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Comorbidity Profile of Head and Neck Cancer Patients With and Without Depression

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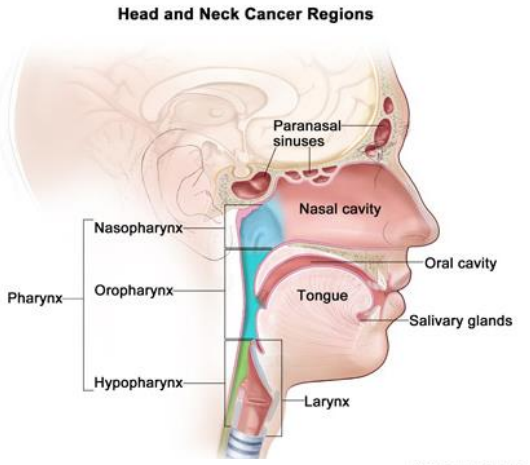
Abstract

This population-based retrospective study used SEER-Medicare data from 2002-2010 to assess depression, comorbidity, and substance use in the elderly head and neck cancer population. Out of 3,533 head and neck cancer patients, 10.6% had depression diagnoses two years prior to cancer diagnosis, 8.9% were newly diagnosed with depression within one year after cancer diagnosis, and 44.5% of those with preexisting depression had an additional depression diagnosis within one year following cancer diagnosis. Comorbid conditions ($p<0.0001$) and substance use ($p=0.0017$) showed associations with depression prior to cancer diagnosis yet, no significant associations with incidence of depression in this head and neck cancer population. This study affirms the need for continual depression screenings in head and neck cancer patients and suggests the need for increased research into the burden of comorbid conditions and substance use within the head and neck cancer population.

Chapter 1 – Introduction

Head and neck cancers are a group of cancers within certain areas of the body, such as oral cavity, pharynx, larynx, nasal cavity, and paranasal sinuses. Although not the most common type of cancer, head and neck cancers account for about 4% of all cancers in the United States (American Society of Clinical Oncology (ASCO), 2017; National Cancer Institute



NCI, 2017

(NCI), 2017). Each year, approximately 63,000 people are diagnosed with head and neck cancer, with diagnoses primarily occurring in individuals over the age of 50 (ASCO, 2017). It is estimated that about 14,000 people die each year from head and neck cancers, with men being 2-3 times more likely than women to develop these cancers (ASCO, 2017).

The 5-year survival rate for head and neck cancers vary greatly, ranging from 35-80%, and mainly depend on location of cancer and stage of diagnosis, with an average 5-year survival rate across all locations of about 60% (ASCO, 2017). Later stage diagnosis is often associated with preexisting depression for cancer patients along with poorer survival rates and less definitive treatments (Baillargeon et al., 2011; Boyd et al., 2012). Depression following diagnosis is also associated with advanced stages of cancer and is highly prevalent in elderly populations (Spoletini et al., 2008; Parpa, Tsilika, Gennimata, & Mystakidou, 2015). Higher rates of depression are common in head and neck cancer patients, often related to disfigurement or dysfunctional eating and communication abilities, and depressive symptoms have been associated with lower survival rates (Haisfield-Wolfe, 2009; Zimmaro et al., 2018). Additionally, comorbidities are known to affect treatment plans for head and neck cancer patients and the severity of comorbidities has been associated with poorer outcomes and lower survival rates in this population (Piccirillo, 2000).

Since patients diagnosed with head and neck cancer are particularly at risk for depression and other comorbidities before and after cancer diagnosis, it is important to understand the associations between additional comorbidities and depression in this population. However, little has been shown in the literature aimed at analyzing these connections. The purpose of this research report is to examine the associations between

comorbidities and depression status in patients with head and neck cancers using the Surveillance, Epidemiology and End Results (SEER)-Medicare linked data. The specific aims of this study are to: (1) estimate the prevalence of depression and common comorbidities before cancer diagnosis, (2) estimate the incidence of depression 1 year after cancer diagnosis, (3) compare comorbidity distributions between patients with and without depression, and (4) examine common comorbidities and other factors associated with prevalence and incidence of depression.

Chapter 2 – Background and Literature Review

Overall, head and neck cancers have been known to be more emotionally taxing than other cancer types (Koster & Bergsma, 1990). Often associated with a higher prevalence of depression compared to other cancers, patients with head and neck cancer share many risk factors between the two diseases. The most notable shared risk factors for depression and head and neck cancer are excessive tobacco and/or alcohol use and poor lifestyle choices, including unhealthy diet. Such shared risk factors create higher risk for this cancer population to develop depression after diagnosis along with having an increased risk for depression prior to diagnosis. Additionally, negative impacts of head and neck cancer often result from the location of cancer near the face and the treatment process. Patients may experience severe disfigurement related to the cancer itself or due to the treatment process which can impact physical and mental health (Massie et al., 2011). Patients may also experience distress from issues such as eating, breathing, and communication which may be affected in this cancer population (Haisfield-Wolfe, 2009). Treatment options often include the use of radiation

therapy which has been associated with increased psychiatric disorders, including depression, which can greatly affect patient outcomes (Frick, 2007; Kelly et al., 2007).

Since head and neck cancers are typically diagnosed in individuals over the age of 50, it is more likely comorbidities play a role in patient outcomes. Prevalence of comorbidity increases with age and is known to impact treatment and treatment selection in head and neck cancer patients (Boje, 2014). Within populations of older adults aged 65 years or older, hypertension, hyperlipidemia, heart disease, arthritis, and diabetes are some of the most prevalent comorbid conditions, which are similarly seen in cancer populations (Williams et al., 2016). Higher rates of comorbidity have been observed in patients with head and neck cancer in particular and additional diseases create difficulties when selecting treatment modalities, thus affecting outcomes. Previous research has shown hypertension, pulmonary disease, diabetes to be highly prevalent in the head and neck cancer population, with prevalence of 28%, 13%, and 10%, respectively (Piccirillo & Vlahiotis, 2006). Such comorbid diseases are consistent with elderly populations, with higher impacts on those with head and neck cancer as an added disease. Additionally, high amounts of comorbidity and increased severity are known to increase mortality and have dramatic impacts on patient quality of life, especially for elderly cancer populations (Piccirillo & Vlahiotis, 2006; Williams et al., 2016; Paleri et al., 2010).

Substance use disorders are a highly prevalent comorbidity among patients with cancer, especially for head and neck cancer patients. Tobacco and alcohol use are well known risk factors for developing head and neck cancer and many patients continue use following diagnosis (Hashibe et al., 2009). Previous research has shown that in patients diagnosed with head and neck cancer over 30% continue to smoke and 16% continue hazardous alcohol

consumption, despite major impacts on treatment and quality of life related to depression (Duffy et al., 2007). Use of other substances have also been shown to be strongly associated with depression (Swendsen, J. D. & Merikangas, K. R., 2000; Moussas, G. I. & Papadopoulou, A. G., 2017). However, less is known about related impacts on cancer due to large numbers of drug subtypes and complications in research related to polysubstance use.

Implications of depression, substance use and additional comorbidities in head and neck cancer patients can be serious. Individuals with head and neck cancer have been shown to have higher risk for suicide compared to patients with other cancers and the general population (Zeller, 2006) while other studies have shown associations between mental illness, such as depression, and fewer cancer screenings, leading to later stage diagnosis (Baillargeon et al., 2011; Boyd et al., 2012). Differences in survival rates have been noted by recent studies for head and neck cancer patients with severe comorbidity conditions as well as more negative outcomes for individuals with an increased number of comorbidities (Boje, 2014; Yang & Warnakulasuriya, 2016). Substance use, especially alcohol and tobacco abuse, are known risk factors of head and neck cancer while being highly associated with mood disorders, like depression (Lai, Cleary, Sitharthan & Hunt, 2015; Duffy et al., 2007) However, even with the known impacts of depression, substance use, and other comorbidities, there are gaps in the research concerning the additive effects of substance use and other comorbid conditions on depression in head and neck cancer populations.

Chapter 3 – Data and Methods

This was a population-based retrospective study that used records from the SEER-Medicare database from 2002-2010. The SEER-Medicare linked database utilizes two large population-based sources of data to provide information on elderly adults with cancer diagnoses (NCI, 2019). The SEER database provides clinical, demographic, and death information on cancer patients while the Medicare databased provides information on claims for health care services provided while the patient was using Medicare insurance (NCI, 2019). From the database, the records of more than 10,000 individuals diagnosed with head and neck cancer in 2004-2005 were analyzed and those meeting certain criteria were included in the study sample.

For inclusion in the study sample, patients had to have head and neck cancer as their only cancer diagnosis and be aged 67 years or older, to guarantee at least two years of Medicare enrollment prior to cancer diagnosis (Figure 1). Additionally, patients could not be enrolled in a health maintenance organization (HMO) during the two years prior or one year following diagnosis along with continual enrollment in Medicare Parts A and B for two years before their cancer diagnosis, to ensure complete claim records. Head and neck cancer diagnosis was identified using International Classification of Disease for Oncology, Version 3 codes (ICD-O3) for lip, oral cavity, oropharynx, nasopharynx, hypopharynx, and larynx cancers.

The study sample was further separated by depression status using ICD-9-CM codes for depression, including: dysthymic disorder, major depression (single or recurrent episode), adjustment disorder (with depressive symptoms or prolonged depressive reaction), depressive disorder (not otherwise classified), bipolar I disorder (most recent episode or current depressed), depressive type psychosis, affective personality disorder (unspecified), chronic

depressive personality disorder, and cyclothymic disorder. Preexisting depression groups, post-cancer diagnosis depression groups, and a preexisting cancer with additional post-cancer depression diagnosis groups were created. Preexisting depression was defined as those with at least one depression diagnosis within two years prior to their cancer diagnosis. Post-cancer diagnosis depression was defined at least one depression diagnosis within one year following cancer diagnosis and those with preexisting depression were excluded. Preexisting depression with additional post-cancer depression diagnosis was defined as those having preexisting cancer and at least one addition diagnosis of depression following cancer diagnosis. For all analyses on the post-cancer diagnosis depression group, individuals diagnosed with head and neck cancers at death or autopsy were excluded since depression could not develop.

Sociodemographic information (sex, race, age, education, income, marital status, and cancer stage) was taken from SEER data with education and income based on census tract. Comorbidity diagnoses were determined using ICD-9-CM diagnostic codes based on the Deyo method for Medicare data (Deyo, Cherkin, & Ciol, 1992). Claims were used for diagnoses twelve months prior to head and neck cancer diagnosis and included myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, rheumatologic disease, peptic ulcer disease, mild live disease, diabetes (complicated and non-complicated), hemiplegia/paraplegia, moderate to severe renal disease, moderate-severe liver disease, and AIDS. Diagnoses of moderate to severe liver disease and AIDS were included for sample demographics but were excluded from final analyses due to extremely low frequencies within the study sample. Comorbidity groups were defined by the number of unique comorbidity types each patient had based on the separated comorbidities

listed above. Groups were divided into those with no comorbid conditions, one comorbidity type, two comorbidity types, three comorbidity types, and four or more comorbidity types.

Substance use disorder status was determined using Medicare data based on ICD-9-CM diagnostic codes. The codes included diagnoses for alcohol induced mental disorders, drug induced mental disorders, alcohol dependence, drug dependence, and non-dependence drug abuse (including tobacco use). Substance use was categorized by drug use type into alcohol use, tobacco use, and all other drugs.

Chi-square tests were used to determine differences in demographics between depression status groups, before and after cancer diagnosis. Further chi-square tests were used to determine differences in frequency of comorbid conditions and substance use disorders between depression status groups, before and after cancer diagnosis. Additional analysis of factors associated with depression diagnosis were completed with multivariable logistic regression models using stepwise selection. All analyses were completed using SAS version 9.4.

Chapter 4 – Results

A total of 12,175 patients were diagnosed with head and neck cancer from 2004-2005. From these individuals, 2,951 were excluded due to additional cancer diagnoses, 4,315 were excluded for age of diagnosis below 67 years, 151 were excluded for lacking continuous enrollment in Medicare Parts A and B, and 1,225 were excluded for enrollment in an HMO at some point during the study. The final sample included 3,533 patients.

Depression prior to cancer diagnosis. Of the 3,533 patients, 375 (10.6%) patients were diagnosed with depression within two years prior to head and neck cancer diagnosis. Table 1

provides demographics of these individuals by depression status prior to head and neck cancer diagnosis. These groups had significant differences by age, gender, race, marital status, and number of unique comorbidities. The preexisting depression group had a higher percentage of patients in the two oldest age group, 80-84: (18.7% vs 15.3%) and 85+: (16.3% vs 12.9%), and a lower percentage of patients in the youngest age group, 67-69: (16.3% vs 21.3%). Additionally, the preexisting depression group had a higher percentage of females (45.9% vs 32.5%) and Non-Hispanic whites (86.9% vs 80.2%), compared to the non-depressed group. Differences in marital status were seen between the groups such that the preexisting depression group had a higher percentage of widowed patients (34.1% vs 24.5%) and a lower percentage of married or living as married patients (40.5% vs 52%). The number of unique comorbidities was different between depression groups such that patients with preexisting depression had a higher percentage of patients with more comorbidity types. The preexisting depression group had a higher percentage of patients with 4 or more comorbidity types (24.8% vs 9.5%) and a lower percentage of patients with no comorbid conditions (18.4% vs 37.6%). For those 375 individuals with preexisting depression, 267 (44.5%) had an additional depression diagnosis following head and neck cancer diagnosis.

Comorbidity comparison by depression status prior to cancer diagnosis. Table 2 provides the comorbidity characteristics of the study sample by depression status prior to head and neck cancer diagnosis. The preexisting depression group had a significantly higher percentage of individuals with each comorbidity category, except moderate to severe liver disease and AIDS, which were about equal between preexisting depression and non-depression groups. Table 2a provides the distribution of substance use disorders in the sample prior to

cancer diagnosis. The groups differed significantly by alcohol use, with a higher percentage of alcohol users in the preexisting depression group (8.3% vs 4.7%). Both groups had similar percentages of individuals using tobacco. Additionally, there was a trending difference in use of other drugs with a slightly higher percentage other drug users in the preexisting depression group (1.1% vs 0.4%).

Multivariable logistic regression of factors associated with preexisting depression. The odds of having depression compared to no depression prior to cancer diagnosis differs significantly by gender, race/ethnicity, number of comorbidities, and alcohol use (Table 3). Females have 1.88 (95% CI=1.50, 2.35) times the odds of having preexisting depression compared to males after adjusting for all other variables in the model. Non-white individuals have 0.57 (95% CI=0.41, 0.79) times the odds of having preexisting depression compared to Non-Hispanic Whites after adjusting for other variables in the model. Additionally, increasing the number of comorbidities is associated with increasing odds of preexisting depression such that one additional comorbidity has 1.28 (95% CI=0.91, 1.81) times the odds, two additional comorbidities have 2.51 (95% CI=1.78, 3.55) times the odds, three additional comorbidities have 3.79 (95% CI=2.63, 5.46) times the odds, and four or more additional comorbidities have 5.32 (95% CI=3.78, 7.49) times the odds after adjusting for other model variables. Finally, alcohol use was associated with preexisting depression such that individuals using alcohol had 1.97 (95% CI=1.29, 3.01) time the odds of preexisting depression when compared to those not using alcohol after adjusting for other model variables. No significant associations were found with interactions between gender, race/ethnicity, comorbidity group, and alcohol.

Additional depression diagnosis following cancer diagnosis. A further analysis was conducted on the sample of 375 patients who had preexisting depression. During the one-year period following head and neck cancer diagnosis, 167 or 44.5% received at least one additional depression diagnosis. Table 4 compares demographics of patients with additional depression diagnosis (n=167) and patients without additional depression diagnosis (n=208). These groups differ by race/ethnicity, with a higher percentage of Non-Hispanic Whites in the depression group (92.8% vs 82.2%). Table 5 compares the comorbidity characteristics of these two samples. These groups have significant difference in prevalence of myocardial infarction, non-complicated diabetes, and moderate to severe renal disease. Individuals with an additional diagnosis of depression have a lower percentage of myocardial infarction (5.4% vs 12.5%), a lower percentage of non-complicated diabetes (23.4% vs 33.2%) and a lower percentage of moderate to severe renal disease (6.0% vs 13.0%). Table 5a provides the distribution of substance use disorders for patients with preexisting depression by status of additional depression diagnoses following cancer diagnosis. These groups have no significant differences in alcohol, tobacco, or other drug use.

New depression case development following cancer diagnosis. There were 3,158 patients who had no depression diagnosis during the two years before head and neck cancer diagnosis. Within one year after the head and neck cancer diagnosis, 281 (8.9%) developed depression. Table 6 provides demographics of these individuals by depression status following cancer diagnosis. These groups differed significantly by age and gender. The depression group had a higher percentage of females (40.6% vs 31.7%) compared to the non-depressed group and a higher percentage of patients aged 70-74 (35.2% vs 27.8%).

Comorbidity comparison by depression status following cancer diagnosis. Table 7 provides the comorbidity characteristics of the study sample by depression status following head and neck cancer diagnosis. There were no significant differences between groups on any comorbidity categories. Table 7a provides the substance use characteristics by depression status following head and neck cancer diagnosis. Trending differences were shown for other drug use with a slightly higher percentage of depressed patients using other drugs (1.1% vs 0.3%). There were no significant differences between groups for alcohol or tobacco use following cancer diagnosis.

Multivariable logistic regression for factors associated with new depression development. Gender was significantly associated with depression following cancer diagnosis with females having 1.49 (95% CI=1.15, 1.92) times the odds of developing depression compared to males, when adjusting for age (Table 8). Additionally, age was associated with depression following cancer diagnosis with those aged 70-74 having 1.43 (95% CI: 1.01, 2.04) times the odds of developing depression compared to those aged 67-69, when adjusting for gender. No significant interactions were found between age and gender.

Chapter 5 – Discussion

The results of this study show the prevalence of depression to be approximately 10.6% for elderly adults during the two years prior to head and neck cancer diagnosis. Similar studies have shown slightly lower prevalence of depression for other cancers such as pancreatic adenocarcinoma (7.9%), breast cancer (7.5%), and prostate cancer (5%), suggesting a higher burden of depression on head and neck cancer populations (Boyd et al., 2012; Goodwin, Zhang,

& Ostir, 2004; Prasad et al., 2014). Our findings replicate previous research results showing incidence rates of depression ranging from 15% to 50% in head and neck cancer populations, which is among the highest rates for cancer patients (Lydiatt, Moran & Burke, 2009). We found that one in ten patients (8.9%) with no depression diagnosis during the two years prior to head and neck cancer diagnosis received a diagnosis of depression within one year following cancer diagnosis. Interestingly, close to half (44.5%) of patients with pre-existing depression received additional diagnosis of depression within one year following cancer diagnosis.

These results indicate an increased need for depression screening following cancer diagnosis, especially in patients known to have depressive symptoms prior to head and neck cancer diagnosis. Depression is a highly recurrent disorder and cancer diagnosis can be considered a stressful life event, creating higher risk of depressive disorders (Burcusa & Iacono, 2007). Following diagnosis with head and neck cancer, patients with a history of depression may need symptoms monitored closely to avoid missed depression diagnoses which could be overlooked as normal grief. Focusing on such symptoms can hopefully minimize the impact of depression on treatment and overall quality of life in this population.

The present study showed high prevalence of comorbidity in the head and neck cancer patient sample. The overall prevalence of comorbidity was 64.5% with 62.4% of patients with preexisting depression having at least two types of comorbidity and 34.1% of patients without preexisting depression having at least two types of comorbidity. Since only unique comorbidity types were used in this sample, these percentages are likely a conservative measure of the burden of comorbidity on this population. However, the increased burden is notable and

follows previous research showing associations between high rates of comorbidity and depression in elderly cancer populations (Spoletini et al., 2008).

More specifically, the comorbidities with the highest prevalence for this sample were chronic obstructive pulmonary disease (32.8%), non-complicated diabetes (22.8%), peripheral vascular disease (19.1%), cerebrovascular disease (17.9%), and chronic heart failure (16.1%). As expected, patients with preexisting depression had higher percentages of most comorbidity types, however, patients developing depression after head and neck cancer diagnosis showed no difference in types of comorbidities compared to those who did not develop depression. Since comorbid conditions did not differ between patients that did and did not develop depression following head and neck cancer diagnosis, other factors likely had greater influence on a patient's likelihood of developing depression. For those patients without preexisting depression, gender and age were the only significant predictors of depression which suggests other factors may be better for predicting depression in this sample. Since age and gender have previously been shown to be risk factors for depression across many populations, it's possible that other factors have greater predictive abilities within this sample that were not assess in this study.

The present study found prevalence of alcohol use disorder to be 5.0% for head and neck cancer patients. Previous research has shown the overall prevalence of alcohol use disorder to be 2.6% for Medicare recipients suggesting higher rates of alcohol use disorder in the head and neck cancer population (Centers for Medicare and Medicaid Services, 2017). Differences were found in prevalence of alcohol use disorder between those with and without preexisting depression. However, no differences were found in substance use disorders

between patients that did and did not develop depression after diagnosis, regardless of their depression history. The lack of difference in substance use following cancer diagnosis suggests a lack of association between substance use and depression in this sample, however the prevalence of substance use shown in this data was likely not representative of the entire head and neck cancer population. This study was limited to reports of substance use disorders based on diagnostic codes which do not account for other types of substance use beyond clinical diagnoses. Most likely a higher percentage of the sample had history of substance use which was not document with Medicare codes and could not be accounted for in these analyses.

This study had limitations based on the data set used for analyses. The SEER-Medicare database only offers diagnostic codes for identification of depression, comorbidities, and substance use. Previous research has shown higher estimates of prevalence and incidence of depression, substance use, and other comorbid conditions which suggests that diagnostic codes used in the SEER-Medicare database do not account for all forms of these diseases. Additionally, this sample only included individuals strictly relying on Medicare for their health care. According to the AARP Public Policy Institute (2009), over 90% of Medicare beneficiaries have supplemental insurance coverage and those individuals would not be accounted for in these analyses. This sample also only included individuals over the age of 67 so, interpretation is limited to older patients and should not be generalized to younger populations of head and neck cancer patients. Based on the limitations associated with SEER-Medicare data, more research needs to be done with less restrictive samples to further assess the impacts of comorbidity and substance use on depression in head and neck cancer patients. Further research should aim to include substance use information beyond claim data and an increased

variety of comorbid conditions to get a more well-rounded view of the burdens on head and neck cancer patients.

Table 1. Demographics by depression status prior to HNC diagnosis.

	Depression (N=375)		No Depression (N=3158)		
Variable	Count	%	Count	%	p-value
Age					0.0425
67-69	61	16.3%	671	21.3%	
70-74	108	28.8%	899	28.5%	
75-79	75	20.0%	696	22.0%	
80-84	70	18.7%	484	15.3%	
85+	61	16.3%	408	12.9%	
Gender					<0.0001
Male	203	54.1%	2133	67.5%	
Female	172	45.9%	1025	32.5%	
Race					0.0014
Non-Hispanic White	326	86.9%	2533	80.2%	
Other	49	13.1%	625	19.8%	
% of Census Tract with 4 Year College Degree					0.1845
0-33%	254	67.73%	2260	71.56%	
34+%	93	24.80%	723	22.89%	
Unknown	28	7.47%	175	5.54%	
Marital Status					0.0001
Married/Living as Married	152	40.5%	1642	52.0%	
Divorced/Separated	43	11.5%	284	9.0%	
Single	32	8.5%	274	8.7%	
Widowed	128	34.1%	775	24.5%	
Unknown	20	5.3%	183	5.8%	
Median Income (census tract)					0.9341
<$35,000 or Missing	124	33.1%	1005	31.8%	
$35,000-$44,999	87	23.2%	723	22.9%	
$45,000-$59,999	80	21.3%	714	22.6%	
$60,000+	84	22.4%	716	22.7%	
Cancer Stage					0.1805
Unstaged	150	40.0%	1394	44.1%	
In Situ/Localized	84	22.4%	657	20.8%	
Regional	102	27.2%	865	27.4%	
Distant	39	10.4%	242	7.7%	
Comorbidity Group					<0.0001
0	69	18.4%	1186	37.6%	
1	72	19.2%	896	28.4%	
2	75	20.0%	486	15.4%	
3	66	17.6%	291	9.2%	
4+	93	24.8%	299	9.5%	
Additional Depression DX[a]					N/A
Yes	167	44.5%	-	-	
No	208	55.5%	-	-	

[a] Additional Depression DX indicates individuals with preexisting depression with at least one diagnosis of depression following head and neck cancer diagnosis

Table 2. Comorbidities by depression status prior to HNC diagnosis.

	Depression (N=375)		No Depression (N=3158)		
Variable	Count	%	Count	%	p-value
Myocardial Infarction					0.0085
Yes	35	9.3%	181	5.7%	
No	340	90.7%	2977	94.3%	
Congestive Heart Failure					<0.0001
Yes	122	32.5%	445	14.1%	
No	253	67.5%	2713	85.9%	
Peripheral Vascular Disease					<0.0001
Yes	114	30.4%	559	17.7%	
No	261	69.6%	2599	82.3%	
Cerebrovascular Disease					<0.0001
Yes	124	33.1%	508	16.1%	
No	251	66.9%	2650	83.9%	
Dementia					<0.0001
Yes	56	14.9%	102	3.2%	
No	319	85.1%	3056	96.8%	
Chronic Obstructive Pulmonary Disease					<0.0001
Yes	182	48.5%	978	31.0%	
No	193	51.5%	2180	69.0%	
Rheumatologic Disease					0.0049
Yes	24	6.4%	104	3.3%	
No	351	93.6%	3054	96.7%	
Peptic Ulcer Disease					0.0065
Yes	23	6.1%	100	3.2%	
No	352	93.9%	3058	96.8%	
Mild Liver Disease					0.0289
Yes	24	6.4%	124	3.9%	
No	351	93.6%	3034	96.1%	
Diabetes (Complicated)					0.0030
Yes	33	8.8%	153	4.8%	
No	342	91.2%	3005	95.2%	
Diabetes (Non-complicated)					0.0042
Yes	108	28.8%	698	22.1%	
No	267	71.2%	2460	77.9%	
Hemiplegia/Paraplegia					<0.0001
Yes	13	3.5%	25	0.8%	
No	362	96.5%	3133	99.2%	
Moderate/Severe Renal Disease					0.0009
Yes	37	9.9%	166	5.3%	
No	338	90.1%	2992	94.7%	
Moderate/Severe Liver Disease					0.4296
Yes	1	0.3%	4	0.1%	
No	374	99.7%	3154	99.9%	
AIDS					0.2010
Yes	1	0.3%	1	>0.1%	
No	374	99.7%	3157	<99.9%	

Table 2a. Substance use disorders by depression status prior to HNC diagnosis.

Variable	Depression (N=375) Count	Depression (N=375) %	No Depression (N=3087)[b] Count	No Depression (N=3087)[b] %	p-value
Alcohol					0.0057
Yes	31	8.3%	145	4.7%	
No	344	91.7%	2942	95.3%	
Tobacco					0.3025
Yes	41	10.9%	285	9.2%	
No	334	89.1%	2802	90.8%	
Other Drugs					0.0862
Yes	4	1.1%	12	0.4%	
No	371	98.9%	3075	99.6%	

[b] 71 patients missing substance use data

Table 3. Multivariate logistic regression of depression prior to HNC diagnosis.

Variable	OR	95%	CI	p-value
Gender				<0.0001
Male	REF	-	-	
Female	1.88	1.50	2.35	
Race/Ethnicity				0.0006
Non-Hispanic White	REF	-	-	
Other	0.57	0.41	0.79	
Comorbidity Group				<0.0001
0	REF	-	-	
1	1.28	0.91	1.81	
2	2.51	1.78	3.55	
3	3.79	2.63	5.46	
4+	5.32	3.78	7.49	
Alcohol				0.0017
Yes	1.97	1.29	3.01	
No	REF	-	-	

Table 4. Demographics for patients with preexisting depression by status of additional depression diagnoses following HNC diagnosis.

Variable	Additional Depression (N=167) Count	%	No Additional Depression (N=208) Count	%	p-value
Age					0.3137
67-69	27	16.2%	34	16.4%	
70-74	57	34.1%	51	24.5%	
75-79	32	19.2%	43	20.7%	
80-84	27	16.2%	43	20.7%	
85+	24	14.4%	37	17.8%	
Gender					0.8349
Male	89	53.3%	114	54.8%	
Female	78	46.7%	94	45.2%	
Race					0.0031
Non-Hispanic White	155	92.8%	171	82.2%	
Other	12	7.2%	37	17.8%	
% of Census Tract with 4 Year College Degree					0.2189
0-33%	109	65.3%	145	69.7%	
34+%	48	28.7%	45	21.6%	
Unknown	10	6.0%	18	8.7%	
Marital Status					0.7952
Married/Living as Married	64	38.3%	88	42.3%	
Divorced/Separated	21	12.57%	22	10.6%	
Single	17	10.2%	15	7.2%	
Widowed	56	33.5%	72	34.6%	
Unknown	9	5.4%	11	5.3%	
Median Income (census tract)					0.9733
<$35,000 or Missing	55	32.9%	69	33.2%	
$35,000-$44,999	40	24.0%	47	22.6%	
$45,000-$59,999	34	20.4%	46	22.1%	
$60,000+	38	22.7%	46	22.1%	
Cancer Stage					0.2988
Unstaged	62	37.1%	88	42.3%	
In Situ/Localized	45	27.0%	39	18.7%	
Regional	44	26.3%	58	27.9%	
Distant	16	9.6%	23	11.1%	
Comorbidity Group					0.4778
0	36	21.6%	33	15.9%	
1	33	19.8%	39	18.8%	
2	34	20.4%	41	19.7%	
3	29	17.4%	37	17.8%	
4+	35	21.0%	58	27.9%	

Table 5. Comorbidities for patients with preexisting depression by status of additional depression diagnoses following HNC diagnosis.

Variable	Additional Depression (N=167) Count	%	No Additional Depression (N=208) Count	%	p-value
Myocardial Infarction					0.0203
Yes	9	5.4%	26	12.5%	
No	158	94.6%	182	87.5%	
Congestive Heart Failure					0.6577
Yes	52	31.1%	70	33.7%	
No	115	68.9%	138	66.3%	
Peripheral Vascular Disease					0.4988
Yes	54	32.3%	60	28.9%	
No	113	67.7%	148	71.1%	
Cerebrovascular Disease					0.3780
Yes	51	30.5%	73	35.1%	
No	116	69.5%	135	64.9%	
Dementia					0.5628
Yes	27	16.2%	29	13.9%	
No	140	83.8%	179	86.1%	
Chronic Obstructive Pulmonary Disease					0.5347
Yes	78	46.7%	104	50.0%	
No	89	53.3%	104	50.0%	
Rheumatologic Disease					0.3972
Yes	13	7.8%	11	5.3%	
No	154	92.25	197	94.7%	
Peptic Ulcer Disease					0.3907
Yes	8	4.8%	15	7.2%	
No	159	95.2%	193	92.8%	
Mild Liver Disease					0.8343
Yes	10	6.0%	14	6.7%	
No	157	94.0%	194	93.3%	
Diabetes (Complicated)					0.2018
Yes	11	6.6%	22	10.6%	
No	156	93.4%	186	89.4%	
Diabetes (Non-complicated)					0.0394
Yes	39	23.4%	69	33.2%	
No	128	76.6%	139	66.8%	
Hemiplegia/Paraplegia					0.5752
Yes	7	4.2%	6	2.9%	
No	160	95.8%	202	97.1%	
Moderate/Severe Renal Disease					0.0245
Yes	10	6.0%	27	13.0%	
No	157	94.0%	181	87.0%	
Moderate/Severe Liver Disease					0.4453
Yes	1	0.6%	0	0%	
No	166	99.4%	208	100%	
AIDS					0.4453
Yes	1	0.6%	0	0%	
No	166	99.4%	208	100%	

Table 5a. Substance use disorders for patients with preexisting depression by status of additional depression diagnoses following HNC diagnosis.

	Additional Depression (N=167)		No Additional Depression (N=208)		
Variable	Count	%	Count	%	p-value
Alcohol					1.0000
Yes	14	8.4%	17	8.2%	
No	153	91.6%	191	91.8%	
Tobacco					0.6188
Yes	20	12.0%	21	10.1%	
No	147	88.0%	187	89.9%	
Other Drugs					0.6320
Yes	1	0.6%	3	1.4%	
No	166	99.4%	205	98.6%	

Table 6. Demographics by depression status following HNC diagnosis, excluding those with preexisting depression.

	Depression (N=281)		No Depression (N=2877)		
Variable	Count	%	Count	%	p-value
Age					0.0111
67-69	52	18.5%	619	21.5%	
70-74	99	35.2%	800	27.8%	
75-79	52	18.5%	644	22.4%	
80-84	52	18.5%	432	15.0%	
85+	26	9.3%	382	13.3%	
Gender					0.0027
Male	167	59.4%	1966	68.3%	
Female	114	40.6%	911	31.7%	
Race					0.4327
Non-Hispanic White	231	82.2%	2302	80.0%	
Other	50	17.8%	575	20.0%	
% of Census Tract with 4 Year College Degree					0.3601
0-33%	197	70.1%	2072	71.7%	
34+%	72	25.6%	654	22.6%	
Unknown	12	4.3%	165	5.7%	
Marital Status					0.1884
Married/Living as Married	131	46.6%	1511	52.5%	
Divorced/Separated	23	8.2%	261	9.1%	
Single	29	10.3%	245	8.5%	
Widowed	83	29.5%	692	24.1%	
Unknown	15	5.3%	168	5.8%	
Median Income (census tract)					0.8207
<$35,000 or Missing	84	29.9%	921	32.0%	
$35,000-$44,999	63	22.4%	660	23.0%	
$45,000-$59,999	69	24.6%	645	22.4%	
$60,000+	65	23.1%	651	22.6%	
Cancer Stage					0.2895
Unstaged	115	40.9%	1279	44.5%	
In Situ/Localized	54	19.2%	603	21.0%	
Regional	85	30.3%	780	27.1%	
Distant	27	9.6%	215	7.5%	
Comorbidity Group					0.0734
0	102	36.3%	1084	37.7%	
1	67	23.8%	829	28.8%	
2	57	20.3%	429	14.9%	
3	31	11.0%	260	9.0%	
4+	24	8.5%	275	9.6%	

Table 7. Comorbidities by depression status following HNC diagnosis, excluding those with preexisting depression.

	Depression (N=281)		No Depression (N=2877)		
Variable	Count	%	Count	%	p-value
Myocardial Infarction					0.5907
Yes	18	6.4%	163	5.7%	
No	263	93.6%	2714	94.3%	
Congestive Heart Failure					0.1788
Yes	47	16.7%	398	13.8%	
No	234	83.3%	2479	86.2%	
Peripheral Vascular Disease					0.6231
Yes	53	18.9%	506	17.6%	
No	228	81.1%	2371	82.4%	
Cerebrovascular Disease					0.4973
Yes	49	17.4%	459	16.0%	
No	232	82.6%	2418	84.0%	
Dementia					0.7229
Yes	10	3.6%	92	3.2%	
No	271	96.4%	2785	96.8%	
Chronic Obstructive Pulmonary Disease					0.3447
Yes	94	33.5%	884	30.7%	
No	187	66.5%	1993	69.3%	
Rheumatologic Disease					1.0000
Yes	9	3.2%	95	3.3%	
No	272	96.8%	2782	96.7%	
Peptic Ulcer Disease					0.7197
Yes	10	3.6%	90	3.1%	
No	271	96.4%	2787	96.9%	
Mild Liver Disease					0.8724
Yes	10	3.6%	114	4.0%	
No	271	96.4%	2763	96.0%	
Diabetes (Complicated)					0.7708
Yes	12	4.3%	141	4.9%	
No	269	95.7%	2736	95.1%	
Diabetes (Non-complicated)					0.7636
Yes	64	22.8%	634	22.0%	
No	217	77.2%	2243	78.0%	
Hemiplegia/Paraplegia					0.4831
Yes	3	1.1%	22	0.8%	
No	278	98.9%	2855	99.2%	
Moderate/Severe Renal Disease					0.5742
Yes	12	4.3%	154	5.3%	
No	269	95.7%	2723	94.7%	
Moderate/Severe Liver Disease					1.0000
Yes	0	0%	4	0.1%	
No	281	100%	2873	99.9%	
AIDS					1.0000
Yes	0	0%	1	>0.1%	
No	281	100%	2876	>99.9%	

Table 7a. Substance use disorders by depression status following HNC diagnosis, excluding those with preexisting depression.

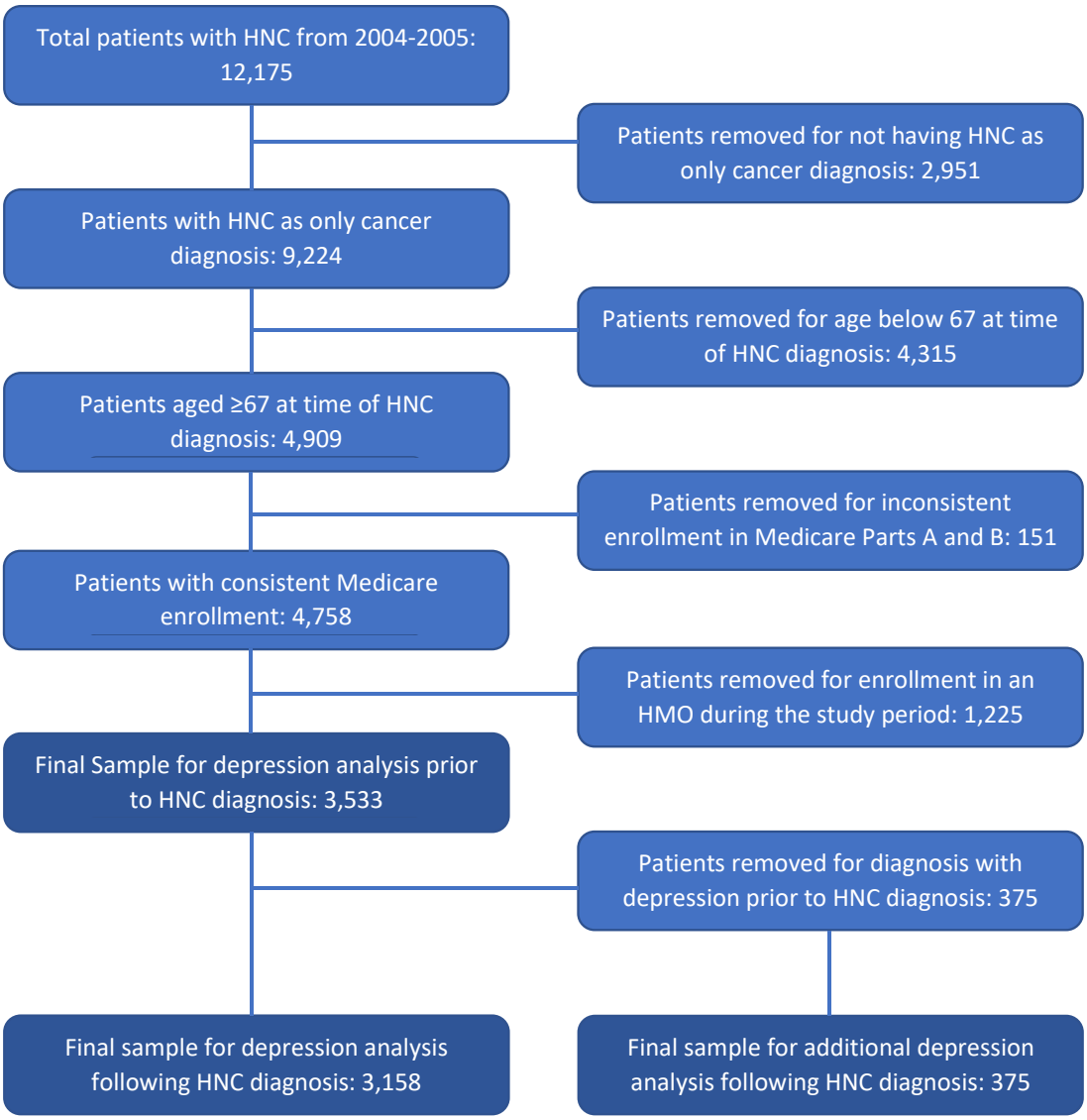
Variable	Depression (N=281) Count	Depression (N=281) %	No Depression (N=2820)[c] Count	No Depression (N=2820)[c] %	p-value
Alcohol					0.7670
Yes	14	5.0%	131	4.7%	
No	267	95%	2689	95.3%	
Tobacco					0.1930
Yes	32	11.4%	253	9.0%	
No	249	88.6%	2567	91.0%	
Other Drugs					0.0877
Yes	3	1.1%	9	0.3%	
No	278	98.9%	2811	99.7%	

[c] 71 patients missing substance use data

Table 8. Multivariate logistic regression of depression following HNC diagnosis.

Variable	OR	95%	CI	p-value
Gender				0.0023
Male	REF	-	-	
Female	1.49	1.15	1.92	
Age Group				0.0089
67-69	REF	-	-	
70-74	1.43	1.01	2.04	
75-79	0.92	0.62	1.38	
80-84	1.32	0.88	1.97	
85+	0.72	0.44	1.18	

Figure 1. Study sample selection flowchart.



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