SMOKING AND DRINKING IN RELATION TO DEPRESSIVE SYMPTOMS AMONG PERSONS WITH ORAL CANCER OR ORAL EPITHELIAL DYSPLASIA

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Abstract

Background—We examined whether smoking or drinking during or before the diagnosis-year of oral cancer or oral epithelial dysplasia (OED) was related to "subsequent depression" measured months after the oral diagnosis.

Methods—Incident cases of oral cancer or OED were identified via 3 oral pathology laboratories. A telephone-administered questionnaire included questions on smoking/drinking history through the diagnosis-year and measured depressive symptoms using the Center for Epidemiologic Studies-Depression Scale (CES-D); scores of 16+ indicated clinical depression. "Subsequent depression" was defined as a CES-D score of 16+, measured at the time of assessment several months after the diagnosis of oral cancer or OED.

Results—Patients who smoked during their diagnosis-year had twice the odds of subsequent depression relative to former/never smokers. Diagnosis-year (vs never/former) drinking was not associated with depression; however, average alcohol consumption of >1.5 drinks/week was negatively associated with subsequent depression for both diagnosis-year and ex-drinkers (past reported drinking) even among heavy drinkers.

Conclusion—Our findings suggest that subsequent depression is positively associated with diagnosis-year smoking and negatively associated with alcohol consumption of >1.5 drinks/week among both diagnosis-year and ex-drinkers.

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Smoking tobacco and heavy alcohol use are associated with an increased risk of oral cancer, and at least 1 report has identified both smoking and drinking as risk factors for oral epithelial dysplasia (OED), a histopathologic diagnosis associated with an increased risk of oral cancer. [1–5] Nevertheless, although a growing body of literature has explored the occurrence and correlates of depressive symptoms among head and neck cancer patients,[6–12] and although depression has been linked to both alcohol abuse and smoking in a variety of diverse populations,[10,13–25] only limited information is available on the relationship between depression and either smoking or drinking among persons diagnosed with oral cancer or precancer.[10]

As part of a larger retrospective investigation focusing on risk factors for oral cancer and OED, [26] we obtained information on depressive symptoms at the time the study interview was administered.[6] In a previous report, we identified young age (<50 years old), a low level of social support, lack of employment outside the home, and a diagnosis of oral cancer relative to OED as being associated with elevated odds of depressive symptoms indicative of clinical depression.[6] In that analysis, based upon patients whose diagnostic biopsy was performed by either a dentist or an oral and maxillofacial surgeon, we controlled for the potentially confounding effects of smoking and drinking during the year of diagnosis, but did not further explore the relationship between depressive symptoms and either smoking or drinking.[6]

Because the relationship between depressive symptoms and both smoking and drinking among persons with oral cancer or precancer has received little previous attention, we utilized our data to examine whether a history of smoking or drinking during or before the year of oral cancer or OED diagnosis is related to depressive symptoms presenting several months after the diagnosis. If such relationships do exist, their identification could improve our understanding of depression in these patients and may assist in predicting which patients are at the greatest risk of depression. On an a priori basis, we hypothesized that smoking would be positively associated with depressive symptoms and that the association between drinking and clinical depression would follow a J- or U-shaped curve, with low and moderate drinkers having the lowest, and heavy drinkers having the greatest risk of depression.

MATERIALS AND METHODS

Incident cases of oral cancer and OED were identified by reviewing pathology reports generated generated by oral pathology laboratories at the University of Florida College of Dentistry, the New Jersey Dental School, and the University of Connecticut School of Dental Medicine. These pathology laboratories serve primarily community-based oral and maxillofacial surgeons and other dental specialists and general dentists. Persons were eligible for inclusion in the study if they had been diagnosed with an invasive cancer or epithelial dysplasia of the oral cavity (eligible anatomic sites: tongue, gingiva, floor of mouth, palate, and other unspecified parts of the mouth [ICD-0–3 C01.9–C06.9]; excluded sites: the lip and major salivary glands), were 30 to 79 years of age at diagnosis, and could speak and read English.

After obtaining surgeon permission, study personnel contacted potentially eligible subjects, first via mail and subsequently by telephone. Consenting individuals were interviewed over the telephone by trained interviewers blinded to study hypotheses and oral diagnostic status. The study utilized a standardized, structured questionnaire that, in addition to obtaining

demographic/environmental risk factor information, included questions regarding depressive symptoms and social support. Surrogate interviews were not conducted, and data collected were based solely on the subject's self-report.

Depressive symptoms were measured using the Center for Epidemiologic Studies-Depression Scale (CES-D),27 a 20-item scale that assesses symptom frequency over the 2-week period preceding the interview; scores range from 0 to 60. In keeping with previous studies, we defined a CES-D score of 16 or above as indicative of clinical depression.28 Because depressive symptoms were assessed several months subsequent to the oral cancer or OED diagnosis (mean SD, 13.4 [4.2]), we will refer to a CES-D score of 16+ at the time of the interview as "subsequent depression."

The study questionnaire obtained comprehensive smoking and drinking histories and was closely adapted from questionnaires used in previous epidemiologic studies of oral cancer and oral dysplasia.[2,4] Because the parent study was designed to investigate risk factors for oral cancer and dysplasia, questions related to smoking and alcohol consumption intentionally addressed years before and up to the year in which the cancer or OED was diagnosed, but did not capture smoking and drinking information after diagnosis. Questions included the usual amount of tobacco and alcohol consumed by product type, when the use of tobacco and alcohol began, and, if applicable, when it had ended.

Information on smoking tobacco use was obtained individually for cigarettes, pipes, and cigars. An "ever-smoker" was defined as a person who reported smoking at least 100 cigarettes over his/her lifetime or who reported smoking a pipe or cigar for 6 months or more. A "diagnosis-year smoker" was defined as an individual who reported smoking during the calendar year in which the oral diagnosis was made, whereas an "ex-smoker" was defined as an ever-smoker who had discontinued smoking before the year of diagnosis. Cigarette equivalents were calculated using the conversion factor 1 cigarette = 1/2 pipe = 1/4 cigar; the average number of cigarette equivalents smoked/day was categorically defined as 0, 1–19, 20–39, and 40+.[4,26]

The consumption of alcoholic beverages was obtained separately for beer, wine, and hard liquor. Because drinking patterns can vary for weekdays (Monday–Thursday) and weekends (Friday–Sunday), questions pertaining to alcohol consumption for a given alcoholic beverage were grouped separately for weekdays and weekends. For example, study participants were asked to report the usual number of weekends/month or year that a given type of alcoholic beverage (eg, beer) had been consumed, followed by a question regarding the usual number of drinks consumed on those weekends in which that product type was consumed. A "drink" was defined for the study participants as a 12-ounce beer, a 4-ounce glass of wine, and a 1.5-ounce shot of hard liquor.[2,4] The mean total number of drinks consumed/week was calculated by summing the average number of drinks (as defined above) of beer, wine, and hard liquor that were reportedly consumed/week.[2,4] An "ever-drinker" was defined as a person who reported drinking 20 or more drinks of beer, wine, or hard liquor over his/her lifetime; a "diagnosis-year drinker" was defined as an individual who reported drinking any alcoholic beverage within the calendar year that the oral diagnosis was made; and an "ex-drinker" was defined as an ever-drinker who had discontinued drinking all types of alcoholic beverages before the year of diagnosis. Using a standard epidemiologic approach, alcohol consumption was categorized into quartiles based upon the distribution of reported alcohol intake among persons with a CES-D score of less than 16.29

Based upon the smoking and drinking information obtained, we calculated the number of cigarette equivalents smoked/day for both diagnosis-year and ex-smokers, and the average number of drinks consumed/week for both diagnosis-year and ex-drinkers.

The Berkman Social Network Inventory (BSNI) was used to measure the level of social support.[30] The BSNI assesses the size of the social network and the degree of the individual's integration within the network. Raw scores are calculated based on marital status, number of friends/relatives, and church/group memberships. In accord with the method recommended by Berkman and Syme,[30] scores are categorized into 4 groups, low, medium, medium-high, and high.

Data analyses were conducted using standard statistical methods. Odds ratios (ORs) and their 95% confidence intervals (CIs) were obtained using unconditional logistic regression models in which the CES-D score (<16, 16+) was the dependent variable.[31] Both smoking and alcohol consumption were viewed as independent variables in that their presence preceded the administration of the CES-D, which measures depressive symptoms during the 2 weeks before the interview. In our analyses, we evaluated whether subsequent depression as defined herein was associated with diagnosis-year smoking or drinking and whether there was a dose–response relationship between the level of either smoking or drinking in relation to subsequent depression. If a dose–response was observed, we further evaluated whether the relationship was apparent only for those who used the product during the year their cancer or OED was diagnosed or whether the association also existed for persons who had stopped their consumption before the year of their diagnosis.

The study protocol was approved by the applicable institutional review boards.

RESULTS

Subject Recruitment

Subject recruitment has been discussed in detail previously.[6] Briefly, 735 potentially eligible subjects were identified during the time that the CES-D and BSNI questions were included in the study questionnaire. Of these subjects, 65 were too ill to participate or had died before being contacted regarding the study. An additional 50 subjects were not contacted based upon the wishes of the surgeon of record, and 110 cases could not be reached by letter or telephone. Among the individuals who could be contacted by telephone, 79% (404/510) agreed to participate. Three of the 404 subjects refused to answer all CES-D questions and were excluded from the analysis.

Sociodemographic Characteristics

Table 1 presents sociodemographic characteristics for the study subjects. The majority of participants had a diagnosis of OED, were over 60 years of age, male, white, and non-Hispanic. Subjects generally had good social networks as measured by the BSNI; most scoring in the medium to high level, but with 24% reporting low social support. The majority of interviews were conducted within 15 months of diagnosis (77%). Although not shown in Table 1, most subjects were married (66%), were not employed outside the home (64%), had more than a high school education (62%), and reported incomes of at least $30,000/year (60%). The majority of subjects were diagnosed at the University of Florida (51%). The overall mean CES-D score was 8.2 (SD = 9.6).

For the primary analyses, CES-D scores of 16+ were considered indicative of clinical depression. Using that definition, 19% (76/401) of the respondents were classified as having a subsequent depression. Table 1 presents sociodemographic characteristics of the study participants by depression status. In crude analyses, a CES-D score indicative of depression was statistically significantly associated with age and BSNI score, whereas oral diagnostic status was marginally significant.

Smoking and Drinking

We investigated whether either smoking or drinking during or before the year of diagnosis were related to subsequent depression (ie, a CES-D score of 16+ as measured several months subsequent to the oral cancer or OED diagnosis).

Crude and adjusted ORs are presented in Table 2. The ORs from the adjusted model control for independent variables previously linked to a CES-D score of 16+ in this sample of subjects (ie, oral diagnosis status [oral cancer vs OED], age, employment outside the home, social support, and sex).[6] In addition, the model for smoking also adjusted for level of alcohol consumption, whereas the model for drinking additionally controlled for smoking at diagnosis. We also evaluated other covariates, including education, race, pathology laboratory, and the time interval between diagnosis and interview, as possible confounders of the primary relationships of interest, but these variables when added to the models, were neither statistically significant nor did they meaningfully change the reported ORs for smoking or drinking.

Smoking

The adjusted OR for the association between diagnosis-year smoking and a subsequent depression was 2.30 (95% CI: 1.26–4.21) relative to never- and ex-smokers combined (Table 2). When we stratified ever-smokers on the basis of ex-smokers or diagnosis-year smoking and designated never-smokers as the referent category, the corresponding adjusted ORs (95% CIs) were 0.98 (0.40–2.37) for ex-smokers and 2.27 (0.96–5.35) for diagnosis-year smokers.

To assess a possible dose–response for smoking, we examined the association between subsequent depression in relation to the average level of smoking/day before diagnosis. Relative to never-smokers and after adding a term for diagnosis-year smoking to the adjusted model, the OR point estimates for increasingly higher levels of smoking were all near or below 1.0, whereas the OR for diagnosis-year smoking was unchanged (Table 2).

Drinking

Diagnosis-year drinking (yes/no), per se, was not associated with subsequent depression (OR_{adj} = 0.89; 95% CI: 0.50–1.60; Table 2). In the crude analyses, ORs for depression in relation to increasing levels of drinking produced a U-curve. In the adjusted model, however, the OR for each increasing level of alcohol consumption was inversely associated with a CES-D score indicative of subsequent depression (relative to those drinking <1.5 drinks/week), and the ORs (95% CIs) for drinkers of 8 to <23 drinks/week (OR_{adj} = 0.35, 0.15–0.80) and 23+ drinks/week (OR_{adj} = 0.38, 0.16–0.88) were both clinically and statistically significant (Table 2).

The adjusted ORs for average level of drinking, as reported in Table 2, changed little when we also controlled for diagnosis-year drinking (yes/no). When we included only ever-drinkers (ie, diagnosis-year and ex-drinkers) in our adjusted model and added an interaction term for diagnosis-year drinking (yes/no)* average number of drinks/week, the adjusted ORs for increasing levels of consumption were all negatively associated with a CES-D score of 16+ for both ex-drinkers and diagnosis-year drinkers (Table 3). Finally, to further explore the relationship between a history of heavy drinking before a diagnosis of OED or oral cancer and subsequent depression, we computed the adjusted OR for persons who reported a history of drinking 50+ drinks/week before being diagnosed with oral cancer or OED (the 91st percentile of drinking among the nondepressed) relative to those drinking <1.5 drinks/week; the OR_{adj} was 0.36 (95% CI: 0.10–1.36).

We additionally evaluated the relationship between subsequent depression and the type of alcoholic beverage consumed (beer, wine, hard liquor) before or during the year of diagnosis.

When we dichotomized the drinking of each beverage type at <1.5 and 1.5+ drinks/week and controlled for each other type of alcohol consumption and age, social support, working outside the home, oral diagnostic status, sex, and diagnosis-year smoking, the ORs (95% CIs) for beer, wine, and hard liquor were 0.43 (0.22–0.84), 0.71 (0.37–1.38), and 1.02 (0.57–1.83), respectively. Controlling additionally for diagnosis-year drinking had little impact on these ORs.

Oral Diagnostic Status

Table 4 presents adjusted ORs for diagnosis-year smoking and level of alcohol consumption in relation to subsequent depression separately for the cancer and OED subjects. The associations tended to be somewhat stronger for the cancer series.

CES-D Cut-Scores

We explored the robustness of the CES-D criterion score used to define subsequent depression by evaluating the impact of increasing the CES-D cut-score on ORs obtained from the adjusted model. Using cut-scores of 16, 17, and 20, the adjusted ORs (95% CIs) for diagnosis-year smoking were 2.30 (1.26–4.21), 3.21 (1.66–6.19), and 2.69 (1.27–5.69). Regarding increasing levels of alcohol consumption, the adjusted ORs for cut-points of 17 and 20 varied little from those reported in Table 2 when a cut-point of 16 was used.

DISCUSSION

A diagnosis of oral cancer or precancer can impact quality of life, and Ronis et al[32] recently reported that smoking and depressive symptoms, but not problem drinking, were inversely associated with quality of life in head and neck cancer patients, both before and 1 year after treatment.

We previously identified psychosocial risk indicators for depression in persons with oral cancer or oral dysplasia.[6] In the current paper, based upon the same OED and oral cancer cases that were included in our earlier analysis, we report findings from analyses in which we evaluated whether smoking or drinking during or before the year of diagnosis was associated with depression, as measured by the CES-D several months after the oral cancer or OED diagnosis.

Smoking

Numerous studies from disparate populations and subpopulations have found a positive association between smoking and various measures of depression,[10,13–20,33] with some investigations reporting that current, but not ex-smokers, are more likely to exhibit depressive symptoms than never-smokers.[15,19,20] In the current study, and after controlling for various potential confounders, we found that diagnosis-year smokers, but not persons who had quit smoking before the year of their diagnosis, had twice the odds (relative to never-smokers) of having a subsequent depression. The amount of tobacco smoked/day, however, was not significantly linked to such a depression.

Drinking

Previous reports have linked the misuse of alcohol with an increased risk of depression in various populations,[21–25] and several reports have identified a U- or J-shaped relationship between the level of alcohol intake (low to high) and depressive symptoms.[34–37]

In previous studies of head and neck cancer patients, Duffy et al[10,38] found no association between problem drinking and significant depressive symptoms or quality of life as measured by the SF-36, the SF-36V, and the Head and Neck Quality of Life instruments. On the other hand, and based upon a series of post-treatment head and neck cancer patients, Allison[39]

reported that current alcohol consumers had a better global health-related quality of life than abstainers; however, information on the frequency and quantity of alcohol intake was limited and could not be explored in relation to health-related quality of life.

In our study, diagnosis-year alcohol consumption, per se, was not associated with subsequent depression; however, drinking 1.5 or more drinks/week was associated with reductions in the odds of depression relative to drinking less than that amount, with beer consumption showing the strongest association. Notably, the protective relationship was observed for both diagnosis-year consumers and persons who had quit drinking at least 1 year before their diagnosis, and the ORs were robust and reasonably strong.

Although an inverse relationship between depression status and intermediate levels of drinking was not unexpected, we were surprised to find that elevated levels of drinking were also negatively associated with a subsequent depression, even among drinkers of 50 or more drinks/week. It was also unanticipated that the past level of alcohol consumption among former drinkers would show an inverse relationship. The latter finding suggests that the association between alcohol intake and depression may be mediated, at least in part, via some indirect mechanism, such as personal characteristics (eg, belief systems, personality traits, and genetics) related to both drinking and depressive symptoms. In a similar vein, Lipton[35] suggested that alcohol intake at moderate levels may serve as a marker for other behaviors that reduce the effects of stress on depression. Our findings further suggest that these characteristics continue to be negatively associated with depression even among former drinkers.

Another possible explanation for the anomalous finding regarding alcohol intake and depression, is that the participants in this study were not selected because they were problem drinkers or were seeking treatment for alcohol abuse. Many studies that demonstrate a positive relationship between alcohol use and depression are based on individuals who are problem drinkers. The relationship between alcohol and depression among individuals with chronic and life-threatening conditions, such as oral cancer, has not been studied extensively, and the findings among those who abuse alcohol may not hold for those with such chronic health problems.

Methodologic Considerations

In the current analysis, we found robust associations between smoking and drinking during or before the year of diagnosis in relation to a subsequent depression. When interpreting our findings, however, 1 should consider how the study methodology may have influenced our findings.

Whereas 79% of contacted subjects participated in the study, other potentially eligible subjects could not be interviewed and were not included in our analyses. Further, most study participants were white, non-Hispanic, and all were biopsied by community-based oral surgeons and dentists. The latter is significant in that there is evidence that oral cancers detected by dentists and oral and maxillofacial surgeons are more likely to be early-stage cancers requiring less radical cancer-directed treatment than are cases diagnosed by primary care physicians and otolaryngologists.[40] Consequently, our study results may be most applicable and generalizable to cases of OED and oral cancer detected and biopsied by oral surgeons and dentists.

In our investigation, we used a CES-D score of 16+ as being indicative of depression at the time of the study interview; however, a clinical diagnosis of depression was not obtained. On the other hand, in a recent evaluation of the CES-D in predicting major and minor depression in head and neck cancer patients, a CES-D cut-score of 16 had a sensitivity of 100% and specificity of 78.6% when using an abridged version of the Schedule for Affective Disorders

and Schizophrenia as the gold standard diagnosis.[41] Further, we found that shifting the CES-D cut-point from 16 to 20 had little impact on our estimated ORs.

It is possible that some uncontrolled or residual confounding may have impacted the observed relationships for smoking and drinking in relation to depression status. In our analyses, we adjusted for covariates previously found to be associated with depressive symptoms among these study participants (ie, oral diagnostic status, age, employment status, social support, and sex).[6] Further, because the duration between diagnosis and interview varied across study participants, we evaluated it and other potential confounders (ie, education, race, and pathology laboratory), but the inclusion of these variables in our analyses had no meaningful impact on the reported findings and were excluded from the final models.

Limitations

Among the cancer cases, we did not have information on stage at diagnosis or treatment received, and that precluded the adjustment of our cancer-specific models for those variables. That said, however, it should be reiterated that the oral cancer cases in our series all received their diagnostic biopsy from a dentist or oral surgeon, and, therefore, it is not unlikely that many, if not most, of the respondents, had early-stage cancers, which generally require less radical cancer-directed treatment.[40]

The questionnaire used in the current study obtained detailed information on lifelong smoking and drinking through the year in which the oral cancer or OED was diagnosed. Based upon the information obtained, our analysis suggests that subsequent depression is positively associated with diagnosis-year smoking and negatively associated with even elevated levels of alcohol consumption among both diagnosis-year and ex-drinkers. Our approach was consistent with the clinical situation at the time of diagnosis, (ie, the patient's smoking and drinking history is known), and, therefore, has clinical relevance in terms of identifying persons who may be at an increased risk of a subsequent depression. Notably, our questionnaire did not include questions regarding tobacco and alcohol use after diagnosis, and consequently we could not evaluate the impact of changes in the use of those products after diagnosis in relation to subsequent clinical depressive symptoms. That topic should be addressed in future studies.

Future Studies

Evidence from the current and previous studies suggests that smoking and drinking may be associated with depressive symptoms among persons diagnosed with oral cancer and precancer. Although our findings were highly robust with regard to associations between subsequent depression and both smoking and drinking through the year of diagnosis, it is necessary to confirm our results in other populations of OED cases and among early and late-stage cancer cases. Given our findings, it also seems prudent that future studies, preferably longitudinal in nature, seek to obtain detailed smoking and drinking histories for periods both before and at the time of diagnosis and for specified time-points after diagnosis and treatment. Attention should be given to obtaining information on potentially confounding variables, including stage, treatment, and their proximity to the assessment of depression. In addition, future studies will benefit from measures of personality traits, belief systems, genetic factors that could be related to depressive symptoms, and the use of tobacco and alcohol.

In summary, it is important for healthcare practitioners who treat or care for individuals with head and neck cancer or precancers to be aware of depressive symptoms in their patients and the factors that may contribute to them. In this sample of persons diagnosed with oral cancer or OED, individuals who were smoking during the calendar year of diagnosis had twice the odds of having a CES-D score indicative of depression compared with former and never-smokers combined. Diagnosis-year drinking, per se, was not associated with CES-D scores

suggestive of depression; however, our findings suggest that an average alcohol consumption of greater than 1.5 drinks/week is associated with a protective effect on depression among both diagnosis-year and former drinkers. Beer consumption was most strongly associated with the inverse relationship. Although the relationships between depression status and both smoking and drinking were generally similar for both oral cancer and OED, the associations tended to be stronger for the cancer series.

Acknowledgments

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Table 1

Sociodemographic characteristics of study subjects in total and by Center for Epidemiologic Studies–Depression Scale (CES-D) score dichotomized at ≤15 and 16+ (n = 401).

| | | No. (%) by CES-D score | | |
Variable	Total sample No. (%)	0–15	16+	p value
Oral diagnosis				
OED	234 (58.4)	197 (60.6)	37 (48.7)	
Cancer	167 (41.6)	128 (39.4)	39 (51.3)	.06[*]
Age at interview, y				
≤50	69 (17.2)	46 (14.2)	23 (30.3)	
51–60	81 (20.2)	65 (20.0)	16 (21.1)	
61–70	119 (29.7)	106 (32.6)	13 (17.1)	
71+	132 (32.9)	108 (33.2)	24 (31.6)	.002[*]
Mean (SD)	63.3 (11.9)	64.1 (11.4)	60.2 (13.3)	.04[†]
Sex				
Female	192 (47.9)	159 (48.9)	33 (43.4)	
Male	209 (52.1)	166 (51.1)	43 (56.6)	.39[*]
Race				
White, non-Hispanic	384 (95.8)	313 (96.3)	71 (93.4)	
Other	17 (4.2)	12 (3.4)	5 (6.6)	.26[*]
BSNI score				
Low (0–1)	95 (23.9)	65 (20.2)	30 (39.5)	
Medium (2–5)	160 (40.2)	131 (40.7)	29 (38.2)	
Medium-high (6,7)	55 (13.8)	49 (15.2)	6 (7.9)	
High (8+)	88 (22.1)	77 (23.9)	11 (14.5)	.002[*]
Months between diagnosis and interview[*]				
≤12	121 (30.2)	96 (29.5)	25 (32.9)	
13–15	189 (47.1)	153 (47.1)	36 (47.4)	
16+	91 (22.7)	76 (23.4)	15 (19.7)	.74[*]
Mean (SD)	13.4 (4.2)	13.5 (4.2)	13.0 (4.2)	.31[†]

[*] Based on Pearson chi-square test.

[†] Based on Mann-Whitney test.

Percentages may not total to 100% due to rounding. Three subjects did not answer questions related to the BSNI.

Table 2

Odds ratios for smoking and drinking (during or prior to the year of diagnosis) in relation to a subsequent depression (as measured by a CES-D score of 16 +).

| Variable | No. of Subjects by CES-D Score | | OR$_{crude}$ | 95% CI | OR$_{adj}$* | 95% CI |
	0–15	16+				
Smoking						
Diagnosis-year smoking						
No	193	32	1.00	(Ref)	1.00	(Ref)
Yes	132	44	2.01	1.21–3.34	2.30	1.26–4.21
Smoking status						
Never	62	13	1.00	(Ref)	1.00	(Ref)
Former	131	19	0.69	0.32–1.49	0.98	0.40–2.37
Diagnosis-year	132	44	1.59	0.80–3.16	2.27	0.96–5.35
Average cigarette equivalents per day						
0	62	13	1.00	(Ref)	1.00†	(Ref)
1–19	73	18	1.18	0.53–2.59	1.07	0.40–2.84
20–39	128	31	1.16	0.57–2.36	0.93	0.36–2.44
40+	62	14	1.08	0.47–2.48	0.88	0.29–2.65
Drinking						
Diagnosis-year drinking						
No	97	24	1.00	(Ref)	1.00	(Ref)
Yes	228	52	0.92	0.54–1.58	0.89	0.50–1.60
Drinks/wk in quartiles						
< 1.5	82	24	1.00	(Ref)	1.00	(Ref)
1.5–<8.0	80	16	0.68	0.34–1.38	0.53	0.24–1.15
8–<23	80	14	0.59	0.29–1.24	0.35	0.15–0.80
23+	83	22	0.91	0.47–1.74	0.38	0.16–0.88

*
Odds ratios (ORs) adjusted for diagnostic status (cancer /OED), age (≤50, 51–60, 61–70, 71+), working outside the home, social support (BSNI, >low vs. low), and sex as well as either level of alcohol consumption in quartiles (< 1.5, 1.5–<8, 8–<23, 23+ drinks/week) or diagnosis-year smoking. All adjusted ORs exclude 3 subjects who did not answer BSNI questions.

†
Odds ratios adjusted for diagnostic status (cancer /OED), age (≤50, 51–60, 61–70, 71+), working outside the home, social support (BSNI, >low vs. low), sex, level of alcohol consumption in quartiles (< 1.5, 1.5–<8, 8–<23, 23+ drinks/week) and diagnosis-year smoking.

Table 3

Adjusted odds ratios for alcohol consumption/week in relation to a subsequent depression reported for ex- and diagnosis-year drinkers[*].

Variable	Ex-drinkers		Diagnosis-year drinkers	
	OR	95% CI	OR	95% CI
Drinks/wk in quartiles[*]				
<1.5	1.00	(Ref)	0.56	0.15–2.07
1.5–<8.0	0.57	0.11–2.91	0.35	0.10–1.20
8–<23	0.29	0.04–2.03	0.23	0.07–0.82
23+	0.10	0.10–0.50	0.36	0.10–1.29

[*] Odds ratios from a model containing diagnostic status, age, social support (BSNI), working outside the home, sex, diagnosis-year smoking, diagnosis-year drinking (y/n), average number of drinks/week (4 categories), and the interaction term: diagnosis-year drinking * average number of drinks/week.

Table 4

Adjusted odds ratios for a subsequent depression in relation to diagnosis-year smoking and level of alcohol consumption by oral diagnostic status.[*]

Variable	OED		Cancer	
	OR	95% CI	OR	95% CI
Diagnosis-year smoking				
No	1.00	(Ref)	1.00	(Ref)
Yes	1.73	0.74–4.06	3.10	1.25–7.64
Drinks/wk in quartiles				
<1.5	1.00	(Ref)	1.00	(Ref)
1.5–<8.0	0.46	0.17–1.27	0.76	0.21–2.75
8–<23	0.43	0.14–1.36	0.29	0.08–1.02
23+	0.55	0.17–1.73	0.23	0.06–0.87

[*] Odds ratios (ORs) from separate models for OED and oral cancer cases. Each model included age, social support (BSNI), working outside the home, sex, diagnosis-year smoking, and level of alcohol consumption. Adjusted ORs exclude 3 subjects who did not answer BSNI questions.