Original Article

Differential impact of socioeconomic position across life on oral cancer risk in Kerala, India: An investigation of life-course models under a time-varying framework

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Abstract

Objectives: The incidence of oral cancer has been rapidly increasing in India, calling for evidence contributing to a deeper understanding of its determinants. Although disadvantageous life-course socioeconomic position (SEP) is independently associated with the risk of these cancers, the explanatory mechanisms remain unclear. Possible pathways may be better understood by testing which life-course model most influences oral cancer risk. We estimated the association between life-course SEP and oral cancer risk under three life-course models: critical period, accumulation and social mobility.

Methods: We recruited incident oral cancer cases (N=350) and controls (N=371) frequency-matched by age and sex from two main referral hospitals in Kozhikode, Kerala, India between 2008 and 2012. We collected information on childhood (0-16 years), early adulthood (17-30 years) and late adulthood (above 30 years) SEP and behavioural factors along the life span using interviews and a life-grid technique. Odds ratios (OR) and 95% confidence intervals (CI) were estimated for the association between life-course SEP and oral cancer risk using inverse probability weighted marginal structural models.

Results: Relative to an advantageous SEP in childhood and early adulthood, a disadvantageous SEP was associated with oral cancer risk [(OR=2.76, 95% CI: 1.99, 3.81) and (OR=1.84, 95% CI: 1.21, 2.79), respectively]. In addition, participants who were in a disadvantageous (vs. advantageous) SEP during all three periods of life had an increased oral cancer risk (OR=4.86, 95% CI: 2.61, 9.06). The childhood to early adulthood social mobility model and overall life-course trajectories indicated strong influence of exposure to disadvantageous SEP in childhood on the risk for oral cancer.

Conclusions: Using novel approaches to existing methods, our study provides empirical evidence that disadvantageous childhood SEP is critical for oral cancer risk in this population from Kerala, India.

1. INTRODUCTION

Oral cancer can be broadly defined as cancers affecting the lip, mouth and parts behind the mouth. It is a disease with low survival rates, and high morbidity, and affects roughly 300,000 people each year, leading to approximately 145,000 deaths worldwide.[1, 2] Developing countries bear two-thirds of the global burden, with India accounting for 25% of new cases and 35% of deaths and where incidence rates have increased considerably in the last decade.[2] A comparison of Globocan data from 2008 and 2012 reveals that the incidence of oral cancer surpassed lung cancer in a span of four years to become the 3rd most common cancer in this country after breast and cervical cancers.[2, 3] Most prevention programmes for these cancers are centred around its strongest risk factors such as paan chewing,[4] bidi and cigarette smoking, and alcohol consumption. [4, 5] However, what has not been emphasised are prevention strategies tailored to socioeconomic contexts critical for comprehensive control of cancers.[6] A major reason for this is the lack of deeper understanding of pathways involving social determinants of health such as socioeconomic position (SEP) and oral cancer.

A cumulative disadvantageous SEP over life has been independently associated with increased risk for this disease.[7] However, SEP varies over the life-course of an individual, a characteristic that is well documented, but consistently overlooked by SEP-oral cancer studies.[8] Appreciating the time-varying nature of SEP provides the unique opportunity to explore the pathways underlying its cumulative effect on oral cancer. The dynamic nature of SEP can be well articulated using the life-course framework, which takes into account the effects of several risk factors spread across multiple points in life.[9] Apart from the cumulative effect of SEP on the outcome (accumulation model), the framework allows to estimate the effect of timing of exposure to disadvantageous SEP at key periods of life (critical period model) that could contribute to the initiation of oral cancer. In addition, the framework permits the investigation of life trajectories generated by the interaction of SEP exposures in multiple periods of life (social mobility model) that can alter an individual's risk of cancer.[9] However, although imperative to its understanding, the relation between SEP and oral cancer has not yet been explored through the lens of multiple life-course models within a single study. Such an investigation may be of special relevance to developing countries such as India, as well as specific populations within India, where high socio-economic disparity exists.

The analysis of life-course models poses challenges. For example, the life-course framework implies that the relation between SEP at several time points and behavioural risk factors are likely subject to complex time-varying feedback loops.[10] Yet, investigators often fail to account for these relations between SEP over the life-course and other time-varying covariates.[7, 11] Therefore, by considering the time-varying nature of SEP and these variables, we estimated the association between SEP measured over three periods of life and oral cancer risk using a case-control study from Kerala, India. We further assessed whether the associations conformed better to a critical period, accumulation or social mobility model.

2. METHODS

Data for this analysis were drawn from the Head and Neck Cancer (HeNCe) Life course study, a multicentre hospital-based case-control study investigating the aetiology of head and neck cancers. Adult participants (N=721) were recruited from the outpatient clinics at two major teaching hospitals, the Government Dental and Medical College and Hospitals, Kozhikode, Kerala, South India between 2008 and 2012. The study design, sample and eligibility criteria have been described in detail elsewhere.[12] Briefly, cases (N=350) included incident, histologically confirmed stage I to IV, consecutive, squamous cell carcinoma cases (C01 and C02: tongue, C03: gum, C04 and C06: floor and unspecified parts of mouth respectively, C05: palate, and C09: tonsil, under International Classification of Diseases 10 Version:2016) of oral cavity diagnosed during the study period. Non-cancer controls (N=371), frequency matched to each identified case by 5-year age group and sex, were randomly selected from 8 outpatient clinics in the same hospitals. Controls were recruited from several clinics (distribution reported elsewhere),[13] not strongly associated with tobacco and alcohol consumption (with no single diagnostic group contributing to more than 20% of the total). This was done to mitigate selection bias.[14] The participation rate was 85.6% and 44.3% among cases and controls respectively.

Data were collected through one-on-one semi-structured interviews using a questionnaire with life-grid technique. Help of a proxy respondent was sought for consenting participants who had difficulty speaking due to disease status. Re-interviews were conducted for 46 randomly selected participants, 6 to 12 weeks after the original interview to test the reliability of the data collected. Ethics approval was obtained from Institutional Review Boards of participating hospitals. Informed written consent was obtained from all participants prior to inclusion in this study.

2.2 Life-course socioeconomic position

Information on housing conditions was used to derive an asset/wealth index that has been documented to be a suitable indicator of SEP for low to middle income societies such as India.[15, 16] We created the wealth index using responses to questions about various assets (housing characteristics, durable assets and access to services),[17] available at the participant's longest place of residence during three time periods: childhood (0-16 years), early adulthood (17-30 years), and late adulthood (above 30 years). Responses to each question were binary coded (Supplemental Appendix file, eTable 1) and a tetrachoric correlation matrix was created for each period (Supplemental Appendix file, eTable 2-4). Principal component analysis was conducted on the correlation matrices and the first component that explained maximum variance (approximately 65%) was extracted.[15] Continuous scores were predicted from these components. The scores for each period were then dichotomized (cut-off at 50th percentile among controls), generating a binary SEP variable (0= advantageous SEP, 1= disadvantageous SEP) for childhood, early adulthood and late adulthood periods each. This variable represented the SEP exposure for each of the three respective critical period models. A four-category variable representing the accumulation model was created by summing the number of periods of disadvantageous SEP (0, 1, 2 and 3). Finally, to test the social mobility models (childhood to early adulthood, and early to late adulthood) we combined the binary SEP variables in respective periods into two variables with four categories representing stable advantageous SEP, upward mobility, downward mobility, and stable disadvantageous SEP. Additional details are provided in Supplemental Appendix file, eAppendix and eTables 1-5.

2.3 Potential confounders

Information on potential confounders and mediators was collected from a set of time-invariant and time-varying factors. The factors included baseline exposures [age (continuous), sex (0: female, 1: male), caste i.e., hierarchy in Hindu religion based on occupation, (0=higher caste, 1=middle caste comprising of backward caste, 2=other backward/scheduled caste/scheduled tribe/others)], education (0=high, 1=low), and time-varying exposures (continuous-cigarette smoking, bidi smoking, paan chewing and alcohol consumption). Education was measured by the number of years of schooling and dichotomized based on the participants' birth cohort (participant's year of birth in our study ranged from 1921 to 1979) to

account for the major social and educational reforms in Kerala in the 1950's.[18] We collected detailed lifetime information on risk behaviours (e.g., duration, quantity, and type of cigarette and bidi smoking, paan chewing, and alcohol consumption) as described elsewhere.[13] This information was used to compute continuous measures of pack-years of cigarette and bidi smoked, chew-years of paan, and number of standard drinks of alcohol per week corresponding to multiple life periods.[13] Additional details are provided in Supplemental Appendix file, eAppendix.

The directed acyclic graph in Figure 1 represents the assumed temporal relations between these variables. Although this is a case-control study, our unique data collection procedure allowed us flexibility to appreciate the temporal relation between vectors representing potential confounders (C0: baseline covariates, C1: 0-16 years, C2a: 17-23 years, C2b: 24-30 years, C3a: 31-50 years, C3b: above 50 years), SEP exposure in the three periods of life and oral cancer. We adjusted for categorical and continuous confounders using indicator coding and restricted cubic splines respectively.

2.4 Statistical methods

T-tests and chi-square tests were used to describe the distribution of continuous and categorical variables, respectively. Our primary aim was to assess the relation between life-course SEP and oral cancer under the three conceptual life-course models. Due to their time-varying nature, SEP and related confounders may also act as mediators. Consequently, standard regression methods may produce biased estimates of exposure-outcome association, regardless of the method used to adjust for confounders. We therefore used inverse probability weighted marginal structural models to account for such confounding and derive our estimates.[19] The inverse probability weighting creates a pseudo reweighted sample where the exposure is independent of the measured potential confounders. We assumed that our case-control data arose from an underlying cohort representing the population of interest.[20]

Weights were derived by fitting a separate exposure model for each period of life and were computed as the inverse of the conditional probability of falling in the disadvantageous SEP category at each time period. To account for the case-control design, each exposure model was weighted by sampling fraction. The weights were stabilized by the marginal probability of falling in the disadvantageous SEP category at each time period. Once the stabilized inverse probability weights were computed, they were further

combined with time dependent sampling weights to account for the case-control design.[21] Sampling weights were defined as:

$$\text{Sampling weight} = [(1-\prod)/\prod] * \text{ncases/ncontrols},$$

where $\prod$ is the annual prevalence of oral cancer in India during the four-years of study, and ncases and ncontrols are the number of cases and controls in our sample. Finally, unadjusted logistic regression marginal structural outcome models were fit for each life-course model. In general, the outcome model took the form:

$$\text{Logit } \{Pr[Yg(A)=1]\} = \propto + \beta 1\ g(A)$$

where g(A) is a function of exposure, SEP, specific to each model. Additional technical details including those on exposure models and characteristics of stabilized weights are provided in Supplemental Appendix file, eTables 6 - 8.

We also fit a saturated all-trajectories model in which the other three models are nested. This model contained eight possible trajectories formed by binary SEP exposures measured over three periods of life.

Thirty-seven participants (17 controls and 20 cases) had missing values related to the main exposure. Therefore, we present our results on complete case analysis of 684 participants. Analyses were performed using Stata, version 13 SE (StataCorp. 2013, College Station, TX: StataCorp LP.). Annotated Stata codes are provided in Supplemental Appendix file, eTable 8.

3. RESULTS

Table 1 shows socio-demographic characteristics and measured potential confounders among cases and controls. The participants' age ranged from 32 to 88 years (mean=61 years) and the majority of the cases had a low level of education (78% of cases vs 50% of controls). The help of a proxy respondent was sought more rarely for controls (3%) than cases (14%). The majority of the participants belonged to the middle caste (81% of controls, 70% of cases). On an average, cases had a higher propensity for practicing all habits in each life period except for cigarette smoking. A higher proportion of cases than controls were exposed to disadvantageous SEP (60% vs 36% in childhood, 63% vs 35% in early adulthood, and 62% vs 33% in late adulthood).

Table 2 presents the association between life-course SEP and oral cancer under each conceptual model (IP weighted adjusted estimates. Crude estimates are presented in Supplemental Appendix file, eTable 9). Among the critical period models, being exposed to disadvantageous (vs. advantageous) SEP in childhood and early adulthood was associated with an increased odd of oral cancer (childhood: OR = 2.76, 95% CI: 1.99, 3.81; early adulthood: OR=1.84, 95% CI: 1.21, 2.79). In contrast, relative to an advantageous SEP, exposure to disadvantageous SEP in late adulthood was not associated with the disease (OR=0.92, 95% CI: 0.55, 1.54).

For the accumulation model, the odds of oral cancer increased with additional periods of socioeconomic disadvantage. Relative to never experiencing a period of disadvantageous SEP, experiencing one, two, and three periods of disadvantageous SEP yielded ORs of 2.56 (95% CI: 1.34, 4.87), 2.71 (95% CI: 1.44, 5.09), and 4.86 (95% CI: 2.61, 9.06), respectively.

Under the social mobility models, for childhood to early adulthood mobility, compared to stable advantageous SEP group, downward mobile (OR=2.75, 95% CI: 1.57, 4.83), upward mobile (OR=3.19, 95% CI: 1.83, 5.55) and stable disadvantageous (OR=4.06, 95% CI: 2.62, 6.28) trajectories were associated with increased odds for oral cancer.

The all-trajectories model (Table 2) showed that compared to non-exposure to disadvantageous SEP in all periods (0, 0, 0), the magnitude of ORs associated with trajectories in which individuals were exposed to disadvantageous SEP in childhood (1, 0, 0: OR= 4.37, 95% CI:1.83, 10.85 ; 1, 1, 0: OR=3.36, 95% CI 1.61, 6.99; 1, 0, 1: OR= 2.61, 95% CI: 1.16, 5.89; 1, 1, 1: OR=4.86, 95% CI: 2.61, 9.06) were larger than those of trajectories where participants were never exposed in childhood (0, 1, 0: OR=2.58, 95% CI: 1.15,5.80; 0, 0, 1: OR =1.00, 95% CI: 0.40, 2.53; 0, 1, 1: OR=2.25, 95% CI: 0.82, 6.21).

4. DISCUSSION

In this study, we examined the role of lifetime SEP on oral cancer risk comparing different life-course models and taking well-known behavioural risk factors into account under a time varying framework. Our findings indicate that an exposure to disadvantageous SEP in childhood may play a critical role in the development of oral cancer later in life.

Considered as the most fundamental of all life-course models,[22] the accumulation model implies cross-sectional clustering of (dis)advantages driven by social structure that accumulate longitudinally.[23] In our study, we found that the risk for oral cancer increased with the accumulation of disadvantageous SEP periods over the course of life. This finding is similar to the monotonically increasing risk pattern identified in life-course studies investigating other health outcomes.[24, 25] However, exploring other life-course models within this study provided further insight into this overall exposure-outcome relationship.

In line with studies investigating other chronic diseases including cancers,[24, 26, 27] our findings indicated that disadvantageous SEP during childhood and early adulthood increased the risk of oral cancer. The magnitude of association was higher for childhood. Interestingly, our findings from other models tested as well converged to indicate that childhood is a critical period for the risk of oral cancer. In our social mobility analyses, the magnitude of the OR associated with upward mobility from childhood to early adulthood was higher than that of downward mobility. This reflects the higher impact of disadvantageous SEP in childhood compared to the same exposure in early adulthood as observed from the critical period models. Also, the estimates from the all-trajectories model provided further evidence for the critical role an exposure to disadvantageous SEP in childhood may play in the increased risk for oral cancer later in life. A recent smaller study of 180 oral cancer cases and 272 controls from the nearby state of Karnataka, India, reported that a disadvantageous socioeconomic condition (measured using occupation of head of the household) in childhood had a significant effect on oral cancer risk that was not mediated through smoking, alcohol or paan chewing habits.[26]

The risk behaviours considered as time-varying variables in our study are usually considered to be affected by SEP and hence as mediators of the relationship between SEP and adult health outcomes. However, such behaviours (e.g., alcohol consumption) have been considered as determinants of socioeconomic consequences, especially in developing societies.[28] Although the state of Kerala ranks high in social development relative to other states, the state has one of the highest alcohol consumption levels in India.[29] Furthermore, alcohol consumption is highly correlated with tobacco habits. This strengthens our analytical approach considering the dual nature of these exposures as potential confounders and mediators.

The statistical evidence presented here does have biological plausibility. The adverse effects of an accumulation of socioeconomic disadvantage over an individual's life span can manifest biologically through increased allostatic load, impaired immune response, and specific genetic or epigenetic changes resulting in oral cancer.[9, 30] Of particular relevance to the critical period model, childhood represents a specific time of rapid development and vulnerability when exposures produce irreversible biological damage.[31] Childhood SEP captures different dimensions of adversity (e.g., poor nutrition) that may initiate the above carcinogenic processes in the oral cavity.[32]

There are several challenges in interpreting the results of our study. For example, although the results from the mobility models were in line with the gradient constraint hypothesis of social mobility,[33] the empirical difficulty in defining social mobility and associated life-course trajectories from limited time periods has been discussed in the literature.[24] In addition, although our sample size did exceed that of the majority of case-control studies exploring the SEP-oral cancer association,[7, 26] the results from social mobility and all-trajectories models tested were limited by the low numbers in some of the trajectories. There is also the potential for measurement error affecting our results. Our measure of SEP, an asset index,[17] may not have captured all aspects of SEP. However, asset indices serve as indicators of wealth and are particularly relevant to less industrialized societies.[16] Developing countries like India are more prone to high rates of short-term economic shock, and lack concrete socioeconomic classification systems such as those used in developed countries.[16, 17, 34] In addition, the cut-off points chosen to divide confounder vectors C2 into C2a and C2b (23 years) and C3 into C3a and C3b (50 years) were not based on statistical modelling, which might be a source of potential misclassification. However, we expect this to be negligible as our cut-off selection was based on the assumption that disadvantageous SEP during earlier stages of life (e.g., 17-23 years for early adulthood and 31-50 for late adulthood) is less likely to drive risk behaviours during these early stages (Figure 1). Moreover, behavioural factors in these earlier stages have higher probability to causally effect SEP later in life. Finally, recall bias is a well-recognized problem in case-control studies. Although, not a substitute for more reliable methods, we attempted to mitigate this bias by using a life-grid tool (in both cases and controls) that has been shown to improve recall.[35] We expect this to increase the expectation of non-differential misclassification of exposures, resulting in any bias towards the null. Relative measures of test-retest reliability for housing assets from this study are presented in Supplemental Appendix file, eTables5.

Several methodological strengths of our study also merit consideration. Cohort studies are not always feasible to investigate rare health outcomes. Our rigorous data collection procedures allowed us to analyse the temporal associations between exposures and potential confounders, as well as their time-varying nature. Leffondre et al,[21] developed weighted partial likelihood estimators for time-dependent exposures in a case-control setting. However, these estimators have not been extended to time-varying confounders. In this study, we employed a novel approach by combining these estimators with inverse probability weighting to account for both time-varying exposures and confounders. An additional complication in social epidemiology stems from the non-manipulable nature of social exposures such as SEP. We believe that, as there are numerous ways in which an individual may be "assigned" to a given level of SEP, each of which may have different impacts on the risk of oral cancer, interpreting associational estimates as causal effects is not possible.[36] However, our results do provide valid estimates of the socioeconomic distribution of oral cancer risk in Kerala, India. Furthermore, although the participation rate for controls were low in our study, a comparison of the housing assets of controls and data from the Census of India 2011, Kozhikode district, Kerala, showed that the distributions were similar (presented in Supplemental Appendix file, eTable 10) increasing the validity of our findings.[37]

4.1 Public health implications

Approximately 80% of oral cancer patients in India approaching health care facilities present with advanced disease, decreasing the success of treatments and overall survival rates.[38] The optimal solution to decrease the impact of these cancers on morbidity and mortality is to focus on comprehensive screening for these cancers (considered most amenable to early detection and treatment along with cervical and breast cancers), tailored to socioeconomic contexts in the population. Dentists, dental residents, nurses and dental hygienists can support such programmes by targeting populations with disadvantageous SEP. In its current form (e.g., use of toluidine blue dye, fluorescent imaging, brush biopsy), population-based screening for oral cancer is not cost-effective.[39] Furthermore, evidence on the effectiveness of the visual screening method is insufficient. However, the systematic examination of the oral cavity by dentists and physicians with particular attention to high-risk socioeconomic sub-groups (e.g., those exposed to a disadvantageous childhood SEP) is largely recommended. The coverage of such programmes can be increased through regular outreach programmes in dental schools (e.g., dental camps conducted by Government Dental College, Kozhikode, Kerala, in partnership with the National Service

Scheme of India). The opportunistic screening of high-risk group individuals and their referral to secondary prevention programs (e.g., alcohol and tobacco cessation) by medical service providers play a central role in a multi-disciplinary approach to the prevention of oral cancer.[39] Also, valid indicators of childhood SEP may be incorporated into oral cancer risk calculations and screening tools. Factoring in the negative effect of low SEP on oral cancer, specifically childhood SEP, can increase the precision of risk calculations and enhance the effectiveness of opportunistic screening.

5. CONCLUSIONS

To our knowledge, this is the first case-control study investigating the association between SEP over the life-course and oral cancer through the lens of multiple life-course models within a single study, and by considering the time-varying nature of SEP and multiple associated confounders over several periods of life. We used novel analytical approaches to existing methods adapted for a case-control study design to calculate our associational estimates. Multiple life-course models provided empirical evidence for the independent association of SEP during childhood with oral cancer risk in this Indian population. Addressing issues related to unfavourable social circumstances early in life may be beneficial in reducing the long-term burden of oral cancer in high-risk regions such as India.

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Conflicts of Interest: The authors declare that they have no conflict of interest.

Ethical approval: The study was approved by IRB and ethics committees of Government Dental and Medical colleges, Calicut, Kerala, India. All procedures performed in this study which involved human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Figure caption

Figure 1. Directed acyclic graph (DAG) representing the relationship between exposure, covariates and outcome, in the study from Kerala, India, 2008-2012 (n=684). **Oral cancer**: Outcome; **SEP:** Socioeconomic position, main exposure; **CH SEP**: SEP during childhood; **EAH SEP**: SEP during early adulthood; **LAH SEP**: SEP during late adulthood; **C0**: Vector representing baseline covariates, age, sex, caste i.e., hierarchy in Hindu religion (potential time-invariant confounders); **C1**: Vector representing education, health related behaviours (time-varying) of cigarette smoking, bidi smoking, paan chewing and alcohol consumption recorded during 0-16 years of age; **C2a**: Vector representing health related behaviours recorded during 17-23 years of age; **C2b**- Vector representing health related behaviours recorded during 24-30 years age; **C3a**- Vector representing health related behaviours recorded during 31-50 years of age; **C3b**- Vector representing health related behaviours recorded above 50 years

Table 1. Descriptive characteristics of oral cancer cases and controls from Kerala, India, 2008-12, (n=684)

	Controls (n=354)		Cases (n=330)	
	N (%)	**mean (SD)**	**N (%)**	**mean (SD)**
Age in years		61 (11)		61 (11)
Sex				
Female	163 (46)		149 (45)	
Male	191 (54)		181 (55)	
Education				
High	178 (50)		74 (22)	
Low	176 (50)		256 (78)	
Respondent type				
Use of proxy	11 (3)		46 (14)	
No use of proxy	343 (97)		284 (86)	
Caste				
Higher	51 (14)		26 (8)	
Middle	285 (81)		231 (70)	
Lower	18 (5)		73 (22)	
Time-varying risk behaviours				
During childhood (0-16 years)				
Cigarette smoking (pack-years)	25 (7)	0.08 (0.59)	13 (4)	0.05 (0.36)
Bidi smoking (pack-years)	45 (13)	0.14 (0.59)	66 (20)	0.23 (0.78)
Paan chewing (chew-years)	16 (5)	0.41 (3.50)	96 (29)	4.09 (9.29)
Alcohol consumption (drinks per week)	3 (0.8)	0.17 (2.29)	10 (3)	0.38 (2.70)
During early adulthood (17-23 years)				
Cigarette smoking (pack-years)	67 (19)	0.57 (1.73)	35 (11)	0.36 (1.87)
Bidi smoking (pack-years)	75 (21)	0.59 (1.94)	108 (33)	0.88 (2.10)
Paan chewing (chew-years)	30 (8)	1.72 (6.80)	156 (47)	12.44 (18.39)
Alcohol consumption (drinks per week)	32 (9)	2.54 (12.52)	50 (15)	4.30 (15.15)
During early adulthood (24-30 years)				
Cigarette smoking (pack-years)	97 (27)	1.26 (3.46)	63 (19)	0.88 (3.26)
Bidi smoking (pack-years)	81 (23)	0.91 (2.73)	120 (36)	1.60 (3.44)
Paan chewing (chew-years)	42 (12)	3.51 (11.67)	207 (63)	22.27 (28.24)
Alcohol consumption (drinks per week)	48 (14)	5.52 (33.18)	77 (23)	11.17 (43.33)
During late adulthood (31-50 years)				
Cigarette smoking (pack-years)	104 (29)	5.56 (14.33)	83 (25)	3.32 (9.58)
Bidi smoking (pack-years)	65 (18)	2.20 (7.59)	109 (33)	4.45 (9.19)
Paan chewing (chew-years)	57 (16)	15.76 (49.06)	237 (72)	94.95 (94.06)
Alcohol consumption (drinks per week)	59 (17)	6.65 (40.27)	90 (27)	15.37 (48.38)

Table 1 *Continued …*

	Controls (n=354)		Cases (n=330)	
	N (%)	**mean (SD)**	**N (%)**	**mean (SD)**
During late adulthood (51 years & above)				
Cigarette smoking (pack-years)	71 (20)	2.44 (9.77)	59 (18)	1.56 (5.34)
Bidi smoking (pack-years)	31 (9)	0.57 (2.63)	74 (22)	1.51 (4.24)
Paan chewing (chew-years)	52 (15)	15.76 (59.29)	183 (55)	60.41 (90.55)
Alcohol consumption (drinks per week)	42 (12)	2.47 (11.97)	60 (18)	11.71 (44.82)
SEP over the life-course				
Childhood SEP (0-16 years)				
Advantageous SEP	227 (64)		131 (40)	
Disadvantageous SEP	127 (36)		199 (60)	
Early adulthood SEP (17-30 years)				
Advantageous SEP	230 (65)		121 (37)	
Disadvantageous SEP	124 (35)		209 (63)	
Late adulthood SEP (above 30 years)				
Advantageous SEP	237 (67)		125 (38)	
Disadvantageous SEP	117 (33)		205 (62)	

SD: Standard deviation; SEP: Socioeconomic position.

Table 2. Odds ratios (adjusted for confounders using IP weighting) and 95% confidence intervals for risk of oral cancer under different life-course socioeconomic models in the study sample from Kerala, India, 2008-2012 (n=684)

Life-course SEP models	Levels of SEP (0 = Advantageous, 1= Disadvantageous)	Controls /Cases N	OR (95% CI)
Critical period models			
Childhood SEP	0[a]	227/131	Ref
	1	127/199	2.76 (1.99, 3.81)
Early adulthood SEP	0[a]	230/121	Ref
	1	124/209	1.84 (1.21, 2.79)
Late adulthood SEP	0[a]	237/125	Ref
	1	117/205	0.92 (0.55, 1.54)
Accumulation model			
Number of periods spent	0 periods[a]	162/53	Ref
in disadvantageous SEP	1 period	71/63	2.56 (1.34, 4.87)
over the life course	2 periods	66/92	2.71 (1.44, 5.09)
	3 periods	55/122	4.86 (2.61, 9.06)
Social mobility models			
Childhood-early adulthood SEP			
Stable advantageous	0,0[a]	190/79	Ref
Upward mobility	1, 0	40/42	3.19 (1.83, 5.55)
Downward mobility	0, 1	37/52	2.75 (1.57, 4.83)
Stable disadvantageous	1,1	87/157	4.06 (2.62, 6.28)
Early adulthood-late adulthood SEP			
Stable advantageous	0,0[a]	183/71	Ref
Upward mobility	1, 0	54/54	1.52 (0.80,2.87)
Downward mobility	0, 1	47/50	0.81 (0.40, 1.62)
Stable disadvantageous	1,1	70/155	1.53 (0.68, 3.41)
Saturated all-trajectories	0, 0, 0[a]	162/53	Ref
model[b]	1, 0, 0	21/18	4.37 (1.83,10.85)
(All SEP trajectories	0, 1, 0	22/19	2.58 (1.15,5.80)
across 3 life periods)	0, 0, 1	28/26	1.00 (0.40,2.53)
	1, 1, 0	32/35	3.36 (1.61,6.99)
	1, 0, 1	19/24	2.61 (1.16,5.89)
	0, 1, 1	15/33	2.25 (0.82,6.21)
	1, 1, 1	55/122	4.86 (2.61, 9.06)

SEP: socioeconomic position

[a] Reference category/ level within each SEP variable representing the specific life-course model.

[b] Categories/levels in the saturated all-trajectories model variable represents all possible 8 trajectories created from each binary SEP measure representing the three time periods.

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