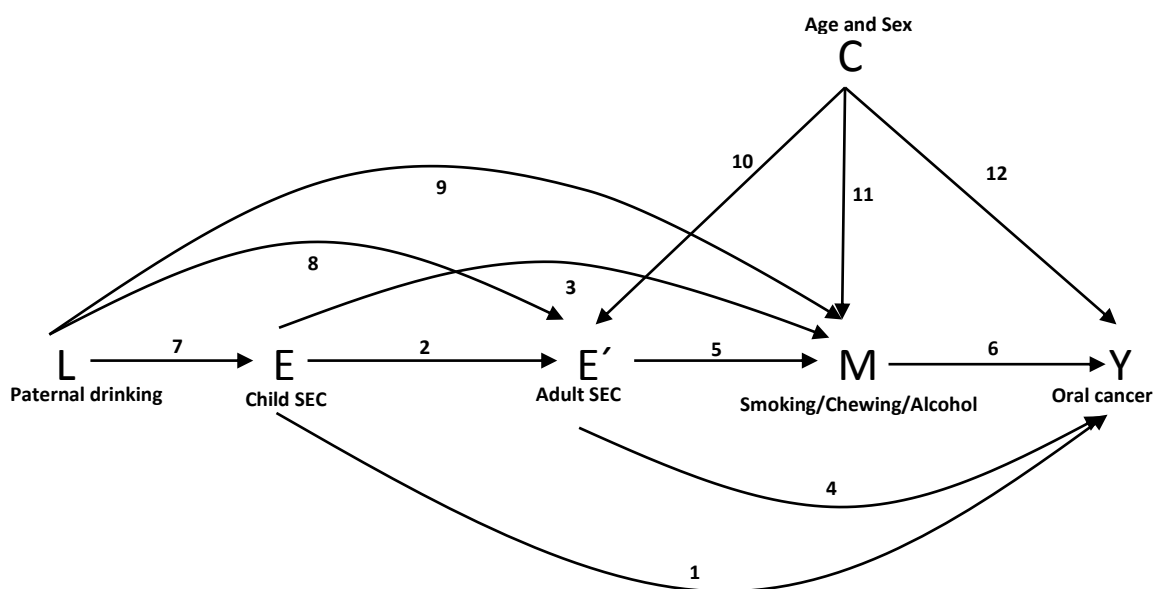


Figure 5.1 Conceptual framework

- L**- Confounder of E— E' and E'—M relation
- E**- Exposure of interest
- E'**- Endogenous confounder (M—Y relation)
- M**- Risk factors such as tobacco, quid, alcohol and diet
- Y**- Outcome
- C**- Confounders of E'—M and M—Y relation

5.4 Methods

A case-control study was conducted at four major cancer hospitals situated in Karnataka state (India) between July 2011 and August 2012. Ethics approval was obtained from the ethics committees of the University of Adelaide and the selected cancer hospitals. Informed consent was obtained from all participants.

5.4.1 Participant recruitment

Cases: Incident cases, diagnosed histopathologically with oral and/or oropharyngeal cancer [International Classification of Diseases (ICD) -10: C00–C10] during the study period, attending the selected cancer hospitals and aged 18 years or more were identified, selected consecutively and recruited. Sarcomas, secondary cancers and skin cancers of external lip were excluded because of pre-existing comorbidity or different etiopathology.

Controls: The controls selected were carers/visitors of cancer patients (excluding UADT, lung and liver cancers to avoid overmatching on SEC, tobacco and alcohol) or those seeking medical care for medical conditions not related to tobacco and/or alcohol, ≥ 18 years, not diagnosed with cancer, and not having memory loss. Controls were selected from the same cancer hospitals and their medical health/referral centers so that the exposure patterns reflected the base population (Wacholder et al., 1992a). Recruitment was at a steady rate per unit time during the same period as that of cases, also known as density method of sampling (Rothman et al., 2011a). Oral examination was done to screen for possible presence of oral cancer among controls.

5.4.2 Data collection

Life course data were collected through direct interviews. Hospital records were abstracted for histopathological confirmation of cases. The interview took place in a regional Indian language (Kannada) at the hospitals/medical health centers within one to seven days of participant recruitment. Interviews were completed within an hour and with some assistance (from siblings/spouse/children/parents) for respondents experiencing difficulty in speaking due to cancer. A semi-structured questionnaire was used to collect data on paternal alcohol habit, education, occupation, housing conditions, area of residence, diet, oral hygiene practices, tobacco, alcohol and quid use throughout the life course. A life grid was used to improve recall (Berney and Blane, 2003). Initially, the questionnaire was developed in English and then translated to the local language. The questionnaire was pilot tested with the first fifteen cases and controls. Because no changes were required, the pilot participants were included in the analysis.

5.4.3 Measures

5.4.3.1 Outcome

The outcome was oral cancer, according to the case definition explained above.

5.4.3.2 Exposure

Child SEC was determined from the longest-held occupation of the HH³ at childhood (6–10 years of age). In childhood, HH was usually the participant's father in nuclear families and sometimes an uncle or grandfather in joint families. Occupation was recorded and later dichotomized into 'Low' and 'High' SEC indicative of social standing. The low group included the unemployed, farmers, fishermen, and manual laborers, considered to occupy the lowest SEC in the Indian context (Karnataka, 2005; Bhattacharya, 2011; Muggur, 2013). The high category involved tradesmen, craftsmen, industrial workers, white-collared workers, professionals and owners of business/establishments.

5.4.3.3 Confounders and mediators

Adult socioeconomic measures included the current occupation of the HH at the time of initial diagnosis and the participant's highest educational attainment. The HH in adulthood was a participant himself if male and others if female. Adult SEC was categorized in a similar way to child SEC. Participants' education was dichotomized as 'Secondary school/less' and 'Post-secondary school'. The paternal alcohol drinking habit was considered as a confounder of the *E – M* path since parental drinking could influence offspring's behaviour as well as family circumstances (Ellis et al., 1997; Handley and Chassin, 2009; Kerr et al., 2012). Paternal

³HH was usually an elder male family member that financially supported and maintained the household.

drinking was either ‘Yes’/‘No’. Age was dichotomized into ‘ ≤ 55 years’ and ‘ > 55 years’ across the median (54 yrs).

Mediators (smoking, chewing quid and/or tobacco and alcohol) were kept as binary– ‘Yes’/ ‘No’. Participants who had regularly smoked at least 3–5 days per week for ≥ 1 year were regarded as smokers and others rarely smoking or never as non-smokers. Those who had regularly chewed quid/tobacco at least 3–5 days per week for ≥ 1 year were considered as chewers and others rarely chewing or never as non-chewers. Participants who had regularly consumed alcohol at least one day per week for ≥ 1 year were considered as drinkers and others rarely drinking or never as non-drinkers. The exposure and mediators were kept at a binary level for simplicity, so that there would be only two counterfactual scenarios for the potential outcome framework. This also enables easier interpretation.

5.4.4 Statistical analyses

Missing data were less than 5% and were hence excluded from analysis. The aim was to estimate the CDE of the child SEC (E) on oral cancer (Y) given by path 1 (in fig. 1) not mediated by behavioral risk factors (M), that is, smoking, chewing quid and/or tobacco and alcohol given by paths 3&6 and 2&5&6. As hypothesized in the DAG (fig. 1), adult socioeconomic measures (E') that were successors of child SEC (E), confounded the mediator-outcome ($M-Y$) relation. The presence of a causal intermediate (E') confounding the mediator-outcome relation allows for estimation of the CDE of the exposure (E) on the outcome (Y) (VanderWeele, 2009). All analyses were done using SAS[®] software (SAS Institute Inc., Cary, NC, USA) version [9.2].

5.4.5 Outcome models

Risk ratio (RR) was used to estimate the effect. CDE of the child SEC from MSM were compared with the adjusted effect from conventional regression. The data were cluster correlated because of the multicentre design. Risk ratios estimated before and after accounting for clustering were also compared. Accounting of cluster variance was done by averaging the estimates over clusters.

$$\log [P (Y = 1|E = e, L = l)] = \beta_0 + \beta_1 E + \beta_2 L \quad (1)$$

Initially, a log-linear model was built by regressing the outcome ($Y = 1$) on child SEC and the confounder (L) of the exposure–mediator ($E - M$) relation, since there were no measured confounders of the exposure-outcome ($E - Y$) relation according to the conceptual framework (fig.1). From Model (1) the total effect of child SEC is given by β_1 assuming that the measured confounder (L) is sufficient to control for confounding.

$$\begin{aligned} \log [P (Y = 1|E = e, E' = e', M = m, L = l, C = c)] \\ = \beta_0 + \beta_1 E + \beta_2 E' + \beta_3 M + \beta_4 L + \beta_5 C \end{aligned} \quad (2)$$

The adjusted effect of the child SEC on oral cancer from conventional regression, given by β_1 in Model (2), was estimated by adjusting for all mediators and confounders (Baron and Kenny, 1986).

The CDE measured by RR using MSM for the counterfactual outcome $y(e, m)$, is given as

$$RR^m (e, e^*) = \frac{P[y(e, m) = 1]}{P[y(e^*, m) = 1]} \quad (3)$$

where E is set to e , $E = e^*$ for counterfactual and M is set to m .

To estimate the CDE of child SEC not mediated by each of the risk factors, three separate MSMs were used for smoking, chewing and alcohol despite the knowledge that there would be possible combined effects. In addition, currently available methods also restrict their use marginally (VanderWeele and Vansteelandt, 2012). Furthermore, for practical reasons controlling one mediator at a time would be desirable; it would not be possible to fix all the mediators to one level simultaneously as total abstinence from habits is not seen even in people diagnosed with cancer (Simmons et al., 2013; Aalen et al., Online first on March 28, 2014).

$$\log [P (Y = 1|E = e, M = m)] = \beta_0 + \beta_1 E + \beta_2 M \quad (4)$$

The average CDE with MSM was calculated using stabilized inverse probability weight (SW) in the log-linear regression in Model (4). Based on the assumption of no unmeasured confounders of $E-Y$, $E-M$ and $M-Y$ relations, β_1 in Model (4) gives the CDE of child SEC not mediated through M (paths 3&6 and 2&5&6) but could be mediated through E' (path 2&4).

CDE may be equal to natural direct effect when there are no interactions between child SEC and each of the risk factors (De Stavola and Daniel, 2012). Interactions between the exposure and each of the mediators were examined on both additive and multiplicative scales (Robins and Greenland, 1992; VanderWeele, 2009). The interaction on a multiplicative scale was examined using a cross-product term and on an additive scale by estimating the relative excess risk due to interaction (RERI) using RR, adopting a weighting approach for case-control data similar to that described by VanderWeele and Vansteelandt (VanderWeele and Vansteelandt, 2011). RERI between the exposure and each of the three mediators indicated no departures from additivity (**Table 5.5, 5.8 and 5.11**). However, there was an interaction of child SEC with alcohol on a multiplicative scale, but not with smoking and chewing (**Tables 5.6, 5.9 and 5.12**). Since the aim was to estimate CDE considering the counterfactual scenario

that if drinkers were non-drinkers, we estimated only the independent effect without considering the interaction term in Model (4).

5.4.6 Estimating stabilised weights

Inverse probability weights assist in handling the confounders in the MSM. SWs are more efficient than IPW because SW avoid extreme differences in weights for the exposed and unexposed while maintaining the original sample size in the weighted dataset and reducing type I error (Xu et al., 2010). For the case-control data, SW were calculated for cases and controls, while logistic regression was fitted only for controls (Newman, 2006; VanderWeele and Vansteelandt, 2011). SWs were created using unconditional logistic regression for the case where clustering was ignored and conditional logistic regression was used where clustering was considered.

SW for each model is given by $W = sw_i^e * sw_i^m$ where Z is the clusters (hospitals)

$$sw_i^e = \frac{P(E=e)}{P(E=e | L=l)} \Big| Z \quad (5)$$

and

$$sw_i^m = \frac{P(M_x=m_x | E=e)}{P(M_x=m_x | E=e, E'=e', M_y=m_y, M_z=m_z, L=l, C=c)} \Big| Z \quad (6)$$

Models (5) and (6) describe the creation of weights for child SEC and each mediator respectively. SW were calculated separately for smoking, chewing quid and/or tobacco and alcohol (M_x, M_y, M_z). For each mediator, the other two mediators were regarded as confounders of the M - Y relation and were included in the weight calculation, in addition to a vector of measured confounders denoted by L, C and E' .

5.4.7 Sensitivity analysis

Sensitivity analysis was performed to test the assumption of no unmeasured confounder (U). The presence of U that is correlated with M and Y will violate the assumption of no unmeasured confounder of the $M - Y$ relation provided E is randomized and U is not correlated with E . However, U could be correlated with E , M and Y , a likely situation in the real world that would violate the assumption of no unmeasured confounding of the $E - M$, $M - Y$ and $E - Y$ paths. Then, conditioning on the collider ‘ M ’ without accounting for U in the weight estimation would result in ‘collider stratification’ inducing an association between E and Y (Kim et al., 2004; Matthews and Gallo, 2011). An assumption of the sensitivity analysis was “no RERI” between the effects of E and effects of U and that U was correlated with E , M and Y . Sensitivity parameters of U such as γ (conditional increase in risk for oral cancer), $P1$ (prevalence in smokers/chewers drinkers) and $P2$ (prevalence among non-smokers/non-chewers/non-drinkers) were specified. The bias introduced by U that may entirely invalidate the CDE was calculated using the Model (7) given by VanderWeele (Vanderweele, 2010).

$$\text{Bias} \left(CDE_{e,e^*|c}^{RR}(m) \right) = \frac{1 + (\gamma - 1)(P1)}{1 + (\gamma - 1)(P2)} \quad (7)$$

5.5 Results

Of the total 452 participants, 180 were cases and 272 were controls. The participation rates were 95.8% for cases and 81% for controls.

Table 5.1 presents descriptive data on the study variables among cases and controls. The crude RR estimates indicate that paternal drinking, sex, child SEC, adult socioeconomic

measures, and participants' risk factors such as smoking, chewing quid and/or tobacco and alcohol were associated with oral cancer.

Table 5.1 Distribution of life course socioeconomic measures, paternal and own habits among cases and controls, and crude risk ratio estimates with 95% confidence intervals

	Cases (n=180)	Controls (n=272)	Total (n=452)	Crude RR (95% CI)
	n (%)	n (%)	n (%)	
Paternal alcohol drinking				
Yes	77 (44.3)	87 (33.2)	164 (37.6)	1.32 (1.05–1.65)
No	97 (55.7)	175 (66.8)	272 (62.4)	1.00
Age (years)				
18-55	95 (52.8)	156 (57.4)	251 (55.5)	1.00
≥ 56	85 (47.2)	116 (42.6)	201 (44.5)	1.12 (0.89–1.40)
Sex				
Males	143 (79.4)	149 (54.8)	292 (64.6)	2.12 (1.56–2.88)
Females	37 (20.6)	123 (45.2)	160 (35.4)	1.00
SEC in childhood				
Low	140 (79.1)	170 (62.5)	310 (69.0)	1.70 (1.25–2.30)
High	37 (20.9)	102 (37.5)	139 (31.0)	1.00
SEC in adulthood				
Low	105 (58.3)	119 (43.8)	224 (49.6)	1.43 (1.13–1.80)
High	75 (41.7)	153 (56.2)	228 (50.4)	1.00
Education				
Secondary/less	149 (82.8)	194 (71.3)	343 (75.9)	1.53 (1.11–2.11)
Post-secondary	31 (17.2)	78 (28.7)	109 (24.1)	1.00
Own habits:				
Smoking				
Yes	77 (42.8)	54 (19.8)	131 (29.0)	1.83 (1.48–2.27)
No	103 (57.2)	218 (80.2)	321 (71.0)	1.00
Chewing quid and/or tobacco				
Yes	122 (67.8)	63 (23.2)	185 (40.9)	3.04 (2.36–3.90)
No	58 (32.2)	209 (76.8)	267 (59.1)	1.00
Alcohol drinking				
Yes	96 (53.3)	57 (21.0)	153 (33.8)	2.23 (1.80–2.78)
No	84 (46.7)	215 (79.0)	299 (66.2)	1.00

The results obtained from conventional regression and MSM are presented in **Table 5.2**

According to the total effects Model (1), people from low SEC in childhood had 63%

(RR=1.63 [95% CI=1.38–1.92]) higher risk for oral cancer than those in the high SEC group.

This association disappeared (RR=1.09 [95% CI= 0.94–1.26]) after adjusting for adult SEC, education, risk factors and other confounders in the conventional regression. CDE of early-life SEC estimated from MSMs showed that people with low child SEC had 48% (RR=1.48 [95% CI= 1.43–1.53]), 24% (RR=1.24 [95% CI= 0.88–1.74]) and 94% (RR=1.94 [95% CI=1.66–2.27]) higher risk for oral cancer that was not mediated by smoking, chewing quid and/or tobacco and alcohol respectively, than those with high SEC in childhood. However, the 95% CI of CDE not mediated by quid chewing did include unity. Accounting for clustering improved the precision of RR estimates.

Table 5.2 Total effect, adjusted effect from conventional regression, and controlled direct effect from the marginal structural model for oral cancer

			Without accounting for clustering RR (95% CI)	Accounting for clustering RR (95% CI)
(Model 1)	Total effect^a			
	Child SEC	Low	1.60 (1.17–2.17)	1.63 (1.38–1.92)
		High	1.00	1.00
Conventional regression (Model 2)	Adjusted effect^b			
	Child SEC	Low	1.08 (0.72–1.63)	1.09 (0.94–1.26)
		High	1.00	1.00
MSM (Model 4)	Direct effect controlled for smoking^c			
	Child SEC	Low	1.38 (1.02–1.86)	1.48 (1.43–1.53)
		High	1.00	1.00
	Direct effect controlled for chewing quid and/or tobacco^d			
	Child SEC	Low	1.21 (0.92–1.59)	1.24 (0.88–1.74)
		High	1.00	1.00
	Direct effect controlled for alcohol^e			
	Child SEC	Low	1.89 (1.30–2.75)	1.94 (1.66–2.27)
		High	1.00	1.00

^aadjusted for paternal alcohol;

^badjusted for paternal alcohol, adult SEC, smoking, chewing quid and/ or tobacco, alcohol, age and sex

^c stabilized weight accounting for paternal alcohol, adult SEC, chewing quid and/or tobacco, alcohol, age and sex

^d stabilized weight accounting for paternal alcohol, adult SEC, smoking, alcohol, age and sex

^e stabilized weight accounting for paternal alcohol, adult SEC, smoking and chewing quid and/or tobacco, age and sex

The results of sensitivity analysis for unmeasured confounder ' U ' are presented in **Table 5.3**. In order to eliminate the CDE not mediated by smoking, the probability of U being present is 33% (53% Vs 20%) higher among smokers(P_{1_1}) than in non-smokers(P_{2_1}) across strata of child SEC, i.e., $[P(U = 1|m_1, e) - P(U = 1|m_0, e) = 0.33]$ and the risk of oral cancer to be increased by three times across all strata of child SEC and smoking. However, the presence of U increasing the oral cancer risk by 3 fold is impossible; therefore, CDE cannot be attributed to unmeasured confounders. Similarly, when considering the scenarios for alcohol, U increasing the risk of oral cancer by 3 or 4 times is also implausible. Most of the sensitivity parameters hypothesized in Table 5.3 to nullify the CDE of the child SEC on oral cancer are not plausible and hence we could consider with some confidence that child SEC conditionally affects oral cancer.

Table 5.3 Sensitivity analysis for unmeasured confounding considering three estimates of controlled direct effect of early-life socioeconomic conditions on oral cancer

Sensitivity analysis for unmeasured confounder that would invalidate CDE not mediated by smoking				Sensitivity analysis for unmeasured confounder that would invalidate CDE not mediated by chewing				Sensitivity analysis for unmeasured confounder that would invalidate CDE not mediated by drinking			
γ_1	P1 ₁	P2 ₁	RR ₁	γ_2	P1 ₂	P2 ₂	RR ₂	γ_3	P1 ₃	P2 ₃	RR ₃
2	0.5	0.02	1.48	2	0.26	0.02	1.24	-	-	-	-
2	0.51	0.025	1.48	2	0.27	0.025	1.24	-	-	-	-
2	0.52	0.03	1.48	2	0.27	0.03	1.24	-	-	-	-
2	0.53	0.04	1.48	2	0.28	0.04	1.24	-	-	-	-
2	0.55	0.05	1.48	2	0.3	0.05	1.24	-	-	-	-
2	0.62	0.1	1.48	2	0.36	0.1	1.24	-	-	-	-
2	0.77	0.2	1.48	2	0.48	0.2	1.24	-	-	-	-
2	0.9	0.29	1.48	2	0.61	0.3	1.24	-	-	-	-
-	-	-	-	2	0.6	0.3	1.24	-	-	-	-
3	0.265	0.02	1.48	3	0.14	0.02	1.24	3	0.51	0.023	1.94
3	0.28	0.028	1.48	3	0.15	0.025	1.24	3	0.52	0.027	1.94
3	0.28	0.03	1.48	3	0.16	0.035	1.24	3	0.53	0.033	1.94
3	0.3	0.042	1.48	3	0.17	0.042	1.24	3	0.55	0.043	1.94
3	0.31	0.05	1.48	3	0.18	0.05	1.24	3	0.57	0.054	1.94
3	0.39	0.105	1.48	3	0.24	0.1	1.24	3	0.66	0.1	1.94
3	0.53	0.2	1.48	3	0.37	0.205	1.24	3	0.86	0.204	1.94
3	0.68	0.3	1.48	3	0.49	0.3	1.24	-	-	-	-
3	0.83	0.4	1.48	3	0.61	0.4	1.24	-	-	-	-
-	-	-	-	3	0.74	0.5	1.24	-	-	-	-
-	-	-	-	3	0.86	0.6	1.24	-	-	-	-
4	0.19	0.022	1.48	4	0.11	0.025	1.24	4	0.35	0.02	1.94
4	0.2	0.028	1.48	4	0.11	0.025	1.24	4	0.36	0.025	1.94
4	0.21	0.035	1.48	4	0.12	0.035	1.24	4	0.37	0.03	1.94
4	0.22	0.042	1.48	4	0.13	0.043	1.24	4	0.39	0.04	1.94
4	0.24	0.055	1.48	4	0.14	0.05	1.24	4	0.41	0.05	1.94
4	0.31	0.104	1.48	4	0.2	0.1	1.24	4	0.7	0.2	1.94
4	0.46	0.205	1.48	4	0.33	0.205	1.24	4	0.9	0.305	1.94
4	0.6	0.3	1.48	4	0.45	0.3	1.24	-	-	-	-
4	0.75	0.4	1.48	4	0.57	0.4	1.24	-	-	-	-
4	0.9	0.5	1.48	4	0.7	0.5	1.24	-	-	-	-
-	-	-	-	4	0.82	0.6	1.24	-	-	-	-

Note: Bias formula for CDE given by VanderWeeleTJ²⁷ was used by specifying sensitivity parameters γ , P1 and P2 to calculate RR;

γ_1 = conditional increase in the risk for oral cancer when smoking is the mediator in model 4;

γ_2 = conditional increase in the risk for oral cancer when chewing is the mediator in model 4;

γ_3 = conditional increase in the risk for oral cancer when drinking is the mediator in model 4;

P1₁= prevalence in smokers and P2₁= prevalence in non-smokers;

P1₂= prevalence in chewers and P2₂= prevalence in non-chewers;

P1₃= prevalence in drinkers and P2₃= prevalence in non-drinkers;

RR₁ = direct effect of child SEC controlled for smoking;

RR₂ = direct effect of child SEC controlled for chewing;

RR₃ = direct effect of child SEC controlled for drinking;

Table 5.4 Frequency distribution of cases and controls according to joint exposure to childhood SEC (CHSEC) and smoking

	Cases (n)	Controls (n)
CHSEC ₁ SMOKING ₁	64	39
CHSEC ₁ SMOKING ₀	76	131
CHSEC ₀ SMOKING ₁	11	15
CHSEC ₀ SMOKING ₀	26	87

The frequency distribution of cases and controls by childhood SEC and smoking is presented in **Table 5.4**. Smokers were more common among cases than controls that were in low SEC.

Table 5.5 shows that there is no additive interaction between childhood SEC and smoking on the RR scale.

Table 5.5 RERI between childhood SEC and smoking on the risk ratio scale

	Estimate	SE	95% CI		t Value	Pr > t
			Lower	Upper		
	β					
Intercept	-1.01	0.21	-1.42	-0.59	-4.76	<0.001
Childhood SEC	0.46	0.26	-0.05	0.97	1.78	0.076
Smoking	0.84	0.56	-0.26	1.94	1.50	0.135
Childhood SEC*Smoking	0.30	0.64	-0.95	1.55	0.47	0.638
	RR					
RERI	0.32	0.56	-0.77	1.420	0.58	0.561

Table 5.6 shows that there is no multiplicative interaction of childhood SEC and smoking on the RR scale.

Table 5.6 Multiplicative interaction between childhood SEC and smoking on risk ratio scale

	β estimate	SE	95% CI		Z	Pr> Z
			Lower	Upper		
Intercept	-1.34	0.21	-1.74	-0.93	-6.40	<0.001
Child SEC	0.32	0.08	0.16	0.48	3.97	<0.001
Smoking	0.54	0.07	0.40	0.68	7.52	<0.001
Childhood SEC*Smoking	0.03	0.05	-0.07	0.14	0.60	0.548

Table 5.7 Frequency distribution of cases and controls according to joint exposure to childhood SEC and chewing quid/tobacco (CHEWING)

	Cases (n)	Controls (n)
CHSEC ₁ CHEWING ₁	101	50
CHSEC ₁ CHEWING ₀	39	120
CHSEC ₀ CHEWING ₁	20	13
CHSEC ₀ CHEWING ₀	17	89

Table 5.7 shows that quid/tobacco chewers were more common among cases, who lived in low SEC in their childhood when compared with controls of low child SEC.

As seen from Table 5.8 there is no interaction of childhood SEC and chewing on additive scale considering RR.

Table 5.8 RERI between childhood SEC and chewing quid/tobacco on risk ratio scale

Parameter	Estimate	SE	95% CI		t Value	Pr > t
			Lower	Upper		
β						
Intercept	-1.45	0.25	-1.94	-0.96	-5.82	<0.001
Childhood SEC	0.32	0.31	-0.29	0.93	1.02	0.307
Chewing	1.73	0.44	0.87	2.60	3.93	<0.001
Childhood SEC*chewing	0.10	0.51	-0.91	1.10	0.19	0.851
RR						
RERI	0.23	0.56	-0.88	1.33	0.4	0.687

Table 5.9 shows that multiplicative interaction between childhood SEC and chewing quid if any is merely due to chance.

Table 5.9 Multiplicative interaction between childhood SEC and chewing on risk ratio scale

	β Estimate	SE	95% CI		Z	Pr > Z
			Lower	Upper		
Intercept	-1.68	0.47	-2.59	-0.77	-3.60	<0.001
Child SEC	0.29	0.33	-0.35	0.93	0.90	0.368
Chewing	1.13	0.70	-0.24	2.50	1.61	0.106
Child SEC*Chewing	-0.15	0.60	-1.32	1.03	-0.24	0.810

Table 5.10 Frequency distribution of cases and controls according to joint exposure to childhood SEC and alcohol

	Cases (n)	Controls (n)
CHSEC₁ALCOHOL₁	74	43
CHSEC₁ALCOHOL₀	66	127
CHSEC₀ALCOHOL₁	19	14
CHSEC₀ALCOHOL₀	18	88

Alcohol users were more common among cases than controls considering low child SEC strata (Table 5.10).

Additive interaction of childhood SEC and alcohol on RR scale is not present in the study population (Table 5.11).

Table 5.11 RERI between childhood SEC and alcohol on risk ratio scale

	Estimate	SE	95% CI		t Value	Pr > t
			Lower	Upper		
	β					
Intercept	-1.78	0.28	-2.34	-1.23	-6.32	<0.001
Childhood SEC	1.28	0.32	0.65	1.91	3.99	<0.001
Alcohol	2.01	0.55	0.94	3.08	3.68	<0.001
Childhood SEC*Alcohol	-0.81	0.61	-2.00	0.39	-1.32	0.187
	RR					
RERI	-0.84	1.01	-2.82	1.15	-0.83	0.668

As observed from the **Table 5.12**, there is sub-multiplicative interaction of childhood SEC and alcohol on the risk ratio scale.

Table 5.12 Multiplicative interaction between childhood SEC and alcohol on risk ratio scale

	β estimate	SE	95% CI		Z	Pr> Z
			Lower	Upper		
Intercept	-1.94	0.35	-2.63	-1.25	-5.51	<0.001
Child SEC	0.97	0.18	0.63	1.31	5.54	<0.001
Alcohol	1.34	0.39	0.57	2.10	3.41	<0.001
Child SEC*Alcohol	-0.77	0.27	-1.30	-0.25	-2.90	0.004

5.6 Discussion

The aim of the study was to estimate the CDE of child SEC on oral cancer. To the best of our knowledge, this is the first study that makes use of MSM in oral cancer research. Although cohort designs are suited for life course research, for a relatively infrequent chronic disease like oral cancer, a case-control study is a feasible option (Maheshwaran et al., 2002; Lynch and Smith, 2005; Nicolau et al., 2007).

The present study provides evidence to support the hypothesis that childhood socioeconomic disadvantage has a long-term effect on oral cancer occurrence in adulthood independent of individual risk factors. The findings are similar to those of other studies, which show that childhood socioeconomic disadvantage adversely affects general health in the adult stage (Nandi et al., 2012).

The conventional regression (Model (2)) indicated that childhood SEC was not independently associated with oral cancer. Adjusting for all mediators and confounders in the model would block the pathways through all three risk factors and adulthood SEC, thus showing a null effect.

This problem was overcome by fitting MSM that handles confounders with SW, while controlling for a mediator in Model (4). The CDE highlights the lasting effect of childhood socioeconomic disadvantage on development of oral cancer for those who lived in low SEC when they were 6–10 years old, regardless of the development of risk factors in later life.

In this paper, the occupation of HH was used to measure SEC in childhood. The HH is responsible for financially supporting and maintaining the family. Moreover, the occupation of HH determines the income and living conditions that can influence a child's health. Socioeconomic disadvantage in childhood, a sensitive period of growth and development, could permanently alter the physiological constitution that could subsequently affect health in adulthood.

Estimates from the MSM are valid, provided the assumptions for model building are satisfied. Firstly, there should be 'no unmeasured confounders' of the $E-Y$, $E-M$ and $M-Y$ paths. As observed from the sensitivity analysis, the CDEs are less likely to be invalidated until a strong confounder in the source population with specified parameters is discovered. With paternal alcohol drinking being measured in this study, the potential confounding bias of the $E-M$ relation was lower. Moreover, to the best of our knowledge, there were no confounders of the child SEC and oral cancer outcome relation identified from the literature review. Secondly, assumptions such as positivity and correct model specification are required for weight estimation, which may be violated if the means of SW are far from 1. Since the means of SWs in this study varied between 0.91 and 1.00, the above mentioned assumptions can be considered to be valid. Lastly, the assumption of 'no interaction' means that the effect measure (β) is equal across all levels of a mediator. The measure of RERI signifies the absence of public health interactions, meaning the benefits of intervention on the exposure would be similar across all subgroups (VanderWeele and Vansteelandt, 2014). Interaction on

a multiplicative scale between child SEC and alcohol shows that the CDE of child SEC mediated through alcohol may not be equated to a natural direct effect. Future studies may employ approaches unifying mediation and interaction or estimating natural direct effects (VanderWeele, 2009; Xu et al., 2010). It is possible to demonstrate that child SEC is causally associated with oral cancer from the evidence obtained with the above assumptions, along with consistency and the logistic regression and marginal structural models being correctly specified.

There are some limitations to this study. Early-life socioeconomic disadvantage in general may include various aspects which may relate to oral cancer through various pathways independent of risk factors, but we have considered only occupation. There could be misclassification of early-life SEC due to error in recall. However, by using the life-grid method, we assumed that the error in recall would be less. People of various age groups were included in the study; there could be some cohort effect that was not considered.

Measurement error of risk factors would be lower because smoking, chewing quid/tobacco and alcohol were based on exposure history over the entire life course. If two or more risk factors are present in an individual simultaneously, they may interact with each other. Some of the indirect effect may be mediated by HPV, which was not measured in this study.

5.7 Conclusion

In conclusion, early-life socioeconomic disadvantage has a lasting effect on oral cancer outcome in adulthood when examined using marginal structural model. Further research should focus on social mobility and accumulation of socioeconomic disadvantage, including other mediators such as diet and HPV.

Chapter 6

6 A screening model for oral cancer using risk scores: Development and validation

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6.2 Abstract

Objective: A study was conducted to develop and validate a screening model for oral cancer using risk scores to identify high-risk individuals in an Indian population.

Methods: Life-course data collected from a multicentre case-control study in India were used. Interviews were conducted to collect information on predictors limiting to the time before the onset of symptoms of cancer/pre-cancer or cancer diagnosis. Predictors included statistically significant risk factors in the multivariable model. A risk score for each predictor was derived from respective OR. Discrimination of the final model, risk scores and various risk score cut-offs were examined using the *c* statistic. The optimal cut-off was determined as the one with good area under curve (AUC) and high sensitivity. The predictive ability of the regression model and cut-off risk score were determined by calculating sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The models were validated from a bootstrap sample.

Results: Smoking, chewing quid and/or tobacco, alcohol, family history of upper aerodigestive tract cancer, diet and oral hygiene behaviour were significant predictors. Risk scores ranged from 0 to 28. The AUC of the ROC curve for risk scores was good (0.866). The sensitivity (0.928) and NPV (0.927) were higher while specificity (0.603) and PPV (0.607) were lower for a risk score cut-off of 6.

Conclusions: A risk score model to screen for oral cancer with satisfactory predictive ability was developed in the Indian population. Validation of the model in other populations is necessary before it can be recommended to identify subgroups of the population to be directed towards more extensive clinical evaluation.

6.3 Introduction

Oral cancer is the sixth leading cancer in the world. Although a rare disease, oral cancer is the fourth most frequent cancer in India, with the majority of cases being SCC (Bhurgri et al., 2003; Bhurgri, 2005; Ferlay et al., 2010b). The stage at diagnosis has implications for prognosis; if diagnosed at initial stages the mortality rate reduces (Sankaranarayanan et al., 2000). Oral cancer can progress rapidly to advanced stages, with a delay in diagnosis ranging from a few weeks to years (Llewellyn et al., 2004). Diagnostic delay is mainly due to delay in presentation and sometimes because of failure to follow-up after initial examination by a professional (Kantola et al., 2001; Kumar et al., 2001). The five year survival rate is lowered when oral cancer is diagnosed at advanced stages (Yeole et al., 2000).

In countries where a high proportion of the population live in rural areas with poor access to health care services and have a high prevalence of risk factors for oral cancer, that is, tobacco, quid and alcohol use (Yen et al., 2008b; Petti, 2009), early detection and timely treatment could improve the survival rate, reducing the psychological and economic burden on the patient and his/her family as well as reducing physical disability. Community-based visual screening for oral cancer using the existing workforce, such as community/primary health care workers, is a feasible option (Warnakulasuriya et al., 1984; Sankaranarayanan et al., 2000). Some visual screening programs have a high sensitivity rate and reduce the oral cancer related death rate (Sankaranarayanan et al., 2000; Sankaranarayanan et al., 2013). However, in rural/remote areas, community health workers trained to perform visual screening are limited. Therefore, there is a need to develop a method that would be economical and easy to adopt, that is, by asking simple questions that do not require intense, systematic training of the personnel to perform visual oral screening. Such a method would help in utilising the existing untrained personnel to identify target groups when resources are limited.

Risk scores are model-based scores that predict the outcome and, therefore, assist in decision making in diagnosis and prognosis (Steyerberg et al., 2010). Risk scores based on the history of exposure to risk factors have been used to identify high-risk individuals for prostate and colorectal cancer (Driver et al., 2007; Roudgari et al., 2012). The Harvard cancer risk index is based on such a model (Colditz et al., 2000). A similar model was developed and validated in Sri Lanka for detecting *OPMD* in a high-risk population (Amarasinghe et al., 2010). Though *OPMD* can give rise to oral cancer, the rate of malignant transformation varies (Yen et al., 2008a). Moreover, oral cancer can arise from normal appearing mucosa. To the best of our knowledge, there are no models that use risk scores in screening for oral cancer. Therefore, the aim was to develop and validate a screening model using risk scores that could be used to identify adults at high-risk for developing oral cancer in the Indian population.

6.4 Methods

6.4.1 Study design

A multicentre hospital based unmatched case-control study was conducted between July 2011 and August 2012. Data was collected for a larger life-course study on oral cancer from four major cancer hospitals located in Karnataka, India. These hospitals draw patients from both rural and urban areas of India and majorly from South India. A risk score model was developed using data collected for the life-course study. Ethics approval was obtained from the ethics committees of the University of Adelaide and the selected cancer hospitals. Informed consent was obtained from all the participants. Interviews were conducted after the diagnosis of cancer, in hospitals for all participants to collect information on sociodemographic details, exposure history for tobacco, quid, alcohol, diet and oral hygiene practices over their life-course using a semi-structured questionnaire. A life-grid was used to improve recall (Berney and Blane, 2003). Oral examination was done to record oral mucosal

lesions for all participants. Medical records were abstracted for histopathological confirmation of cases.

6.4.2 Participant selection and recruitment

6.4.2.1 Cases

‘Oral cancer’ included cancers of the oral cavity and oropharynx [International classification of Diseases (ICD)- 10 codes: C00–C10]. Cases were identified from outpatient clinics, hospital wards and treatment plan/surgery registers maintained in the hospitals. Incident cases histopathologically diagnosed with oral cancer between July 2011 and August 2012, visiting selected cancer hospitals, and ≥ 18 years of age were included. Secondaries, sarcomas and skin cancer of the lips were excluded because of co-morbidity or different etiopathology. The eligible cases providing consent were recruited. Some cases receiving diagnostic work-up at the participating hospitals could not be included in the study, if they did not return to the same hospital for further consultation or treatment.

6.4.2.2 Controls

They were from the same cancer hospitals and their referral/health centres so that the exposure patterns would reflect the source population that gave rise to cases (Rothman et al., 2011a). People in waiting places, wards and out-patient clinics were selected and approached. The eligible controls providing consent were recruited throughout the same period as cases (density sampling) (Rothman et al., 2011a). The selection criteria for controls were: ≥ 18 years, not diagnosed with cancer, were carers/visitors of cancer patients (excluding UADT), lung and liver cancers to avoid overmatching on exposure characteristics such as SEC, tobacco, quid or alcohol use) or those seeking health care for medical conditions not related to

tobacco and/or alcohol and those not suffering from memory loss. Controls were confirmed to be negative of oral cancer by oral examination.

6.4.3 Potential predictors

The predictors were chosen based on a literature search for plausible risk factors for oral cancer (Rao et al., 2013). Data collected on all the predictors through the interview were restricted to the time point prior to the onset of symptoms of OPMD or cancer. Predictors included sociodemographic factors, habits, diet, and oral hygiene behaviour. They were dichotomised into broad categories so that questions are easily administered. Paternal and maternal education was collected as the highest level of education attained by participants' parents and dichotomised as 'primary/less' and 'higher than primary'. Adult SEC was based on the head of the household's occupation, classified by authors into three groups (low, middle and high) indicative of social standing. The 'low' level group included unemployed, farmers, fishermen, and manual labourers. The 'middle' category involved small time tradesmen, craftsmen and industrial workers. White collared workers, professionals and business/establishment owners were categorised as 'high'. The paternal alcohol drinking habit was considered as 'present'/'absent'. The participants' own habits were dichotomised as 'Yes'/'No'. Participants who regularly smoked at least 3-5 days per week for one year were considered as smokers and others rarely smoking or never as non-smokers. Chewing included three separate predictors such as chewing tobacco, chewing quid with tobacco and chewing quid without tobacco. Participants who regularly chewed tobacco and/or quid at least 3-5 days per week for one year were considered as 'Yes' and others rarely chewing or never as 'No' for their respective categories. For alcohol, participants who regularly consumed alcohol at least one day per week for one year were considered as drinkers and others rarely drinking or never as non-drinkers. BMI was derived from self-reported height and body weight five years ago (weight loss may be related to long existing oral cancer/ OPMD) using the relationship -

kg/m² and categorised into underweight (≤ 18.4) and normal/above (≥ 18.5). Spiciness of food was self-rated on a schematic ladder of 1-10 scale. It was dichotomised into 'Less spicy' (1-5) and 'More spicy' (≥ 6). Frequency of fruit consumption was dichotomised into 'at least once weekly' and 'less than once a week'. Family history of UADT cancer in first or second degree relatives, irrespective of age was included as 'Yes'/'No'. The practice of rinsing the mouth with water after eating and/or chewing was collected as a general measure for oral hygiene and was dichotomised into 'Yes'/'No'. Eating/chewing referred to either food or quid.

6.5 Statistical analyses

6.5.1 Model development

Statistical significance at $p < 0.05$ was determined with the chi-square test for OR. Missing data were excluded because it was less than 10%. Odds ratios were adjusted for clustering using a generalised estimating equation. Statistically significant predictors at the bivariate level were included in the multivariable logistic regression. Nevertheless, a predictor not significant at the bivariate level, but which was a risk factor according to the literature review was, still included in the multivariable model. The predictors to be included in the multivariable prediction model were assessed for correlation using Spearman's rho. Of the predictors that were highly correlated ($r \geq 0.3$), the one with a stronger association with oral cancer was retained and others were dropped. Starting with a full model, statistically insignificant predictors were removed backwards manually to obtain a final model. Only significant variables remained in the final model. The fit of models was assessed with the Hosmer-Lemeshow goodness of fit test. A risk score for each predictor was derived from the predictors' corresponding OR. Receiver Operating Characteristic (ROC) curves were plotted to examine the discrimination of the final model, risk scores and various risk score cut-offs (Pepe et al., 2006). Since the risk scores are continuous and range between a minimum and a

maximum, a cut-off is required to make decisions for further referral. The optimal cut-off was determined as the one with good specificity and a higher sensitivity.

6.5.2 Model validation

The final and the risk score models developed from the original data set were validated in 200 bootstrap samples drawn with replacement from the same data set by checking for the reliability of the *c* statistics. The sensitivity, specificity, PPV and NPV calculated for the final regression model and a range of cut-off risk scores in the original and bootstrap samples were compared.

6.5.3 Analysis of prevalence

The prevalence of the disease affects predictive values and sensitivity (Brenner and Gefeller, 1997). Given the case-control design of this study, prevalence is unmeasurable. Therefore, it was necessary to adjust the results for the sampling fraction of control and prevalence in India (Ferlay et al., 2010b). Data were analysed using SAS[®] software (SAS Institute Inc., Cary, NC, USA) version [9.2].

6.6 Results

Of the eligible 188 incident cases and 336 controls approached, 180 (95.8%) cases and 272 (81.0%) controls consented and participated in the study.

Sex, paternal and maternal education, adult SEC, paternal drinking, own habits such as smoking, chewing tobacco, quid with tobacco, alcohol, low frequency of fruit consumption, spiciness of food, not rinsing the mouth with water after chewing/eating, and family history of UADT cancer in first or second degree relatives were significant predictors at the bivariate level (**Table 6.1**).

Table 6.1 Characteristics of cases and controls and unadjusted odds ratios

Characteristics	Cases (n=180) n (%)	Controls (n=272) n (%)	Unadjusted OR (95% CI)	p value*
Age (years)				
18-55	95 (52.8)	156 (57.4)	Ref	
>55	85 (47.2)	116 (43.6)	1.14 (0.73-1.79)	0.573
Sex				
Males	143 (79.4)	149 (54.8)	3.23 (2.89-3.61)	<0.001
Females	37 (20.6)	123 (45.2)	Ref	
Paternal education				
Primary/less	139 (77.6)	171 (63.6)	2.07 (1.32-3.25)	0.002
Higher than primary	40 (22.4)	98 (36.4)	Ref	
Maternal education				
Primary/less	159 (88.3)	210 (78.1)	2.24 (1.34-3.75)	0.002
Higher than primary	21 (11.7)	59 (21.9)	Ref	
Adult SEC				
Low	105 (58.3)	119 (43.8)	2.17 (1.23-3.81)	0.007
Middle	47 (26.1)	89 (32.7)	1.29 (0.95-1.76)	0.099
High	28 (15.6)	64 (23.5)	Ref	
Paternal alcohol drinking				
Yes	77 (44.3)	87 (33.2)	1.57 (1.24-2.00)	0.018
No	97 (55.7)	175 (66.8)	Ref	
Smoking				
Yes	77 (42.8)	54 (19.8)	3.06 (2.78-3.37)	<0.001
No	103 (57.2)	218 (80.2)	Ref	
Chewing tobacco				
Yes	57 (31.7)	23 (8.5)	4.96 (3.42-7.17)	<0.001
No	123 (68.3)	249 (91.5)	Ref	
Chewing quid with tobacco				
Yes	74 (41.1)	22 (8.1)	7.77 (7.03-8.61)	<0.001
No	106 (58.9)	250 (91.9)	Ref	
Chewing quid without tobacco				
Yes	25 (13.9)	26 (9.6)	1.58 (0.88-2.84)	0.125
No	155 (86.1)	246 (90.4)	Ref	
Alcohol				
Yes	96 (53.3)	57 (21.0)	4.22 (3.08-5.79)	<0.001
No	84 (46.7)	215 (79.0)	Ref	
BMI				
Underweight	27 (15.4)	35 (13.5)	1.15 (0.94-1.41)	0.169
Normal and above	148 (84.6)	224 (86.5)	Ref	
Spiciness of food				

More spicy	111 (61.6)	110 (40.6)	2.32 (1.83-2.95)	<0.001
Less spicy	69 (38.3)	161 (59.4)	Ref	
Fruit consumption				
At least once weekly	42 (23.3)	140 (51.8)	Ref	<0.001
Less than once a week	138 (76.7)	130 (48.2)	3.76 (2.87-4.92)	
Family history of UADT cancer				
Yes	26 (14.7)	16 (6.1)	2.63 (2.07-3.32)	<0.001
No	151 (85.3)	246 (93.9)	Ref	
Rinsing mouth with water after eating and/or chewing				
Yes	24 (13.3)	103 (38.0)	Ref	
No	156 (86.7)	168 (62.0)	4.12 (3.02-5.60)	<0.001

***from chi-square test**

Table 6.2 presents all predictors included in the full model. Adult SEC, smoking, chewing tobacco, quid with tobacco, quid without tobacco, spicy food, not rinsing mouth with water and family history of UADT cancer were associated with oral cancer.

Table 6.2 Multivariable logistic regression with all predictors of oral cancer included in the full model

Predictors	Categories	Adjusted OR (95% CI)	Chi-sq	p
Paternal education	Primary/less	1.22 (0.66-2.29)	0.40	0.529
	Higher than primary	Ref		
Maternal education	Primary/less	0.49 (0.22-1.09)	3.04	0.081
	Higher than primary	Ref		
Adult SEC	Low	2.27 (1.62-3.18)	22.66	<0.001
	Middle	1.30 (0.68-2.46)		
	High	Ref		
Age (Years)	>55	0.94 (0.35-2.50)	0.02	0.894
	18-55	Ref		
Smoking	Yes	3.50 (2.71-4.52)	91.66	<0.001
	No	Ref		
Chewing tobacco	Yes	3.31 (2.26-4.86)	37.60	<0.001
	No	Ref		
Chewing quid with tobacco	Yes	10.13 (8.71-11.78)	898.69	<0.001
	No	Ref		
Chewing quid without tobacco	Yes	2.05 (1.11-3.80)	5.23	0.022
	No	Ref		
Alcohol	Yes	2.20 (0.96-5.03)	3.45	0.063
	No	Ref		
Spiciness of food	More spicy	2.28 (1.88-2.75)	72.06	<0.001
	Less spicy	Ref		
Fruit consumption	Less than once/week	3.06 (2.04-4.61)	28.83	<0.001
	At least once/week	Ref		
BMI	Underweight	1.09 (0.80-1.47)	0.30	0.586
	Normal and above	Ref		
Rinsing mouth with water after eating/chewing	No	4.19 (1.90-9.20)	12.70	<0.001
	Yes	Ref		
Family history of UADT cancer	Yes	2.05 (1.82-2.31)	139.51	<0.001
	No	Ref		

Table 6.3 presents the multivariable model for the final set of predictors. Sex and paternal alcohol drinking were not included in the model because they were highly correlated with participant's own habits. Based on the literature review, age and chewing quid without tobacco (Warnakulasuriya et al., 2002; Lee et al., 2011) were risk factors and therefore included in the multivariable model. In the final model, smoking, chewing tobacco, quid with tobacco, quid without tobacco and alcohol were associated with oral cancer. Participants with a family history of UADT cancer had a higher OR (2.45, 95% CI = 2.01–2.97) for oral cancer than those with no family history. Dietary factors such as eating more spicy food and not eating fruits at least once a week were associated with oral cancer. Those not rinsing the mouth with water after eating/chewing had an OR that was four times that of people who did rinse their mouth. Chewing quid with tobacco was the strongest (OR = 8.25, 95% CI = 6.53-10.43) of all the predictors. The Hosmer-Lemeshow test showed that the model fit the data adequately ($p = 0.390$). The AUC for ROC curve for the final regression model was good (0.870). Discrimination in a bootstrap sample with 200 repetitions showed a similar AUC (0.869). The total individual risk score ranged from 0 to 28. The AUC of the ROC curve for risk scores was good (0.866) and similar to that of the logistic model (See **Figures 6.1 to 6.4**).

Table 6.3 Multivariable regression model for predictors of oral cancer and risk scores for the predictors

Covariates	Adjusted OR	95% CI for Adjusted OR	p value†	Risk score
Smoking				
Yes	3.03	2.38-3.86	<0.001	3
No	Ref			
Chewing tobacco				
Yes	3.12	1.92-5.07	<0.001	3
No	Ref			
Chewing quid with tobacco				
Yes	8.25	6.53-10.43	<0.001	8
No	Ref			
Chewing quid without tobacco				
Yes	1.89	1.16-3.07	0.011	2
No	Ref			
Alcohol				
Yes	2.22	1.30-3.76	0.003	2
No	Ref			
Spiciness of food				
More spicy	2.15	1.91-2.42	<0.001	2
Less spicy	Ref			
Fruit consumption				
At least once weekly	Ref			
Less than once a week	2.47	1.64-3.73	<0.001	2
Family history of UADT cancer				
Yes	2.45	2.01-2.97	<0.001	2
No	Ref			
Rinsing mouth with water after eating/chewing				
Yes	Ref			
No	3.63	2.23-5.89	<0.001	4
AUC	0.870 (0.869)*			0.866 (0.865)*
Hosmer-Lemeshow Goodness of fit	Chi-sq= 8.46		0.390	

* AUC for bootstrap sample; †from Chi-sq

Figure 6.1 ROC curve for the multivariable model

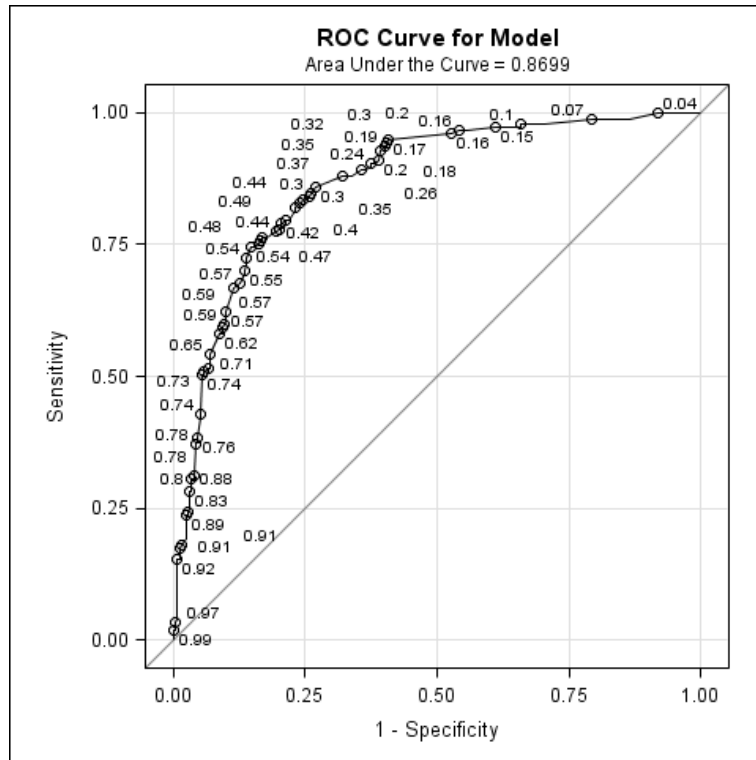
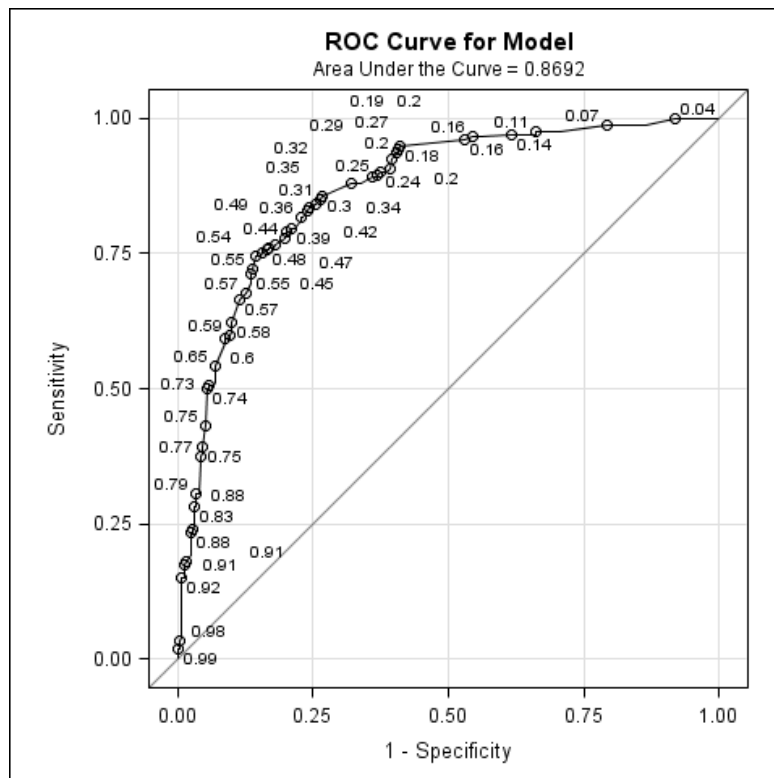


Figure 6.2 ROC curve for the multivariable model using the bootstrap sample



The plotted points on the ROC curves represent the predicted probabilities from the model for each threshold.

Figure 6.3 ROC curve for risk scores

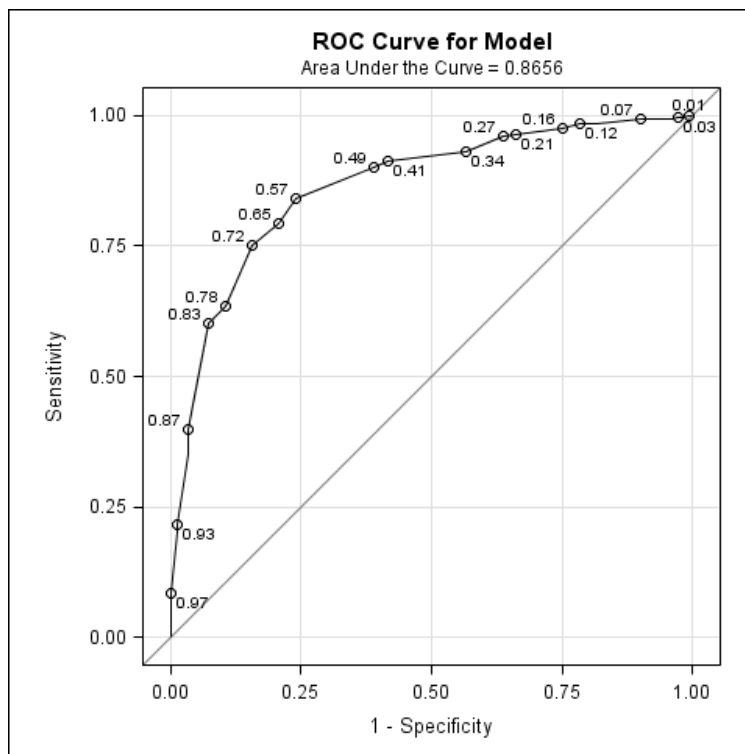
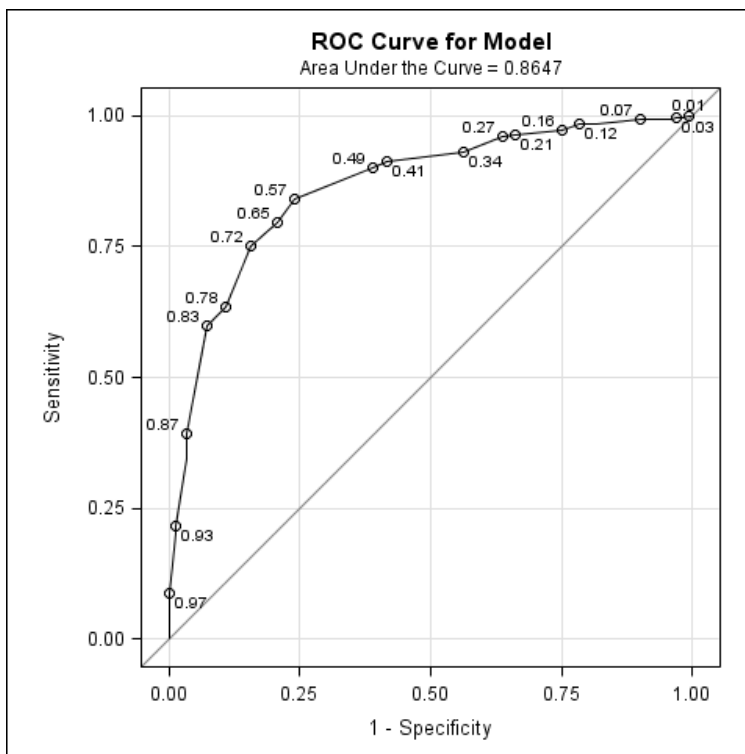


Figure 6.4 ROC curve for risk scores using the bootstrap sample



The plotted points on the ROC curves represent the predicted probabilities from the model for each threshold

Comparison of sensitivity and specificity of risk score cut-offs at 5, 6 and 7 shows that the cut-off score 5 has a higher sensitivity (0.967) and lower specificity (0.397) than the cut-off scores of 6 and 7. The cut-off score 6 has a higher sensitivity but marginally lower specificity than that of 7 (Table 6.4).

Table 6.4 Comparison of sensitivity and specificity of risk score cut-offs of 5, 6 and 7

Cut-off risk score	5	6	7
Sensitivity (95% CI)	0.967 (0.940-0.988)	0.928 (0.890-0.966)	0.894 (0.850-0.939)
Specificity (95% CI)	0.397 (0.339-0.455)	0.603 (0.545-0.661)	0.636 (0.579-0.693)

Table 6.5 shows the accuracy and predictive ability of the final regression model and the risk score cut-off at 6. The sensitivity and NPV of risk score cut-off at 6 in the study population showed good concordance with the bootstrap sample. Specificity and PPV were lower in the validation sample than in the study population. However, the sensitivity, specificity, PPV and NPV of the multivariable models were similar in the original and validation samples. The sensitivity (0.928) and NPV (0.927) were higher while specificity (0.603) and PPV (0.607) were lower when than in the logistic model (Table 6.6 below for frequency distribution by risk score cut-off).

Table 6.5 Comparison of predictive ability of multivariable model and risk scores with the cut-off as 6 in the study and bootstrap samples

Measures	Final multivariable model (95% CI)		Risk scores with cut-off at 6 (95% CI)	
	Study population	Bootstrap sample [‡]	Study population	Bootstrap sample [‡]
Sensitivity	0.746 (0.682-0.810)	0.744 (0.740-0.750)	0.928 (0.890-0.966)	0.966 (0.964-0.968)
Specificity	0.846 (0.802-0.890)	0.851(0.848-0.854)	0.603 (0.545-0.661)	0.393 (0.388-0.397)
PPV	0.767 (0.704-0.831)	0.773 (0.768-0.777)	0.607 (0.550-0.665)	0.514 (0.510-0.517)
NPV	0.830 (0.785-0.875)	0.830 (0.827-0.833)	0.927 (0.888-0.965)	0.946 (0.943-0.949)

[‡] Bootstrap sample of 200 iterations with replacement was drawn from original sample

Table 6.6 presents the frequency distribution of cases and controls as classified by the cut-off risk score. There were 13 false negative cases and 108 false positive controls.

Table 6.6 Frequency distribution of cases and controls by risk score cut-off at 6

Risk score cut-off	Cases	Controls	Total
≤ 6	13	164	177
> 6	167	108	275
Total	180	272	452

Variation in the predictive values according to the proportion of cases in the study population and prevalence is presented in **Table 6.7**. The PPV was lower and NPV was higher for lower prevalence of oral cancer at national level (6.3%) when compared to the proportion of cases (35.9%) among the total number of eligible study participants approached.

Table 6.7 Expected PPV and NPV according to proportion of cases in the study population and prevalence at national level

	Proportion of oral cancer cases	PPV	NPV
Study population	35.9%	0.567	0.937
National level prevalence[†]	6.3%	0.136	0.992

[†] GLOBOCAN 2008 database for India

6.7 Discussion

The aim was to develop and validate a screening model using risk scores to identify high-risk individuals for oral cancer. Predictors strongly associated with oral cancer were selected to derive the screening model. In this population, smoking, chewing tobacco/quid and alcohol were strongly associated proximate factors. These findings are similar to previous studies on risk factors of oral cancer (Ko et al., 1995). Higher OR for oral cancer was observed among those reporting presence of UADT cancer in their family. An association of positive family

history of cancer with OC has been seen in studies from other countries (Brown et al., 2001; Garavello et al., 2008). People who rated the spiciness of their diet as being high had higher odds (OR = 2.15) for developing oral cancer than those rating the spiciness as five or less. This is a subjective measure, but it is an easier method to collect information on the spiciness of food at a population level and in a hospital setting. In India and other South Asian countries, red chilli powder or red/green chillies are added to increase the spiciness of food. These findings support the results of other studies conducted in India that showed red chillies in diet increases the risk by two-three times for UADT cancers including oral cancer (Notani and Jayant, 1987). Similarly, a higher risk has been observed for gall bladder (Serra et al., 2002), liver and gastric cancers (López-Carnllo et al., 1994; Archer and Jones, 2002) in other countries. Although the association of spicy food with oral cancer could be due to the carcinogenicity of capsaicin found in chillies (Bode and Dong, 2011), it could be a marker for some underlying dietary aspect in this population. Low frequency of fruit intake was associated with higher OR. This is in agreement with recent studies showing the protective effect of fruits (Bravi et al., 2013). BMI was not associated with oral cancer in our study population which is contrary to other studies showing an association of oral cancer with underweight (Radoi et al., 2013b). This could be due to recall bias because the recalled body weight was 5 years previous to the time of interview. Rinsing the mouth with water after eating is a common mouth-cleansing practice in India. Not rinsing the mouth with water after chewing/eating was a strong predictor for oral cancer. We speculate that the practice of mouth rinsing with water indicates the participants' care for oral hygiene, and lack of the practice could be related to poor oral hygiene and that has been shown to be associated with oral cancer in other studies (Balaram et al., 2002; Rajamanickam et al., 2007). Probably, rinsing mouth with water cleanses off the oral mucosa of some of the adherent carcinogens among quid/tobacco chewers. However, this is the first study to report an association between the

lack of cleansing the mouth with water after chewing/eating and an enhanced predisposition to oral cancer. This relation requires to be explored further. Socioeconomic predictors were not statistically associated with oral cancer after adjusting for other factors.

A risk score model with strong predictive ability (AUC = 0.866) was developed using a set of predictors obtained through interviews. The AUC or the *c* statistics refer to the probability of the model to predict the outcome. A model is considered to have a reasonable predictive ability if the *c* statistic is greater than 0.7 and strong if it is greater than 0.8 (Hosmer and Lemeshow, 1989; Hosmer and Lemeshow, 2000). Internal validation in a bootstrapped sample of the same dataset showed similar findings (AUC = 0.865). Identification of high-risk individuals is essential in settings with limited/restricted resources. The risk score model developed is simple to administer using minimally available resources and logistics. For a serious disease like oral cancer, a risk assessment method for mass screening should be simple and accurate, although there is a trade-off between simplicity and accuracy. This model did not include continuous variables or transformations. Moreover, the model did not consist of any oral examination component. Hence, information can be collected using screening questions on predictors to directly calculate risk scores. Such a model to identify high-risk individuals using screening questions would be desirable in rural and remote settings with limited resources, where there are no health care workers trained to do a visual examination. The optimal cut-off with high sensitivity (0.928) and moderate specificity (0.603) was chosen. The present model had similar sensitivity but a lower specificity compared to OPMD model developed in Sri Lanka (Amarasinghe et al., 2010). A screening model for fatal diseases like oral cancer should have higher sensitivity than specificity in order to reduce false negatives at the initial screening (Lalkhen and McCluskey, 2008). The identified high-risk individuals could be further evaluated with more specific diagnostic tests in the hospitals.

The feasibility and success of a screening program are determined by PPV and NPV, which depend on the disease prevalence in the population (Lalkhen and McCluskey, 2008). In the study sample nearly 93% of the adults with a risk score lower than the cut-off at 6 did not have oral cancer. The NPV of the oral cancer risk score was greater than PPV (nearly 61%). In a population with high prevalence of oral cancer, a higher NPV is preferable to reassure an individual with a low score (negative test) that he/she is very unlikely to have the disease. However, it will be uninformative in populations with low prevalence (Loong, 2003). This model could be useful in plausibly related population (Justice et al., 1999) with similar practices (of smoking, betel quid/tobacco chewing and alcohol consumption) such as in Asia or Asian migrants in western countries that are at a higher risk for developing oral and oropharyngeal cancer.

Some of the drawbacks of the screening model come with the errors. False positive (FP) results might create apprehension in individuals and their families until they are clinically diagnosed with negative results. Conversely, the false negative (FN) cases miss out referrals. With the cut-off at 6, the FP rate was high (38.6%) but the FN was low (7.8%). The FNs were mainly because of the absence of known risk factors (9 out of 13 FN had no habits). On the contrary, risk factors were present in a high percentage of FP cases and they also included five people with OPMD. Although the model was developed including oral cancer cases in all stages, it could identify individuals with pre-cancer. This calls for intervention/monitoring of subgroups with a potential to develop oral cancer. Other than cases with no known risk factors, a proportion related to human papillomavirus infection could go undetected. In this study, other potential biases such as recall bias and information bias due to differential recall between cases and controls, though cannot be eliminated, it is considered to be reduced with the use of life-grid, restricting the information collection before the onset of symptoms of OPMD/cancer and by interviewing cases and controls in similar settings. There could be

potential selection bias because there were more men as cases and more females as controls. The model was developed using case-control data in which the cases-control ratio is higher than the prevalence of the disease that affects the prediction accuracy. This has been addressed to some extent by adjusting the predictive values for the prevalence estimates. Furthermore, methods are being developed to address the issues related to low prevalence of the disease.

Despite its limitations, primary health care workers in rural/remote areas can use this model as an initial screening method, due to ease in application and its simplicity. This does not imply to dismiss the visual screening, but could be used where there are no such programmes. The screened high-risk individuals could be further referred for clinical evaluation by trained health professionals, thereby encouraging them to make contact with the health care system. However, there could be compliance issues. Development of this risk score model is an initial effort towards identifying target groups in controlling the burden of oral cancer. The model can also create a sense of awareness of risk factors and oral cancer among the screened. It has the potential for integration into ongoing cancer control programmes and possibly help clinicians to identify high-risk individuals to do a thorough oral examination using other diagnostic aids.

6.8 Conclusion

A screening model using risk scores with the satisfactory predictive ability was developed and validated in a population of the country with a high incidence of oral cancer. Further studies are necessary to validate this model in other populations before its implementation can be recommended to identify subgroups of the population to be directed towards more extensive screening approaches.

Chapter 7: Discussion

7 Discussion

This chapter presents the strengths and limitations related to the methodology, and a discussion of the results presented in the three papers (Chapters 4, 5 and 6), and conclusions.

7.1 Summary

The present epidemiological study was undertaken in India, where the incidence rate of oral cancer is high. A hospital-based case-control study was conducted with the focus on:

1. Examining the life course SEC in relation to oral cancer, with special emphasis on the early-life social origin of oral cancer.
2. Development of a practically applicable screening model to triage asymptomatic adults with oral cancer.

These two aspects have been addressed in Chapters 4, 5 and 6.

Life course SEC at childhood, early and later adulthood was associated with oral cancer. People in low SEC had higher odds for oral cancer. Socially mobile groups had ORs intermediate to that of stable-high, and stable-low groups. An inverse association between accruing disadvantages from living in low SEC throughout the life course and oral cancer was a more valid explanation found from life course models. Moreover, the observed disparities of oral cancer in adulthood were a direct effect of early-life low SEC that was not mediated by individual risk factors.

A screening model was developed using inputs from life-course risk factors such as tobacco, quid chewing, alcohol use, diet, family history of UADT cancer and oral hygiene practices to

identify adults with oral cancer. The model was found to have good predictive ability in the study population.

7.2 Why life course epidemiology of oral cancer?

A large body of scientific evidence is available on a number of behavioural and biological factors associated with oral cancer. Furthermore, individuals' biological and behavioural factors are patterned by social factors, and their interaction with the surrounding environment (Krieger, 2005). Understanding the social factors is needed in adopting a holistic approach towards the prevention and control of oral cancer, a frequently fatal disease. Implementation of public health reforms to bring about social changes is complicated and requires concerted efforts from different disciplines.

Knowledge about the social causes is essential in epidemiology, because ignoring the SEC will bias the epidemiological evidence in understanding disease causation (Krieger, 2007). People's health is influenced by their material resources, social factors and the environment in which they live and interact. Looking at people as social and biological beings, it is essential that the disease or health be observed and understood within the context in which they were born, grew and lived. Exposure to detrimental social processes in childhood could alter the biological development process and could be damaging to health in the long-term (Kuh and Ben-Shlomo, 2004).

In addition to studying social epidemiology, epidemiologists can help by offering an interventional solution towards the prevention and control of the disease. As Rothman and colleagues point out, when not much can be done by epidemiologists to bring about social equality, the goal should be to find a practical solution (Rothman et al., 1998).

Therefore a life-course study was conducted, with a social perspective, and to seek a practical solution towards reducing the burden from oral cancer.

7.3 What are the study findings?

This section discusses the study findings of Chapters 4, 5 and 6.

7.3.1 Which life course models can explain the association of oral cancer with socioeconomic conditions at various stages in life?

Chapter 4 is aimed at exploring the life-course models with regard to the association between SEC and oral cancer. The underlying hypothesis was that accumulation of socioeconomic disadvantage over the life course is associated with oral cancer in the Indian population. The findings from Chapter 4 show that there are inequalities in the occurrence of oral cancer in adulthood. Life course models offer alternative explanations for the association of life course SEC with oral cancer.

As seen from various models below, the findings supported the hypothesis.

7.3.1.1 The critical period model

Socioeconomic conditions at the three stages (childhood, early adulthood and later adulthood) were associated oral cancer occurring in later adulthood. Among the three stages, early adulthood SEC was more strongly related to oral cancer. The findings suggest an inverse relation between SEC and oral cancer that is similar to that for general health outcomes (Vagero and Leon, 1994; Smith and Hart, 2002; Hallqvist et al., 2004). In the present study, paternal and maternal education was inversely associated with oral cancer in the offspring (Table 6.1). A review of 49 studies found that early-life SEC measured by parental education or occupation were inversely associated with cardiovascular disease (Pollitt et al., 2005). However, when their own education, current SEC and risk factors were included, the association was null. The methodological issues of multivariable models are related to mediators (risk factors and adult SEC) and are discussed in greater detail elsewhere (section

7.4). The methodological problem was overcome by undertaking a causal analytical approach using marginal structural modelling.

7.3.1.2 The social mobility model

According to the social mobility model, health is affected by SEC at all stages. The socially mobile subgroups carry with them the advantage or disadvantage of the SEC that they move away from, and the one they attain (Hallqvist et al., 2004). Hence, the mobile subgroups have an intermediate level of health between those of the always disadvantaged and advantaged groups. The findings of the present study support the findings of previous studies, where the socially mobile subgroups had a greater risk in general health and longevity (Hart et al., 1998; Hallqvist et al., 2004) and oral health (Poulton et al., 2002; Peres et al., 2011a) than the subgroup stable at high SEC. In the present study, the greatest difference was observed between the stable groups. Those who remained stable in the low SEC had the highest odds for oral cancer than those stable at a high SEC.

7.3.1.3 The accumulation model

The accumulation of life course SEC experiences was examined for its association with oral cancer. A gradient was observed in the OR with an increase in the number of occasions of low SEC in a lifetime. These findings indicate that the disadvantages of low SEC are cumulative and stable-low group has the highest odds for oral cancer. Other cohort studies on oral health (Thomson et al., 2004; Peres et al., 2011a), general health and cancer mortality (Hart et al., 1998) show similar findings.

7.3.2 Does low SEC during childhood have a long-term effect on oral cancer in adulthood?

This life course study's emphasis was on the long-term effect of SEC in early-life on oral cancer. In the previous section (7.3.1) on life course models, childhood SEC was associated

with oral cancer when age and sex was adjusted. However, people in the later years of their life may develop some habits that are detrimental to health. Some of the behaviour may be risk factors for oral cancer, such as tobacco, quid and alcohol, which mediate the effect of SEC on oral cancer. Similarly, SEC in childhood and adulthood when correlated may affect the risk factors. In such a situation when there is mediation by other factors, to infer causality, a MSM is useful in decomposing the direct and indirect effects of exposure on the outcome (Robins et al., 2000).

In the present study, by using MSM, evidence was found to support the hypothesis that the effect of low SEC in childhood had a long-lasting effect on oral cancer. It has been shown that various health outcomes in adulthood are associated with childhood SEC (Cohen et al., 2010). The findings of this study suggest that there is early origin of risk for oral cancer during the childhood, a critical period of growth and development. The long term effect of socioeconomic disadvantage can be explained to some extent by behavioural and biological factors.

7.3.2.1 Mediation through behavioural factors

Many years of research have shown that socioeconomic factors have pathways through behavioural factors such as tobacco, alcohol use and diet, and that they play a crucial role in determining health (Berkman and Kawachi, 2000; Adler and Newman, 2002; Cutler et al., 2008). Smoking, quid with/without tobacco, alcohol, diet and oral hygiene behaviour all have been shown to be strongly associated with oral cancer in Chapter 6. Tobacco, quid and alcohol have been classified as carcinogens by the IARC.

Behavioural and lifestyle factors also have social origins. Children of parents from low SEC are more likely to attain lower levels of education and work in manual or blue-collar jobs, and

they are also more likely to take up tobacco and alcohol habits early in life (Lynch et al., 1997). People with low occupational status are more likely to develop health-risk behaviours.

A diet deficient in nutrients and antioxidants, low intake of fruits and vegetables, and poor oral health are known risk factors of oral cancer (Levi et al., 1998; De Stefani et al., 1999; Amtha et al., 2009; Helen-Ng et al., 2012). Due to a low dietary intake of fruits and vegetables, and the lack of a well-balanced diet, the children of poor parents are more likely to experience malnutrition (Kanjilal et al., 2010); this can have an impact on their physiologic constitution and increase sensitivity to endogenous and exogenous carcinogens (Lutz, 1999). These risk factors could cause genetic alterations that lead to the development of oral cancer.

7.3.2.2 Genetic and epigenetic explanation for long-term effect of childhood low SEC on oral cancer

Developmental origin of health supports prenatal exposure and is of relevance to cardiovascular diseases (CVD) and cancers (Barker and Bagby, 2005). Identification of genotypes, behavioural and environmental factors responsible for CVD and cancers has helped in understanding that many genetic and epigenetic changes take place because of environmental changes (Knox, 2010). Epigenetic and physiological explanations have been suggested as evidence for social disparities in chronic disease (Schooling and Leung, 2010).

The social environment interacts with genes that influence the biological responses of an individual (Manuck et al., 2005). Experiencing adverse SEC in childhood has been found to deplete some seven biological systems such as nervous, endocrine, immune, lipid and glucose metabolism, which is also known as allostatic load, in adulthood (Gruenewald et al., 2012).

The allostatic load is greatest for cumulative experience of low SEC over the life course (Gruenewald et al., 2012). More support for this theory may be drawn from research that indicated a link between abnormal glucose metabolism and oral cancer (Ujpal et al., 2004;

Suba and Ujpal, 2007). It is also known that diabetes is increasing in India. Moreover, in an Indian population, association between OPMD, precursors of oral cancer, and diabetes mellitus have been found especially among women (Dikshit et al., 2006). However, the exact pathways through epigenetic changes are yet to be elucidated.

Another plausible pathway is embedding of early-life socioeconomic experiences in physiologic responses where epigenetic alterations play a role. Research has shown substantial correlation between early-life poverty and genetic-epigenetic changes such as DNA methylation (Lam et al., 2012). DNA methylation is an important step in the onset and progression of oral cancer (Shaw, 2006; Radhakrishnan et al., 2011).

7.3.3 How well can the risk score model predict oral cancer?

Risk prediction is of special interest in epidemiology. Having known the risk factors, the next step would be to predict the risk for oral cancer, for its practical application in clinics or public health. Statistical methods could be used to combine multiple risk factors for predicting the risk. The known risk factors such as social (parental education, own education, occupation), health behaviour (smoking, chewing quid with or without tobacco, alcohol), dietary (spiciness of diet consumed, frequency of fruit consumption) and biological factors (BMI) were included in the initial model. Some of the predictors were carefully removed before arriving at a final model that included only those variables that predicted oral cancer quite well. The risk scores were derived from ORs for each variable. The total risk score for a person depended on the risk factors he/she had. Risk scores are similar to a continuous measure of a risk factor used as a screening test (e.g., blood cholesterol) to screen for ischemic heart disease. Since individuals' total risk score ranged between 0 and 28, the cut-point was chosen as 6 to make a clinical decision for the presence of oral cancer based on its good predictive ability.

The performance of such statistical predictive models is examined using several traditional and novel measures (Steyerberg et al., 2010). The performance of the final model measured with 'goodness of fit', and ROC curve or *c* statistic (Steyerberg et al., 2010) was found to be adequate. The performance of a classifier (risk score cut-point) was measured using specificity and sensitivity (Pepe et al., 2006), and a cut-point was chosen that had high sensitivity (0.93) and reasonable specificity (0.60). The predictive values (PPV and NPV) that depend on the prevalence of oral cancer are the other dimensions to measure a classifier (Pepe et al., 2006). Since the inputs on various risk predictors were obtained from a case-control study that limited the estimation of prevalence of oral cancer, PPV and NPV could not be directly estimated (Brenner and Gefeller, 1997). However, in the initial stages, case-control designs are frequently used to develop a prediction model, or for risk stratification (Pepe et al., 2004). Prospective studies are used in later stages for the evaluation of the prediction tool (Pepe et al., 2001).

The PPV and NPV were estimated indirectly using the formulae by inputting the values of prevalence of oral cancer, available from GLOBOCAN (Ferlay et al., 2010b), and sensitivity and specificity (Brenner and Gefeller, 1997) of the risk score cut point. The estimation of PPV and NPV was carried out using GLOBOCAN data since actual data on the prevalence of oral cancer in India, from observational studies, is lacking. The GLOBOCAN data on the prevalence of oral cancer in India is estimated from incidence of diagnosed cases of oral cancer at Registries and mortality of the diagnosed cases, but not the observed prevalence. Furthermore, oral cancer has a high mortality rate and, therefore, even when the incidence is high the prevalence may be lower. The actual prevalence may be different since there would be undiagnosed cases and some people with oral cancer who are not seeking care. This estimation of PPV and NPV was only an attempt to show how the predictive values would change with the prevalence of disease and should not be confused as actual PPV and NPV.

Applicability of a risk prediction tool is good if it is easy to administer and non-invasive. The developed screening model is simple and can be easily administered by people with minimal training. It does not require extensive training like that of visual screening. The present model could be used by untrained personnel in rural and remote areas to screen asymptomatic individuals at high-risk for developing oral cancer.

The screening model was tested for internal validity using a bootstrap sample of 200 iterations. Split-sample, cross-validation, jack-knife and bootstrapping methods have been considered for internal validation of predictive models. Among them bootstrapping is an efficient method because of the random re-sampling procedure with replacement from the original dataset to generate a sample (Steyerberg et al., 2001).

The present risk model may be applicable for the study population, some of the countries in South and Southeast Asia, and migrant communities in Asia with similar risk factors. Further studies in different settings are required before generalising the screening model to other populations (Justice et al., 1999).

7.4 How methodological issues have been addressed?

To answer the research questions, appropriate methodological approaches have to be followed. The methodological issues related to three study objectives have been described below.

7.4.1 Using a case-control design for life course research on oral cancer

Life course epidemiology originated from cohort studies conducted in European countries and was later followed in other developed countries, and recently in developing countries.

Conducting cohort studies is laborious, time-consuming and expensive. For a rare disease such as oral cancer, that has a long induction period, a cohort study is not a feasible option.

Moreover, in India, where the population-level data suitable for life course study is

insufficient and it is difficult to establish a cohort, the most feasible option is a case-control study to answer the research questions that require a life course approach.

A hospital-based case-control study was conducted in the major cancer hospitals because many cases could be recruited in a short duration stipulated for data collection. Further, to avoid prevalence-incidence bias, only incident cases were included in the study. A case-control study could be regarded as being easily and efficiently mounted in a cohort (Rothman et al., 2011a; Vandenbroucke and Pearce, 2012). The efficiency comes from the selection of controls from the same source population that gave rise to cases. According to modern understanding, if the controls are selected following basic principles, then valuable findings can be obtained from case-control studies. The controls should be representative of the source population rather than the general population (Wacholder et al., 1992a). Since the cases in the selected cancer hospitals came from various states of India, it was difficult to geographically define the primary source population. Therefore, the hospital and visitor controls were chosen from the same hospitals and their health/referral centres, to reflect the prevalence of risk factors and covariates in the underlying source population.

Selection of neighbourhood controls or random selection of controls from the general population was not possible because of the difficulty in enumerating people on the roster and lack of resources. Furthermore, such controls would not be representative of the source population (Wacholder et al., 1992a; Wacholder et al., 1992b; Rothman et al., 2011a).

For relatives, friends and neighbours of the patients, visiting during hospitalisation is a social obligation in India. A pool of patient visitors in the hospitals provided an excellent opportunity for the selection of controls not related to exposure (Armenian et al., 1988). Hospital visitors have been selected in other studies and shown to be a valid and feasible alternative for control series (Armenian et al., 1988; Ngelangel, 1989; Mendonca and Eluf-

Neto, 2001). The control series in the present study were selected from visitors, those seeking health care for reasons other than cancer, and conditions not related to tobacco and alcohol, to avoid selection bias (Hernan et al., 2004; Rothman et al., 2011a). Anticipating that selection of controls could be related to exposure to risk factors, relatives or friends of UADT, lung and liver cancers were not included. In addition, hospital controls (exclusive of cancer patients) seeking care for reasons not related to tobacco or alcohol, were included.

The incidence-density sampling of controls provides an opportunity to include the controls as cases, if they were to be diagnosed with oral cancer. This method of control selection is similar to selecting the participants at the beginning of follow-up who could contribute to both numerator and denominator (Rothman et al., 2011a). Thus, the incidence case-control study does not require a rare disease assumption (Rothman et al., 2011a; Vandenbroucke and Pearce, 2012).

The cases and controls were not matched for confounders (such as age and sex) because restrictive selection of controls could reduce the study size and sometimes matching itself may induce selection bias (Rothman et al., 2011b). If a confounder is quantifiable, then it can be adjusted in the analysis (Wacholder et al., 1992c). Despite careful selection of controls, there could be some bias related to gender, age and visiting pattern. However, age, sex, and hospital centres were adjusted for in the analysis. Since the controls selected were not matched, conditional logistic regression has not been used.

7.4.2 Causal and predictive modelling in life course research

Conventional multivariable regression models are commonly being used in epidemiology. There is a need to clearly understand the purpose when using conventional regression models (Zalpuri et al., 2013). In epidemiology, statistical modelling for an outcome is done for two

purposes –causal modelling to investigate causality of an exposure, and predictive modelling to empirically predict the outcome (Shmueli, 2010).

In social epidemiology, as in the life course approach, causal modelling was applied mainly because of the need to test the theory of causation of oral cancer by childhood SEC, where time-dependent confounders, such as later life SEC are an issue. The causal modelling is driven by theory, while the data are used to test the proposed theoretical model, thus explaining the causal hypothesis. In Chapter 5, the causal model was based on the DAG developed from prior knowledge (the Literature Review), and regression modelling was followed to suit the theory. The causal inference requires special techniques such as marginal structural modelling (Robins, 1999), structural nested modelling (Robins et al., 1992) or g-computation (Robins, 1986) as applied to observational or experimental data, assisted by causal diagrams and a counterfactual framework (Pearl, 1995; Hernan et al., 2000; Robins et al., 2000). Furthermore, when causal analysis includes mediation, confounders and mediators have to be distinguished to avoid collider bias (Hernan et al., 2004). It has been shown in Chapter 5, that when all variables were included in the multivariable model, irrespective of their status (exposure, mediators and confounders), there was no effect of childhood SEC on oral cancer. However, when MSM was used, there was a direct effect of early-life low SEC on oral cancer in adulthood. MSM manages for adjusting of confounders effectively by using stabilised inverse probability weights. The sensitivity analysis further recognised the causal association by showing that the direct effect of childhood SEC cannot be attributed completely to any unmeasured confounders.

The goal of predictive modelling is to predict the outcome based on independent variables. As described in Chapter 6, the aim was to predict oral cancer given the inputs on various risk predictors. Although many of the risk predictors (tobacco, alcohol, quid, diet, oral hygiene practice, family history) chosen were risk factors in the screening model, good predictors

need not necessarily be causal factors (Moons et al., 2009). In predictive modelling, variable selection procedures (for variable inclusion or exclusion) are more important (Greenland, 1989). A variable could be included as a covariate if it improved the predictive ability (Fletcher et al., 2012). In this thesis, predictive or causal modelling was used appropriately depending on the aim.

7.4.3 Measures of association and effect measures used

In epidemiological studies, prevalence ratios, odds ratios, risk ratios and rate ratios are used as measures of association, depending on the aim and the study design. In the present study, ORs were used when strength of association was important, as estimated from conventional regression/prediction models. The RR was used as the effect measure when the causality had to be inferred. The interest was in estimation of the RR as a summary measure for the causal association because of its usefulness and convenience in communicating the results in terms of ‘risk’ compared to ‘odds’ (Greenland, 2004; Lumley et al., 2006). The estimates (RR and OR) obtained from incidence-density case-control study will be approximately similar (Pearce, 1993; Vansteelandt, 2009; Rothman et al., 2011b). Moreover, RR estimation was possible since the control selection was not conditional on the absence of oral cancer (Rothman et al., 2011b). The precision of the RR estimates would, however, be inferior to those from cohort studies and could be improved if the disease is rare (Pearce, 1993; Rothman et al., 2011a; Vandembroucke and Pearce, 2012).

7.5 What are the strengths and limitations of the study?

It is essential to examine the strengths and limitations of the study for right interpretation of the results. In this part of the thesis, the strengths and limitations of the methodological approaches followed in chapters 4, 5 and 6 will be discussed.

7.5.1 Strengths

1. The present study was conducted at multiple major cancer hospitals that provide care to patients of different socioeconomic strata.
2. The study was primarily designed to address the aims of the study. The statistical procedures conformed to the study aims and design.
3. The life course approach adopted in the present case-control study did facilitate examining for the causal effect of SEC on oral cancer. The timing of exposures (SEC) and behavioural factors (tobacco, alcohol, quid and dietary factors) among cases, and controls over the life course helped in determining the temporality of exposure, mediators, and outcome to establish a causal relation.
4. The high response rate achieved in the study minimised the missing data. Direct interviews and use of a life-grid helped to build a positive rapport with the participants that minimised missing data.
5. Control selection was carefully done so as to reduce bias. Incidence-density sampling allowed for inclusion of a person selected as a control to become a case if he/she developed the disease. This is similar to the cohort design where a person contributes to both numerator and denominator. Density sampling of controls facilitated the estimation of relative risk.
6. Appropriate statistical methods (causal and prediction analyses) were employed to address the research aims. MSM was employed for causal analysis in which the confounders were efficiently handled using SW. Furthermore, sensitivity analysis showed that a causal relation between early-life SEC and oral cancer cannot be invalidated by unmeasured confounders. The multivariable prediction model assisted in developing a screening model for oral cancer using risk scores.

7.5.2 Limitations

1. As the interviews were conducted following the diagnosis, there could be some recall bias due to differences between cases and controls, especially in remembering the details related to behaviour. Although the differences were considered to be less with the use of a life-grid and interviewing cases and controls in similar settings, they cannot be completely avoided.
2. Potential interviewer bias may be anticipated because a single dentist interviewed and examined the participants. Even if a separate examiner and interviewer were employed, blinding the interviewer to case/control status was not possible. The case status would be evident as the lesions would be visible due to gross changes in facial structures in most cases.
3. Adults of different age groups were included in the study. There could be some cohort effect on oral cancer incidence. However, age was controlled in the analysis. It is also known that separation of age-period-cohort effect is difficult.
4. Controls comprised more women than did the case group. The greater number of female controls was due to the inclusion criteria for control selection in this study; many hospital visitors and carers of patients were women. However, gender was adjusted in the analysis where it was considered a confounder. In future research, investigators planning to select patient visitors and carers as controls have to be aware of this issue, that is, the possibility of there being more female controls.
5. The estimated sample size could not be achieved within the stipulated time for data collection. Post-hoc power calculation showed that the power ranged between 74% and 95% for considering unadjusted odds ratios for SEC at different stages over the life course. The power was still higher for risk factors such as chewing quid that had an OR of 7.77.

6. The estimates could be assumed to be biased because of the complete case analysis. The discrepancy in estimates would be minimal because the missing data ranged from 3 to 5%. If missing data is less than 5% one could choose to exclude missing data for analysis (Fichman and Cummings, 2003).
7. There could be some misclassification bias relating to the outcome. Among the controls, five were clinically diagnosed with OPMD and one with suspected oral cancer lesion. However, all of the six people did not complete the histopathological examination (due to the time of their recruitment being during the last few months of the study, or because of non-compliance). Five of the selected controls (even when found to have OPMD on oral examination) were included as controls according to the protocol because there were no suspicious lesions found during the oral examination. Any control participant experiencing the causal intermediate should not be excluded from the analysis. Such exclusion may underestimate the exposure in the control group (Poole, 1999). Inclusion or exclusion of the suspected case, as a case, during the analysis did not alter the estimates. However, all of the cases were histopathologically confirmed with oral cancer.
8. As with the most observational studies, in particular case-control designs, there is a potential for recall bias since the information on exposures was obtained by having participants recollect details of exposure over their life course. In epidemiological research conducted with limited resources, recall is a feasible method of collecting data on exposures such as occupation, education and behaviour. Recall is also a predominant method of data collection in many studies including cohort studies when the data is required for the period in-between follow-ups. A life-grid was used to improve the accuracy of recall. Berney and Blane (1997) have shown the accuracy of

recollecting an occupation after 50 years is nearly 80% for occupation and housing conditions with the use of a life-grid.

7.6 What are the study implications?

The study findings are of public health and future research relevance. The study implications of social epidemiological findings and the screening model for public health consideration will be discussed. Some more questions that arise from the present study findings that could be considered for future research will also be discussed.

7.6.1 Implications for public health consideration

The present research provided the evidence for the origin of socioeconomic inequalities in oral cancer occurrence in childhood. Experiencing adverse SEC in early and later stages of a life course is associated with oral cancer in adulthood. Socioeconomic inequality that commences in the early years of life accumulates over the life course, increasing the odds for oral cancer in adulthood.

The MSMs facilitated estimating the direct effect of childhood SEC on oral cancer. Childhood is a sensitive period and adverse SEC has a long-lasting effect on oral health in adulthood.

With advancing economy and urbanisation in India, there is room for widening socioeconomic inequality that could have further detrimental effects on the health of people facing adversity. Improvement of SEC, providing quality education, and safe and healthy living conditions during the childhood is essential not only for oral health, but also for overall health in adulthood.

The present study findings show that being in low SEC throughout the life course was more common among cases, thus suggesting the low SEC at one stage links to low SEC in the next

stage of life. This chain has to be broken as early as possible in childhood and emphasis placed on tackling socioeconomic determinants in childhood.

In the present study, the association of oral cancer with smoking, the use of quid (with or without tobacco), diet and oral hygiene practices was strong. These risk factors act conjointly with SEC reiterating that addressing behavioural problems and socioeconomic development should go hand-in-hand.

The screening model has been shown to predict oral cancer with greater sensitivity and consistency as seen with its validation findings. The model could even pick some controls with OPMD and suspicious lesions. On the contrary, the specificity was lower and could not screen out cases without known risk factors. This screening model has the potential for being implemented in public health programs using Primary Health Care Workers, without additional training, to screen and refer asymptomatic and high-risk individuals for further evaluation. The potential of the model to screen for early-stage malignant and pre-malignant lesions is advantageous in assisting early diagnosis and improving the treatment outcome.

7.6.2 Implications for future research considerations

The study findings contribute to the causal knowledge of the socioeconomic inequalities of oral cancer. It also supported the previous findings of the association between behavioural, dietary and oral hygiene factors associated with oral cancer. However, the study limitations and some of the findings pave the way for further research to answer the questions arising from this research.

This study found that childhood SEC and oral cancer are directly related when the mediators such as smoking, quid (with or without tobacco) and alcohol were controlled. The mediators were controlled individually in each of the models. Future research should consider mediators

such as diet, human papillomavirus, and concurrence of other mediators to estimate the natural direct effect.

The study found an interaction between alcohol and childhood SEC. Further research has to be undertaken to investigate the interaction between SEC, tobacco, quid and alcohol and associated genetic or epigenetic changes predisposing to oral cancer. Understanding social-genetic interaction and underlying biological pathways can have an impact on oral cancer prevention, control and treatment outcome.

Although three life course models were explored in relation to oral cancer, only the critical period model, which relates to the time of exposure, was examined for greater understanding. Further, the accumulation model has to be researched for cumulative risk considering the timing and duration of exposure to various risk factors and adverse SEC.

A screening model was developed that has a practical application. The predictive accuracy was valid for the study sample. External validation studies are required to test the model in other populations under different settings before implementation.

Recall could be different for cases and controls. The bias in estimates obtained due to recall differences have to be determined.

7.7 Conclusions

This study examined socioeconomic inequalities in oral cancer by adopting a life course approach, and developed and validated a screening model for oral cancer in the Indian population. The conclusions drawn are:

1. Socioeconomic conditions in childhood, early adulthood and later adulthood were inversely associated with oral cancer in later adulthood.

2. The socioeconomic disparities in relation to oral cancer showed a gradient, with an increase in the number of occasions of experiencing of adverse SEC, beginning from childhood to later adulthood. People who were always socioeconomically disadvantaged had the highest odds for oral cancer compared with the stably high or socially mobile groups. The socially mobile groups had an intermediate level of OR compared to stable groups.
3. The conventional regression model found a null association between childhood SEC and oral cancer. This was due to the collider bias introduced by including many mediators.
4. Low SEC in childhood increased the relative risk for oral cancer in adulthood that was not mediated individually by smoking, chewing quid and alcohol when MSM was used. Since the temporal relationship of childhood SEC, risk factors and oral cancer was known from life course data, the causality could be established after efficient adjustment of confounding by using stabilised inverse probability weight.
5. Social and behavioural factors interact to affect oral cancer as seen from relative excess risk due to interaction between childhood SEC and alcohol consumption in later life on the RR scale. Any effect of public health intervention to address socioeconomic determinants would not be similar among alcohol users and non-alcohol users.
6. Smoking, chewing quid with or without tobacco, and alcohol were strongly associated with oral cancer. Chewing quid with tobacco was the most strongly associated factor among all the risk predictors of oral cancer.
7. A low frequency of fruit consumption (i.e. less than once a week) increased the odds for oral cancer. Oral cancer was more common among those who reported consuming more spicy food than those who reported eating less spicy food.

8. Body mass index five years prior to the interview was not associated with oral cancer.
9. A simple oral hygiene practice (i.e. rinsing the mouth with water after eating or chewing) was negatively associated with oral cancer.
10. The risk prediction model had reasonable accuracy in predicting oral cancer. At cut-point 6 for risk scores, the model had high sensitivity and lower specificity.
Information on several predictors can be collected by asking simple questions.

8 References

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9 Appendices

1. Ethics approval



RESEARCH BRANCH
RESEARCH ETHICS AND COMPLIANCE UNIT

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07 April 2011

Associate Professor K Roberts-Thomson
School of Dentistry

Dear Associate Professor Roberts-Thomson

PROJECT NO: H-064-2011
Oral cancer - a life course approach

I write to advise you that the Human Research Ethics Committee has approved the above project. Please refer to the enclosed endorsement sheet for further details and conditions that may be applicable to this approval.

Approval is current for one year. The expiry date for this project is: 30 April 2012

Where possible, participants taking part in the study should be given a copy of the Information Sheet and the signed Consent Form to retain.

Please note that any changes to the project which might affect its continued ethical acceptability will invalidate the project's approval. In such cases an amended protocol must be submitted to the Committee for further approval. It is a condition of approval that you immediately report anything which might warrant review of ethical approval including (a) serious or unexpected adverse effects on participants (b) proposed changes in the protocol; and (c) unforeseen events that might affect continued ethical acceptability of the project. It is also a condition of approval that you inform the Committee, giving reasons, if the project is discontinued before the expected date of completion.

A reporting form is available from the Committee's website. This may be used to renew ethical approval or report on project status including completion.

Yours sincerely

 **PROFESSOR GARRETT CULLITY**
Convenor
Human Research Ethics Committee



RESEARCH BRANCH
RESEARCH ETHICS AND COMPLIANCE UNIT

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23 May 2012

Associate Professor K Roberts-Thomson
School of Dentistry

Dear Associate Professor Roberts-Thomson

PROJECT NO: H-064-2011
Oral Cancer – a life course approach

Thank you for the annual renewal report which included a request to amend the above project. I write to advise you that on behalf of the Human Research Ethics Committee I have approved renewal of ethical approval for the project and the amendment request to: (i) no longer conduct the HPV analysis; (ii) conduct telephone interviews for cases and controls; and (iii) expand the selection criteria for controls as detailed in your report. Thank you for forwarding copies of the modified participant consent form and questionnaire.

The ethical endorsement for the project applies for the period until: 30 April 2013

Please note that any changes to the project which might affect its continued ethical acceptability will invalidate the project's approval. In such cases an amended protocol must be submitted to the Committee for further approval. It is a condition of approval that you immediately report anything which might warrant review of ethical approval including (a) serious or unexpected adverse effects on participants (b) proposed changes in the protocol; and (c) unforeseen events that might affect continued ethical acceptability of the project. It is also a condition of approval that you inform the Committee, giving reasons, if the project is discontinued before the expected date of completion.

A reporting form is available from the Committee's website. This may be used to renew ethical approval or report on project status including completion.

Yours sincerely

PROFESSOR GARRETT CULLITY
Convenor
Human Research Ethics Committee



RESEARCH BRANCH
OFFICE OF RESEARCH ETHICS, COMPLIANCE AND
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09 April 2013

Professor K Roberts-Thomson
School of Dentistry

Dear Professor Roberts-Thomson

PROJECT NO: H-064-2011
Oral cancer - a life course approach

Thank you for your report on the above project. I write to advise you that I have endorsed renewal of ethical approval for the study on behalf of the Human Research Ethics Committee.

The expiry date for this project is: 30 April 2016

Where possible, participants taking part in the study should be given a copy of the Information Sheet and the signed Consent Form to retain.

Please note that any changes to the project which might affect its continued ethical acceptability will invalidate the project's approval. In such cases an amended protocol must be submitted to the Committee for further approval. It is a condition of approval that you immediately report anything which might warrant review of ethical approval including (a) serious or unexpected adverse effects on participants (b) proposed changes in the protocol; and (c) unforeseen events that might affect continued ethical acceptability of the project. It is also a condition of approval that you inform the Committee, giving reasons, if the project is discontinued before the expected date of completion.

A reporting form is available from the Committee's website. This may be used to renew ethical approval or report on project status including completion.

Yours sincerely

 **Dr John Semmler**
Convenor
Human Research Ethics Committee



Kasturba Hospital, Manipal

(ISO 9001:2000 certified)
(An associate hospital of the Manipal University, Manipal)

Communication of the Decision of the Institutional Ethics Committee

Saturday 13th August 2011

IEC228 / 2011

Protocol title	: Oral Cancer – A life course approach
Principal Investigator	: Dr. Muralidhar M.K
Guide/ Co Guide/ Co Investigators	: Dr. Veena G Kamath, Dr. Donald J Fernandes, Dr. Satadru Ray, Dr. Narendra H, Dr. Krishna Sharan, Dr. Sree Vidya Krishna Rao, Prof. Kaye Roberts-Thomson, Dr. Gloria Mejia, Dr. Richard Logan
Name & Address of Institution	: Dept. of Community Medicine, Dept. of Radiation Oncology and Dept. of Surgical Oncology, KMC, Manipal, and Australian Research Centre for Population Oral Health, Adelaide-South Australia
New review	: New
Date of review (DD/M/YYYY)	: 09/08/2011
Decision of the IEC ➤ Approved ➤ Pending ➤ Revision ➤ Rejected	: Approved from 09.08.2011
Remarks	: Approved for the study period as mentioned in protocol

Please note*

- Inform IEC immediately in case of any Adverse events and Serious adverse event
- Inform IEC in case of any amendments to the protocol, change of study procedure, site and Investigator and premature termination of study with reasons along with summary.
- Final & Six month Reports to be submitted to IEC.
- Members of IEC have right to monitor the trial with prior intimation.
- A copy of the consent document to be given to the study participant giving the consent.

Dr. Joseph Thomas
MEMBER SECRETARY- IEC



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MR-447

Approval Letter
Central Ethics Committee

HCG Tower, 1 Floor, Board Room, # 8.P. Kalinga Rao Road, Sampangiramnagar, Bangalore – 560027

To,
Dr. Sree Vidya Rao,
Principal Investigator
Adelaide University
Australia

30 Jan 2012

Sub: CEC comment on Thesis study

Protocol Title: *“Oral cancer- A life course approach”*

Dear Dr. Sree Vidya Rao,

The HCG-Central Ethics Committee held a meeting on 27 Jan 2012, at 4:00 pm in Board Room of Health Care Global - Bangalore Institute of Oncology Specialty Centre. The following members were present in CEC meeting:

Sr. No.	Name	Sex	Designation (Responsibility)	Conflict of Interest
1.	Justice Rajendra Babu S	Male	Chairman (Legal Person)	No
2.	Dr. Ganesh Nayak	Male	Member Secretary	No
3.	Dr. B. M. Agadi	Male	Member (Clinician)	No
4.	Dr. Sameer Khatri	Male	Member (Clinician)	No
5.	Dr. Shilpa Prabhu Desai	Female	Member (Clinician)	No
6.	Dr. Keerti Tewari	Female	Member (Social Activist)	No
7.	Mrs. Bhushani Kumar	Female	Member (Legal Person)	No
8.	Dr. Sudha Suresh	Female	Member (Basic Medical Scientist)	No
9.	Dr. Raghavendra Rao	Male	Member (Ethicist)	No
10.	Ms. Rekha Hande	Female	Member (Lay Person)	No

Page 1 of 3

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Tel / Fax : +91-80-4020 6000 www.hcgoncology.com

Excellence in Cancer Care and Research

The Central Ethics Committee reviewed the following documents related to the study:

Sr No	Document description	Version	Date
1	Approval of Research Protocol.		
2	Information Sheet for the participant and Informed Consent Form in English and Kannada.		
3	Oral examination form & form for record extraction.		
4	Questionnaire/Data Collection Form in English and Kannada.		
5	Notification of Ethics approval from the university of Adelaide, Australia		

Discussion: The protocol was presented by Dr. Sree Vidya Rao; this study was approved in the CEC meeting.

Decision: Documents in section 1 to 4 are approved and document in section 5 is notified.

Decision of Central Ethics Committee

Please tick (✓) any one of the following

SR. NO.	COMMENTS	TICK (✓) ANY ONE
1.	Approve with no changes	✓
2.	Approvable with minor changes to be reviewed by the member secretary	
3.	Approvable with substantive changes	
4.	Deferred pending receipt of additional substantive information	
5.	Disapproved	

"Any study getting approved in the HCG CEC can be initiated in other sites of the HCG group of Hospitals with concerned specialty, experience and prior notification to the CEC"

Note:

1. The "HCG-Central Ethics Committee" expects to be informed about the progress of the study, any SAE occurring in the course of the study and Suspected Unexpected Serious Adverse Reaction (SUSAR), any changes in the protocol and patient information / informed consent and request you to provide periodic study reports at least annually and a copy of final report of the study.

2. Kindly note that "HCG-Central Ethics Committee" is constituted in accordance with Ethical Guidelines for Biomedical Research on Human Participants (ICMR), ICH-GCP and Schedule Y.

Cordially,

Dr. Ganesh Nayak
Member Secretary,
HCG-Central Ethics Committee
Bangalore

2. Information sheet and consent form



Information Sheet for oral examination

Introduction:

This study will provide important information on factors responsible for oral cancer. The study will try to find if there is any relation between the socioeconomic conditions, habits, diet, poor oral health and oral cancer. This will be done by conducting interviews, oral examination and collecting information from medical records.

The information obtained from the study will help in better understanding of the causes for oral cancer. Your participation and the information provided will help us greatly in adopting strategies for improving oral health and preventing oral cancer.

Right of refusal to participate and withdrawal

You are free to choose to participate in the study. You may choose not to participate without providing us any reason. It is your right to decide whether you wish to participate or not. Your choice to not participate in this study will not affect your course of treatment.

Purpose of this research study

The purpose of our study is to find the reasons for poor oral health and development of oral cancer.

Who is conducting the study?

Dr. Sree Vidya Krishna Rao who is with you here and other researchers from the Australian Research Centre for Population Oral Health, University of Adelaide, Australia, Kidwai Memorial Institute of Oncology and Shri Shirdi Sai Baba Cancer Hospital, Kasturba Medical college.

What is involved?

The study shall begin by conducting an interview where questions related to your oral hygiene and teeth cleaning habits, monthly income, occupation, food habits, and adverse habits if any, will be asked. The interview will take around 40 minutes. You may choose not to answer questions which you do not feel like answering.

This will be followed by an oral examination which will not take more than 20 minutes. Your medical records may be accessed to obtain information on your medical condition and treatment received. You will be informed of the results of your examination and we will try to clarify anything which is related to your oral health and you would like to know. If you need any additional information we would be happy to provide you with the same or refer you to people who could help you.

As we are trained in examining the mouth we shall make every effort to examine your mouth with care causing very minimal or no discomfort to you.

No treatment will be provided and no X-rays will be taken as a part of this study. You will be informed if we feel that you need urgent treatment and we shall refer you to the concerned department.

Possible risks or benefits

There are no health risks to you if you participate in the study.

No money will be provided to you for participating in the study.

Confidentiality

The information given to us in the study will not be revealed to anyone but will be used to study on how we could improve your oral health and prevent and control oral cancer. The results of this study may be published in scientific articles and supplied to the health care officials in your hospital and the Department of Health and Family welfare. We would like to assure you that your names will not be revealed in any of the reports or scientific articles.

You will be provided with oral health education at the end of the examination.

Contact Details of the Researchers

Dr. Sree Vidya Krishna Rao

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Manipal – 576104

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ಬಾಯಿಯ ತಪಾಸಣೆಗೆ ಮಾಹಿತಿ ಹಾಳೆ

ಪೀಠಿಕೆ

ಈ ಅಧ್ಯಯನವು ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್ ಗೆ ಕಾರಣವಾದ ಅಂಶಗಳನ್ನು ಕುರಿತು ಮುಖ್ಯವಾದ ಮಾಹಿತಿಯನ್ನು ಒದಗಿಸುತ್ತದೆ. ಕಾರಣಗಳನ್ನು ಸಂಶೋಧಿಸಲು ಪ್ರಯತ್ನಿಸುತ್ತದೆ. ಈ ಅಧ್ಯಯನವು ಸಾಮಜಿಕ-ಆರ್ಥಿಕ ಪರಿಸ್ಥಿತಿಗಳು, ಅಭ್ಯಾಸಗಳು, ಆಹಾರ, ಕೆಳಮಟ್ಟದ ಬಾಯಿಯ ಆರೋಗ್ಯ ಮತ್ತು ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್ ಇವುಗಳ ನಡುವೆ ಏನಾದರೂ ಸಂಬಂಧವಿದೆಯೇ ಎಂದು ಪರಿಶೀಲಿಸಲು ಪ್ರಯತ್ನಿಸುತ್ತದೆ. ಇದನ್ನು ನಿಮ್ಮ ಸಂದರ್ಶನೆ, ಬಾಯಿಯ ತಪಾಸಣೆ, ಹಾಗೂ ಆಸ್ಪತ್ರೆಯ ದಾಖಲೆಯನ್ನು ಸಂಗ್ರಹಿಸುವುದರ ಮೂಲಕ ಮಾಡಲ್ಪಡುತ್ತದೆ.

ಈ ಅಧ್ಯಯನದಿಂದ ದೊರೆತ ಮಾಹಿತಿಯು ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್ ನ ಕಾರಣಗಳನ್ನು ಉತ್ತಮವಾಗಿ ತಿಳಿಯಲು ಸಹಾಯ ಮಾಡುತ್ತದೆ. ನಿಮ್ಮ ಸಹಯೋಗ ಹಾಗೂ ನೀವು ನೀಡಿದ ಮಾಹಿತಿಯು ಬಾಯಿಯ ಆರೋಗ್ಯ ಸುಧಾರಿಸಲು ಹಾಗೂ ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್‌ನ್ನು ತಡೆಗಟ್ಟಲು ಯೋಜನಾ ನೀತಿಗಳನ್ನು ಅಳವಡಿಸುವಲ್ಲಿ ನಮಗೆ ಬಹಳವಾಗಿ ಸಹಾಯ ಮಾಡುತ್ತದೆ.

ಭಾಗವಹಿಸಲು ನಿರಾಕರಿಸುವ ಹಾಗೂ ಹಿಂತೆಗೆದುಕೊಳ್ಳುವ ಹಕ್ಕು:

ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಆಯ್ಕೆಮಾಡುವುದಕ್ಕೆ ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ನಮಗೆ ಯಾವುದೇ ಕಾರಣ ನೀಡದೆ ನೀವು ಭಾಗವಹಿಸಲು ನಿರಾಕರಿಸಬಹುದು. ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸುವುದು ಅಥವಾ ಇಲ್ಲದಿರುವುದು ಎಂದು ನಿಶ್ಚಯಿಸುವುದು ನಿಮ್ಮ ಹಕ್ಕು. ನಮ್ಮ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಬಾರದೆಂದು ಆಯ್ಕೆ ಮಾಡಿದರೂ ಸಹ ನಿಮ್ಮ ಚಿಕಿತ್ಸಾಕ್ರಮದ ಮೇಲೆ ಯಾವುದೇ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ.

ಈ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ:

ಈ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ ಬಾಯಿಯ ಕೆಳಮಟ್ಟದ ಆರೋಗ್ಯ ಹಾಗೂ ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್ ನ ಬೆಳವಣಿಗೆಗೆ ಕಾರಣಗಳನ್ನು ಶೋಧಿಸುತ್ತದೆ.

ಈ ಅಧ್ಯಯನವನ್ನು ಯಾರು ಮಾಡುತ್ತಾರೆ?

ಇಲ್ಲಿ ನಮ್ಮ ಜ್ಯೋತಿಯಲ್ಲಿರುವ ಡಾ. ಶ್ರೀವಿದ್ಯಾ ಕೃಷ್ಣರಾವ್, ಆಸ್ಟ್ರೇಲಿಯನ್ ರಿಸರ್ಚ್ ಸೆಂಟರ್ ಫಾರ್ ಪಾಪ್ಯುಲೇಷನ್ ಓರಲ್ ಹೆಲ್ತ್, ಕಿಡ್ನಿಯ್ ಆಸ್ಪತ್ರೆ ಹಾಗೂ ಶಿರಡಿ ಸಾಯ್ಬಾ ಆಸ್ಪತ್ರೆಯ ಇತರ ಸಂಶೋಧಕರು.

ಏನನ್ನು ಒಳಗೊಂಡಿದೆ?

ಈ ಅಧ್ಯಯನವು ಸಂದರ್ಶನದಿಂದ ಶುರುವಾಗಿ, ಬಾಯಿಯ ನೈರ್ಮಲ್ಯ, ಬಾಯಿಯನ್ನು ಸ್ವಚ್ಛಗೊಳಿಸುವ ಅಭ್ಯಾಸಗಳು, ಮಾಸಿಕ ಆದಾಯ, ಉದ್ಯೋಗ, ಆಹಾರಾಭ್ಯಾಸಗಳು, ಹಾಗೂ ಪ್ರತಿಕೂಲ ಅಭ್ಯಾಸಗಳು ಇದ್ದಲ್ಲಿ ಅವುಗಳ ಬಗ್ಗೆ ಪ್ರಶ್ನೆಗಳು ಕೇಳಲ್ಪಡುತ್ತವೆ. ಸಂದರ್ಶನೆಯ ಸಮಯ ಸುಮಾರು ೪೦ ನಿಮಿಷಗಳು. ನೀವು ಉತ್ತರಿಸಲು ಇಚ್ಛಿಸದ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರ ನೀಡದೇ ಇರಬಹುದು. ಇದನ್ನು ಅನುಸರಿಸಿ ಬಾಯಿಯ ತಪಾಸಣೆ ಸುಮಾರು ೨೦ ನಿಮಿಷಗಳ ಕಾಲ ಮಾಡಲಾಗುವುದು.

ನಿಮ್ಮ ದೇಹದ ಸ್ಥಿತಿ ಹಾಗೂ ಪಡೆಯಲ್ಪಟ್ಟಿರುವ ಚಿಕಿತ್ಸೆ ಬಗ್ಗಿನ ಮಾಹಿತಿಗಳನ್ನು ನಿಮ್ಮ ಆಸ್ಪತ್ರೆಯ ದಾಖಲೆಗಳನ್ನು ಸಂಗ್ರಹಿಸುವುದರ ಮೂಲಕ ಮಾಡಬಹುದು. ನಿಮ್ಮ ಬಾಯಿಯ ತಪಾಸಣೆಯ ಫಲಿತಾಂಶವನ್ನು ನಿಮಗೆ ತಿಳಿಸಲಾಗುವುದು ಮತ್ತು ನಿಮ್ಮ ಬಾಯಿಯ ಆರೋಗ್ಯಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ಏನನ್ನಾದರೂ ನೀವು ಅರಿಯಲು ಇಷ್ಟಪಟ್ಟಲ್ಲಿ ನಾವು ಅದನ್ನು ತಿಳಿಸಿಕೊಡಲು ಪ್ರಯತ್ನಿಸುತ್ತೇವೆ. ನಿಮಗೆ ಅಧಿಕ ಮಾಹಿತಿ ಬೇಕಾದರೆ ನಾವು ಅದನ್ನು ಒದಗಿಸಲು ಯತ್ನಿಸುತ್ತೇವೆ ಅಥವಾ ನಿಮಗೆ ಸಹಾಯ ಮಾಡಬಹುದಾದ ಜನರ ಬಳಿಗೆ ಕಳುಹಿಸುತ್ತೇವೆ. ನಾವು ಬಾಯಿಯ ತಪಾಸಣೆ ಮಾಡುವುದರಲ್ಲಿ ಪರಿಣತರಾದವರಿಂದ ನಾವು ನಿಮಗೆ ಅತ್ಯಂತ ಕಡಿಮೆ ಅಥವಾ ಅಹಿತಕರವಾಗಿರದಂತೆ ನಿಮ್ಮ ಬಾಯಿಯ ತಪಾಸಣೆಯನ್ನು ಮಾಡಲು ಪ್ರಯತ್ನಿಸುತ್ತೇವೆ.

ಈ ಸಂಶೋಧನೆಯ ಭಾಗವಾಗಿ ಯಾವುದೇ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುವುದಿಲ್ಲ ಹಾಗೂ ಎಕ್ಸ್‌ರೇ ತೆಗೆಯಲಾಗುವುದಿಲ್ಲ. ನಿಮಗೆ ಯಾವುದೇ ತುರ್ತು ಚಿಕಿತ್ಸೆಯ ಅವಶ್ಯಕತೆ ಇದೆ ಎಂದು ನಮಗೆ ತಿಳಿದು ಬಂದಲ್ಲಿ ನಿಮಗೆ ನಾವು ತಿಳಿಸುತ್ತೇವೆ ಹಾಗೂ ಸಂಬಂಧಪಟ್ಟ ವಿಭಾಗಕ್ಕೆ ನಿಮ್ಮನ್ನು ನಿರ್ದೇಶಿಸುತ್ತೇವೆ.

ಸಾಧ್ಯವಾಗಬಹುದಾದತೊಂದರೆಹಾಗೂಪ್ರಯೋಜನ:

ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದರಿಂದ ನಿಮ್ಮ ಆರೋಗ್ಯಕ್ಕೆ ಯಾವುದೇ ತೊಂದರೆ ಇಲ್ಲ. ನಿಮಗೆ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದಕ್ಕೆ ಯಾವುದೇ ಹಣ ನೀಡಲಾಗುವುದಿಲ್ಲ.

ಗೋಪ್ಯತೆ:

ನಿಮಗೆ ನೀವು ಒದಗಿಸಿದ ನಿಮ್ಮ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯನ್ನು ಈ ಅಧ್ಯಯನದ ಸಂಶೋಧಕರ ಹೊರತಾಗಿ ಬೇರೆ ಯಾರಿಗೂ ಬಹಿರಂಗ ಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮಿಂದ ಪಡೆದ ಮಾಹಿತಿಯನ್ನು ನಿಮ್ಮ ಬಾಯಿಯ ಆರೋಗ್ಯವನ್ನು ಹೇಗೆ ಸುಧಾರಿಸಬಹುದೆಂದು ಅಧ್ಯಯನ ಮಾಡಲು ಬಳಸಲಾಗುವುದು. ಈ ಅಧ್ಯಯನದ ಫಲಿತಾಂಶವನ್ನು ವೈಜ್ಞಾನಿಕ ಲೇಖನಗಳಲ್ಲಿ ಪ್ರಕಾಶನ ಮಾಡಬಹುದು ಹಾಗೂ ನಿಮ್ಮ ಆಸ್ಪತ್ರೆಯ ಆರೋಗ್ಯಾಧಿಕಾರಿಗಳಿಗೆ ಹಾಗೂ ಆರೋಗ್ಯ ಮತ್ತು ಕುಟುಂಬ ಕಲ್ಯಾಣ ವಿಭಾಗಕ್ಕೆ ಒದಗಿಸಬಹುದು. ನಿಮ್ಮ ಹೆಸರನ್ನು ಯಾವುದೇ ವರದಿಯಲ್ಲಿ ಅಥವಾ ವೈಜ್ಞಾನಿಕ ಲೇಖನಗಳಲ್ಲಿ ಬಹಿರಂಗಪಡಿಸುವುದು ಎಂದು ನಾವು ಆಶ್ಚರ್ಯ ನೀಡುತ್ತೇವೆ. ನಿಮಗೆ ಬಾಯಿಯ ತಪಾಸಣೆಯ ನಂತರ ಬಾಯಿಯ ಆರೋಗ್ಯದ ಬಗ್ಗೆ ಶಿಕ್ಷಣ ನೀಡಲಾಗುವುದು.

ಸಂಶೋಧಕರಸಂಪರ್ಕವಿವರಗಳು:

1. ಡಾ. ಶ್ರೀವಿದ್ಯಾ ಕೃಷ್ಣ ರಾವ್,

ಡಿ-೧೧೫, ಆನಂತನಗರ ೨ನೆಯ ಹಂತ,

ಮಣಿಪಾಲ- ೫೭೬೧೦೪,

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ಈಮೈಲ್: sree.rao@adelaide.edu.au

2. ಡಾ. ಕೇಯ್ ರಾಬರ್ಟ್ಸ್-ಥಾಂಸನ್,

ಪ್ರೊಫೆಸರ್,

ಆಸ್ಟ್ರೇಲಿಯನ್ ರಿಸರ್ಚ್ ಸೆಂಟರ್ ಫಾರ್ ಪಾಪ್ಯುಲೇಷನ್ ಓರಲ್ ಹೆಲ್ತ್, ಯೂನಿವರ್ಸಿಟಿ ಆಫ್ ಅಡಲೇಡ್

ಟೆಲಿಫೋನ್: +೬೧-೮೨೧೨-೪೪೫೫,

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3. ಡಾ. ಮುರಳಿಧರ್ ಕುಲಕರ್ಣಿ,

ಕನ್ನೂರಬ ಮೆಡಿಕಲ್ ಕಾಲೇಜ್

ಮಣಿಪಾಲ-೫೭೬೧೦೪

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THE UNIVERSITY OF ADELAIDE HUMAN RESEARCH ETHICS COMMITTEE

And.....

**STANDARD CONSENT FORM
FOR PEOPLE WHO ARE PARTICIPANTS IN A RESEARCH PROJECT**

1. I, *(please print name)*
consent to take part in the research project entitled: **Oral cancer – A life course approach 2011-12**
2. I acknowledge that I have read the attached Information Sheet entitled: **Information Sheet for oral examination**
3. I have had the project, so far as it affects me, fully explained to my satisfaction by the research worker. My consent is given freely. I consent to undergo an examination of my mouth. In addition, I consent to those investigations that I have endorsed with my initials below:

		Initials below if you:	
		consent	Do not consent
3a.	Conducting interview		
3b.	Oral Examination		
3c.	Information extraction from medical records		

4. Although I understand that the purpose of this research project is to improve the understanding of the disease, it has also been explained that my involvement may not be of any benefit to me.
5. I have been given the opportunity to have a member of my family or a friend present while the project was explained to me.
6. I have been informed that, while information gained during the study may be published, I will not be identified and my personal results will not be divulged.
7. I understand that I am free to withdraw from the project at any time and that this will not affect medical advice in the management of my health, now or in the future.
8. I am aware that I should retain a copy of this Consent Form, when completed, and the attached Information Sheet.

.....
(signature) *(date)*

WITNESS	
I have described to <i>(name of subject)</i>	
the nature of the research to be carried out. In my opinion she/he understood the explanation.	
Status in Project:	
Name:	
.....	
<i>(signature)</i>	<i>(date)</i>

ದಿಯೂನಿವರ್ಸಿಟಿಆಫ್‌ಅಡಿಲೇಡ್- ಹ್ಯೂಮನ್‌ನಿರ್ವಹಣೆತಿಕ್ಸೆ ಮಿಟಿ

ಮತ್ತು.....

ನಿರ್ಧಾರಿತಒಪ್ಪಿಗೆಪ್ರಪತ್ರ

ಸಂಶೋಧನಾಯೋಜನೆಯಲ್ಲಿಭಾಗವಹಿಸುವಜನರಿಗೆ

೧. ನಾನು,(ದಯವಿಟ್ಟು ಹೆಸರನ್ನು ಮುದ್ರಿಸಿ) ‘ಓರಲ್ ಕ್ಯಾನ್ಸರ್- ಎ ಲೈಫ್ ಕೋರ್ಸ್ ಅಪ್ರೋಚ್- ೨೦೧೧-೧೨’ ಎಂಬ ಶೀರ್ಷಿಕೆಯುಳ್ಳ ಸಂಶೋಧನಾ ಯೋಜನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಒಪ್ಪಿಕೊಳ್ಳುತ್ತೇನೆ.

೨. ನಾನು ಲಗತ್ತಿಸಿರುವ ‘ಬಾಯಿಯ ತಪಾಸಣೆಗೆ ಮಾಹಿತಿ ಹಾಳೆ’ ಎಂಬ ಹೆಸರುಳ್ಳ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿರುತ್ತೇನೆ.

೩. ನನಗೆ ಎಷ್ಟರವರೆಗೆ ನನ್ನ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರಬಲ್ಲ ಯೋಜನೆಯನ್ನು, ನನಗೆ ಸಂಪೂರ್ಣವಾಗಿ ಸಮಾಧಾನಕರವಾಗುವಂತೆ ಸಂಶೋಧನಾ ಕಾರ್ಯಕರ್ತರು ವಿವರಿಸಿರುತ್ತಾರೆ.

ನಿಮ್ಮ ಸಹಿ/ ಬೆರಳಚ್ಚು	
ಒಪ್ಪಿಗೆ ಇದೆ	ಒಪ್ಪಿಗೆ ಇಲ್ಲ
೩ಅ. ಸಂದರ್ಶನ ನೀಡಲು	
೩ಬಿ. ಬಾಯಿಯತಪಾಸಣೆಗೆ	
೩ಸಿ. ವೈದ್ಯಕೀಯ ದಾಖಲೆಯನ್ನು ಸಂಗ್ರಹಿಸಲು	

೪. ಈ ಸಂಶೋಧನಾ ಯೋಜನೆಯ ಉದ್ದೇಶ ರೋಗದ ತಿಳುವಳಿಕೆಯ ಸುಧಾರಣೆಯಾದರೂ, ನನ್ನ ಒಳಗೊಳ್ಳುವಿಕೆ ನನಗೆ ಯಾವುದೇ ರೀತಿಯಲ್ಲಿ ಉಪಯೋಗಕರವಾಗದಿರಬಹುದೆಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

೫. ನನಗೆ ಯೋಜನೆಯನ್ನು ವಿವರಿಸುವಾಗ ಒಬ್ಬ ಕುಟುಂಬದ ಸದಸ್ಯ/ಸ್ಯೆ ಅಥವಾ ಒಬ್ಬ/ಳು ಸ್ನೇಹಿತ/ತೆ ನನ್ನ ಬಳಿ ಇರಲು ಅವಕಾಶ ಕೊಡಲಾಗಿದೆ.

೬. ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಪಡೆದ ಮಾಹಿತಿ ಪ್ರಕಾಶಿಸಬಹುದಾದರೂ, ನಾನು ಗುರುತಿಸಲ್ಪಡುವುದಿಲ್ಲ ಹಾಗೂ ನನ್ನ ವೈಯಕ್ತಿಕ ಫಲಿತಾಂಶವನ್ನು ಬಹಿರಂಗ ಪಡಿಸುವುದಿಲ್ಲ ಎಂದು ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ.

೭. ನಾನು ಯೋಜನೆಯಿಂದ ಯಾವ ಸಮಯದಲ್ಲಾದರೂ ಹಿಂತೆಗೆದುಕೊಳ್ಳಲು ಮುಕ್ತನಾಗಿದ್ದೇನೆ ಮತ್ತು ಇದು ಈಗ ಅಥವಾ ಭವಿಷ್ಯದಲ್ಲಿ ನನ್ನ ಆರೋಗ್ಯ ನಿರ್ವಹಣೆಯಲ್ಲಿ ಬೇಕಾದ ಸಲಹೆಯ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ ಎಂದು ನನಗೆ ಅರ್ಥವಾಗಿದೆ.

೮. ಪೂರ್ಣಗೊಳಿಸಿದ ನಂತರ ಈ ಒಪ್ಪಿಗೆ ಪ್ರಪತ್ರದ ಪ್ರತಿಯನ್ನು ಹಾಗೂ ಲಗತ್ತಿಸಿದ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ನಾನು ಇಟ್ಟುಕೊಳ್ಳಬೇಕೆಂದು ನನಗೆ ಗೊತ್ತಿದೆ.

.....

(ಸಹಿ)

(ದಿನಾಂಕ)

ಸಾಕ್ಷಿ,

.....(ಒಳಪಟ್ಟವರ ಹೆಸರು) ಇವರಿಗೆ ನಾನು ಮಾಡಲ್ಪಡುವ ಸಂಶೋಧನೆಯ ಬಗೆಯನ್ನು ವಿವರಿಸಿದ್ದೇನೆ.ನನ್ನ ಅನಿಸಿಕೆಯ ಪ್ರಕಾರ ಇವರು ವಿವರಣೆಯನ್ನು ಅರ್ಥ ಮಾಡಿಕೊಂಡಿರುತ್ತಾರೆ.

ಯೋಜನೆಯಲ್ಲಿಸ್ಥಾನ:.....ಹೆಸರು:.....

.....

(ಸಹಿ)

(ದಿನಾಂಕ)

3. Questionnaire

ORAL CANCER - A LIFE COURSE APPROACH

ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್- ಒಂದು ಜೀವನಸರಣಿ ಮಾರ್ಗ

IDENTIFICATION DETAILS OF THE PARTICIPANT

ಭಾಗವಹಿಸುವವರ ಗುರುತಿನ ಸಂಖ್ಯೆ

PARTICIPANT'S ID

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ಸಂದರ್ಶನದ ದಿನಾಂಕ ದಿಡಿ/ಮಾಮಾ/ವವವವ

Date of Interview DD/MM/YYYY

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ಆಸ್ಪತ್ರೆಯ ಹೆಸರು

Name of the Hospital

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ಭಾಗವಹಿಸುವವರ ಹೊರ/ಒಳ ರೋಗಿ

ವಿಭಾಗದ ಸಂಖ್ಯೆ

Participant's OPD number

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ಭಾಗವಹಿಸುವವರ ಗುರುತಿನ ಸಂಖ್ಯೆ

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PARTICIPANT'S ID

ಭಾಗ ೧. ಭಾಗವಹಿಸುವವರ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿ PART I. Personal details of the participant

A1. ವಯಸ್ಸು Age	ವರ್ಷಗಳು Years	<input type="text"/>	<input type="text"/>
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A2. ಲಿಂಗ Gender	ಗಂಡಸು Male	<input type="text"/>	ಹೆಂಗಸು Female	<input type="text"/>
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A3. ಧರ್ಮ Religion	ಹಿಂದೂ Hindu	<input type="text"/>	ಮುಸ್ಲಿಂ Muslim	<input type="text"/>	ಕ್ರೈಸ್ತ Christian	<input type="text"/>	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Others please specify
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A4. ಸದ್ಯದ ವಾಸದ ವಲಯ Current area of residence	ಹಳ್ಳಿ Rural	<input type="text"/>	ನಗರಸುತ್ತ Peri-urban	<input type="text"/>	ನಗರ Urban	<input type="text"/>
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A5. ಮನೆಯಲ್ಲಿ ಮಾತನಾಡುವ ಭಾಷೆ Language spoken at home	ಕನ್ನಡ Kannada	<input type="text"/>	ಇತರೆ Others	<input type="text"/>	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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A6. ಅತ್ಯಂತ ಮೇಲ್ಮಟ್ಟದ ಶಿಕ್ಷಣ Highest level of education	ಔಪಚಾರಿಕ ಶಿಕ್ಷಣ ಇಲ್ಲ ಹಾಗೂ ಅನಕ್ಷರಸ್ಥ No formal education and illiterate	<input type="text"/>	ಔಪಚಾರಿಕ ಶಿಕ್ಷಣ ಇಲ್ಲ ಆದರೆ ಅಕ್ಷರಸ್ಥ No formal education but literate	<input type="text"/>	ಪ್ರಾಥಮಿಕ Primary	<input type="text"/>	ಮಾಧ್ಯಮಿಕ Middle	<input type="text"/>
	ಪ್ರೌಢ ಶಿಕ್ಷಣ Secondary	<input type="text"/>	ಪದವಿಪೂರ್ವ / ಡಿಪ್ಲೊಮಾ Intermediate/ Post high school diploma	<input type="text"/>	ಸ್ನಾತಕ / ಸ್ನಾತಕೋತ್ತರ ಪದವೀಧರ Graduation/ Post- Graduation	<input type="text"/>	ವೃತ್ತಿ / ಆನರ್ಸ್ Profession/ Honours	<input type="text"/>

A7. ಶಾಲಾಶಿಕ್ಷಣವನ್ನು ಸಂಪೂರ್ಣಗೊಳಿಸಿದ ವರ್ಷಗಳ ಸಂಖ್ಯೆ Number of years of schooling completed	<input type="text"/>	<input type="text"/>	ಸಂಖ್ಯೆ Number
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A8. ಮನೆಯ ಯಜಮಾನರ ಉದ್ಯೋಗ Occupation of the head of the household	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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A9. ಕುಟುಂಬದ ಸದ್ಯದ ಒಟ್ಟು ಮಾಸಿಕ ಆದಾಯ Current household income per month	ರೂ/- <input type="text"/>	In rupees
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A10. ವೈವಾಹಿಕ ಸ್ಥಿತಿ Marital status	ಒಬ್ಬಂಟಿ Single	<input type="text"/>	ವಿವಾಹಿತ Married	<input type="text"/>	ಬೇರ್ಪಟ್ಟ Separated	<input type="text"/>	ವಿಚ್ಛೇದಿತ Divorced	<input type="text"/>	ವೈಧವ್ಯ Widowed	<input type="text"/>
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A11. ಕುಟುಂಬದ ರಚನೆ Family structure	ಅವಿಭಕ್ತ ಕುಟುಂಬ Joint family	<input type="checkbox"/> 1	ಅಣು-ವಿಭಕ್ತ ಕುಟುಂಬ Nuclear Family	<input type="checkbox"/> 2
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A12. ನಿಮಗೆ ಎಷ್ಟು ಜನ ಮಕ್ಕಳಿದ್ದಾರೆ? How many children do you have?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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A13. ನಿಮಗೆ ಎಷ್ಟು ಜನ ಒಡಹುಟ್ಟಿದವರು ಇದ್ದಾರೆ? How many siblings do you have?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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ಭಾಗ ೨ . ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ನಿಮ್ಮ ಅಭ್ಯಾಸ ಹಾಗೂ ಆಹಾರದ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿದೆ:
PART II. The following questions ask about the habits and diet

B. ಮುಂದಿನವುಗಳಲ್ಲಿ ಯಾವುದು ನಿಮ್ಮ ಅಭ್ಯಾಸಗಳ ವಿದ್ಯಮಾನವನ್ನು ಉತ್ತಮವಾಗಿ ವಿವರಿಸುತ್ತದೆ? Which of the following best describes status of your habits?

B1. ಧೂಮಪಾನ Smoking	ಎಂದಿಗೂಇಲ್ಲ Never	<input type="checkbox"/> 1	ಈಹಿಂದೆ Former	<input type="checkbox"/> 2	ಈಗಲೂ Current	<input type="checkbox"/> 3
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B2. ತಂಬಾಕು ಅಗೆಯುವುದು Chewing tobacco	ಎಂದಿಗೂಇಲ್ಲ Never	<input type="checkbox"/> 1	ಈಹಿಂದೆ Former	<input type="checkbox"/> 2	ಈಗಲೂ Current	<input type="checkbox"/> 3
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B3. ತಂಬಾಕು ಸಹಿತ ಎಲೆ-ಅಡಿಕೆ ಅಗೆಯುವುದು Chewing quid with tobacco	ಎಂದಿಗೂಇಲ್ಲ Never	<input type="checkbox"/> 1	ಈಹಿಂದೆ Former	<input type="checkbox"/> 2	ಈಗಲೂ Current	<input type="checkbox"/> 3
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B4. ತಂಬಾಕು ರಹಿತ ಎಲೆ-ಅಡಿಕೆ ಅಗೆಯುವುದು Chewing quid without tobacco	ಎಂದಿಗೂಇಲ್ಲ Never	<input type="checkbox"/> 1	ಈಹಿಂದೆ Former	<input type="checkbox"/> 2	ಈಗಲೂ Current	<input type="checkbox"/> 3
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B5. ನಷ್ಟ ಸೇವನೆ Snuff dipping	ಎಂದಿಗೂಇಲ್ಲ Never	<input type="checkbox"/> 1	ಈಹಿಂದೆ Former	<input type="checkbox"/> 2	ಈಗಲೂ Current	<input type="checkbox"/> 3
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B6. ಮದ್ಯಪಾನ Alcohol	ಎಂದಿಗೂಇಲ್ಲ Never	<input type="checkbox"/> 1	ಈಹಿಂದೆ Former	<input type="checkbox"/> 2	ಈಗಲೂ Current	<input type="checkbox"/> 3
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B7. ಯಾವ ತರಹದ ಆಹಾರ ನೀವು ಸೇವಿಸುತ್ತೀರಿ? What is the type of diet that you consume?	ಸಸ್ಯಾಹಾರ Vegetarian	<input type="checkbox"/> 1	ಮಿಶ್ರಿತ Mixed	<input type="checkbox"/> 2
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vcಭಾಗ ೨. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ನಿಮ್ಮ ಕುಟುಂಬದವರ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿದೆ:

PART III. The following questions ask about family history

C1. ನಿಮ್ಮ ತಂದೆಯ ಅತ್ಯಂತ ಮೇಲ್ಮಟ್ಟದ ಶಿಕ್ಷಣ ಏನು? What is your father's Highest level of education?	ಔಪಚಾರಿಕ ಶಿಕ್ಷಣ ಇಲ್ಲ ಹಾಗೂ ಅನಕ್ಷರಸ್ಥ No formal education and illiterate <input type="checkbox"/> 1	ಔಪಚಾರಿಕ ಶಿಕ್ಷಣ ಇಲ್ಲ ಆದರೆ ಅಕ್ಷರಸ್ಥ No formal education but literate <input type="checkbox"/> 2	ಪ್ರಾಥಮಿಕ Primary <input type="checkbox"/> 3	ಮಾಧ್ಯಮಿಕ Middle <input type="checkbox"/> 4
	ಪ್ರೌಢ ಶಿಕ್ಷಣ Secondary <input type="checkbox"/> 5	ಪದವಿಪೂರ್ವ/ ಡಿಪ್ಲೊಮಾ Intermediate/ Post high school diploma <input type="checkbox"/> 6	ಸ್ನಾತಕ/ ಸ್ನಾತಕೋತ್ತರ ಪದವೀಧರ Graduation/ Post-Graduation <input type="checkbox"/> 7	ವೃತ್ತಿ / ಆನರ್ಸ್ Profession/ Honours <input type="checkbox"/> 8

C2. ನಿಮ್ಮ ತಾಯಿಯ ಅತ್ಯಂತ ಮೇಲ್ಮಟ್ಟದ ಶಿಕ್ಷಣ ಏನು? What is your mother's highest level of education?	ಔಪಚಾರಿಕ ಶಿಕ್ಷಣ ಇಲ್ಲ ಹಾಗೂ ಅನಕ್ಷರಸ್ಥ No formal education and illiterate <input type="checkbox"/> 1	ಔಪಚಾರಿಕ ಶಿಕ್ಷಣ ಇಲ್ಲ ಆದರೆ ಅಕ್ಷರಸ್ಥ No formal education but literate <input type="checkbox"/> 2	ಪ್ರಾಥಮಿಕ Primary <input type="checkbox"/> 3	ಮಾಧ್ಯಮಿಕ Middle <input type="checkbox"/> 4
	ಪ್ರೌಢ ಶಿಕ್ಷಣ Secondary <input type="checkbox"/> 5	ಪದವಿಪೂರ್ವ/ ಡಿಪ್ಲೊಮಾ Intermediate/ Post high school diploma <input type="checkbox"/> 6	ಸ್ನಾತಕ/ ಸ್ನಾತಕೋತ್ತರ ಪದವೀಧರ Graduation/ Post-Graduation <input type="checkbox"/> 7	ವೃತ್ತಿ / ಆನರ್ಸ್ Profession/ Honours <input type="checkbox"/> 8

C3. ನಿಮ್ಮ ತಂದೆಗೆ ಮುಂದಿನವುಗಳಲ್ಲಿ ಯಾವುದಾದರೂ ಅಭ್ಯಾಸಗಳು ಇದ್ದವೆ? Did your father have any of the following habits?	ಧೂಮಪಾನ Smoking <input type="checkbox"/> 1	ತಂಬಾಕು ಅಗೆಯುವುದು Chewing tobacco <input type="checkbox"/> 2	ತಂಬಾಕು ಸಹಿತ ಎಲೆ-ಅಡಿಕೆ ಅಗೆಯುವುದು Chewing quid with tobacco <input type="checkbox"/> 3
	ತಂಬಾಕು ರಹಿತ ಎಲೆ-ಅಡಿಕೆ ಅ Chewing quid without tobacco <input type="checkbox"/> 4	ನಷ್ಟ ಸೇವನೆ Snuff dipping <input type="checkbox"/> 5	ಮದ್ಯಪಾನ Alcohol use <input type="checkbox"/> 6

C4. ನಿಮ್ಮ ತಾಯಿಗೆ ಮುಂದಿನವುಗಳಲ್ಲಿ ಯಾವುದಾದರೂ ಅಭ್ಯಾಸಗಳು ಇದ್ದವೆ? Did your mother have any of the following habits?	ಧೂಮಪಾನ Smoking <input type="checkbox"/> 1	ತಂಬಾಕು ಅಗೆಯುವುದು Chewing tobacco <input type="checkbox"/> 2	ತಂಬಾಕು ಸಹಿತ ಎಲೆ-ಅಡಿಕೆ ಅಗೆಯುವುದು Chewing quid <input type="checkbox"/> 3
	ತಂಬಾಕು ರಹಿತ ಎಲೆ-ಅಡಿಕೆ ಅ Chewing quid without tobacco <input type="checkbox"/> 4	ನಷ್ಟ ಸೇವನೆ Snuff dipping <input type="checkbox"/> 5	ಮದ್ಯಪಾನ Alcohol use <input type="checkbox"/> 6

C5. ನಿಮ್ಮ ಕುಟುಂಬದವರಲ್ಲಿ ಯಾರಾದರೂ ಕ್ಯಾನ್ಸರ್ ಇಂದ ಬಾಧಿಸಲ್ಪಟ್ಟಿದ್ದಾರೆಯೇ? Did/ Does anybody in your family suffer from cancer?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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C6. ಹೌದು, ಎಂದರೆ ವೇಹದ ಯಾವ ಭಾಗ ಎಂದು ದಯವಿಟ್ಟು ತಿಳಿಸಿ. If yes, please specify the site	ದಯವಿಟ್ಟು ತಿಳಿಸಿ Please specify
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C7. ಅವರು ನಿಮಗೆ ಹೇಗೆ ಸಂಬಂಧಿಸಿರುತ್ತಾರೆ? How are they related to you?	ತಂದೆ-ತಾಯಿ Parents <input type="checkbox"/> 1	ಒಡಹುಟ್ಟಿದವರು Siblings <input type="checkbox"/> 2	ಮಕ್ಕಳು Children <input type="checkbox"/> 3	ಇತರೆ Others <input type="checkbox"/> 4
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ಭಾಗ ೪: ಲೈಫ್ ಗ್ರಿಡ್ **PART IV. LIFE GRID**

ವರ್ಷ Year	ಬಾಹ್ಯ ಘಟನೆಗಳು External events	ವಯಸ್ಸು Age	ಜೀವನದ ಘಟನೆಗಳು Life events	ವಾಸಸ್ಥಳ Residence	ಉದ್ಯೋಗ Occupation	ಆದಾಯ Income
1930						
1940						
1950						
1960						
1970						
1980						
1990						
2000						
2010						

ವರ್ಷ Year	ಆಹಾರ Diet	ಧೂಮಪಾನ Smoking	ತಂಬಾಕು Smokeless tobacco	ಎಲೆ-ಅಡಿಕೆ Quid	ಮದ್ಯಪಾನ Alcohol
1930					
1940					
1950					
1960					
1970					
1980					
1990					
2000					
2010					

ಭಾಗ ೫. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ನಿಮ್ಮ ಜೀವನದ ವಿವಿಧ ಘಟ್ಟಗಳಲ್ಲಿ ಅಧಿಕ ಸಮಯ ವಾಸಿಸಿದ ಮನೆಯ ಪರಿಸ್ಥಿತಿಯ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿವೆ

PART V. The following questions ask about the conditions of the house you have lived in for longest period at different stages of life

ಬಾಲ್ಯಾವಸ್ಥೆಯಲ್ಲಿ (೬-೧೦ ವರ್ಷಗಳು) **At childhood (6-10 years)**

E1a. ವಾಸದ ವಲಯ Area of residence	ಹಳ್ಳಿ Rural <input type="checkbox"/> 1	ನಗರ ಸುತ್ತ Peri-urban <input type="checkbox"/> 2	ನಗರ Urban <input type="checkbox"/> 3
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E2a. ನೀವು ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಆ ವಲಯದಲ್ಲಿ ವಾಸಿಸಿದ್ದೀರಿ? For how many years did you live in the area?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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E3a. ಅದು ಯಾವ ತರಹದ ಮನೆಯಾಗಿತ್ತು? What was the type of house?	ಕಚ್ಚು Kuccha <input type="checkbox"/> 1	ಮಧ್ಯಮ Semi-pucca <input type="checkbox"/> 2	ಪಕ್ಕು Pucca <input type="checkbox"/> 3
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E4a. ಆ ಮನೆ ನಿಮ್ಮ ಸ್ವಂತದ್ದಾ ಅಥವಾ ಬಾಡಿಗೆಯದಾ? Was the house your own or rented?	ಬಾಡಿಗೆ Rented <input type="checkbox"/> 1	ಸ್ವಂತ Own <input type="checkbox"/> 2
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E5a. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಜನ ವಾಸಿಸುತ್ತಿದ್ದೀರಿ? How many people resided in the house?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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E6a. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಕೋಣೆಗಳಿದ್ದವು? How many rooms were present in the house?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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E7a. ಅಡುಗೆ ಮಾಡಲು ಬಳಸುತ್ತಿದ್ದ ಇಂಧನ ಶಕ್ತಿ ಯಾವುದು? What was the energy source for cooking?	ಕಟ್ಟಿಗೆ Wood <input type="checkbox"/> 1	ಇದ್ದಲು Charcoal <input type="checkbox"/> 2	ಜೈವಿಕ ಅನಿಲ Biogas <input type="checkbox"/> 3	ಸೂರ್ಯನ ಶಕ್ತಿ Solar <input type="checkbox"/> 4
	ವಿದ್ಯುಚ್ಛಕ್ತಿ Electricity <input type="checkbox"/> 5	ಅಡುಗೆ ಅನಿಲ LPG <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify

E8a. ಕುಡಿಯುವ ನೀರಿನ ಲಭ್ಯತೆ Availability of drinking water	೫ ಕಿ.ಮಿ.ಗಿಂತಲೂ ದೂರ More than 5km away <input type="checkbox"/> 1	೫ ಕಿ.ಮಿ. ಗಿಂತಲೂ ಕಡಿಮೆ ದೂರದಲ್ಲಿ Within 5 km <input type="checkbox"/> 2	ಮನೆಯಲ್ಲಿಯೇ Inside the house <input type="checkbox"/> 3
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E9a. ಶೌಚಾಲಯದ ವಸತಿ Access to toilet facility	ಇಲ್ಲ None <input type="checkbox"/> 1	ಮನೆಯಿಂದ ಹೊರಗೆ Outside the house <input type="checkbox"/> 2	ಮನೆಯೊಳಗೆ Inside the house <input type="checkbox"/> 3
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E10a. ಮನೆಯ ಯಜಮಾನರ ಉದ್ಯೋಗ (ಬಾಲ್ಯಾವಸ್ಥೆಯಲ್ಲಿ ೬-೧೦ ವರ್ಷಗಳು) Occupation of the head of the household At childhood (6-10 years)	ದಯವಿಟ್ಟು ತಿಳಿಸಿ Please specify
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ತಾರುಣ್ಯದಲ್ಲಿ (೧೧-೧೮ ವರ್ಷಗಳು) **At adolescence (11-18 years)**

E1b. ವಾಸದ ವಲಯ Area of residence	ಹಳ್ಳಿ Rural	<input type="checkbox"/> 1	ನಗರ ಸುತ್ತ Peri-urban	<input type="checkbox"/> 2	ನಗರ Urban	<input type="checkbox"/> 3
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E2b. ನೀವು ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಆ ವಲಯದಲ್ಲಿ ವಾಸಿಸಿದ್ದೀರಿ? For how many years did you live in the area?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E3b. ಅದು ಯಾವ ತರಹದ ಮನೆಯಾಗಿತ್ತು? What was the type of house?	ಕಚ್ಚ Kuccha	<input type="checkbox"/> 1	ಮಧ್ಯಮ Semi-pucca	<input type="checkbox"/> 2	ಪಕ್ಕ Pucca	<input type="checkbox"/> 3
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E4b. ಆ ಮನೆ ನಿಮ್ಮ ಸ್ವಂತದ್ದಾ ಅಥವಾ ಬಾಡಿಗೆಯದಾ? Was the house your own or rented?	ಬಾಡಿಗೆ Rented	<input type="checkbox"/> 1	ಸ್ವಂತ Own	<input type="checkbox"/> 2
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E5b. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಜನ ವಾಸಿಸುತ್ತಿದ್ದೀರಿ? How many people resided in the house?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E6b. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಕೋಣೆಗಳಿದ್ದವು? How many rooms were present in the house?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E7b. ಅಡುಗೆ ಮಾಡಲು ಬಳಸುತ್ತಿದ್ದ ಇಂಧನ ಶಕ್ತಿ ಯಾವುದು? What was the energy source for cooking?	ಕಟ್ಟಿಗೆ Wood	<input type="checkbox"/> 1	ಇದ್ದಲು Charcoal	<input type="checkbox"/> 2	ಜೈವಿಕ ಅನಿಲ Biogas	<input type="checkbox"/> 3	ಸೂರ್ಯನ ಶಕ್ತಿ Solar	<input type="checkbox"/> 4
	ವಿದ್ಯುಚ್ಛಕ್ತಿ Electricity	<input type="checkbox"/> 5	ಅಡುಗೆ ಅನಿಲ LPG	<input type="checkbox"/> 6	ಇತರೆ Others	<input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify	

E8b. ಕುಡಿಯುವ ನೀರಿನ ಲಭ್ಯತೆ Availability of drinking water	೫ ಕಿ.ಮಿ.ಗಿಂತಲೂ ದೂರ More than 5km away	<input type="checkbox"/> 1	೫ ಕಿ.ಮಿ. ಗಿಂತಲೂ ಕಡಿಮೆ ದೂರದಲ್ಲಿ Within 5 km	<input type="checkbox"/> 2	ಮನೆಯಲ್ಲಿಯೇ Inside the house	<input type="checkbox"/> 3
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E9b. ಶೌಚಾಲಯದ ವಸತಿ Access to toilet facility	ಇಲ್ಲ None	<input type="checkbox"/> 1	ಮನೆಯಿಂದ ಹೊರಗೆ Outside the house	<input type="checkbox"/> 2	ಮನೆಯೊಳಗೆ Inside the house	<input type="checkbox"/> 3
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E10b. ಮನೆಯ ಯಜಮಾನರ ಉದ್ಯೋಗ (ತಾರುಣ್ಯದಲ್ಲಿ ೧೧- ೧೮ವರ್ಷಗಳು) Occupation of the head of the household (At adolescence 11-18 years)	ದಯವಿಟ್ಟು ತಿಳಿಸಿ Please specify
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ಎಳೆಯ ಪ್ರೌಢಾವಸ್ಥೆಯಲ್ಲಿ (೧೯-೩೫ ವರ್ಷಗಳು) At young adulthood (19-35 years)

E1C. ವಾಸದ ವಲಯ Area of residence	ಹಳ್ಳಿ Rural	<input type="checkbox"/> 1	ನಗರ ಸುತ್ತ Peri-urban	<input type="checkbox"/> 2	ನಗರ Urban	<input type="checkbox"/> 3
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E2C. ನೀವು ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಆ ವಲಯದಲ್ಲಿ ವಾಸಿಸಿದ್ದೀರಿ? For how many years did you live in the area?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E3C. ಅದು ಯಾವ ತರಹದ ಮನೆಯಾಗಿತ್ತು? What was the type of house?	ಕಚ್ಚು Kuccha	<input type="checkbox"/> 1	ಮಧ್ಯಮ Semi-pucca	<input type="checkbox"/> 2	ಪಕ್ಕ Pucca	<input type="checkbox"/> 3
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E4C. ಆ ಮನೆ ನಿಮ್ಮ ಸ್ವಂತದ್ದಾ ಅಥವಾ ಬಾಡಿಗೆಯದಾ? Was the house your own or rented?	ಬಾಡಿಗೆ Rented	<input type="checkbox"/> 1	ಸ್ವಂತ Own	<input type="checkbox"/> 2
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E5C. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಜನ ವಾಸಿಸುತ್ತಿದ್ದೀರಿ? How many people resided in the house?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E6C. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಕೋಣೆಗಳಿದ್ದವು? How many rooms were present in the house?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E7C. ಅಡುಗೆ ಮಾಡಲು ಬಳಸುತ್ತಿದ್ದ ಇಂಧನ ಶಕ್ತಿ ಯಾವುದು? What was the energy source for cooking?	ಕಟ್ಟಿಗೆ Wood	<input type="checkbox"/> 1	ಇದ್ದಲು Charcoal	<input type="checkbox"/> 2	ಜೈವಿಕ ಅನಿಲ Biogas	<input type="checkbox"/> 3	ಸೂರ್ಯನ ಶಕ್ತಿ Solar	<input type="checkbox"/> 4
	ವಿದ್ಯುಚ್ಛಕ್ತಿ Electricity	<input type="checkbox"/> 5	ಅಡುಗೆ ಅನಿಲ LPG	<input type="checkbox"/> 6	ಇತರೆ Others	<input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify	

E8C. ಕುಡಿಯುವ ನೀರಿನ ಲಭ್ಯತೆ Availability of drinking water	೫ ಕಿ.ಮಿ.ಗಿಂತಲೂ ದೂರ More than 5km away	<input type="checkbox"/> 1	೫ ಕಿ.ಮಿ. ಗಿಂತಲೂ ಕಡಿಮೆ ದೂರದಲ್ಲಿ Within 5 km	<input type="checkbox"/> 2	ಮನೆಯಲ್ಲಿಯೇ Inside the house	<input type="checkbox"/> 3
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E9C. ಶೌಚಾಲಯದ ವಸತಿ Access to toilet facility	ಇಲ್ಲ None	<input type="checkbox"/> 1	ಮನೆಯಿಂದ ಹೊರಗೆ Outside the house	<input type="checkbox"/> 2	ಮನೆಯೊಳಗೆ Inside the house	<input type="checkbox"/> 3
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ನಂತರದ ಪ್ರೌಢಾವಸ್ಥೆಯಲ್ಲಿ (೩೫ ವರ್ಷಗಳ ನಂತರ) **At late adulthood (more than 35 years)**

E1d. ವಾಸದ ವಲಯ Area of residence	ಹಳ್ಳಿ Rural	<input type="checkbox"/> 1	ನಗರ ಸುತ್ತ Peri-urban	<input type="checkbox"/> 2	ನಗರ Urban	<input type="checkbox"/> 3
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E2d. ನೀವು ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಆ ವಲಯದಲ್ಲಿ ವಾಸಿಸಿದ್ದೀರಿ? For how many years did you live in the area?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E3d. ಅದು ಯಾವ ತರಹದ ಮನೆಯಾಗಿತ್ತು? What was the type of house?	ಕಚ್ಚು Kuccha	<input type="checkbox"/> 1	ಮಧ್ಯಮ Semi-pucca	<input type="checkbox"/> 2	ಪಕ್ಕು Pucca	<input type="checkbox"/> 3
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E4d. ಆ ಮನೆ ನಿಮ್ಮ ಸ್ವಂತದ್ದಾ ಅಥವಾ ಬಾಡಿಗೆಯದಾ? Was the house your own or rented?	ಬಾಡಿಗೆ Rented	<input type="checkbox"/> 1	ಸ್ವಂತ Own	<input type="checkbox"/> 2
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E5d. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಜನ ವಾಸಿಸುತ್ತಿದ್ದೀರಿ? How many people resided in the house?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E6d. ಆ ಮನೆಯಲ್ಲಿ ಎಷ್ಟು ಕೋಣೆಗಳಿದ್ದವು? How many rooms were present in the house?	ಸಂಖ್ಯೆ Number	<input type="text"/>	<input type="text"/>
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E7d. ಅಡುಗೆ ಮಾಡಲು ಬಳಸುತ್ತಿದ್ದ ಇಂಧನ ಶಕ್ತಿ ಯಾವುದು? What was the energy source for cooking?	ಕಟ್ಟಿಗೆ Wood	<input type="checkbox"/> 1	ಇದ್ದಲು Charcoal	<input type="checkbox"/> 2	ಜೈವಿಕ ಅನಿಲ Biogas	<input type="checkbox"/> 3	ಸೂರ್ಯನ ಶಕ್ತಿ Solar	<input type="checkbox"/> 4
	ವಿದ್ಯುಚ್ಛಕ್ತಿ Electricity	<input type="checkbox"/> 5	ಅಡುಗೆ ಅನಿಲ LPG	<input type="checkbox"/> 6	ಇತರೆ Others	<input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify	

E8d. ಕುಡಿಯುವ ನೀರಿನ ಲಭ್ಯತೆ Availability of drinking water	೫ ಕಿ.ಮಿ.ಗಿಂತಲೂ ದೂರ More than 5km away	<input type="checkbox"/> 1	೫ ಕಿ.ಮಿ. ಗಿಂತಲೂ ಕಡಿಮೆ ದೂರದಲ್ಲಿ Within 5 km	<input type="checkbox"/> 2	ಮನೆಯಲ್ಲಿಯೇ Inside the house	<input type="checkbox"/> 3
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E9d. ಶೌಚಾಲಯದ ವಸತಿ Access to toilet facility	ಇಲ್ಲ None	<input type="checkbox"/> 1	ಮನೆಯಿಂದ ಹೊರಗೆ Outside the house	<input type="checkbox"/> 2	ಮನೆಯೊಳಗೆ Inside the house	<input type="checkbox"/> 3
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ಭಾಗ ೬. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ಧೂಮಪಾನದ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿವೆ **PART VI. The following questions ask about**

F1a. ನೀವು ಮೊದಲು ಯಾವುದನ್ನು ಸೇದುತ್ತಿದ್ದಿರಿ? What did you smoke initially?	ಬೀಡಿ <input type="checkbox"/> 1 Beedi	ಫಿಲ್ಟರ್ ಇಲ್ಲದ ಸಿಗರೇಟು <input type="checkbox"/> 2 Unfiltered cigarette	ಫಿಲ್ಟರ್ ಇದ್ದ ಸಿಗರೇಟು <input type="checkbox"/> 3 Filtered cigarette
	ಸಿಗಾರ್ <input type="checkbox"/> 4 Cigar	ಇತರೆ <input type="checkbox"/> 5 Other	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
F2a. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸೇದುತ್ತಿದ್ದಿರಿ? How many did you smoke on a usual day?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F3a. ನೀವು ಎಷ್ಟು ಸಲ ಸೇದುತ್ತಿದ್ದಿರಿ? How frequently did you smoke?	ಅಪರೂಪವಾಗಿ <input type="checkbox"/> 1 Rarely	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು <input type="checkbox"/> 2 1-3 days a month	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು <input type="checkbox"/> 3 1-2 days a Week
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು <input type="checkbox"/> 4 3-5 days a week		ಪ್ರತಿದಿನ <input type="checkbox"/> 5 Everyday
F4a. ಇದೇ ರೀತಿ ಎಷ್ಟು ವರ್ಷಗಳು ಸೇದುತ್ತಿದ್ದಿರಿ? For how many years did you smoke the same quantity?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F5a. ಸೇದುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in smoking habit?	ಇಲ್ಲ <input type="checkbox"/> 1 No	ಹೌದು <input type="checkbox"/> 2 Yes	

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ:

If yes, please answer the following questions:

F1b. ನೀವು ಯಾವುದನ್ನು ಸೇದುತ್ತಿದ್ದಿರಿ? What did you smoke?	ಬೀಡಿ <input type="checkbox"/> 1 Beedi	ಫಿಲ್ಟರ್ ಇಲ್ಲದ ಸಿಗರೇಟು <input type="checkbox"/> 2 Unfiltered cigarette	ಫಿಲ್ಟರ್ ಇದ್ದ ಸಿಗರೇಟು <input type="checkbox"/> 3 Filtered cigarette
	ಸಿಗಾರ್ <input type="checkbox"/> 4 Cigar	ಇತರೆ <input type="checkbox"/> 5 Other	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
F2b. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸೇದುತ್ತಿದ್ದಿರಿ? How many did you smoke on a usual day?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F3b. ನೀವು ಎಷ್ಟು ಸಲ ಸೇದುತ್ತಿದ್ದಿರಿ? How frequently did you smoke?	ಅಪರೂಪವಾಗಿ <input type="checkbox"/> 1 Rarely	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು <input type="checkbox"/> 2 1-3 days a month	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು <input type="checkbox"/> 3 1-2 days a Week
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು <input type="checkbox"/> 4 3-5 days a week		ಪ್ರತಿದಿನ <input type="checkbox"/> 5 Everyday
F4b. ಇದೇ ರೀತಿ ಎಷ್ಟು ವರ್ಷಗಳು ಸೇದುತ್ತಿದ್ದಿರಿ? For how many years did you smoke the same quantity?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F5b. ಸೇದುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in smoking habit?	ಇಲ್ಲ <input type="checkbox"/> 1 No	ಹೌದು <input type="checkbox"/> 2 Yes	

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ:			
If yes, please answer the following questions:			
F1c. ನೀವು ಯಾವುದನ್ನು ಸೇದುತ್ತಿದ್ದಿರಿ? What did you smoke?	ಬೀಡಿ <input type="checkbox"/> 1 Beedi	ಫಿಲ್ಟರ್ ಇಲ್ಲದ ಸಿಗರೇಟು <input type="checkbox"/> 2 Unfiltered cigarette	ಫಿಲ್ಟರ್ ಇದ್ದ ಸಿಗರೇಟು <input type="checkbox"/> 3 Filtered cigarette
	ಸಿಗಾರ್ <input type="checkbox"/> 4 Cigar	ಇತರೆ <input type="checkbox"/> 5 Other	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
F2c. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸೇದುತ್ತಿದ್ದಿರಿ? How many did you smoke on a usual day?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F3c. ನೀವು ಎಷ್ಟು ಸಲ ಸೇದುತ್ತಿದ್ದಿರಿ? How frequently did you smoke?	ಅಪರೂಪವಾಗಿ <input type="checkbox"/> 1 Rarely	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು <input type="checkbox"/> 2 1-3 days a month	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು <input type="checkbox"/> 3 1-2 days a Week
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು <input type="checkbox"/> 4 3-5 days a week		ಪ್ರತಿದಿನ <input type="checkbox"/> 5 Everyday
F4c. ಇದೇ ರೀತಿ ಎಷ್ಟು ವರ್ಷಗಳು ಸೇದುತ್ತಿದ್ದಿರಿ? For how many years did you smoke the same quantity?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F5c. ಸೇರುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in smoking habit?		ಇಲ್ಲ <input type="checkbox"/> 1 No	ಹೌದು <input type="checkbox"/> 2 Yes

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ:			
If yes, please answer the following questions:			
F1d. ನೀವು ಯಾವುದನ್ನು ಸೇದುತ್ತಿದ್ದಿರಿ? What did you smoke?	ಬೀಡಿ <input type="checkbox"/> 1 Beedi	ಫಿಲ್ಟರ್ ಇಲ್ಲದ ಸಿಗರೇಟು <input type="checkbox"/> 2 Unfiltered cigarette	ಫಿಲ್ಟರ್ ಇದ್ದ ಸಿಗರೇಟು <input type="checkbox"/> 3 Filtered cigarette
	ಸಿಗಾರ್ <input type="checkbox"/> 4 Cigar	ಇತರೆ <input type="checkbox"/> 5 Other	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
F2d. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸೇದುತ್ತಿದ್ದಿರಿ? How many did you smoke on a usual day?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F3d. ನೀವು ಎಷ್ಟು ಸಲ ಸೇದುತ್ತಿದ್ದಿರಿ? How frequently did you smoke?	ಅಪರೂಪವಾಗಿ <input type="checkbox"/> 1 Rarely	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು <input type="checkbox"/> 2 1-3 days a month	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು <input type="checkbox"/> 3 1-2 days a Week
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು <input type="checkbox"/> 4 3-5 days a week		ಪ್ರತಿದಿನ <input type="checkbox"/> 5 Everyday
F4d. ಇದೇ ರೀತಿ ಎಷ್ಟು ವರ್ಷಗಳು ಸೇದುತ್ತಿದ್ದಿರಿ? For how many years did you smoke the same quantity?			ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
F5d. ಸೇರುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in smoking habit?		ಇಲ್ಲ <input type="checkbox"/> 1 No	ಹೌದು <input type="checkbox"/> 2 Yes

ಭಾಗ ೭. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ತಂಬಾಕು ಸೇವನೆಯ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿದೆ. **PART VII. The following questions ask about**

G1a. ನಿಮ್ಮ ಅಭ್ಯಾಸ ಶುರುವಾದಾಗ ಏನನ್ನು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What did you chew when you started with the habit?	ಬಿಡಿ ತಂಬಾಕು ಎಲೆಗಳು Loose tobacco leaves <input type="checkbox"/> 1	ಪಾನ್ ಮಸಾಲ Panmasala <input type="checkbox"/> 2	ಗುಟ್ಟು Gutkha <input type="checkbox"/> 3
	ಮಾವ Mawa <input type="checkbox"/> 4	ಇತರೆ Other <input type="checkbox"/> 5	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify

G2a. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸಲ ತಂಬಾಕು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many times did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G3a. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

G4a. ಪ್ರತಿಸಲ ಎಷ್ಟು ಹೊತ್ತು ತಂಬಾಕನ್ನು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	<input type="text"/> <input type="text"/> Min	ಘಂ <input type="text"/> <input type="text"/> Hrs
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G5a. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಪ್ಯಾಕೆಟ್ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many packets of tobacco did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G6a. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ತಂಬಾಕನ್ನು ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the tobacco?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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G7a. ಅಗದೆ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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G8a. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ತಂಬಾಕನ್ನು ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep tobacco in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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G9a. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ತಂಬಾಕನ್ನು ಸೇವಿಸಿದಿರಿ? For how many years did you chew the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G10a. ತಂಬಾಕು ಸೇವನೆಯ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಹೌದು ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

G1b. ನಿಮ್ಮ ಏನನ್ನು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What did you chew?	ಬಿಡಿ ತಂಬಾಕು ಎಲೆಗಳು Loose tobacco leaves <input type="checkbox"/> 1	ಪಾನ್ ಮಸಾಲ Panmasala <input type="checkbox"/> 2	ಗುಟ್ಟು Gutkha <input type="checkbox"/> 3
	ಮಾವ Mawa <input type="checkbox"/> 4	ಇತರೆ Other <input type="checkbox"/> 5	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify

G2b. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸಲ ತಂಬಾಕು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many times did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G3b. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧-೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

G4b. ಪ್ರತಿಸಲ ಎಷ್ಟು ಹೊತ್ತು ತಂಬಾಕನ್ನು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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G5b. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಪ್ಯಾಕೆಟ್ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many packets of tobacco did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G6b. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ತಂಬಾಕನ್ನು ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the tobacco?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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G7b. ಅಗದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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G8b. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ತಂಬಾಕನ್ನು ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep tobacco in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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G9b. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ತಂಬಾಕನ್ನು ಸೇವಿಸಿದಿರಿ? For how many years did you chew the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G10b. ತಂಬಾಕು ಸೇವನೆಯ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಹೌದು ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

G1c. ನಿಮ್ಮ ಏನನ್ನು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What did you chew?	ಬಿಡಿ ತಂಬಾಕು ಎಲೆಗಳು Loose tobacco leaves <input type="checkbox"/> 1	ಪಾನ್ ಮಸಾಲ Panmasala <input type="checkbox"/> 2	ಗುಟ್ಟು Gutkha <input type="checkbox"/> 3
	ಮಾವ Mawa <input type="checkbox"/> 4	ಇತರೆ Other <input type="checkbox"/> 5	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify

G2c. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸಲ ತಂಬಾಕು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many times did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G3c. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

G4c. ಪ್ರತಿಸಲ ಎಷ್ಟು ಹೊತ್ತು ತಂಬಾಕನ್ನು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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G5c. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಪ್ಯಾಕೆಟ್ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many packets of tobacco did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G6c. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ತಂಬಾಕನ್ನು ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the tobacco?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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G7c. ಅಗೆದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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G8c. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ತಂಬಾಕನ್ನು ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep tobacco in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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G9c. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ತಂಬಾಕನ್ನು ಸೇವಿಸಿದಿರಿ? For how many years did you chew the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G10c. ತಂಬಾಕು ಸೇವನೆಯ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಹೌದು ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

G1d. ನಿಮ್ಮ ಏನನ್ನು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What did you chew?	ಬಿಡಿ ತಂಬಾಕು ಎಲೆಗಳು Loose tobacco leaves <input type="checkbox"/> 1	ಪಾನ್ ಮಸಾಲ Panmasala <input type="checkbox"/> 2	ಗುಟ್ಟು Gutkha <input type="checkbox"/> 3
	ಮಾವ Mawa <input type="checkbox"/> 4	ಇತರೆ Other <input type="checkbox"/> 5	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify

G2d. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಸಲ ತಂಬಾಕು ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many times did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G3d. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

G4d. ಪ್ರತಿಸಲ ಎಷ್ಟು ಹೊತ್ತು ತಂಬಾಕನ್ನು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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G5d. ಒಂದು ದಿನದಲ್ಲಿ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಪ್ಯಾಕೆಟ್ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How many packets of tobacco did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G6d. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ತಂಬಾಕನ್ನು ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the tobacco?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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G7d. ಅಗೆದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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G8d. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ತಂಬಾಕನ್ನು ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep tobacco in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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G9d. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ತಂಬಾಕನ್ನು ಸೇವಿಸಿದಿರಿ? For how many years did you chew the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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G10d. ತಂಬಾಕು ಸೇವನೆಯ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಭಾಗ ಲ. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ಎಲೆ-ಅಡಿಕೆ ಸೇವನೆ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿವೆ

PART VIII. The following questions ask about quid chewing

H1a. ನೀವು ಶುರು ಮಾಡಿದಾಗ ಎಲೆ-ಅಡಿಕೆಗೆ ಏನೇನು ಸೇರಿಸುತ್ತಿದ್ದಿರಿ? What did the quid contain when you started the habit?	ವಿಳೆದಲೆ Beetle leaf <input type="checkbox"/> 1	ಒಣ ಅಡಿಕೆ Arecanut dry <input type="checkbox"/> 2	ಹಸಿ ಅಡಿಕೆ Fresh Arecanut <input type="checkbox"/> 3	ಕಾಡು, ಕ್ರಯ, ಕಗ್ಗಲಿ, ಕಾಜು Catechu <input type="checkbox"/> 4
	ಸುಣ್ಣ Lime <input type="checkbox"/> 5	ತಂಬಾಕು Tobacco <input type="checkbox"/> 6	ಮಸಾಲೆ Spice <input type="checkbox"/> 7	ಸಿಹಿ Sweeteners <input type="checkbox"/> 8

H2a. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಎಲೆ-ಅಡಿಕೆ ಚೂರುಗಳನ್ನು ತಿನ್ನುತ್ತಿದ್ದಿರಿ? How many pieces of quid did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H3a. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

H4a. ಪ್ರತಿಸಲ ಸಲ ಎಷ್ಟು ಹೊತ್ತು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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H5a. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the quid?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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H6a. ಅಗೆದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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H7a. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ಎಲೆ-ಅಡಿಕೆ ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep quid in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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H8a. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸಿದಿರಿ? For how many years did you chew quid in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H9a. ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

H1b. ನೀವು ಶುರು ಮಾಡಿದಾಗ ಎಲೆ-ಅಡಿಕೆಗೆ ಏನೇನು ಸೇರಿಸುತ್ತಿದ್ದಿರಿ? What did the quid contain when you started the habit?	ವಿಳೆದಲೆ Beetle leaf <input type="checkbox"/> 1	ಒಣ ಅಡಿಕೆ Arecanut dry <input type="checkbox"/> 2	ಹಸಿ ಅಡಿಕೆ Fresh Arecanut <input type="checkbox"/> 3	ಕಾಡು, ಕ್ರೆಯ, ಕಗ್ಗಲಿ, ಕಾಜು Catechu <input type="checkbox"/> 4
	ಸುಣ್ಣ Lime <input type="checkbox"/> 5	ತಂಬಾಕು Tobacco <input type="checkbox"/> 6	ಮಸಾಲೆ Spice <input type="checkbox"/> 7	ಸಿಹಿ Sweeteners <input type="checkbox"/> 8

H2b. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಎಲೆ-ಅಡಿಕೆ ಚೂರುಗಳನ್ನು ತಿನ್ನುತ್ತಿದ್ದಿರಿ? How many pieces of quid did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H3b. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

H4b. ಪ್ರತಿಸಲ ಸಲ ಎಷ್ಟು ಹೊತ್ತು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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H5b. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the quid?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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H6b. ಅಗದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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H7b. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ಎಲೆ-ಅಡಿಕೆ ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep quid in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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H8b. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸಿದಿರಿ? For how many years did you chew quid in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H9b. ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

H1c. ನೀವು ಶುರು ಮಾಡಿದಾಗ ಎಲೆ-ಅಡಿಕೆಗೆ ಏನೇನು ಸೇರಿಸುತ್ತಿದ್ದಿರಿ? What did the quid contain when you started the habit?	ವಿಳೆದಲೆ Beetle leaf <input type="checkbox"/> 1	ಬಣ ಅಡಿಕೆ Arecanut dry <input type="checkbox"/> 2	ಹಸಿ ಅಡಿಕೆ Fresh Arecanut <input type="checkbox"/> 3	ಕಾಡು, ಕ್ರಯ, ಕಗ್ಗಲಿ, ಕಾಜು Catechu <input type="checkbox"/> 4
	ಸುಣ್ಣ Lime <input type="checkbox"/> 5	ತಂಬಾಕು Tobacco <input type="checkbox"/> 6	ಮಸಾಲೆ Spice <input type="checkbox"/> 7	ಸಿಹಿ Sweeteners <input type="checkbox"/> 8

H2c. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಎಲೆ-ಅಡಿಕೆ ಚೂರುಗಳನ್ನು ತಿನ್ನುತ್ತಿದ್ದಿರಿ? How many pieces of quid did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H3c. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

H4c. ಪ್ರತಿಸಲ ಸಲ ಎಷ್ಟು ಹೊತ್ತು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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H5c. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the quid?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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H6c. ಅಗೆದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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H7c. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ಎಲೆ-ಅಡಿಕೆ ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep quid in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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H8c. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸಿದಿರಿ? For how many years did you chew quid in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H9c. ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

H1d. ನೀವು ಶುರು ಮಾಡಿದಾಗ ಎಲೆ-ಅಡಿಕೆಗೆ ಏನೇನು ಸೇರಿಸುತ್ತಿದ್ದಿರಿ? What did the quid contain when you started the habit?	ವಿಳೆದಲೆ Beetle leaf <input type="checkbox"/> 1	ಒಣ ಅಡಿಕೆ Arecanut dry <input type="checkbox"/> 2	ಹಸಿ ಅಡಿಕೆ Fresh Arecanut <input type="checkbox"/> 3	ಕಾಡು, ಕ್ರಯ, ಕಗ್ಗಲಿ, ಕಾಜು Catechu <input type="checkbox"/> 4
	ಸುಣ್ಣ Lime <input type="checkbox"/> 5	ತಂಬಾಕು Tobacco <input type="checkbox"/> 6	ಮಸಾಲೆ Spice <input type="checkbox"/> 7	ಸಿಹಿ Sweeteners <input type="checkbox"/> 8

H2d. ಒಂದು ದಿನಕ್ಕೆ ಸಾಮಾನ್ಯವಾಗಿ ಎಷ್ಟು ಎಲೆ-ಅಡಿಕೆ ಚೂರುಗಳನ್ನು ತಿನ್ನುತ್ತಿದ್ದಿರಿ? How many pieces of quid did you chew on a usual day?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H3d. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you chew?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	

H4d. ಪ್ರತಿಸಲ ಸಲ ಎಷ್ಟು ಹೊತ್ತು ಅಗೆಯುತ್ತಿದ್ದಿರಿ? For how long did you chew everytime?	ನಿಮಿಷ <input type="text"/> <input type="text"/> Min	ಘಂಟೆ <input type="text"/> <input type="text"/> Hrs
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H5d. ಬಾಯಿಯ ಯಾವ ಭಾಗದಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಿ? Where in the mouth did you place the quid?	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
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H6d. ಅಗದ ನಂತರ ಏನು ಮಾಡುತ್ತಿದ್ದಿರಿ? What did you do after chewing?	ತಂಬಾಕು ಮತ್ತು ರಸವನ್ನು ಉಗುಳುವುದು Spit saliva and tobacco <input type="checkbox"/> 1	ರಸವನ್ನು ನುಂಗಿ ತಂಬಾಕನ್ನು ಉಗುಳುವುದು Swallow saliva and spit tobacco <input type="checkbox"/> 2	ರಸ ಮತ್ತು ತಂಬಾಕನ್ನು ನುಂಗುವುದು Swallow saliva and tobacco <input type="checkbox"/> 3
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H7d. ರಾತ್ರಿ ಮಲಗಿದಾಗಲೂ ಎಲೆ-ಅಡಿಕೆ ಬಾಯಿಯಲ್ಲಿ ಇಟ್ಟುಕೊಳ್ಳುತ್ತಿದ್ದಿರಾ? Did you keep quid in your mouth overnight?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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H8d. ಎಷ್ಟು ವರ್ಷಗಳು ಇದೇ ರೀತಿಯಲ್ಲಿ ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸಿದಿರಿ? For how many years did you chew quid in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number
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H9d. ಎಲೆ-ಅಡಿಕೆ ಸೇವಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in chewing habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2
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ಭಾಗ ೯. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ನಷ್ಟ ಸೇವನೆ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿದೆ **PART IX. The following questions ask about Snuff use**

11a. ನೀವು ಸಾಮಾನ್ಯವಾಗಿ ಒಂದು ದಿನದಲ್ಲಿ ಎಷ್ಟು ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? When you started the habit how many times did you use snuff on a usual day?	<input type="text"/> <input type="text"/> ಸಂಖ್ಯೆ Number
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12a. ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣದ (ಚಿಟಿಕೆ) ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? ಸಂಖ್ಯೆ What was the quantity (in pinches) of snuff that you used every time?	<input type="text"/> <input type="text"/> ಸಂಖ್ಯೆ Number
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13a. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? How frequently did you use snuff?	ಅಪರೂಪವಾಗಿ Rarely <input type="text"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="text"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="text"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="text"/> 4		ಪ್ರತಿದಿನ Everyday <input type="text"/> 5

14a. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿಯಲ್ಲಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? For how many years did you use snuff in the same quantity?	<input type="text"/> <input type="text"/> ಸಂಖ್ಯೆ Number
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15a. ನಷ್ಟ ಉಪಯೋಗಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in snuff use habit?	ಇಲ್ಲ No <input type="text"/> 1	ಹೌದು Yes <input type="text"/> 2
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ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

11b. ನೀವು ಸಾಮಾನ್ಯವಾಗಿ ಒಂದು ದಿನದಲ್ಲಿ ಎಷ್ಟು ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? How many times did you use snuff on a usual day?	<input type="text"/> <input type="text"/> ಸಂಖ್ಯೆ Number
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12b. ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣದ (ಚಿಟಿಕೆ) ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? ಸಂಖ್ಯೆ What was the quantity (in pinches) of snuff that you used every time?	<input type="text"/> <input type="text"/> ಸಂಖ್ಯೆ Number
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13b. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? How frequently did you use snuff?	ಅಪರೂಪವಾಗಿ Rarely <input type="text"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="text"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="text"/> 3
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="text"/> 4		ಪ್ರತಿದಿನ Everyday <input type="text"/> 5

14b. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿಯಲ್ಲಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? For how many years did you use snuff in the same quantity?	<input type="text"/> <input type="text"/> ಸಂಖ್ಯೆ Number
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15b. ನಷ್ಟ ಉಪಯೋಗಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in snuff use habit?	ಇಲ್ಲ No <input type="text"/> 1	ಹೌದು Yes <input type="text"/> 2
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ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

11c. ನೀವು ಸಾಮಾನ್ಯವಾಗಿ ಒಂದು ದಿನದಲ್ಲಿ ಎಷ್ಟು ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ?
How many times did you use snuff on a usual day?

ಸಂಖ್ಯೆ
Number

12c. ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣದ (ಚೀಟಿಕೆ) ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? ಸಂಖ್ಯೆ
What was the quantity (in pinches) of snuff that you used every time?

ಸಂಖ್ಯೆ
Number

13c. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ?
How frequently did you use snuff?

ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4		ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5

14c. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿಯಲ್ಲಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ?
For how many years did you use snuff in the same quantity?

ಸಂಖ್ಯೆ
Number

15c. ನಷ್ಟ ಉಪಯೋಗಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ?
Were there any changes in snuff use habit?

ಇಲ್ಲ 1 ಹೌದು 2
No Yes

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

11d. ನೀವು ಸಾಮಾನ್ಯವಾಗಿ ಒಂದು ದಿನದಲ್ಲಿ ಎಷ್ಟು ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ?
How many times did you use snuff on a usual day?

ಸಂಖ್ಯೆ
Number

12d. ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣದ (ಚೀಟಿಕೆ) ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? ಸಂಖ್ಯೆ
What was the quantity (in pinches) of snuff that you used every time?

ಸಂಖ್ಯೆ
Number

13d. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ?
How frequently did you use snuff?

ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3
ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4		ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5

14d. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿಯಲ್ಲಿ ನಷ್ಟ ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ?
For how many years did you use snuff in the same quantity?

ಸಂಖ್ಯೆ
Number

15d. ನಷ್ಟ ಉಪಯೋಗಿಸುವ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ?
Were there any changes in snuff use habit?

ಇಲ್ಲ 1 ಹೌದು 2
No Yes

ಭಾಗ ೧೦. ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ಮದ್ಯಪಾನದ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿವೆ **PART X. The following questions ask about alcohol**

J1a. ನೀವು ಅಭ್ಯಾಸ ಶುರು ಮಾಡಿದಾಗ ಏನನ್ನು ಕುಡಿಯುತ್ತಿದ್ದಿರಿ? What did you drink initially?	ಸಾರಾಯಿ Locally brewed arrack <input type="checkbox"/> 1	ನೀರ, ಸೇಂದಿ, ಹೆಂಡ Toddy <input type="checkbox"/> 2	ರಂ Rum <input type="checkbox"/> 3	ಬ್ರಾಂಡಿ Brandy <input type="checkbox"/> 4
	ಬೀರ್ Beer <input type="checkbox"/> 5	ವಿಸ್ಕಿ Whisky <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
J2a. ನೀವು ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣ (ಮಿ.ಲಿ) ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What was the quantity (in ml) that you consumed every time?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> Number			
J3a. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you drink alcohol?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3	
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5		
J4a. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿ ಮದ್ಯಪಾನ ಮಾಡುತ್ತಿದ್ದಿರಿ? For how many years did you drink alcohol in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number			
J5a. ಮದ್ಯಪಾನ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in alcohol drinking habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2		

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

J1b. ನೀವು ಏನನ್ನು ಕುಡಿಯುತ್ತಿದ್ದಿರಿ? What did you drink?	ಸಾರಾಯಿ Locally brewed arrack <input type="checkbox"/> 1	ನೀರ, ಸೇಂದಿ, ಹೆಂಡ Toddy <input type="checkbox"/> 2	ರಂ Rum <input type="checkbox"/> 3	ಬ್ರಾಂಡಿ Brandy <input type="checkbox"/> 4
	ಬೀರ್ Beer <input type="checkbox"/> 5	ವಿಸ್ಕಿ Whisky <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
J2b. ನೀವು ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣ (ಮಿ.ಲಿ) ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What was the quantity (in ml) that you consumed every time?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> Number			
J3b. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you drink alcohol?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3	
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4	ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5		
J4b. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿ ಮದ್ಯಪಾನ ಮಾಡುತ್ತಿದ್ದಿರಿ? For how many years did you drink alcohol in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> Number			
J5b. ಮದ್ಯಪಾನ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in alcohol drinking habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2		

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

J1c. ನೀವು ಏನನ್ನು ಕುಡಿಯುತ್ತಿದ್ದಿರಿ? What did you drink?	ಸಾರಾಯಿ Locally brewed arrack <input type="checkbox"/> 1	ನೀರ, ಸೇಂದಿ, ಹೆಂಡ Toddy <input type="checkbox"/> 2	ರಂ Rum <input type="checkbox"/> 3	ಬ್ರಾಂಡಿ Brandy <input type="checkbox"/> 4
	ಬೀರ್ Beer <input type="checkbox"/> 5	ವಿಸ್ಕಿ Whisky <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
J2c. ನೀವು ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣ (ಮಿ.ಲಿ) ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What was the quantity (in ml) that you consumed every time?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>			Number
J3c. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you drink alcohol?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3	
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4		ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	
J4c. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿ ಮದ್ಯಪಾನ ಮಾಡುತ್ತಿದ್ದಿರಿ? For how many years did you drink alcohol in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/>			Number
J5c. ಮದ್ಯಪಾನ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in alcohol drinking habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2		

ಹೌದು, ಎಂದರೆ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳನ್ನು ಉತ್ತರಿಸಿ: **If yes, please answer the following questions:**

J1d. ನೀವು ಏನನ್ನು ಕುಡಿಯುತ್ತಿದ್ದಿರಿ? What did you drink?	ಸಾರಾಯಿ Locally brewed arrack <input type="checkbox"/> 1	ನೀರ, ಸೇಂದಿ, ಹೆಂಡ Toddy <input type="checkbox"/> 2	ರಂ Rum <input type="checkbox"/> 3	ಬ್ರಾಂಡಿ Brandy <input type="checkbox"/> 4
	ಬೀರ್ Beer <input type="checkbox"/> 5	ವಿಸ್ಕಿ Whisky <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
J2d. ನೀವು ಪ್ರತಿಸಲ ಎಷ್ಟು ಪ್ರಮಾಣ (ಮಿ.ಲಿ) ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? What was the quantity (in ml) that you consumed every time?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>			Number
J3d. ನೀವು ಎಷ್ಟು ಆವರ್ತಿ ಸೇವಿಸುತ್ತಿದ್ದಿರಿ? How frequently did you drink alcohol?	ಅಪರೂಪವಾಗಿ Rarely <input type="checkbox"/> 1	ತಿಂಗಳಲ್ಲಿ ೧-೩ ದಿನಗಳು 1-3 days a month <input type="checkbox"/> 2	ವಾರದಲ್ಲಿ ೧- ೨ ದಿನಗಳು 1-2 days a Week <input type="checkbox"/> 3	
	ವಾರದಲ್ಲಿ ೩-೫ ದಿನಗಳು 3-5 days a week <input type="checkbox"/> 4		ಪ್ರತಿದಿನ Everyday <input type="checkbox"/> 5	
J4d. ಎಷ್ಟು ವರ್ಷಗಳ ಕಾಲ ಇದೇ ರೀತಿ ಮದ್ಯಪಾನ ಮಾಡುತ್ತಿದ್ದಿರಿ? For how many years did you drink alcohol in the same quantity?	ಸಂಖ್ಯೆ <input type="text"/> <input type="text"/>			Number
J5d. ಮದ್ಯಪಾನ ಅಭ್ಯಾಸದಲ್ಲಿ ಏನಾದರೂ ಬದಲಾವಣೆ ಆಯಿತೇ? Were there any changes in alcohol drinking habit?	ಇಲ್ಲ No <input type="checkbox"/> 1	ಹೌದು Yes <input type="checkbox"/> 2		

PART XIa. The following questions ask about dietary intake at childhood (6-10 years)

ಪದಾರ್ಥ Items	ಆವರ್ತನೆ Frequency							
	Never	1-3 times a month	Once a week	2-4 times a week	Once a day	2-3 times a day	4-5 times a day	≥6 times a day
ಅನ್ನ Rice	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಗೋಧಿ Wheat	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ರಾಗಿ Ragi (cereal)	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಜೋಳ Jowar (cereal)	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಸೊಪ್ಪು Greens	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಎಲೆಕೋಸು ಮುಂತಾದ ತರಕಾರಿ Leafy veg	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕ್ಯಾರೆಟ್ Carrots	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಟೊಮೇಟೋ Tomatoes	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಗಡ್ಡೆಗಿಣಿಸು Tubers	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಪದವಲಕಾಯಿ, ಹಾಗಲಕಾಯಿ ಮುಂತಾದವು Gourds	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬೀನ್ಸ್ Beans	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಈರುಳ್ಳಿ Onions	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬೆಳ್ಳುಳ್ಳಿ Garlic	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕಾಳು-ಬೇಳೆ Pulses & grains	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಅರಿಶಿನ Turmeric	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬಿಸಿ ಚಹಾ Hot tea	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬಿಸಿ ಕಾಫಿ Hot coffee	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕೋಳಿ Chicken	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕುರಿ/ಮೇಕೆ Lamb	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಸುವಿನ ಮಾಂಸ Beef	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಂದಿ ಮಾಂಸ Pork	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೀನು Fish	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಸಮುದ್ರ ಆಹಾರ Sea food	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೊಟ್ಟೆ Eggs	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಾಲು Milk	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೊಸರು Curds	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>

PART XIb. Following questions ask about dietary intake at adolescence (11-18 years)

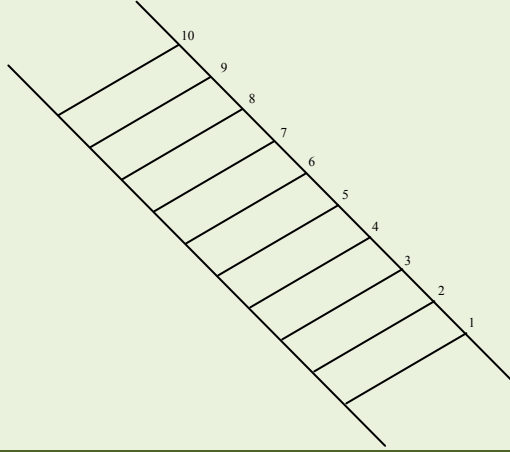
ಪದಾರ್ಥ Items	ಆವರ್ತನೆ Frequency							
	Never	1-3 times a month	Once a week	2-4 times a week	Once a day	2-3 times a day	4-5 times a day	≥6 times a day
ಅನ್ನ Rice	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಗೋಧಿ Wheat	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ರಾಗಿ Ragi (cereal)	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಜೋಳ Jowar (cereal)	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಸೊಪ್ಪು Greens	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಎಲೆಕೋಸು ಮುಂತಾದ ತರಕಾರಿ Leafy veg	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕ್ಯಾರೋಟ್ Carrots	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಟೊಮೇಟೋ Tomatoes	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಗಡ್ಡೆಗೊಣಸು Tubers	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಪಡವಲಕಾಯಿ, ಹಾಗಲಕಾಯಿ ಮುಂತಾದವು Gourds	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬೀನ್ಸ್ Beans	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಈರುಳ್ಳಿ Onions	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬೆಳ್ಳುಳ್ಳಿ Garlic	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕಾಳು-ಬೇಳೆ Pulses & grains	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಅರಿಶಿನ Turmeric	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬಿಸಿ ಚಹಾ Hot tea	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬಿಸಿ ಕಾಫಿ Hot coffee	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕೋಳಿ Chicken	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕುರಿ/ಮೇಕೆ Lamb	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಸುವಿನ ಮಾಂಸ Beef	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಂದಿ ಮಾಂಸ Pork	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೀನು Fish	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಸಮುದ್ರ ಆಹಾರ Sea food	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೊಟ್ಟೆ Eggs	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಾಲು Milk	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೊಸರು Curds	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>

PART XIc. Following questions ask about dietary intake at adulthood (≥19 years)

ಪದಾರ್ಥ Items	ಆವರ್ತನೆ Frequency							
	Never	1-3 times a month	Once a week	2-4 times a week	Once a day	2-3 times a day	4-5 times a day	≥6 times a day
ಅನ್ನ Rice	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಗೋಧಿ Wheat	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ರಾಗಿ Ragi (cereal)	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಜೋಳ Jowar (cereal)	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಸೊಪ್ಪು Greens	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಎಲೆಕೋಸು ಮುಂತಾದ ತರಕಾರಿ Leafy veg	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕ್ಯಾರೆಟ್ Carrots	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಟೊಮೇಟೋ Tomatoes	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಗಡ್ಡೆಗೇಣಸು Tubers	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಪದವಲಕಾಯಿ, ಹಾಗಲಕಾಯಿ ಮುಂತಾದವು Gourds	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬೀನ್ಸ್ Beans	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಈರುಳ್ಳಿ Onions	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬೆಳ್ಳುಳ್ಳಿ Garlic	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕಾಳು-ಬೇಳೆ Pulses & grains	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಅರಿಶಿನ Turmeric	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬಿಸಿ ಚಹಾ Hot tea	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಬಿಸಿ ಕಾಫಿ Hot coffee	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕೋಳಿ Chicken	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಕುರಿ/ಮೇಕೆ Lamb	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಸುವಿನ ಮಾಂಸ Beef	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಂದಿ ಮಾಂಸ Pork	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೀನು Fish	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಸಮುದ್ರ ಆಹಾರ Sea food	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೊಟ್ಟೆ Eggs	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಹಾಲು Milk	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>
ಮೊಸರು Curds	1 <input type="checkbox"/>	2 <input type="checkbox"/>	3 <input type="checkbox"/>	4 <input type="checkbox"/>	5 <input type="checkbox"/>	6 <input type="checkbox"/>	7 <input type="checkbox"/>	8 <input type="checkbox"/>

K1. ನೀವು ಸೇವಿಸುವ ಆಹಾರದ ಮಸಾಲೆ ಪ್ರಮಾಣವನ್ನು ಹೇಗೆ ಸೂಚಿಸುತ್ತೀರಿ?

How would you rate spiciness of food you consume?



K2. ಐದು ವರ್ಷಗಳ ಹಿಂದೆ ನಿಮ್ಮ ದೇಹದ ತೂಕ ಎಷ್ಟು?

What was your body weight 5 yrs ago?

ಕೆ.ಜಿ kg

K3. ಪಾದರಕ್ಷೆ ಇಲ್ಲದೆ ನಿಮ್ಮ ದೇಹದ ಎತ್ತರ ಎಷ್ಟು?

What is your height (in cms) without foot wear?

ಸೆಂ.ಮಿ.
cms

ಭಾಗ ೧೨ ಮುಂದಿನ ಪ್ರಶ್ನೆಗಳು ನಿಮ್ಮ ಬಾಯಿಯ ಸ್ವಚ್ಛತೆಯ ಅಭ್ಯಾಸಗಳ ಬಗ್ಗೆ ಕೇಳಲ್ಪಟ್ಟಿವೆ

PART XII. Following questions ask about oral hygiene practices

ಬಾಲ್ಯದಲ್ಲಿ At childhood (6-10 Yrs)

L1a. ನೀವು ಎಷ್ಟು ಆವೃತ್ತಿ ಹಲ್ಲು ತೊಳೆಯುತ್ತಿದ್ದೀರಿ? How frequently did you clean your teeth?	ದಿನಕ್ಕೆ ಒಂದು ಸಲಕ್ಕಿಂತಲೂ ಕಡಿಮೆ Less than once a day <input type="text"/> 1	ದಿನದಲ್ಲಿ ಒಂದು ಸಲ Once a day <input type="text"/> 2	ದಿನದಲ್ಲಿ ಎರಡು ಸಲ Twice a day <input type="text"/> 3	ದಿನದಲ್ಲಿ ಎರಡು ಸಲಕ್ಕಿಂತಲೂ ಹೆಚ್ಚು More than twice a day <input type="text"/> 4
	L2a. ನೀವು ಹೇಗೆ ಹಲ್ಲು ತೊಳೆಯುತ್ತಿದ್ದೀರಿ? How did you clean your teeth?	ಟೂತ್ ಬ್ರಶ್ Toothbrush <input type="text"/> 1	ಬೆರಳು Finger <input type="text"/> 2	ಕಡ್ಡಿ Twigs <input type="text"/> 3
L3a. ನೀವು ಹಲ್ಲು ತೊಳೆಯಲು ಏನನ್ನು ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? What did you use to clean your teeth?	ಟೂತ್ ಪೇಸ್ಟ್ Toothpaste <input type="text"/> 1	ಹಲ್ಲು ಪುಡಿ Tooth powder <input type="text"/> 2	ತಂಬಾಕು Tobacco <input type="text"/> 3	ಉಪ್ಪು Salt <input type="text"/> 4
	ಮರಳು Sand <input type="text"/> 5	ಇದ್ದಲು Charcoal <input type="text"/> 6	ಇತರೆ Others <input type="text"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
L4a. ನಿಮಗೆ ಬಾಯಿ ಮುಕ್ಕಳಿಸುವ ಅಭ್ಯಾಸ ಇದ್ದಿತೇ? Did you have the habit of rinsing mouth?	ಇಲ್ಲ No <input type="text"/> 1		ಹೌದು Yes <input type="text"/> 2	
L5a. ನೀವು ಬಾಯಿ ಮುಕ್ಕಳಿಸಲು ಏನನ್ನು ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? What did you use for rinsing your mouth?	ನೀರು Water <input type="text"/> 1	ಉಪ್ಪಿನ ನೀರು Salt water <input type="text"/> 2	ಗಿಡಮಾಲಿಕೆಯಿಂದ ಮಾಡಿದ್ದು Herbal mouth wash <input type="text"/> 3	
	ಮಾರುಕಟ್ಟೆಯಲ್ಲಿ ದೊರಕುವ Commercial mouthwash <input type="text"/> 4		ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify	

ಹದಿಹರೆಯದಲ್ಲಿ At adolescence (11-18 Yrs)

L1b. ನೀವು ಎಷ್ಟು ಆವೃತ್ತಿ ಹಲ್ಲು ತೊಳೆಯುತ್ತಿದ್ದೀರಿ? How frequently did you clean your teeth?	ದಿನಕ್ಕೆ ಒಂದು ಸಲಕ್ಕಿಂತಲೂ ಕಡಿಮೆ Less than once a day <input type="checkbox"/> 1	ದಿನದಲ್ಲಿ ಒಂದು ಸಲ Once a day <input type="checkbox"/> 2	ದಿನದಲ್ಲಿ ಎರಡು ಸಲ Twice a day <input type="checkbox"/> 3	ದಿನದಲ್ಲಿ ಎರಡು ಸಲಕ್ಕಿಂತಲೂ ಹೆಚ್ಚು More than twice a day <input type="checkbox"/> 4
L2b. ನೀವು ಹೇಗೆ ಹಲ್ಲು ತೊಳೆಯುತ್ತಿದ್ದೀರಿ? How did you clean your teeth?	ಟೂತ್ ಬ್ರಶ್ Toothbrush <input type="checkbox"/> 1	ಬೆರಳು Finger <input type="checkbox"/> 2	ಕಡ್ಡಿ Twigs <input type="checkbox"/> 3	ಇತರೆ ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Others please specify
L3b. ನೀವು ಹಲ್ಲು ತೊಳೆಯಲು ಏನನ್ನು ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? What did you use to clean your teeth?	ಟೂತ್ ಪೇಸ್ಟ್ Toothpaste <input type="checkbox"/> 1	ಹಲ್ಲು ಪುಡಿ Tooth powder <input type="checkbox"/> 2	ತಂಬಾಕು Tobacco <input type="checkbox"/> 3	ಉಪ್ಪು Salt <input type="checkbox"/> 4
	ಮರಳು Sand <input type="checkbox"/> 5	ಇದ್ದಲು Charcoal <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
L4b. ನಿಮಗೆ ಬಾಯಿ ಮುಕ್ಕಳಿಸುವ ಅಭ್ಯಾಸ ಇದ್ದಿತೇ? Did you have the habit of rinsing mouth?	ಇಲ್ಲ No <input type="checkbox"/> 1		ಹೌದು Yes <input type="checkbox"/> 2	
L5b. ನೀವು ಬಾಯಿ ಮುಕ್ಕಳಿಸಲು ಏನನ್ನು ಉಪಯೋಗಿಸುತ್ತಿದ್ದೀರಿ? What did you use for rinsing your mouth?	ನೀರು Water <input type="checkbox"/> 1	ಉಪ್ಪಿನ ನೀರು Salt water <input type="checkbox"/> 2	ಗಿಡಮೂಲಿಕೆಯಿಂದ ಮಾಡಿದ್ದು Herbal mouth wash <input type="checkbox"/> 3	
	ಮಾರುಕಟ್ಟೆಯಲ್ಲಿ ದೊರಕುವ Commercial mouthwash <input type="checkbox"/> 4		ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify	

ಪೌಢಾವಸ್ಥೆಯಲ್ಲಿ At adulthood (≥19 Yrs)

L1c. ನೀವು ಎಷ್ಟು ಆವೃತ್ತಿ ಹಲ್ಲು ತೊಳೆಯುತ್ತೀರಿ? How frequently do you clean your teeth?	ದಿನಕ್ಕೆ ಒಂದು ಸಲಕ್ಕಿಂತಲೂ ಕಡಿಮೆ Less than once a day <input type="checkbox"/> 1	ದಿನದಲ್ಲಿ ಒಂದು ಸಲ Once a day <input type="checkbox"/> 2	ದಿನದಲ್ಲಿ ಎರಡು ಸಲ Twice a day <input type="checkbox"/> 3	ದಿನದಲ್ಲಿ ಎರಡು ಸಲಕ್ಕಿಂತಲೂ ಹೆಚ್ಚು More than twice a day <input type="checkbox"/> 4
L2c. ನೀವು ಹೇಗೆ ಹಲ್ಲು ತೊಳೆಯುತ್ತೀರಿ? How do you clean your teeth?	ಟೂತ್ ಬ್ರಶ್ Toothbrush <input type="checkbox"/> 1	ಬೆರಳು Finger <input type="checkbox"/> 2	ಕಡ್ಡಿ Twigs <input type="checkbox"/> 3	ಇತರೆ ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Others please specify
L3c. ನೀವು ಹಲ್ಲು ತೊಳೆಯಲು ಏನನ್ನು ಉಪಯೋಗಿಸುತ್ತೀರಿ? What do you use to clean your teeth?	ಟೂತ್ ಪೇಸ್ಟ್ Toothpaste <input type="checkbox"/> 1	ಹಲ್ಲು ಪುಡಿ Tooth powder <input type="checkbox"/> 2	ತಂಬಾಕು Tobacco <input type="checkbox"/> 3	ಉಪ್ಪು Salt <input type="checkbox"/> 4
	ಮರಳು Sand <input type="checkbox"/> 5	ಇದ್ದಲು Charcoal <input type="checkbox"/> 6	ಇತರೆ Others <input type="checkbox"/> 7	ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify
L4c. ನಿಮಗೆ ಬಾಯಿ ಮುಕ್ಕಳಿಸುವ ಅಭ್ಯಾಸ ಇದೆಯೇ? Do you have the habit of rinsing mouth?	ಇಲ್ಲ No <input type="checkbox"/> 1		ಹೌದು Yes <input type="checkbox"/> 2	
L5c. ನೀವು ಬಾಯಿ ಮುಕ್ಕಳಿಸಲು ಏನನ್ನು ಉಪಯೋಗಿಸುತ್ತೀರಿ? What do you use for rinsing your mouth?	ನೀರು Water <input type="checkbox"/> 1	ಉಪ್ಪಿನ ನೀರು Salt water <input type="checkbox"/> 2	ಗಿಡಮೂಲಿಕೆಯಿಂದ ಮಾಡಿದ್ದು Herbal mouth wash <input type="checkbox"/> 3	
	ಮಾರುಕಟ್ಟೆಯಲ್ಲಿ ದೊರಕುವ Commercial mouthwash <input type="checkbox"/> 4		ದಯವಿಟ್ಟು ಹೆಸರಿಸಿ Please specify	

M1. ನಿಮ್ಮ ಅನಿಸಿಕೆಯ ಪ್ರಕಾರ ನಿಮ್ಮ ಈ ಪರಿಸ್ಥಿತಿಗೆ ಕಾರಣವೇನು? What do you think has led to your present condition?

ನೀವು ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಭಾಗವಹಿಸಿದ ಕೃತಜ್ಞತೆಗಳನ್ನು ವ್ಯಕ್ತಪಡಿಸುವುದು.

ನಿಮ್ಮ ಸಹಾಯ ಬಹಳ ಮೆಚ್ಚುವಂತಹುದು ಮತ್ತು ಇದು ಜನರಲ್ಲಿ ಬಾಯಿಯ ಆರೋಗ್ಯಕ್ಕೆ ಮತ್ತು ಬಾಯಿಯ ಕ್ಯಾನ್ಸರ್ ಗೆ ಸಂಬಂಧಿಸಿದಂತೆ ಅದರ ಮೇಲೆ ಪ್ರಭಾವ ಬೀರುವ ಅಂಶಗಳನ್ನು ಅರ್ಥಮಾಡಿಕೊಳ್ಳಲು ಅಮೂಲ್ಯವಾದ ಕೊಡುಗೆಯಾಗಿದೆ.

Thank you for participating in this study.

Your assistance is greatly appreciated and will make a valuable contribution to understanding the role that behavioural and social factors make in explaining differences in oral cancer outcomes.

4. Oral examination and record abstraction forms

Case

Control

Friend
Relative
Neighbour

Prevalent

Incident

NOTES:

Form for record extraction

Hospital name: _____

Date of record extraction: _____

Patient ID: _____

Age: _____

Gender: _____

Address: _____

----- (To be detached at this point) -----

Date of diagnosis: _____ Participant ID _____

Histopathological diagnosis: _____

Type of oral cancer lesion: _____

TNM staging: _____

Medical conditions: _____

Treatment provided: _____

5. Manual

ORAL CANCER – A LIFE COURSE APPROACH

Epidemiological Oral Examination Protocol

(Modified from NSAOH Guidelines and PNG National Oral health Survey)

2011-12

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1 Introduction

1.1 Aim of the study

This study will be conducted with the aim to assess the strength of association between oral cancer and risk factors like socioeconomic conditions, adverse health behaviours and diet throughout life course in an Indian population.

1.2 Methods

This is an unmatched case control study conducted in cancer hospitals in Karnataka state, India. The data collection methods include conducting an interview, oral examination and record extraction.

The study participants (SP) in this study will include cases and controls. SPs will be interviewed directly on socioeconomic conditions, health behaviour, diet and oral hygiene habits at various stages in life. On completion of the interview the SP will be requested to undergo oral epidemiological examination- to record details of oral cancer lesion, presence of other mucosal lesions, tooth loss and oral hygiene status by a dental clinician using standardized epidemiological criteria. The dental clinician will be a qualified and registered dentist in India who will be trained and calibrated in survey procedures. Examination will take approximately 20 minutes. Dental mirrors and periodontal (gum) probes will be used for oral examination. SP reporting presence of any condition/disease contraindicating for periodontal probing will be excluded. Examinations will be conducted in the cancer hospital. No X-Rays will be taken and no treatment will be provided as a part of the study. SPs will be informed of any conditions that in the examiner's opinion require a dentist's diagnosis and or treatment and advice of its urgency.

The order in which the procedures followed will be:

1. Obtaining informed consent
2. Conducting interview
3. Oral examination
4. Record extraction

1.3 Questionnaire completion (Direct interview)

The semi-structured questionnaire designed for the study will seek information from the SPs about the socioeconomic conditions, living conditions, behaviour and diet throughout their life.

1.4 Purpose of this manual

This manual describes the tasks that the staff involved will be expected to perform during the study. It mainly includes oral examination procedures, diagnostic coding systems and diagnostic criteria to be used in this study.

1.5 Conventions used in this Manual

Study participants refer to both cases and controls in this manual.

Each section is described in three subsections:

- Clinical procedures
- Diagnostic codes
- Diagnostic criteria

2 Protection of human subjects and ethical conduct of research

This section is an excerpt from “National Statement on Ethical Conduct in Research Involving Humans” published by the National Health and Medical Research Council (Commonwealth of Australia 1999)

The primary purpose of this ‘Statement of ethical principles and associated guidelines for research involving humans’ is the protection of the welfare and rights of participants in research. The ethical and legal responsibilities which researchers have towards participants in research reflect basic ethical values of integrity, respect for persons, beneficence and justice.

2.1 Integrity, respect for persons, beneficence and justice

2.1.1 The guiding value for researchers is integrity, which is expressed in a commitment to the search for knowledge, to recognised principles of research conduct and in the honest and ethical conduct of research and dissemination and communication of results.

2.1.2 When conducting research involving humans, the guiding ethical principle for researchers is respect for persons which is expressed as regard for the welfare, rights, beliefs, perceptions, customs and cultural heritage, both individual and collective, of persons involved in research.

2.1.3 In research involving humans, the ethical principle of beneficence is expressed in researchers’ responsibility to minimise risks of harm or discomfort to participants in research projects.

Each research protocol must be designed to ensure that respect for the dignity and well-being of the participants takes precedence over the expected benefits to knowledge.

The ethical value of justice requires that, within a population, there is a fair distribution of the benefits and burdens of participation in research and, for any research participant, a balance of burdens and benefits. Accordingly, a researcher must:

- (a) avoid imposing on particular groups, who are likely to be subject to over researching, an unfair burden of participation in research;
- (b) design research so that the selection, recruitment, exclusion and inclusion of research participants is fair; and
- (c) not discriminate in the selection and recruitment of actual and future participants by including or excluding them on the grounds of race, age, sex, disability or religious or spiritual beliefs except where the exclusion or inclusion of particular groups is essential to the purpose of the research.

2.1.4 The proportion of burdens to benefits for any research participant will vary. In clinical research, where patient care is combined with intent to contribute to knowledge, the risks of participation must be balanced by the possibility of intended benefits for the participants. In other research involving humans that is undertaken solely to contribute to knowledge, the absence of intended benefits to a participant should justly be balanced by the absence of all but minimal risk.

2.2 Consent

2.2.1 Before research is undertaken, whether involving individuals or collectivities, the consent of the participants must be obtained, except in specific circumstances defined elsewhere in this Statement.

The ethical and legal requirements of consent have two aspects: the provision of information and the capacity to make a voluntary choice. So as to conform with ethical and legal requirements, obtaining consent should involve:

- (a) provision to participants, at their level of comprehension, of information about the purpose, methods, demands, risks, inconveniences, discomforts, and possible outcomes of the research (including the likelihood and form of publication of research results); and

(b) the exercise of a voluntary choice to participate.

Where a participant lacks competence to consent, a person with lawful authority to decide for that participant must be provided with that information and exercise that choice.

2.2.2 A person may refuse to participate in a research project and need give no reasons nor justification for that decision.

2.2.3 Where consent to participate is required, research must be so designed that each participant's consent is clearly established, whether by a signed form, return of a survey, recorded agreement for interview or other sufficient means.

In some circumstances and some communities, consent is not only a matter of individual agreement, but involves other properly interested parties, such as formally constituted bodies of various kinds, collectivities or community elders. In such cases the researcher needs to obtain the consent of all properly interested parties before beginning the research.

2.2.4 The consent of a person to participate in research must not be subject to any coercion, or to any inducement or influence which could impair its voluntary character.

2.2.5 It is ethically acceptable to conduct certain types of research without obtaining consent from participants in some circumstances, for example, the use of de-identified data in epidemiological research, observational research in public places, or the use of anonymous surveys.

2.2.6 A participant must be free at any time to withdraw consent to further involvement in the research. If any consequences may arise from such withdrawal, advice must be given to participants about these before consent to involvement in the research is obtained.

3 Armamentarium and infection control

The armamentarium for conducting the survey is as follows:

3.1 Paperwork and office supplies

This Examination protocol, including a sheet of codes

Pens, indelible marker pen

- Extra information sheets
- Consent forms
- Folders for completed documents
- Clip board

3.2 Examination instruments

- Stainless steel mouth mirror
- PCP2 probe
- Tweezers
- Chip syringes

3.3 Examination supplies

- Portable lighting and recharging equipment
- Examiner's mask, gloves, eye protection
- Gauze, cotton rolls
- Saline
- Cotton swabs
- Infection control supplies (containers, trays, bags, detergent etc)

3.4 Infection control guidelines

The Infection Control procedures conform to "Infection control guidelines for the prevention of transmission of infectious diseases in the health care setting" amended 19 September 2002 (accessible at

http://www.health.gov.au/pubhlth/strateg/communic/review/icg_pdf/icg_guide.pdf)

Generally, the Infection Control procedures must follow the State/Territory Infection Control Guidelines in every jurisdiction. This section provides general guidelines and guidelines which are specifically for particular equipment used in this survey. Standard precautions for infection control apply.

Standard precautions to be followed are

- Aseptic technique, including appropriate use of skin disinfectants
- Personal hygiene practices, particularly hand washing before and after patient contacts
- Use of personal protective equipment, which include gloves, masks and eye protection

- Appropriate handling and disposal of sharps and other clinical waste
- Appropriate reprocessing of reusable equipment and instruments, including appropriate use of disinfectants

3.5 Sterilisation of reusable instruments

Sterilisation of examination instruments (periodontal probes, tweezers, air syringe tips) are according to the guidelines for instrument sterilisation. Used instruments should be sterilised after the oral examination when and where applicable.

3.6 Transport of instruments

The probes, tweezers and chip syringes are to be bagged and sterilized together in the sterilisation facility.

Separate storage containers are to be used for consumables and non-consumables.

3.7 On site

The tables for instruments and consumables are wiped clean with detergent and wipes.

Instruments are opened only in the presence of the SP and placed on a green clean wiped instrument tray and then it is covered with clean paper towel. Instruments are picked up by gloved examiner as needed.

3.8 Infection control procedures

The dental examiner and recorder are responsible for the infection control procedures described in this section.

4 Selection of participants

The participants of this study will be selected from cancer hospitals and their referral centres in Karnataka state, India. These are the hospitals where most of the oral cancer cases are referred for treatment in the state. From each hospital cases and controls will be selected.

Cases will be those patients diagnosed with oral cancer attending cancer hospitals. Controls will be relatives/friends/neighbours accompanying the patients diagnosed with other cancers like breast cancer, prostate cancer, ovarian cancers, and lymphoma, to the same hospitals and during the same period of time. Other controls will include patients or their visitors attending hospitals not related to tobacco or alcohol.

[Note: prevalent cases include those diagnosed with oral cancer prior to the start of the study and incident cases include those diagnosed with oral cancer during the study period]

For prevalent cases, controls will be chosen based on their time of visit to the hospital accompanying other patients (who would have been diagnosed prior to the start of the study). For incident cases, controls will be selected from those who are visiting the hospital for the first time along with other incident cancer patients (being diagnosed during the study period).

Record all the subjects contacted and note if they have agreed or refused to participate.

5 Examination schedule

The outcome of the contact of cases and controls will be recorded on the examination schedule as complete or incomplete for interview, examination and record extraction.

The reasons may be recorded in the last column.

The schedule must be kept together with questionnaire and examination form.

6 Procedures before examination

6.1 Consent, interviews and scheduling of appointments

The potential participants will be explained about the procedures by providing verbal and written information. These patients/ family members will be given 24 hours time to hand over the consent forms to the administrative staff at their respective wards. Patients who have agreed to participate in the interview and examination will be approached at their convenient time after consulting the patients and family with the help of the administrative staff of the respective wards. Those visiting hospitals as out-patients will be interviewed and examined on the same day or during the next appointment.

Prior to their examination, subjects to be examined will be interviewed by the investigator on the factors which relate to oral health.

6.2 Duties of investigator

Prior to commencement of each session, the researcher is responsible for:

- Transporting equipment, instruments and supplies to the examination area
- Setting up the examination area
- Check all equipment, instruments and supplies

- Making sure enough supplies are available for the session. Sequence of procedures for each examination
- Welcoming SP and asking them to complete consent form.
- Finding and opening the SP's examination form

Conducting the examination (subject to SP's consent):

- Oral Mucosal Tissues Assessment and Tooth presence
- Oral hygiene index-Simplified
- Edentulism and denture use

Informing study participants of the findings of the oral examination.

7 Examination criteria

Clinical procedures

7.1 Oral Mucosa (WHO 1980)

Every subject will be assessed for mucosal lesions. Each observed lesion will be recorded by its location. There might be several lesions in one location or/and one lesion in several locations.

1 : Cancer

2 : Leukoplakia

3 : Erythroplakia

4 : Lichen planus

5 : Submucosal fibrosis

6: Candidiasis

7: Oral hairy leukoplakia

8: Necrotising gingivitis

8a: Necrotising periodontitis

9: Ulceration herpes, aphthous trauma

10: Cancum oris

11: Viral warts

12: Others

Using the mouth mirror and gauze to help retract tissues, visually examine the lips and intra-oral mucosa.

Lips: should be examined with the mouth both closed and open. Note the colour, texture and any surface abnormalities of the vermilion border.

Labial mucosa and sulcus: Examine visually the mandibular and maxillary vestibule and frenum with the mouth partially open. Observe the colour and any swelling of vestibular mucosa and gingiva.

Commissures, buccal mucosa and sulcus (upper and lower): Using mouth mirror as retractor and with the mouth wide open, examine the entire buccal mucosa extending from the commissures and back to the anterior tonsillar pillar. Note any change in pigmentation, colour, texture and mobility of the mucosa, make sure that the commissures are examined carefully and are not covered by the mouth mirror during retraction of the cheeks.

Alveolar ridges: Check from all sides (buccally, palatally, lingually).

Tongue: With the tongue at rest and mouth partially open inspect the dorsum of the tongue for any swelling, ulceration, coating or variation in size, colour or texture. Also, note any change in the pattern of the papillae covering the surface of the tongue. The SP should then protrude the tongue and the examiner should note any abnormality of mobility. With the aid of mouth mirror, inspect the margins of the tongue. Then observe the ventral surface.

If adequate precautions can be taken by the examiner, the tongue can be examined more efficiently by grasping the tip with a piece of gauze to assist full protrusion and to aid examination of the margins.

Floor of the mouth: With the tongue still elevated, inspect the floor of the mouth for swelling or other abnormalities.

Hard and soft palate: With the mouth wide open and the SP's head tilted backward, gently depress the base of the tongue with a mouth mirror. First inspect the hard then the soft palate.

Clinical criteria: (from WHO Guide to epidemiology and diagnosis of oral mucosal diseases and conditions)

7.1.1 Cancer: Malignant tumour (carcinoma)

The most important oral mucosal lesion is the carcinoma, in most cases a squamous cell carcinoma, because it may cause death if not treated at an early stage. The location of an oral carcinoma is often associated with various smoking and/or chewing habits involving tobacco and/or areca (betel) nut. Depending upon where the quid is kept, the carcinoma may be located in a buccal or labial sulcus. Reverse smoking is associated with carcinoma of the palate and posterior part of the dorsum of the tongue.

The carcinoma may develop in a white patch (an area of leukoplakia) or in a red area (an erythroplakia) but many carcinomas arise in an area of mucosa that previously appeared normal.

Despite the serious nature of the lesion, there may be little or no pain.

Except in some early and small lesions, there is usually induration - the tissue feels firm and thickened - either throughout the lesion or at the margins if there is ulceration. Where the tumour occurs on a mobile part of the mucosa, there may be fixation and loss of mobility because the tumour has involved the deeper tissues.

The appearance of the surface of the tumour is very variable: it may be relatively smooth and white or red, but commonly the surface is nodular or ulcerated and the ulcer may have a raised rolled margin. In the later stages there may be a soft fungating mass that bleeds readily. If the carcinoma arises on the lip, where the surface can become dry, there is often a crusted or scaly appearance or the surface can appear warty.

7.1.2 Leukoplakia

For the purpose of this guide, leukoplakia is defined as a white patch, or plaque, that cannot be characterized clinically or pathologically as any other disease.

These lesions are characterized by the presence of a white patch anywhere on the oral mucosa; they may vary from a quite small and circumscribed area to an extensive lesion involving a large area of mucosa. The appearance is variable; the surface may be smooth or wrinkled and sometimes smooth-surfaced lesions may be traversed by small cracks or fissures giving an appearance aptly likened to cracked mud. Lesions may be white, whitish-yellow or grey and some appear homogeneous, while others are nodular, showing white areas intermingled with red zones; this is often called a nodular (speckled) leukoplakia. In those lesions in which there is much epithelial hyperplasia, the affected mucosa may lose

some of its normal softness and flexibility

7.1.3 Erythroplakia

Whilst leukoplakia is a relatively common condition, erythroplakia is rare. In contrast to leukoplakia, erythroplakia is almost always associated with premalignant changes histologically and is therefore a most important precancerous lesion.

The term 'erythroplakia' is used analogously to leukoplakia to designate lesions of the oral mucosa that present as bright red velvety plaques which cannot be characterized clinically or pathologically as due to any other condition. Just as there are many oral lesions that present clinically as white patches on the mucosa, so there are a number of conditions that appear as red areas. These include some dermatoses, inflammatory conditions due to local infection, or a more general subacute or chronic stomatitis associated with the presence of dentures, tuberculosis, fungus infections and other conditions. Some red plaques prove to be early squamous cell carcinomas. The red patches that cannot be classified in any of these categories fall into the group of erythroplakias.

The lesions of erythroplakia are usually irregular in outline though well-defined and have a bright red velvety surface. Occasionally the surface is granular. If red areas are intermingled with white, the lesion should be classified under leukoplakia.

7.1.4 Lichen Planus

This disease commonly affects the oral mucosa and lesions may *occur* in the mouth in the absence of skin lesions. Whilst a number of reports have referred to cancer arising in the oral lesions of lichen planus, especially of the erosive or atrophic types, there remains considerable uncertainty about the risk of this occurrence.

Oral mucosal lesions are usually multiple and often have a symmetrical distribution. They commonly take the form of minute white papules that gradually enlarge and coalesce to form a reticular, annular or plaque pattern. A characteristic feature is the presence of slender white lines (Wickham's striae) radiating from the papules. In the reticular form there is a lace-like network of slightly raised grey-white lines, often interspersed with papules or rings. The plaque form maybe difficult to distinguish from leukoplakia, but in lichen planus there is usually no change in the flexibility of the affected mucosa.

7.1.5 Submucosal fibrosis

This condition, which is found almost exclusively among Indians and Pakistanis, is a slowly

progressive disease of unknown aetiology. There are several indications that oral submucous fibrosis predisposes to cancer; superimposed leukoplakias, occasionally of the speckled type, are often present and a considerable number of submucous fibrosis cases are associated with epithelial dysplasia.

The disease is characterized by the presence of palpable fibrous bands in the oral mucosa, ultimately leading to severe restriction of the movements of the mouth, including that of the tongue. On clinical examination, limitation of opening of the mouth may be obvious. In addition, the tongue may be small and exhibit very limited mobility and show a marked loss of papillae. In the earlier stages of the disease it will usually be possible to detect vertical fibrous bands in the cheek, which can be felt by running the blunt edge of the mouth mirror backwards and forwards along the cheek mucosa. The palate may appear abnormally pale and the uvula may be shrunken. Other characteristic clinical features of submucous fibrosis are loss of normal oral pigmentation and, as previously noted, there may be areas of leukoplakia.

7.1.6 Candidiasis

In several populations it has been found that about 50% of normal individuals are carriers of *Candida*. A variety of oral lesions are caused by the fungus *Candida albicans*. The term "candidiasis" is used when lesions are present. The disease is also known as "moniliasis" and "candidosis".

Acute candidiasis may be pseudomembranous or atrophic. The former, also known as thrush, consists of creamy, pearly-white or bluish-white patches which can be removed by gentle scraping. Thrush may occur in all areas of the oral mucosa, although the sites of predilection are the buccal mucosa, palate and tongue. The atrophic variety, a red and painful lesion, may occur during treatment with antibiotics. *Chronic* candidiasis may manifest itself in several forms. As persistent angular cheilitis, as denture stomatitis, as a median rhomboid glossitis like lesion and as a retrocommissural hyperplastic lesion. The latter may often resemble a leukoplakia.

7.1.7 Oral hairy leukoplakia

Hairy leukoplakia appears as white patches, nearly always on the lateral border (outside edges) of the tongue. The lesions usually have an irregular surface and may have hair-like

projections. While this condition may resemble that of candidiasis, hairy leukoplakia lesions cannot be wiped off. Occasionally candidiasis may superimpose on hairy leukoplakia.

7.1.8 Necrotising ulcerative gingivitis (ANUG)

The oral lesions are characterized by a necrosis at the tips of the interdental papillae and along the marginal gingivae. The ulcers are covered by a greyish-yellow pseudomembrane. The gingivae bleed very easily and are painful. There is a distinctive oral odour.

7.1.9 Necrotising periodontitis

A severe form of necrotising ulcerative gingivitis but associated with periodontal pocketing. Severe interdental and marginal necrosis is seen sometimes with exposed bone. Severe, deep pain is present and it may affect single or multiple sites.

7.1.10 Ulceration (aphthous, herpetic, traumatic)

Ulceration is defined as a break of the oral mucosa. The clinical appearance of ulcerations shows great variation. The most common form is minor aphthae. There are typically 1–4 ulcers in each attack. These are usually confined to the non-keratinised parts of the mucosa. The ulcers are shallow, but painful.

Herpetic ulcers are characterised by a large number of small shallow ulcers occurring in any part of the mucosa. Although each individual ulcer may not exceed 2 mm in diameter, groups of ulcers may coalesce to form compound ulcers with irregular outlines. Herpetic ulcers are more commonly seen on the hard palate and attached gingiva. They appear as solitary ulcers or clusters, frequently found on vermilion border of the lip.

7.1.11 Cancrum oris

The etiology of cancrum oris is unknown, but the bacteriological and histological findings are like those in acute necrotizing gingivitis. However, cancrum oris is not confined to the gingiva: the necrosis is relentlessly progressive and ultimately there may be massive destruction of the mouth, jaws and face. Diseases such as measles, smallpox, malaria, acute herpetic gingivostomatitis and protein malnutrition maybe associated or predisposing factors. Cancrum oris, which is commonly preceded by an acute necrotizing gingivitis, begins as an ulceration of the oral mucous membrane which extends outwards and causes a well demarcated necrosis of the overlying skin. The necrotic area may become large, the gangrenous tissue separates and may expose necrotic bone. Later, the dead bone and the

associated teeth may sequestrate.

7.1.12 Warts

Viral wart lesions in the oral cavity may appear as solitary or multiple nodules. They may be sessile or pedunculated and appear as multiple, smooth-surfaced raised masses resembling focal epithelial hyperplasia or as multiple, small papilliferous or cauliflower-like projections. Any lesion if present is ticked in the single box. The site of occurrence is entered by noting the number present on the topograph of mouth present on the right side. Simultaneously the site is encircled on the figure.

7.2 Presence or absence of tooth

A tooth present or absent is noted under this section. A tooth if present is marked as 'P'. When a tooth is missing due to any reason is represented using 'M'.

7.3 Edentulism

Edentulism is marked separately for upper and lower jaws when one or both jaws have no natural teeth present; or present teeth are all indicated for extraction. Tick in appropriate box(es).

7.4 Denture

Denture is marked as Full, Partial, Fixed separately for upper and lower jaws when subject wears denture(s) on daily basis. Tick in appropriate box(es).

7.5 Oral hygiene index- Simplified (Greene and Vermillion, 1964)

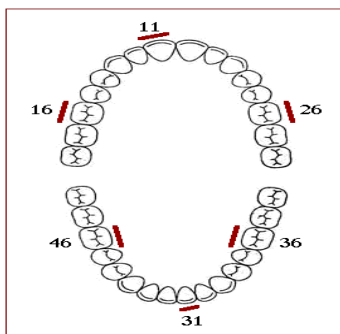
The Oral Hygiene Index is a method for classifying the oral hygiene status of a patient.

- Oral debris defined as the soft foreign matter on the surface of the teeth, consisting of mucin, bacteria and food, and varying in color from grayish white to green or orange.
- Dental calculus is defined as a deposit of inorganic salts composed primarily of calcium carbonate and phosphate mixed with food debris, bacteria, and desquamated epithelium cells.
- The original oral hygiene was determined to be simple, sensitive, and useful, it was time consuming and required more decision-making.
- After considerable trial and error, another index was developed. This, index named, Simplified Oral Hygiene Index.

- The OHI-S is composed of the combined **Debris Index** and **Calculus Index**. Each of these indices, in turn, based on 6 numerical determinations representing the amount of debris or calculus found on six preselected tooth surfaces.

7.5.1 Selection of tooth surfaces

- The first fully erupted tooth distal to the second bicuspid (see picture below). The buccal surfaces of the selected upper molars and the lingual surfaces of the selected lower molars are inspected.
- In the anterior portion of the mouth, the labial surfaces of the upper right (11) and the lower left central incisors are scored (31).
- Only fully erupted (occlusal and incisal surface has reached the occlusal plane) permanent teeth are scored.
- Natural teeth with full crown restorations and surfaces reduced in height by caries and trauma are not scored. Instead, an alternate tooth is examined.



7.5.2 Criteria for classifying debris

Scores	Criteria
0	No debris or stain present
1	Soft debris covering not more than one third of the tooth surface, or presence of extrinsic stains without other debris regardless of surface area covered
2	Soft debris covering more than one third, but not more than two thirds, of the exposed tooth surface.
3	Soft debris covering more than two thirds of the exposed tooth surface.

7.5.3 Criteria for classifying calculus

Scores	Criteria
0	No calculus present
1	Supra-gingival calculus covering not more than third of the exposed tooth surface.
2	Supra-gingival calculus covering more than one third but not more than two thirds of the exposed tooth surface or the presence of individual flecks of sub-gingival calculus around the cervical portion of the tooth or both.
3	Supra-gingival calculus covering more than two third of the exposed tooth surface or a continuous heavy band of sub-gingival calculus around the cervical portion of the tooth or both.

The surface area covered by debris is estimated by running the side of the probe along the buccal, labial, and lingual surfaces and noting the occlusal or incisal extent of the debris as it is removed from the tooth surface as shown in figure (1) below

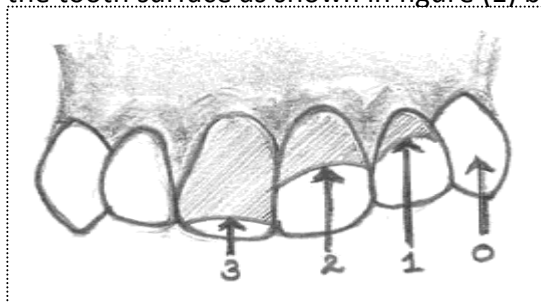


Figure 1.

7.5.4 Calculating the index

- For each individual, the debris (DI-S) and calculus (CI-S) scores are totaled and divided by the number of surfaces scored.
- At least two of the six possible surfaces must have been examined for an individual score to be calculated.
- Group indices are calculated by dividing the sum of the indices determined for individuals by the number of persons for whom indices have been determined.

- The average individual/group debris and calculus score are combined to obtain the OHI-S.
- The (DI-S) and (CI-S) values ranges from 0 – 3;
- The OHI-S values ranges from 0 – 6. These values are just half the score magnitude possible with the OHI.

7.5.5 Interpretation

The (DI-S) and (CI-S) values may range from 0 – 3, which can be interpreted as:

- Excellent – 0.0
- Good – 0.1 to 0.6
- Fair – 0.7 to 1.8
- Poor – 1.9 to 3.0

The OHI-S values range from 0-6, which can be interpreted as:

- Excellent – 0.0
- Good – 0.1 to 1.2
- Fair – 1.3 to 3.0
- Poor – 3.1 to 6.0

8 Record extractions for cases

The hospital records will be accessed by the staff to record histopathological diagnosis, TNM staging, presence of any comorbidity and treatment received/ planned.

The patient's file number and age on the examination form and questionnaire is matched with the patient's file number and age on hospital file. The above details and hospital patient-ID number are recorded from the in-patient file.

9 Completing the examination and discharging the study participants

Following the examination, the examiner must

- inform study participants of the findings from the survey

9.1 Informing study participants of the findings from the survey

After completing the survey examination, each study participant must be advised verbally and in writing of the findings.

9.2 Subjects requiring urgent diagnosis or treatment

Subjects must be referred immediately for care if they have any of the following potentially life-threatening conditions:

- A suspected malignant or pre-cancerous lesion
- Signs of systemic infection or a spreading local infection
- Other life threatening conditions, based on the clinical judgement of the examiner

In these situations, advise the subject that you recommend they obtain immediate attention, complete the appropriate section of the form.

9.3 Subjects not requiring urgent diagnosis or treatment

For all other subjects, advice should be given:

1. Note subjects can be advised to seek care immediately, even if they do not have a life threatening condition – for example, if you find a tooth likely to develop pulpitis. In addition to ticking relevant boxes, provide additional explanation to the subject (e.g. explain that “dental caries” means decay/cavity).
2. Discussion of any additional findings that you believe are relevant to the subject, for example, if the subject asks about prosthodontic replacement of missing teeth, you should endeavour to discuss their query. This does not mean that you need to make any additional diagnoses, or even provide a specific recommendation if you believe you do not have sufficient information. For example, your discussion may explain that a decision about treatment needs would need to be made after undergoing a more detailed dental assessment and discussing treatment options with a dentist.
3. Explanation of the limitations inherent in the survey examination. It is very important to emphasize to subjects the limitations of a survey examination, including:
 - the possibility that the disease may not have been detected (e.g. interproximal caries, periodontitis at lingual sites), and conversely
 - the possibility that a condition noted may not require treatment (e.g. caries that a dentist may choose to control by prevention rather than fill)

9.4 Recording final outcome of examination

Record on the appointment schedule the outcome of the examination. If you do not complete all sections of the examination for which the SP has provided signed consent and is

eligible, record this as “Partly completed” and record the reasons in the “comments” section of the final page of the data entry program. Reasons for partial completion could include “ran out of time”, “SP became uncooperative”, “equipment failure” etc.

If an SP does not consent to part of the examination, or is not eligible for part of the examination (eg. due to medical contraindications) but completes all other parts of the examination, record this as “Exam completed” on the appointment schedule.