

How much do smoking and alcohol consumption explain socioeconomic inequalities in head and neck cancer risk?

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ABSTRACT

Background A higher burden of head and neck cancer has been reported to affect deprived populations. This study assessed the association between socioeconomic status and head and neck cancer, aiming to explore how this association is related to differences of tobacco and alcohol consumption across socioeconomic strata.

Methods We conducted a case-control study in São Paulo, Brazil (1998–2006), including 1017 incident cases of oral, pharyngeal and laryngeal cancer, and 951 sex- and age-matched controls. Education and occupation were distal determinants in the hierarchical approach; cumulative exposure to tobacco and alcohol were proximal risk factors. Outcomes of the hierarchical model were compared with fully adjusted ORs.

Results Individuals with lower education (OR 2.27; 95% CI 1.61 to 3.19) and those performing manual labour (OR 1.55; 95% CI 1.26 to 1.92) had a higher risk of disease. However, 54% of the association with lower education and 45% of the association with manual labour were explained by proximal lifestyle exposures, and socioeconomic status remained significantly associated with disease when adjusted for smoking and alcohol consumption.

Conclusions Socioeconomic differences in head and neck cancer are partially attributable to the distribution of tobacco smoking and alcohol consumption across socioeconomic strata. Additional mediating factors may explain the remaining variation of socioeconomic status on head and neck cancer.

Tumours of the oral cavity, pharynx and larynx, taken together as head and neck cancer (HNC), have a high incidence worldwide and take a high toll on mortality in developing countries. The global burden of HNC accounts for 650 000 new cases and 350 000 deaths worldwide every year.¹ The city of São Paulo, the location of the current study, experiences a particularly high incidence of HNC, which corresponds to 11% of all new cancer cases (not including non-melanoma skin cancer) among men and 2.8% among women.² With more than 10 million inhabitants, this is one of the largest cities in Latin America and capital of the most populous and industrialised Brazilian state. Throughout the last decades, São Paulo experienced relevant improvements in life expectancy and health indicators.³ Notwithstanding, intense inequalities affect the population and affluent and deprived socioeconomic strata co-habit the town,

resembling patterns of heterogeneous socioeconomic conditions at the country level.

More than 70% of squamous cell carcinoma of the head and neck are estimated to be avoidable by lifestyle changes, particularly by effective reduction of exposure to well-known risk factors such as tobacco smoking and alcohol drinking.⁴ Ecological and individual-based studies conducted in several countries have reported higher incidence and mortality by HNC in deprived populations.⁵ In addition, patients with lower education and non-professional occupations usually exhibit a poorer prognosis and lower survival rates.⁶ A recent meta-analysis on socioeconomic inequalities and oral cancer risk concluded that public health strategies should advocate for socioeconomic change in addition to behaviour change.⁷

However, the concurrent association of socioeconomic status (SES) with the risk of HNC and with proximal behavioural risk factors has been scarcely assessed and produced inconclusive results. A critical question related to this subject refers to what extent the variation of smoking and alcohol consumption across social strata could explain socioeconomic differences in the incidence of HNC. Previous studies which have investigated tobacco smoking and alcohol consumption as covariates of cancer incidence did not explain the concurrent relationship of socioeconomic position with proximal risk factors and with disease outcome.^{8 9} However, recent studies^{10 11} have assessed the aetiological chain of HNC using a conceptual framework of covariates that organises distal socioeconomic and proximal behavioural determinants, a strategy aimed at instructing initiatives to reduce both cancer incidence and socioeconomic inequalities in health.

This study aimed to explore the extent to which differences of tobacco smoking and alcohol consumption across socioeconomic strata explain the association between SES and HNC in a large database of patients in the city of São Paulo, Brazil.

METHODS

Participants

This is a hospital-based case-control study involving newly diagnosed patients with HNC and hospital controls participating in two broader multicentre studies: the Latin-American section of the “International study of environment, viruses and cancer of the oral cavity and the larynx”¹² and

the "Clinical Genome of Cancer Project";¹³ The first study involved seven collaborating centres from three Latin-American countries and was coordinated by the International Agency for Research on Cancer. The second study involved 18 collaborating centres in the state of São Paulo. The joint assessment of both databases allowed for merging of consecutive information related to patients assisted in three large hospitals, which comprise referral centres for head and neck surgery in the city of São Paulo. The recruitment of cases and controls encompassed a continuous period from November 1998 to January 2006.

Case inclusion criteria comprised incident, histologically confirmed squamous cell carcinoma of the oral cavity (C00.3–C06, International Classification of Diseases, 10th revision), pharynx (C09, C10, C12–C14) and larynx (C32). Patients with primary tumours of the external lip, salivary glands and nasopharynx were excluded.

Controls were recruited among in- and out-patients of the same hospitals in which cases were assisted. Controls were frequency-matched with cases by sex and age distribution (5-year strata). The control group presented with a large range of clinical diagnoses; patients with diseases related to tobacco smoking or alcohol consumption were excluded as controls. The three hospitals monitored in this study are sponsored by Brazilian state agencies and mostly offer free-of-charge treatment to patients insured by the national healthcare system.

Ethical committees of each participating institution approved the study, and written informed consent was obtained from all participants. Each individual (case or control) was interviewed face-to-face by a trained interviewer using a detailed questionnaire on socioeconomic characteristics and lifestyle exposures. The gathering of data exclusively considered individual-based information.

Covariate categorisation

SES was assessed in terms of years of education and occupation. Education was classified into three categories: more than 8 years of study (individuals that went further than elementary school); from 4 to 8 years (corresponding to completed and partially completed elementary school) and less than 4 years of formal schooling. Occupation classifications were dichotomously defined as manual (IIIM—skilled, IV—partly skilled, and V—unskilled) or non-manual labour (I—professional, II—intermediate, and IIINM—skilled), according to criteria standardised by the *British Registrar General's Social Class*.¹⁴ These job classifications were based on the occupation performed for the longest period of time.

The assessment of tobacco smoking and alcohol drinking considered sequential patterns of frequency, duration and type of product consumed during the subject's lifetime. This assessment observed methodology endorsed by the International Agency for Research on Cancer^{15 16} and has been extensively used in recent epidemiologic studies.

Patients reporting having not smoked at least one daily cigarette during a whole year were considered non-smokers. A cigar was considered equivalent to four cigarettes, and each pipe serve equivalent to three cigarettes.¹⁵ Cumulative doses of tobacco exposure were calculated in terms of pack-years (number of packs with 20 cigarettes smoked per day multiplied by the number of smoking years). @@Categorisation used quartiles of the distribution in the overall sample.

Patients reporting never having consumed at least one drink at a regular monthly basis were considered non-drinkers. Alcohol drinking was measured by grams of ethanol, considering that 1 l of ethanol weighs 798 g and that beer contains 5% ethanol in

volume; wine 12%; liqueurs 30% and distilled spirits 41%.¹⁶ Cumulative exposure to alcohol was expressed in grams-year (grams of ethanol per day multiplied by the number of drinking years). Categorisation used quartiles of the distribution in the overall sample.

Data analysis

OR and 95% CIs (95% CI) were assessed by unconditional logistic regression.¹⁷ The assessment of education considered the group with more than 8 years of study as the reference group, whereas the assessment of occupation considered non-manual jobs as the reference and manual labour jobs as the comparison group. Education and occupation were independently assessed by fitting separate regression models on account of being partially collinear: manual workers mostly correspond to the two lower education groups; only five cases and four controls had manual occupation and more than 8 years of formal education.

Multivariate analysis used a hierarchical framework considering socioeconomic position (education, occupation) as distal covariates and behavioural factors (tobacco, alcohol consumption) as proximal exposures. All associations in the hierarchical model¹⁸ were adjusted for sex and age; SES variables were not adjusted for smoking and drinking; behavioural covariates (smoking and drinking) were adjusted for each other and for SES variables. The subsequent fitting of fully adjusted multivariate models assessed associations concurrently adjusted for all covariates: sex, age, education or occupation (separate models), smoking and alcohol drinking.

The comparison of outcomes of the hierarchical and the fully adjusted models allowed for estimating the proportion of socioeconomic differences in HNC that is explained by the distribution of exposure to alcohol and tobacco among socioeconomic strata. This proportion was calculated as $(OR_h - OR_f)/(OR_h - 1)$,¹⁰ where OR_f refers to the OR for education and occupation in the fully adjusted model and OR_h refers to the OR from the hierarchical model.

Statistical analysis was performed using the Stata V. 10.0 2007 software (Stata Corporation, College Station).

RESULTS

From the initial sample (1200 cases and 1117 controls), 183 cases and 166 controls were excluded due to lack of information for at least one covariate. Consequently, a total of 1017 patients were newly diagnosed with HNC (539 of oral cavity; 247 of pharynx; 231 of larynx), and 951 controls were included in the analysis. The sex ratio was 5.1 men per woman, and the age distribution had quartiles for the following groups: younger than 48, 48–55, 56–64 and ≥ 65 years.

Table 1 describes the distribution of cases and controls according to covariates. Low socioeconomic position were largely prevalent in the sample: 79.5% of cases and 71.0% of controls held manual occupations; 79.6% of cases and 72.9% of controls had up to 8 years of formal education. A small proportion of cases were non-smokers (5.8%) or non-drinkers (10.2%).

Table 2 summarises the assessment of covariates for HNC, according to the hierarchically adjusted framework, specifically considering education (model 1) and occupation (model 2) as SES indices. A higher risk of HNC was indicated for less-educated individuals and those performing primarily manual labour. Tobacco smoking and alcohol consumption were directly related with HNC, with higher levels of cumulative exposure presenting higher figures of OR. The separate assessment of

Table 1 Distribution of 1017 cases and 951 controls by education, occupation, tobacco smoking and alcohol consumption

Covariates	Cases n (%)	Controls n (%)
Distal covariates: socioeconomic status		
<i>Education</i>		
More than 8 years	207 (20.4)	258 (27.1)
4 to 8 years	660 (64.9)	613 (64.5)
Less than 4 years	150 (14.7)	80 (8.4)
<i>Occupation*</i>		
Non-manual (I, II, IIIN)	208 (20.5)	276 (29.0)
Manual (IIIM, IV, V)	809 (79.5)	675 (71.0)
Proximal covariates: lifestyle factors		
<i>Smoking (packs-year)†</i>		
Non-smokers	59 (5.8)	344 (36.2)
Less than 21.8	152 (14.9)	240 (25.2)
21.8 to 37.0	246 (24.2)	150 (15.8)
37.1 to 57.7	273 (26.9)	113 (11.9)
57.8 or more	287 (28.2)	104 (10.9)
<i>Alcohol drinking (grams-year)‡</i>		
Non-drinkers	104 (10.2)	415 (43.7)
Less than 723.4	162 (15.9)	200 (21.0)
723.4 to 2241.18	221 (21.7)	143 (15.0)
2241.19 to 5562.1	260 (25.6)	102 (10.7)
5562.2 or more	270 (26.5)	91 (9.6)

*Classified according to the British Registrar.¹⁰

†Number of packs (20 cigarettes) smoked per day multiplied by the number of years of smoking.

‡Grams of ethanol consumed per day multiplied by the number of years of drinking.

associations involving site-specific (oral cavity, pharynx and larynx) tumours had analogous results to those found for the overall (head and neck) appraisal (non-tabled results).

Table 3 compares associations obtained by the hierarchical and the fully adjusted models. Lower education and manual occupation on HNC had higher ORs in the hierarchical approach than in the fully adjusted model. However, the association of SES covariates remained statistically significant in the fully adjusted model, even after being adjusted for smoking and alcohol consumption.

Table 4 shows the proportion of socioeconomic differences in HNC that is explained when the assessment was adjusted for tobacco and alcohol consumption. The association between education and disease was fully explained for the intermediate category, although the lowest category of education remained significantly associated even after acknowledging that 54% of its effect was due to differences of smoking and alcohol consumption across educational strata. As to manual occupation, 45% of its association with disease was explained by the full adjustment, thus suggesting that near half of this association is independent of differences of tobacco smoking and alcohol drinking across occupational strata.

DISCUSSION

This study examined the effect of socioeconomic inequalities in HNC. Individuals with low educational attainment and those performing manual occupations for long periods showed an increased risk of head and neck cancer. These findings are in agreement with studies conducted in other regions.⁵ A recent systematic review and meta-analysis stated the relevance of socioeconomic inequalities on oral cancer both in high- and low-income countries.⁷

These findings are consistent with previous studies performed in Brazil, which also reported a higher burden of HNC on poorer socioeconomic strata.^{19–24} However, studies conducted thus far

Table 2 Hierarchical assessment of socioeconomic status (education and occupation) in head and neck cancer (1017 cases and 951 controls)

Covariates	Model 1 OR (95% CI)*	Model 2 OR (95% CI)†
Distal covariates: socioeconomic status		
<i>Education</i>		
More than 8 years	1.00	
4 to 8 years	1.23 (0.99 to 1.53)	
less than 4 years	2.27 (1.61 to 3.19)	
<i>Occupation‡</i>		
Non-manual (I, II, IIIN)		1.00
Manual (IIIM, IV, V)		1.55 (1.26 to 1.92)
Proximal covariates: lifestyle factors		
<i>Smoking (packs-year)§</i>		
Non-smokers	1.00	1.00
Less than 21.8	2.67 (1.84 to 3.88)	2.66 (1.83 to 3.86)
21.8 to 37.0	6.25 (4.25 to 9.18)	6.18 (4.21 to 9.07)
37.1 to 57.7	7.92 (5.34 to 11.75)	7.84 (5.29 to 11.63)
57.8 or more	7.78 (5.22 to 11.60)	7.89 (5.30 to 11.76)
<i>Alcohol drinking (grams-year)¶</i>		
Non-drinkers	1.00	1.00
Less than 723.4	3.01 (2.10 to 4.31)	3.02 (2.11 to 4.32)
723.4 to 2241.18	5.40 (3.72 to 7.84)	5.39 (3.72 to 7.82)
2241.19 to 5562.1	7.88 (5.33 to 11.64)	7.88 (5.34 to 11.64)
5562.2 or more	8.47 (5.69 to 12.59)	8.38 (5.64 to 12.45)

*OR, 95% CI, as assessed by unconditional logistic regression. Distal covariates were adjusted for sex and age. Proximal covariates were adjusted for sex, age, education and by themselves.

†OR, 95% CI, as assessed by unconditional logistic regression. Distal covariates were adjusted for sex and age. Proximal covariates adjusted were adjusted for sex, age, occupation and by themselves.

‡Classified according to the British Registrar.¹⁰

§Number of packs (20 cigarettes) smoked per day multiplied by the number of years of smoking.

¶Grams of ethanol consumed per day multiplied by the number of years of drinking.

in the Brazilian context only assessed the association between SES (income, education, household crowding, unemployment rate) and HNC incidence¹⁷ and mortality^{20–22} information aggregated at the area level or used SES as intermediate variables to assess the effect of other covariates.^{23 24} In spite of being appropriate to assess contextual determinants of disease, ecological studies are poor surrogates of individual-based conclusions. Therefore, assessing individual-based information with the main focus on socioeconomic position, and the large number of participants are considered strengths of this study.

Failing to consider the impact of SES on the risk of disease was stated to be a source of bias to epidemiologic knowledge and harm to the public health.²⁵ More educated individuals and

Table 3 Association of education and occupation with head and neck cancer according to the hierarchical model and the fully-adjusted models (1017 cases and 951 controls)

Socioeconomic status	Hierarchical model OR (95% CI)*	Fully adjusted OR (95% CI)†
<i>Education</i>		
>8 years	1.00	1.00
4 to 8 years	1.23 (0.99 to 1.53)	0.95 (0.73 to 1.23)
<4 years	2.27 (1.61 to 3.19)	1.58 (1.06 to 2.36)
<i>Occupation‡</i>		
Non-manual (I, II, IIIN)	1.00	1.00
Manual (IIIM, IV, V)	1.55 (1.26 to 1.92)	1.30 (1.01 to 1.66)

*OR and 95% CI, as adjusted by sex and age, as assessed by unconditional logistic regression.

†OR and 95% CI, as adjusted by sex, age and proximal exposures (smoking and alcohol drinking), as assessed by unconditional logistic regression.

‡Classified according to the British Registrar.¹⁰

Table 4 Proportion of socioeconomic status (education and occupation) explained by tobacco smoking and alcohol consumption in head and neck cancer (1017 cases and 951 controls)

Socioeconomic status	Proportion*
<i>Education</i>	
>8 years	Reference
4 to 8 years	100%
<4 years	54%
<i>Occupation†</i>	
Non-manual (I, II, IIIN)	Reference
Manual (IIIM, IV, V)	45%

*Proportion of differences explained by the differential exposure to tobacco smoking and alcohol consumption across socioeconomic strata.¹⁵

†Classified according to the British Registrar.¹⁰

those performing non-manual labour tend to achieve more control upon their own behaviours and are less amenable to deleterious habits such as tobacco smoking and alcohol consumption. A higher socioeconomic position would also reinforce compliance with healthy dietary habits, oral hygiene and physical activity.^{26 27} Education and higher-level occupations would also promote a larger access to health services and social facilities and reduce occupational exposure to agents already acknowledged as potentially relevant to the risk of HNC.²⁸

The assessment of socioeconomic inequalities in health may contribute to identify opportunities for preventive interventions.²⁹ However, the inference of associations between low socioeconomic status and poor health is complex, and disentangling the concurrent effect of SES on disease and on proximal exposures is a relevant target for research. This subject has been insufficiently explored in previous studies.³⁰

This study considered two analytical pathways and compared a fully adjusted multivariate model with a hierarchical approach integrating SES as distal covariates and behavioural exposures as proximal determinants of HNC. The comparison of these two models underscores the hypothesis that the effect of socioeconomic position on HNC is in part explained by differential patterns of tobacco use and alcohol consumption across social strata.

Socioeconomic differences in HNC were in part explained by the distribution of tobacco smoking and alcohol drinking among groups with different education level. This aspect deserves careful consideration by health authorities because tobacco smoking and alcohol drinking were reported to be more prevalent among less-educated individuals in the city of São Paulo,³¹ and the incidence of cancer reflects the cumulative exposure to these risk factors in the long term.

With that being said, SES variables remained independently associated with disease incidence, even after adjusted by tobacco smoking and alcohol drinking. This observation reinforces the hypothesis that other factors may mediate the effect of socioeconomic status on the aetiology of HNC, such as diet, passive smoking, oral hygiene, sexual behaviour and human papilloma virus infection. The absence of information on these factors in the current database is acknowledged as a limitation of the study. Furthermore, occupation was exclusively considered as a proxy for socioeconomic position, which does not take into account occupational exposures to carcinogens that may represent independent risk factors for HNC.

Additional factors that may explain the association of socioeconomic position and HNC independently of tobacco smoking and alcohol consumption have already been reported.^{32 33} However, this issue has been somewhat controversial with

conflicting results. The absence of remaining association between SES variables and the incidence of tumours in specific head and neck anatomic sites, after controlling for smoking and alcohol consumption, has also been reported.^{34 35} Furthermore, being in a manual occupational social class, having no educational qualifications and living in a deprived area were reported as conditions that independently predict significantly lower consumption of fruit and vegetables,³⁶ a dietary habit acknowledged as conducive to protecting individuals against HNC.³⁷

Further research is needed to assess intervening variables that contribute to socioeconomic inequalities of HNC. Specifically applied to the French context, a previous study¹⁰ stated that a substantial proportion of socioeconomic inequalities in laryngeal and hypopharyngeal cancer could be explained by the differential exposure to occupational agents across social strata. Further research should also explore how SES and cumulative exposure to tobacco and alcohol specifically relate to HNC in adults aged less than 45 years and in women. As our sample was relatively reduced to both characteristics (nearly 12% of young adults and 16% of women), we solely considered sex and age as adjusting factors for regression models.

The enrolment of controls in hospital settings restrains the validity of comparisons in case-control studies.¹⁷ The study design identifies the impact of socioeconomic status (and smoking and drinking) on head and neck cancer relative to the impact on other conditions for which patients seek medical care. It does not identify the impact of socioeconomic status on head and neck cancer in the population at large. Furthermore, public hospitals tend to assist a higher proportion of individuals with low SES; indeed, 72.9% of controls had up to 8 years of education, this figure is higher than the estimate for heads of households in the city as a whole (65.1%). Selection bias is acknowledged as a limitation of hospital-based case-control studies.

Recall bias is another relevant source of bias in case-control studies. However, the choice of covariates to evaluate socioeconomic position may have reduced recall bias, because the number of years of schooling and primary occupation are relatively stable conditions, easy to remember and easy to assess.³⁸ Education has been proposed to be the most relevant component of socioeconomic status in studies assessing health-related determinants,³⁹ and occupation is appraised as a surrogate for income and housing conditions.³⁸

Regarding the assessment of cumulative exposure to tobacco smoking and alcohol consumption, residual confounding associated with intra-category variation is a limitation difficult to overcome when dealing with categorical covariates. Aiming to appraise the potential effect of residual confounding on the proportion of socioeconomic differences of HNC that is explained by behavioural exposures, we explored different categorisations. However, no classification is exempt from residual confusion, and our exploratory approach on classification found no discrepant conclusion, which reinforces the hypothesis that tobacco smoking and alcohol consumption do not fully explain socioeconomic differences in HNC.

The validity of self-reported information on behavioural exposures has also raised some concern. Young adults affected by smoking-related diseases were reported to be more prone to misclassify their history of smoking because of pressure to quit⁴⁰ and the self-report of drinking habits among irregular drinkers may be affected by lower validity due to seasonal variation. The burden of cancer was reported to be influenced by age at starting smoking and duration of ex-smoking⁴¹; such conditions may

What is already known on this subject

Previous studies reported socioeconomic inequalities in the incidence of head and neck cancer both in developing and developed countries. However, the concurrent association of socioeconomic position with disease and with behavioural risk factors has been scarcely assessed and produced inconclusive results.

What does this study add

This study assessed the extent to which socioeconomic inequalities in head and neck cancer may be attributed to differences of tobacco smoking and alcohol consumption across socioeconomic strata. Health programs concurrently aimed at reducing the burden of disease and socioeconomic inequalities in health should consider targeting tobacco smoking and alcohol drinking cessation towards socioeconomically deprived population strata.

vary substantially by SES and confound the association between SES and HNC. These possibilities cannot be ruled out, which is also acknowledged as a limitation of the study. However, the self-report of smoking and alcohol drinking among adults has also been subject of validation studies,^{42, 43} and its use in assessments of cancer risk is largely prevalent.

This study indicated that there is room for reducing the impact of socioeconomic inequalities on HNC risk by addressing intervention programs on several risk factors unequally distributed across socioeconomic strata. Essentially, our results showed that inequalities in the incidence of HNC may be reduced in the long term, if effective prevention against tobacco smoking and alcohol drinking is targeted towards socioeconomically deprived population strata.

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Competing interests None.

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the Faculdade de Odontologia, Universidade de São Paulo, Brazil; Hospital Heliópolis, Secretaria de Estado da Saúde de São Paulo, Brazil; Instituto do Câncer Arnaldo Vieira de Carvalho, Brazil; Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, Brazil.

Contributors A.F. Boing, J.L.F. Antunes and V. Wünsch-Filho conceptualised and coordinated the realisation of the study. The working group was convened by J. Eluf-Neto, P. Boffetta and V. Wünsch-Filho. A.F. Boing and J.L.F. Antunes performed the statistical analysis and wrote the first draft of the manuscript. M.B. Carvalho, J.F. Góis-Filho, L.P. Kowalski, P. Michaluart-Junior and GENCAPO coordinated the gathering of data, discussed and approved the study project. All authors helped to conceptualise ideas and interpret findings and contributed to the final paper.

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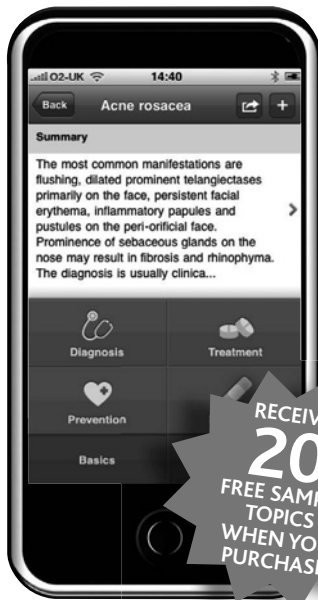
APPENDIX

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