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ORIGINAL RESEARCH

Smoking, depression, and hospital costs of respiratory cancers: Examining race and sex variation

Baqar A. Husaini[1], Robert S. Levine[2], Phillip Lammers[3], Pam Hull[4], Meggan Novotny[5], Majaz Moonis[6]

Abstract

Objective: To investigate the effect of smoking and depression on hospital costs for lung cancer (LC).

Methods: We extracted data on depression, smoking history, demographics, and hospital charges for patients with respiratory cancers (ICD-9 codes 161–163, 165) from the 2008 Tennessee Hospital Discharge Data System. The sample (n=6665) was mostly white (86%) and male (57%). Age-adjusted rates were developed in accordance with Centers for Disease Control and Prevention methods, and hospital costs were compared for patients with LC with versus without depression and a smoking history.

Results: Three findings (P<0.001) emerged: (1) the LC rate was higher among blacks than among whites, and higher among men than among women; (2) while 66% of LC patients smoked (more men than women without racial variation), 24% had depression (more females and whites were depressed); (3) the LC hospital cost was 54% higher than the non-LC hospital cost, and this cost doubled for patients with LC with depression and smoking versus those without such characteristics.

Conclusion: While LC is more prevalent among blacks and men, depression is higher among female and white patients. Since depression with higher costs existed among LC patients, our findings point to (1) the possibility of cost savings by diagnosing and treating depression among LC patients, and (2) implementation of proven smoking cessation programs to reduce LC morbidity and hospital costs.

Keywords: Smoking; depression; lung cancer; race; sex

1. Tennessee State University, Nashville, TN, USA
2. Department of Family and Community Medicine, Baylor College of Medicine, Houston, TX, USA
3. Meharry Medical College, Nashville, TN, USA
4. Division of Epidemiology, Vanderbilt University, Nashville, TN, USA
5. Counseling Psychology, Tennessee State University, Nashville, TN, USA
6. Department of Medicine – Neurology, University of Massachusetts Medical School, Worcester, MA, USA

CORRESPONDING AUTHOR:
Baqar A. Husaini, PhD
Tennessee State University, PO Box 9580, Nashville, TN 37209, USA
E-mail: bhusaini@tnstate.edu

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Background

Respiratory cancers include cancers of the larynx, pleura, bronchus, and lungs. Malignant neoplasm of the trachea, bronchus, and lungs, commonly known as lung cancer, constitutes a large proportion of respiratory cancers in the United States, and according to the Centers for Disease Control and Prevention (CDC), it accounts for 137,000 American deaths annually. Lung cancer is also the most common cancer globally, and is highly correlated with smoking and old age [1, 2]. The average age of US lung cancer patients is around 70 years, and the US lifetime risk of developing lung cancer at age 70 years or older is 1 in 16 (6.4%) for men and 1 in 21 (4.8%) for women [3]. Lung cancer is a leading cause among all causes of US death for individuals aged 60 years or older [3]. Smoking is prevalent in 80%–90% of lung cancer patients

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[4], who occupy 28% of all hospital beds annually [5]. The age-adjusted incidence rate of lung cancer (per 100,000) in the United States is highest in states that produce tobacco or have higher rates of smoking. For example, Utah, a predominantly Mormon non-tobacco-producing state where observant Mormons are not allowed to smoke, has the lowest rates (34.7 for males and 23.7 for females), compared with a high rate (120.4 for males vs. 80.7 for females) in Kentucky, a major tobacco-producing state [3].

Smoking, sex, and lung cancer

According to the CDC [6], while the smoking rate declined from 20.9% in 2005 to nearly 17% in 2014, the proportion of male smokers remained higher than the proportion of female smokers (18.8% and 14.8% respectively)**.** With the decline in smoking, a similar decline in the incidence of lung cancer (per 100,000) has also occurred, from a 2008 rate of 89.0 for males and 55.2 for females [7] to 76.7 for males and 54.1 for females in 2012 [3]. This decline, which has been observed in most states, has been greater for males than for females [3]. However, because of, in part, a higher prevalence of smoking among males [8], lung cancer rates have remained higher for males than for females.

Smoking, race, and lung cancer

In the past, a higher prevalence of smoking has been reported among blacks [9], with different risk factors for lung cancer among blacks who smoked heavily [10]. However, smoking prevalence now appears to be similar between blacks and whites (17.5% vs. 18.2% respectively) [6]. Nonetheless, the incidence of lung cancer in black males was 21% higher in 2012 than that in white males (85.6 vs. 70.9 respectively) [11]. The higher rate of lung cancer among blacks appears to be consistent with their higher rates of smoking in the past [9]. The rate for lung cancer among black females was consistently lower than that among white females from 2008 (51.1 vs. 57.0 respectively) [7] to 2012 (44.3 vs. 69.3 respectively) [11]. Additionally, the 5-year survival rate after a cancer diagnosis is lower among blacks than among whites [12].

Smoking and depression

Recent evidence suggests that 7.6% of the US population has depression, and 43% of seriously depressed individuals have difficulties performing work and activities of daily living [13]. There is also some evidence that indicates that smoking starts in some cases at early ages, while in others it may develop as a coping response to stressors [14–17]. Available data, however, suggest that smoking and depression are highly correlated in that depressed individuals have a higher rate of smoking [18–21]. While the causal direction of the smoking–depression relationship remains unclear, evidence clearly indicates that depressed individuals are more likely to smoke than non-depressed individuals, and that depressed individuals are less likely to be successful in their attempts to quit smoking than non-depressed individuals [18–21]. Further, a recent brief from the CDC noted that more than 60% of depressed individuals had smoked, and that their smoking rate increased with the severity of depression. Moreover, age- and sex-specific data have consistently shown that more depressed adults not only smoked more often but also that they were more likely to be heavy smokers compared with non-depressed adults. Finally, depressed adults have been found to be less likely to quit smoking than non-depressed individuals [22].

Cardiovascular disease risk factors and lung cancer

While cancer, diabetes mellitus, and other CVD risk factors have collectively contributed to 65% of all deaths in recent years [23], the relationships between specific CVD risk factors and lung cancer has remained mixed. For instance, while in six studies lung cancer was unrelated to diabetes [24–29], three studies found significant evidence for such a relationship [30–32]. Other studies have pointed to a higher prevalence of liver, pancreas, endometrium, colon/rectum, breast, and bladder cancers among obese and diabetic patients [33–44]. While cholesterol level was unrelated to lung cancer in two studies [45, 46], hypertension was associated with cancer among male smokers [47]. Lung cancer was also related to angina, myocardial infarction, and stroke that may develop within 14 months after lung cancer diagnosis [48]. These coronary heart disease (CHD) factors (angina, myocardial infarction, or stroke) were characteristic of patients whose cancer had metastasized [49]. Lung cancer also existed among smokers who either self-reported that diagnosis or in whom angina, myocardial infarction, or stroke had been reported [50–52]. Further, lung cancer patients have been reported to develop atrial fibrillation as a result of cancer surgery or other cancer therapies (12%–20% of patients develop atrial fibrillation in the postsurgery period) [53–56]. There is a high prevalence of atrial fibrillation not only among lung cancer patients but also among patients with colorectal cancer [57]. An inflammatory state among these patients is believed to promote atrial fibrillation [58–61].

The occurrence of chronic kidney disease and other comorbidities increases with age [62]. Overall, chronic kidney disease (as measured by estimated glomerular filtration rate) is unrelated to lung, prostate, breast, and colorectal cancers. However, reduced estimated glomerular filtration rate or end-stage renal disease, in particular, is associated with lung cancer [63, 64]. Finally, chronic obstructive pulmonary disease (COPD), which is an accelerated decline in lung functioning, is highly related to lung cancer [65, 66]. Moreover, COPD is also a risk factor for CVD events such as heart failure [62, 66]. In sum, lung cancer is reported to be related to a number of CVD risk factors, including hypertension, diabetes, angina, myocardial infarction, stroke, atrial fibrillation, COPD, and smoking.

While the consequences of smoking relative to CVD and lung cancer are well known [1, 2], and the relationship between smoking and depression has been carefully examined [14–22], what remains unknown is the effect of smoking and depression on hospital costs for lung cancer patients. In our analyses of hospital-discharged patients, we focus on two issues by race and sex: (i) the prevalence of smoking, depression, and lung cancer along with CVD risk factors that characterize lung cancer patients, and (2) variations in the effect of smoking and depression on hospital costs for lung cancer.

Methods

Sample characteristics

We examined 2008 Tennessee Hospital Discharge Data System (HDDS) files for patients (aged 20 years or older) discharged with any diagnosis of respiratory cancer (ICD-9 codes 161, 163, 165), including cancer of the bronchus/lungs (ICD9-9 code 162). There were 6665 patients with respiratory cancers, and 95% of them (6332) had lung cancer, a figure that is closely aligned with the percentage of lung cancer among respiratory cancer deaths in Tennessee among individuals aged 20 years or older for 2008 (98% of 4423 deaths) [67].

The sample patients had a mean age of 67 years (range 20–99 years) and it included 57% men and 86% whites. The sample patients had on average nearly three comorbidities, including conditions such as hypertension, diabetes mellitus, and COPD. There was age variation by race, whereby black patients tended to be younger than white patients (mean age+standard deviation 64.4+11.21 years vs. 67.8+11.21 years respectively).

Data characteristics

HDDS files provide patients' basic demographics such as age, race, sex, county and zip code of residence, ICD-9 diagnostic codes (both primary and secondary diagnoses) for which an inpatient was treated, and the number of admissions, number of days in hospital, and charges (dollars) for each discharge. Only the attending physicians gave diagnoses, which included diagnoses of any smoking history (covering past/present smoking, as well as smoking abuse), depression, and anxiety. Since there is a high overlap in symptoms of depression and anxiety (ranging from 48% to 91%) [68, 69], we combined the diagnoses of depression and anxiety as a single variable for our analyses [70].

The secondary diagnoses (ICD-9 codes) for conditions such as hypertension and diabetes mellitus were used as CVD risk factors for lung cancer. The HDDS files do not provide clinical data on various tests performed or medications administered. Since the Tennessee population is largely composed of whites (77%) and African Americans (16%), we focused on comparing lung cancer rates, risk factors, and estimated costs across African Americans (blacks) and white groups.

We used an index of comorbidity that was simply a sum of all secondary diagnoses identified by ICD-9 codes for each patient. Since HDDS files do not provide information on actual reimbursed dollars for services, we used the submitted charges as an estimated cost of lung cancer for the year 2008. We computed total hospital charges/costs for the year, which included lung cancer cost as well as the cost for the same patient when he/she was readmitted with diagnoses other than lung cancer. These costs included room charges per night, along with the cost of medications, supplies, and tests and procedures done on the patient. Physicians' charges were not included in the hospital costs.

Statistical analysis

Age-adjusted lung cancer prevalence (per 100,000 population, 2010 US Census) were computed for race and sex groups in accordance with CDC methods [71]. Differences in the prevalence of lung cancer risk factors by sex and race were evaluated with the Pearson χ^2 test and the Fisher's exact test. To examine the likelihood of lung cancer association with each CVD risk factor, logistic regression models (odds ratio [OR] and 95% confidence interval [CI]) were used on the total sample first and then for each subgroup separately. Finally, ANOVA and t tests were used to examine group differences for cost variables.

Results

Prevalence of smoking, depression, and lung cancer

Smoking history: The smoking history of the patients was composed of "ever smoked" and "tobacco abuse." We combined these two variables to create a variable of smoking history that included both past smokers and abusers. Our analysis shows that more men than women had a smoking history (68% vs. 64%, $P<0.01$; Table 1), with no racial differences in smoking (67% among blacks vs. 66% among whites).

Depression: One-fourth of patients (24.0%) had depression; the rate of depression was higher among white patients than among black patients (26% vs. 14%, $P<0.001$) and higher among women than among men (32% vs. 18%, $P<0.001$;). Further, a significant ($P<0.001$) proportion of white women (34%) had depression compared with other subgroups, including one-tenth of black men who were depressed. From our data it was not clear whether these patients had depression before their hospital admission or whether their depression developed after hospital admission.

Age-adjusted prevalence: The age-adjusted lung cancer prevalence was 142.9 per 100,000 for the total sample (Table 1), with blacks having a higher rate than whites (146.6 vs. 131.6, $P<0.001$). Prevalence was also higher among men than among women (174.9 vs. 119.9, $P<0.001$), and it was higher, in particular, among black men than among white men (201.2 vs. 171.3, $P<0.001$). Similarly, higher rates existed for black women compared with white women (111.1 vs. 103.4, $P<0.001$). The prevalence is higher among men overall and among blacks of both sexes.

Cardiovascular disease risk factors in lung cancer

We examined risk factors in two ways: (1) by means of a simple comparison of the percentage of risk factors for each lung cancer subgroup (Table 1), and (2) by use of multivariate logistic regression models that predicted lung cancer (Table 2) from various risk factors. Table 1 shows that compared with patients without lung cancer, patients with lung cancer had a higher prevalence of some CVD factors, including hypertension (64% vs. 53%, $P<0.001$), CHD (34% vs. 25%, $P<0.001$), atrial fibrillation (29% vs. 18%, $P<0.001$), COPD (62% vs. 18%, $P<0.001$), smoking history (66% vs. 28%, $P<0.001$), obesity (1.9% vs. 0.4%, $P<0.04$), and depression (24% vs. 20%, $P<0.01$). There were some variations in the CVD predictors by the subgroup of lung cancer patients. For example, depressed patients compared with non-depressed lung cancer patients had a higher prevalence of hypertension (70% vs. 61%, $P<0.001$), diabetes (27% vs. 24%, $P<0.01$), CHD (37% vs. 33%, $P<0.01$), atrial fibrillation (33% vs. 28%, $P<.01$), smoking history (74% vs. 64%, $P<0.001$), and COPD (72% vs. 59%, $P<0.001$). The higher prevalence of both COPD and depression in relation to smoking confirms findings reported by others [22].

Our analysis of those who had both a smoking history and depression revealed that they significantly ($P<0.001$) had a higher prevalence of hypertension, diabetes, CHD, high cholesterol level, atrial fibrillation, and COPD compared with patients without a smoking history and depression (Table 1). However, there were some variations by race, such as black lung cancer patients compared with their white peers had a higher prevalence of hypertension (73% vs. 62%, $P<0.001$), diabetes (30% vs. 24%, $P<0.01$), and chronic kidney disease (13% vs. 10%, $P<0.001$). The white lung cancer patients in comparison had a higher prevalence of CHD (35% vs. 25%, $P<0.001$), atrial fibrillation (29% vs. 25%, $P<0.01$), COPD (63% vs. 52%, $P<0.001$), and depression (26% vs. 14%, $P<0.001$). The higher prevalence of CHD, atrial fibrillation, and COPD among whites was largely contributed by white men (Table 1). There were no racial differences in smoking history, obesity, or myocardial infarction, or stroke (Table 1).

Table 1. Prevalence of lung cancer and risk factors among patients by race and sex

Risk factors	No lung cancer	Lung cancer patients														
		All patients	Smoking history		Depression		Smoking history and depression		Black	White	Male	Female	BM	WM	BF	WF
			Yes	No	Yes	No	Yes	No								
Mean age (years)	56	67	66	70	66	67	67	67	64	68	67	67	64	68	65	68
Lung cancer rate[a]	–	142.9	–	–	–	–	–	–	146.6	131.6	174.9	119.9	201.2	171.3	111.1	103.4
Risk factors																
HTN (%)	53	64*	66†	60	70*	61	70*	57	73*	62	63	64	69	62	78*	62
DM (%)	24	25	25	25	27	24	25	23	30*	24	26	23	28	26	33*	22
High cholesterol level (%)	8	11	12	9	14	10	14*	8	8	11	12	10	18*	12	7	11
CHD (%)	25	34*	35	32	37	33	38*	31	25	34*	39	27	25	41*	24	28
CKD (%)	10	10	9	11	11	10	10	11	13	10	11	9	12	11	13	8
MI (%)	4	4	5	4	5	4	5	4	4	4	5	4	4	5	5	4
Stroke (%)	9	10	10	10	12	9	12	9	11	10	9	10	10	9	13	10
AF (%)	18	29*	29	29	33*	28	33†	28	25	29†	32*	25	27	32*	22	26
COPD (%)	18	62*	70*	46	72*	59	77*	44	52	63*	63†	60	57	64*	46	62
Depression (%)	20	24†	27*	19	–	–	–	–	14	26*	18	32*	10	19	18	34*
Smoking history (%)	28	66*	–	–	74*	64	–	–	67	66	68†	64	72*	67	62	65
Obesity (%)	0.4	1.9†	2.1	1.5	2.1	1.9	2.2	1.5	1.6	2.0	2.0	1.8	2.0	2.0	1.0	1.9

*Differences between adjacent columns are significant at $p<0.001$.

†Differences between adjacent columns are significant at $p<0.05$.

[a]Lung cancer prevalence rate per 100,000 population.

AF, atrial fibrillation; BF, black female; BM, black male; CHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; M, males; MI, myocardial infarction; WF, white female; WM, white male.

In our multivariate logistic regression analyses (Table 2), the association of many of these CVD risk factors with lung cancer was attenuated except for four factors – namely, atrial fibrillation (OR 1.40, 95% CI 1.38–1.48), COPD (OR 5.25, 95% CI 4.96–5.55), smoking (OR 3.03, 95% CI 2.86–3.20), and obesity (OR 2.87, 95% CI 2.37–3.47). These four factors were consistently associated with lung cancer across all lung cancer subgroups (Table 2). Diabetes, CHD, myocardial infarction, or stroke did not emerge as a significant contributor to lung cancer as was previously reported by others [49, 50]. Finally, some racial and sex variations existed in that black lung cancer patients were more likely to have hypertension than whites (OR 1.37, 95% CI 1.16–1.6). This relationship appears to emerge largely because of hypertension among black women (OR 2.00, 95% CI 1.53–2.62). Among whites, cholesterol was related to lung cancer (OR 1.16, 95% CI 1.06–1.27), which largely was due to white women with high cholesterol levels (OR 1.19, 95% CI 104–1.36). Neither smokers nor depressed patients had any other additional risk factor associated with lung cancer besides atrial fibrillation, COPD, obesity, and smoking (Table 2).

Effect of depression and smoking on hospital costs

Overall hospitalization cost: Hospitalization costs in a year are largely affected by three factors: the patients' number of comorbidities, number of hospital admissions, and length of stay (days) in the hospital. Table 3 shows that the average total hospital cost for lung cancer patients was 54% higher than that for patients without lung cancer ($71,850 vs. $41,264, $P<0.001$). Further, among lung cancer patients, hospital costs were 31% higher among blacks than among whites ($94,888 vs. $69,575, $P<0.001$, Table 4), and 5% higher among men than among women ($74,286 vs. 70,829, $P<0.04$). The higher costs among lung cancer patients (total group) compared with patients without lung cancer were due in part to the greater number of comorbidities that lung cancer patients had (2.31 vs. 1.56, $P<0.001$), more admissions (2.24 vs. 1.53, $P<0.001$), and longer hospital stays (14 days vs. 8 days).

Smoking and depression costs: Hospital costs differed significantly by the subgroup of lung cancer patients (Table 4). For instance, the costs were 35% higher for smokers than for nonsmokers ($80,848 vs. $56,931, $P<0.001$), and 40% higher among depressed patients than among non-depressed patients ($97,265 vs. $65,075, $P<0.001$). Clearly, smoking and depression individually contribute to higher hospitalization costs of lung cancer patients.

Combined effect of smoking and depression: Finally, 18% of all lung cancer patients (Table 3) were both smokers and depressed. The costs for these patients doubled compared with those for lung cancer patients who were not smokers or depressed ($104,434 vs. $52,216, $P<0.0001$; Table 3). The effect of these two factors combined (smoking history and depression) was more pronounced for blacks than for whites ($141,480 vs. $101,620, $P<0.001$; Table 4), and also greater for male patients than for female patients ($113,480 vs. $97,324, $P<0.001$; Table 4). Further, these effects were significantly greater for black men and black women compared with their white peers (Table 5).

Discussion

It may be noted that our sample of patients represented serious cases that required hospitalization. These patients included both new cases (diagnosed in 2008) and old cases; that is, those with a prior diagnosis of lung cancer. All diagnoses were made by the attending physicians. The diagnoses appeared in the records only when the patient was treated for those conditions. With this background, our analyses revealed that while there were no racial differences in smoking, significant differences did emerge with regard to depression (24%) that appear to be consistent with previous reports of depression prevalence (11%–44%) among lung cancer patients [72]. In our study, whites and female patients, as in a previous study [13], had a more frequent occurrence of depression than their black and male counterparts. In blacks and men, the depression diagnosis may be made less frequently, in part, because physicians may not ask about their symptoms and these groups of patients do not readily admit to being depressed [73–76].

Racial differences were very pronounced with regard to the prevalence of lung cancer. Here, the rates were higher for blacks than for whites, higher among men than among women; both black men and black women had higher lung cancer rates than white men and white women. These findings in Tennessee

Table 2. Odds ratios and 95% of confidence intervals of cardiovascular disease risk factors predicting lung cancer among subgroups of lung cancer patients

Risk factors	All lung cancer patients	Smoking history	Depression	Black	White	Male	Female	BM	WM	BF	WF	DM	CHD
HTN													
OR	1.05	1.05	0. 90	1.37*	1.01	0.91	1.24*	1.01 (NS)	0.90	2.00*	1.16*	0.89	0.85
CI	0.99–1.11	0.98–1.12	0.87–1.11	1.16–1.62	0.95–1.08	0.84–0.98	1.13–1.35	0.81–1.25	0.83–0.97	1.53–2.62	1.06–1.27	0.76–0.92	0.76–0.96
DM													
OR	0.81	0.80	0.76	0.80	0.81	0.84	0.76	0.81	0.84	0.80	0.75	–	0.78
CI	0.76–0.86	0.74–0.86	0.67–0.85	0.68–0.94	0.76–0.86	0.77–0.90	0.69–0.83	0.66–1.01	0.77–0.91	0.63–1.01	0.67–0.83	–	0.72–0.86
High cholesterol level													
OR	1.15*	1.18*	1.12 (NS)	1.08 (NS)	1.16*	1.38*	1.15†	1.30*	1.13	0.88	1.19*	1.10 (NS)	1.06
CI	1.06–1.24	1.00–1.30	0.96–1.30	0.83–1.30	1.06–1.26	1.02–1.27	1.01–1.30	0.91–1.84	1.01–1.28	0.56–1.29	1.04–1.36	0.96–1.27	0.95–1.19
CHD													
OR	0.90	0.82	0.93	0.78	0.91	0.83	0.85	0.72	0.85	0.83	0.87	0.91	–
CI	0.84–0.95	0.76–0.88	0.82–1.08	0.95–0.93	0.86–0.97	0.77–0.90	0.78–0.92	0.56–0.91	0.78–0.92	0.63–1.10	0.78–0.96	0.82–0.99	–
CKD													
OR	0.77	0.69	0.68	0.51	0.76	0.66	0.76	0.41	0.72	0.65	0.78	0.72	0.73
CI	0.65–0.78	0.58–0.81	0.58–0.81	0.41–0.64	0.69–0.83	0.59–0.74	0.65–0.87	0.31–0.55	0.64–0.81	0.47–0.89	0.66–0.91	0.63–0.82	0.65–0.82
MI													
OR	0.67	0.82	0.82	0.90	0.64	0.63	0.76	0.83	0.61	1.01	0.72	0.58	0.68
CI	0.59–0.76	0.64–1.04	0.64–1.04	0.63–1.30	0.56–0.74	0.53–0.73	0.62–0.94	0.50–1.37	0.51–0.72	0.60–1.72	0.57–0.91	0.46–0.73	0.60–0.77
Stroke													
OR	0.89	0.93	0.92	0.98	0.87	0.81	0.99	0.81	0.81	1.17 (NS)	0.96	0.70	0.86
CI	0.92–0.97	0.79–1.08	0.79–1.08	0.79–1.23	0.80–0.96	0.73–0.91	0.87–1.12	0.59–1.10	0.72–0.92	0.85–1.60	0.83–1.10	0.65–0.84	0.76–0.97
AF													
OR	1.40*	1.38*	1.54*	1.45*	1.39*	1.36*	1.36*	1.43*	1.35*	1.36*	1.36*	1.32*	1.21*
CI	1.38–1.48	1.28–1.48	1.37–1.73	1.23–1.72	1.31–1.48	1.27–1.47	1.24–1.49	1.15–1.78	1.25–1.47	1.04–1.76	1.24–1.50	1.18–1.47	1.11–1.32
COPD													
OR	5.25*	4.47*	4.94*	6.18*	5.11*	5.34*	4.82*	7.36*	5.09*	4.59*	4.86*	3.63*	3.68*
CI	4.96–5.55	4.18–4.79	4.39–5.57	5.32–7.17	4.82–5.43	4.97–5.74	4.42–5.25	6.05–8.91	4.71–5.50	3.65–5.75	4.42–5.33	3.24–4.06	3.33–4.06
Smoking history													
OR	3.03*	–	2.62*	3.72*	2.92*	2.15*	3.80*	2.50*	2.11*	4.30*	3.67*	3.09*	2.53*
CI	2.86–3.20	–	2.33–2.94	3.20–4.32	2.76–3.10	2.00–2.31	3.49–4.12	2.04–3.06	1.95–2.28	3.43–5.38	3.35–4.02	22.76–3.45	2.31–2.79
Depression													
OR	0.82	0.79	–	0.81	0.86	0.81	0.92	0.86	0.91	0.94	0.92	0.84	0.93
CI	0.76–0.87	0.73–0.98	–	0.70–1.05	0.77–0.88	0.74–0.88	0.85–1.01	0.65–1.17	0.74–0.89	0.72–1.23	0.85–1.01	0.75–0.94	0.82–0.90

Table 2 (conitnued)

Risk factors	All lung cancer patients	Smoking history	Depression	Black	White	Male	Female	BM	WM	BF	WF	DM	CHD
Obesity													
OR	2.87*	2.71*	2.03*	2.10*	2.99*	2.98*	2.58*	3.02*	2.07*	1.21 (NS)	2.85*	2.27*	2.77*
CI	2.37–3.47	2.17–3.39	1.41–2.92	1.19–3.70	2.44–3.66	2.33–3.82	1.92–3.47	2.50–6.09	2.28–3.88	1.35–3.56	1.98–3.88	1.58–3.40	1.98–3.91

*Significant at $P<0.001$.

†Significant $P<0.04$.

AF, atrial fibrillation; BF, black female; BM, black male; CHD, coronary heart disease; CI confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction; OR, odds ratio; NS, not significant; WF, white female; WM, white male.

Table 3. Cost factors and effect of smoking and depression on hospital cost of lung cancer

	No lung cancer (*n*=393,570)	Lung cancer patients						
		Total lung cancer patients (*n*=6665)	Smoker		Depressed		Smoker and depressed	
			No (*n*=2246)	Yes (n=4419)	No (*n*=5068)	Yes (*n*=1597)	No (*n*=1824)	Yes (*n*=1175)
Comorbidities	1.56	2.31*	2.44	3.85	3.01	4.54	2.15	4.84
Admissions	1.53	2.24*	1.74	2.43*	1.95	2.99*	1.62	3.26*
Hospital days	7.59	13.90*	11.76	15.32*	12.34	19.77*	10.49	20.66*
Total cost ($)	41,264	71,850*	56,931	80,848*	65,075	97,265*	52,216	104,434*

*Differences between two adjacent columns are significant at $P<0.001$.

The percentage value between two values (e.g., $71,850 and $41,264=54%) was calculated by [(V1−V2)/(V1+V2/2)]×100.

Table 4. Cost factors and total cost of lung cancer alone and with smoking and depression by race and sex

Cost factors	Black			White			Male			Female		
	LC	LC+S+D		LC	LC+S+D		LC	LC+S+D		LC	LC+S+D	
		Yes	No		Yes	No		Yes	No		Yes	No
N	881	83	250	5,784	1092	1574	3,780	517	1045	2,885	659	6,665
Comorbidities	3.21	4.75*	2.28	3.40	4.85	2.13	3.45	5.02*	2.27	3.28	4.70*	1.97
Admissions	2.34+	4.04*	1.70	2.18	3.20	1.61	2.19	3.40*	1.98	2.21	3.09*	1.69
Hospital days	18.20	27.45*	13.9	13.50	20.15	9.96	14.00	21.50*	10.45	14.27	20.00*	10.53
Total cost ($)	94,888	141,480*	69,450	69,575	101,620*	48,479	74,286	113,480*	53,166	70,829	97,324*	50,941

*Differences between two adjacent are significant at $P<0.0001$.

LC, lung cancer patients; LC+S+D, lung cancer patients who are both smokers and depressed.

Table 5. Effect of smoking plus depression by race and sex

	Black male			White male			Black female			White female		
	LC	LC+S+D		LC	LC+S+D		LC	LC+S+D		LC	LC+S+D	
		Yes	No		Yes	No		Yes	No		Yes	No
N	494	36	250	3,286	481	919	387	47	124	2,498	611	655
Comorbidities	3.21	5.08*	2.29	3.49	5.02*	2.11	3.21	4.49*	2.26	3.29	4.72*	1.92
Admissions	2.26	4.39*	1.62	2.18	3.41*	1.57	2.45+	3.71*	1.79	2.17	3.03*	1.66
Hospital days	17.79	29.78*	13.13	13.47	20.88*	10.09	18.97*	25.66*	14.52	13.74	19.57*	9.79
Total cost ($)	91,384	159,950*	64,059	71,716	110,380*	51,673	97,085*	131,160*	74,928	66,758	94,721*	46,400

*Differences between two adjacent columns are significant at $P<0.001$.

LC, lung cancer patients; LC+S+D, lung cancer patients who are both smokers and depressed.

(a tobacco-producing state) are very similar to those for lung cancer in Kentucky (also a tobacco-producing state), and they provide supportive evidence for reported race and sex differences in lung cancer [3, 7].

Our analyses also delineated a set of four risk factors that were consistently related to lung cancer across all subgroups of patients: smoking, atrial fibrillation, COPD, and obesity. These findings substantiated what has been reported previously for lung cancer [53, 54, 57, 67], and they further provide supportive evidence for the inflammation hypothesis linking CVD and cancers [60]. However, our multivariate analyses did not find any additional risk factor in relation to lung cancer except for hypertension among black patients (OR 1.37, 95% CI 1.16–1.62), and high cholesterol level among white patients (OR 1.16, 95% CI 0.06–1.26). Little variation in additional risk factors emerged when separate analyses were conducted for subgroups such as depressed patients or those with a smoking history or those with diabetes mellitus or CHD (Table 2).

The anticipated relationships (e.g., lung cancer and myocardial infarction or stroke as reported earlier) [31, 49, 50] were nonexistent in these analyses. This may have been due to either patients being in treatment or the low prevalence of these risk factors in the present sample. The latter is particularly true for myocardial infarction and stroke, which existed only among less than 10% of our lung cancer patients. Thus CHD did not show a relationship with lung cancer in our analyses (Table 2). However, a relationship between CHD and atrial fibrillation could develop (within 14 months after treatment) because of cancer treatment modalities such as radiation therapy, chemotherapy, and surgery [54, 76]. The occurrence of atrial fibrillation may be higher among cancer patients because of frequent use of aspirin, which reportedly increases atrial fibrillation by 12% [77]. Hence the presence of atrial fibrillation (which existed in 34% of our CHD patients) may occur from nonsteroidal anti-inflammatory drug use. However, it is not clear from our limited data whether these CVD risk factors existed before the onset of lung cancer or developed after the diagnosis of lung cancer. Despite this limitation, our results point to a clear link between the effect of lung cancer and both smoking and depression independently as well as their joint effect (74% of depressed patients had smoked) on increased hospitalization costs (which increased by more than 50%), with some race and sex variation. Since 66% of all lung cancer patients smoked (past or present), an additional observation about its effect needs to be acknowledged—namely, that it is the number of years of smoking (rather than the quantity of cigarettes smoked alone) that may also play a critical role in the development of lung cancer [78].

Finally, the average hospital cost for lung cancer patients was 54% higher than that for patients without lung cancer. This cost among lung cancer patients increased additionally by 35% for smokers and 40% for depressed patients (Table 3). These costs more than doubled (>50%) for patients who were both smokers and depressed (Tables 3 and 4). Further, these higher cost trends held up for race and sex, whereby black and male patients had higher costs than their white and female peers. The higher costs among black lung cancer patients suggest that black patients may have poor access to healthcare providers (because of rates of lower insurance, poor symptom recognition, and/or late referrals [79–82]), may be reluctant to seek medical care during the early stages of disease especially if they are depressed [83], may experience more aggressive disease [84], or may access the healthcare system late in the progression of their disease. In any case, this late involvement may lead to more complex medical conditions that require a longer hospital stay and thus higher costs for blacks. Moreover, these higher hospital costs for male and black patients appear to be consistent with the higher hospital costs reported for blacks with CVD events such as stroke and heart failure [62, 85, 86].

Implications

Our findings relative to smoking and depression have programmatic implications. First, since smoking reduction has contributed to reductions in cancer mortality [87], there is a great need to continue implementing culturally appropriate, evidence-based tobacco cessation programs in the most vulnerable groups; blacks are prominent among such groups. Programs might include American Cancer Society guidelines [83] to reinforce other healthy choices (nutritional and exercise) as well as individualized counseling by service providers that includes both patient empowerment and greater use of the Quit Line services. Lowering smoking rates through such proven programs would not only be beneficial in reducing healthcare costs (estimated at $12.1 billion for lung cancer [88]), but may also reduce cancer morbidity and mortality [82, 87].

Secondly, our analyses showed that 74% of the depressed patients were smokers. Generally, depression, which has a prevalence of 11%–44% among cancer patients [72], is bidirectional in that it may occur before the onset of a disease (lung cancer in this case), or it may develop as a psychosocial response to the diagnosis of lung cancer. In either case, depression should be treated aggressively since it interferes with both self-management and treatment of a medical condition. Additionally, focus must be given to treatment modalities that avoid reoccurrence of depressive episodes. Further, since one-fourth of these patients were depressed and their hospital costs were noticeably higher, significant economic savings might be attainable if these patients were screened and treated for depression in conjunction with cancer treatment.

Finally, if evidence-based smoking cessation programs that incorporate the American Cancer Society guidelines [89] to reinforce a healthy lifestyle (nutritional diet and exercise) are implemented in the minority population, such programs would not only reduce hospitalization costs but would also reduce cancer morbidity significantly [90].

Limitations

Our findings are limited since hospital discharge files (HDDS) do not include veterans or patients from mental institutions. Further, the HDDS data are administrative files that neither provide data pertaining to patients' marital status, education, and annual income nor clinical data regarding medications used, test results, the severity of illness, or symptom indices used for clinical judgments/diagnoses. These files do not provide information on reimbursed dollars for the services provided. For the sake of maintaining confidentiality of records, patients' assigned identification numbers change every year, and hence it is not possible to follow a patient beyond a given year. Given these potential confounders, caution is required in interpreting the racial and sex results. Despite these limitations, we believe the present results provide significant insights into the impact of smoking and depression on hospitalization costs of lung cancer in Tennessee that may have national utility.

Conclusion

Lung cancer rates and hospital costs are higher for blacks and those who smoke and are depressed. Since depression exists among one-quarter of lung cancer patients, greater cost savings might be attained if depression is treated among lung cancer patients as soon as it is diagnosed. Finally, culturally appropriate, evidence-based smoking cessation programs might go a long way toward reducing cancer morbidity in the minority populations.

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Conflict of interest

The authors declare no conflict of interest.

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References

1. US Department of Health and Human Services. The health consequences of smoking – 50 years of progress: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health; 2014.
2. Mons U. Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium. Br Med J 2015;350(apr20 2):h1551.
3. Slegel RL, Miller KD, Jemal A. Cancer statistics. 2016. CA Cancer J Clin 2016;66(1):7–30.
4. Eldridge L. [Internet] Important facts about lung cancer. [accessed 2016 Nov 17]. Available from: https://www.verywell.com/facts-about-lung-cancer-2249396?utm_term=lung+cancer+facts&utm_content=p1-main-1-title&utm_medium=sem&utm_source=msn_s&utm_campaign=adid-8d3c07b3-ff27-4a1b-99a5-a5138ab860ef-0-ab_msb_ocode 31716&ad=semD&an=msn_s&am=broad&q=lung+cancer+facts&o=31716&qsrc=999&l=sem&askid=8d3c07b3-ff27-4a1b-99a5-a5138ab860ef-0-ab_msb.
5. Holmquist L, Russo A, Elixhauser A. Hospital stays for lung cancer, 2006. Statistical brief #63, Healthcare Cost & Utilization Project (HCUP), Agency for Healthcare Research & Quality; 2008.
6. Centers for Disease Control and Prevention. Current cigarette smoking among adults—United States, 2005–2014. Morb Mortal Wkly Rep 2015;64(44):1233–40.
7. Jemal A, Thun MJ, Ries LA, Howe HL, Weir HK, Center MM, et al. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. J Natl Cancer Inst 2008;100(23):1672–94.
8. Peters SAE, Huxley RR, Woodward M. Do smoking habits differ between women and men in contemporary Western populations? Evidence from half a million people in the UK Biobank study. BMJ Open 2014;4(12):e005663.
9. Richardson TL. African American smokers and cancers of the lung and of the upper respiratory and digestive tracts. Is menthol part of the puzzle? West J Med 1997;166(3):189–94.
10. Stellman SD, Chen Y, Muscat JE, Djordjevic MV, Richie JP Jr, Lazarus P, et al. Lung cancer risk in white and black Americans. Ann Epidemiol 2003;13(4):294–302.
11. Centers for Disease Control and Prevention. [Internet] Cancer types grouped by race and ethnicity. 2012. [accessed 2016 July 7]. Available from: www.cdc.gov/cancer/.
12. Bach PB, Schrag D, Brawley OW, Galaznik A, Yakren S, Begg CB. Survival of blacks and whites after a cancer diagnosis. J Am Med Assoc 2002;287(16):2106–2113.

13. Pratt LA, Brody DJ. Depression in the U.S. household population, 2009–2012. NCHS data brief, no 172. Hyattsville, MD: National Center for Health Statistics; 2014.
14. US Department of Health and Human Services. Preventing tobacco use among youth and young adults: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2012.
15. DiFranza JR, Rigotti NA, McNeill AD, Ockene JK, Savageau JA, Cyr DS, et al. Initial symptoms of nicotine dependence in adolescents. Tob Control 2000;9(3):313–19.
16. US Department of Health and Human Services. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2010.
17. Goodman E, Capitman J. Depressive symptoms and cigarette smoking among teens. Pediatrics 2000;106(8):748–55.
18. Glassman AH, Helzer JE, Covey LS, Cottler LB, Stetner F, Tipp JE, et al. Smoking, smoking cessation, and major depression. J Am Med Assoc 1990;264(12):1546–9.
19. Covey LS, Glassman AH, Stetner F. Cigarette smoking and major depression. J Addict Dis 1998;17(1):35–46.
20. Fergusson DM, Goodwin RD, Horwood LJ. Major depression and cigarette smoking: results of a 21-year longitudinal study. Psychol Med 2003;33(8):357–67.
21. Fluharty M, Taylor AE, Grabsski M, Munafo MR. The association of cigarette smoking with depression and anxiety: a systematic review. Nicotine Tob Res 2017;19(1):3–13.
22. Pratt LA, Brody DJ. Depression and smoking in the U.S. household population age 20 and over, 2005–2008. NCHS data brief #34, Hyattsville, MD: National Center for Health Statistics; 2010.
23. Eyre H, Kahn R, Robertson RM. Preventing cancer, cardiovascular disease, and diabetes. Diabetes Care 2004;27(7):1812–24.
24. Hall GC, Roberts CM, Mo J, MacRae KD. Diabetes and the risk of lung cancer. Diabetes Care 2005;28(3):590–4.
25. Wang Z, Bao C, Su C, Xu W, Luo H, Chen L, et al. Association between diabetes or antidiabetic therapy and lung cancer: a meta-analysis. J Diabetes Investig 2013;4(6):659–66.
26. Yang WS, Yang Y, Yang G, Chow WH, Li HL, Gao YT, et al. Pre-existing type 2 diabetes and risk of lung cancer: a report from two prospective cohort studies of 133 024 Chinese adults in urban Shanghai. BMJ Open. 2014;4(7):e004875.
27. Atchison EA, Gridley G, Carreon JD, Leitzmann MF, McGlynn KA. Risk of cancer in a large cohort of U.S. veterans with diabetes. Int J Cancer 2011;128(3):635–43.
28. Ehrlich SF, Quesenberry CP Jr, Van Den Eeden SK, Shan J, Ferrara A. Patients diagnosed with diabetes are at increased risk for asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, and pneumonia but not lung cancer. Diabetes Care 2010;33(1):55–60.
29. Inal A, Kaplan MA, Kucukoner M, Urakcı Z, Kılınc F, Isıkdogan A. Is diabetes mellitus a negative prognostic factor for the treatment of advanced non-small-cell lung cancer? Rev Port Pneumol 2014;20(2):62–8.
30. Lee JY, Jeon I, Lee JM, Moon JM, Park SM. Diabetes mellitus as an independent risk factor for lung cancer: a meta-analysis of observational studies. Eur J Cancer 2013;49(10):2411–23.
31. Lee MY, Lin KD, Hsiao PJ, Shin SJ. The association of diabetes mellitus with liver, colon, lung, and prostate cancer is independent of hypertension, hyperlipidemia, and gout in Taiwanese patients. Metabolism 2012;61(2):242–9.
32. Tseng CH. Diabetes but not insulin increases the risk of lung cancer: a Taiwanese population-based study. PLoS One 2014;9(7):e101553.
33. Cleary MP, Grossmann ME. Minireview: obesity and breast cancer: the estrogen connection. Endocrinology 2009;150(6):2537–42.
34. Larsson SC, Mantzoros CS, Wolk A. Diabetes mellitus and risk of breast cancer: a meta-analysis. Int J Cancer 2007;121(4):856–62.
35. Chow WH, Gridley G, Fraumeni JF, Jarvholm B. Obesity, hypertension, and the risk of kidney cancer in men. N Engl J Med 2000;343(18):1305–11.
36. Zucchetto A, Dal Maso L, Tavani A, Montella M, Ramazzotti V, Talamini R, et al. History of treated hypertension and diabetes mellitus and risk of renal cell cancer. Ann Oncol 2007;18(3):596–600.
37. El-Serag HB, Hampel H, Javadi F. The association between diabetes and hepatocellular carcinoma: a systematic review of epidemiologic evidence. Clin Gastroenterol Hepatol 2006;4(3):369–80.
38. Chari ST, Leibson CL, Rabe KG, Ransom J, de Andrade M, Petersen GM. Probability of pancreatic cancer following diabetes: a population-based study. Gastroenterology 2005;129(2):504–11.
39. Huxley R, Ansary-Moghaddam A, Berrington de Gonzalez A, Barzi F, Woodward M. Type-II diabetes and pancreatic cancer: a meta-analysis of 36 studies. Br J Cancer 2005;92(11):2076–83.

40. Govindarajan R, Ratnasinghe L, Simmons DL, Siegel ER, Midathada MV, Kim L, et al. Thiazolidinediones and the risk of lung, prostate, and colon cancer in patients with diabetes. J Clin Oncol 2007;25(12):1476–81.
41. Elwing JE, Gao F, Davidson NO, Early DS. Type 2 diabetes mellitus: the impact on colorectal adenoma risk in women. Am J Gastroenterol 2006;101(8):1866–71.
42. Kasper JS, Giovannucci E. A meta-analysis of diabetes mellitus and the risk of prostate cancer. Cancer Epidemiol Biomarkers Prev 2006;15(11):2056–62.
43. Friberg E, Orsini N, Mantzoros CS, Wolk A. Diabetes mellitus and risk of endometrial cancer: a meta-analysis. Diabetologia 2007;50(7):1365–74.
44. Larsson SC, Orsini N, Brismar K, Wolk A. Diabetes mellitus and risk of bladder cancer: a meta-analysis. Diabetologia 2006;49(12):2819–23.
45. Jacobs EJ, Gapstur SM. Cholesterol and cancer: answers and new questions. Cancer Epidemiol Biomarkers Prev 2009;28(3):590–4.
46. Tan M, Song X, Zhang G, Peng A, Li X, Li M, et al. Statins and the risk of lung cancer: a meta-analysis. PLoS One 2013;8(2):e57349.
47. Lindgren A, Pukkala E, Nissinen A, Tuomilehto J. Blood pressure, smoking, and the incidence of lung cancer in hypertensive men in North Karelia, Finland. Am J Epidemiol 2003;158(5):442–7.
48. Kocher F, Fiegl M, Mian M, Hilbe W. Cardiovascular comorbidities and events in CLC: often underestimated but worth considering. Clin Lung Cancer 2015;16(4):305–12.
49. Zoller B, Ji J, Sundquist J, Sundquist K. Risk of coronary heart disease in patients with cancer: a nationwide follow-up study from Sweden. Eur J Cancer 2012;48(1):121–8.
50. Hatlin P, Langhammer A, Carlsen SM, Salvesen O, Amundsen T. Self-reported cardiovascular disease and the risk of lung cancer, the HUNT Study. J. Thorasic Oncol 2014;9(7):940–6.
51. Selvik HA, Thomassen L, Bjerkreim AT, Næss H. Cancer-associated stroke: the Bergen NORSTROKE Study. Cerebrovasc Dis Extra 2015;5(3):107–13.
52. Chen PC, Muo CH, Lee YT, Yu YH, Sung FC. Lung cancer and incidence of stroke: a population-based cohort study. Stroke 2011;42(11):3034–9.
53. Beck-Nielsen J, Sorensen HR, Alstrup P. Atrial fibrillation following thoracotomy for non-cardiac diseases, in particular cancer of the lung. Acta Med Scand 1973;193(5):425–9.
54. Gayed IW, Liu HH, Wei X, Liao Z, Yusuf SW, Chang JY, et al. Patterns of cardiac perfusion abnormalities after chemoradiotherapy in patients with lung cancer. J Thorac Oncol 2009;4(2):179–84.
55. Roselli EE, Murthy SC, Rice TW, Houghtaling PL, Pierce CD, Karchmer DP, et al. Atrial fibrillation complicating lung cancer resection. J Thorac Cardiovasc Surg 2005;130(2):438–44.
56. Onaitis M, D'Amico T, Zhao Y, O'Brien S, Harpole D. Risk factors for atrial fibrillation after lung cancer surgery: analysis of the Society of Thoracic Surgeons general thoracic surgery database. Ann Thorac Surg 2010;90(2):368–74.
57. Guzzetti S, Costantino G, Sada S, Fundarò C. Colorectal cancer and atrial fibrillation: a case-control study. Am J Med 2002;112: 587–8.
58. Guzzetti S, Costantino G, Fundarò C. Systemic inflammation, atrial fibrillation, and cancer. Circulation 2002;106(9):e4.
59. Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420(6917):860–7.
60. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and cancer. Circulation 2016;133(11):1104–14.
61. van Leuven SI, Birjmohun RS, Franssen R, Bisoendial RJ, de Kort H, Levels JH, et al. Systemic inflammation as a risk factor for atherothrombosis. Rheumatology 2008;47:3–7.
62. Husaini BA, Levine RS, Norris KC, Cain VA, Bazargan M, Moonis M. Heart failure hospitalization by race/ethnicity, gender, and age in California: implications for prevention. Ethn Dis 2016;26(3):345–54.
63. Lowrance WT, Ordoñez J, Udaltsova N, Russo P, Go AS. CKD and the risk of incident cancer. J Am Soc Nephrol 2014;25(10): 2327–34.
64. Shebl FM, Warren JL, Eggers PW, Engels EA. Cancer risk among elderly persons with end-stage renal disease: a population-based case-control study. BMC Nephrol 2012;26(13):65.
65. Young RP, Hopkins RJ, Christmas T, Black PN, Metcalf P, Gamble GD. COPD prevalence is increased in lung cancer, independent of age, sex and smoking history. Eur Respir J 2009;34(2):380–6.
66. Wang H, Yang L, Zou L, Huang D, Guo Y, Pan M, et al. Association between chronic obstructive pulmonary disease and lung cancer: a case-control study in southern Chinese and a meta-analysis. PLoS One 2012;7:e46144.
67. Rodríguez LA, Wallander MA, Martín-Merino E, Johansson S. Heart failure, myocardial infarction, lung cancer and death in COPD patients: a UK primary care study. Respir Med 2010;104(11):1691–9.
68. Zimmerman M, McDermut W, Mattia JI. Frequency of anxiety disorders in psychiatric outpatients with major depressive disorder. Am J Psychiatry 2000;157(8):1337–40.

69. Bowen RC, Kohout J. The relationship between agoraphobia and primary affective disorders. Can Psychiatr Assoc J 1979;24(4):317–22.
70. Husaini B, Levine R, Sharp L, Cain V, Novotny M, Hull P, et al. Depression increases stroke hospitalization cost: an analysis of 17,010 stroke patients in 2008 by race and gender. Stroke Res Treat 2013;2013:846732.
71. Klein RJ, Schoenborn CA. Age adjustment using the 2000 projected U.S. population. HealthyPeople 2010 Stat Notes 2010;20:1–10.
72. Massie MJ. Prevalence of depression in patients with cancer. J Natl Cancer Inst Monogr 2004;32:57–71.
73. Neighbors HW, Caldwell C, Jackson JS, Thompson EL. Help seeking for depression among African Americans. In: Friedman S, editor. Anxiety disorders in African Americans. New York, NY: Springer Publishing Company; 1994.
74. Vogel DL, Wester SR, Larson LM. Avoidance of counseling: psychological factors that inhibit seeking help. J Clin Psychol 2007;85:410–22.
75. Arcwneaux M. [Internet] Blackman hurting: do doctors fail to diagnose depression in our men? 2012. [accessed 2016 Oct 5]. Available from: www.ebony.com/wellness-empowerment/do-doctors-fail-to-diagnose-depression-in-black-men#axzz4MFW3huOg.
76. Jagsi R, Griffith KA, Koelling T, Roberts R, Pierce LJ. Rates of myocardial infarction and coronary artery disease and risk factors in patients treated with radiation therapy for early-stage breast cancer. Cancer 2007;109:650–7.
77. Liu G, Yan YP, Zheng XX, Xu YL, Lu J, Hui RT, et al. Meta-analysis of nonsteroidal anti-inflammatory drug use and risk of atrial fibrillation. Am J Cardiol 2014;114(10):1523–9.
78. Bach PB, Kattan MW, Thornquist MD, Kris MG, Tate RC, Barnett MJ, et al. Variations in lung cancer risk among smokers. J Natl Cancer Inst 2003;95(6):470–8.
79. Resneck J, Pletcher MJ, Lozano N. Medicare, Medicaid, and access to dermatologists: the effect of patient insurance on appointment access and wait times. J Am Acad Dermatol 2004;50(1):85–92.
80. Devoe JE, Baez A, Angier H, Krois L, Edlund C, Carney PA. Insurance + access not equal to health care: typology of barriers to health care access for low-income families. Ann Fam Med 2007;5(6):511–8.
81. Karve SJ, Balkrishnan R, Mohammad YM, Levine DA. Racial/ethnic disparities in emergency department waiting time for stroke patients in the United States. J Stroke Cerebrovasc Dis 2011;20(1):30–40.
82. Cass A, Cunningham J, Snelling P, Ayanian JZ. Late referral to a nephrologist reduces access to renal transplantation. Am J Kidney Dis 2003;42(5):1043–49.
83. Hankerson SH, Suite D, Bailey RK. Treatment disparities among African American men with depression: implications for clinical practice. J Health Care Poor Underserved 2015;26(1):21–34.
84. Virnig BA, Baxter NN, Habermann E, Feldman RD, Bradley CJ. A matter of race: early- versus late-stage cancer diagnosis. Health Aff 2009;28(1):160–8.
85. Husaini B, Cain V, Novotny M, Samad Z, Levine R, Moonis M. Variation in risk factors of dementia among four elderly patient cohorts. World J Neurol 2014;4(2):7–11.
86. Husaini BA, Levine RS, Novotny ML, Cain VA, Sampson UKA, Moonis M. Depression and race affects hospitalization costs of heart failure patients. Fam Med Community Health 2015;3(2):39–47.
87. Thun MJ, Jemal A. How much of the decrease in cancer death rates in the United States is attributable to reductions in tobacco smoking? Tob Control 2006;15(5):345–7.
88. Yabroff KR, Lund J, Kepka D, Mariotto A. Economic burden of cancer in the US: estimates, projections, and future research. Cancer Epidemiol Biomarkers Prev 2011;20(10):2006–14.
89. Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2012; 62:30–67.
90. Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to diet and physical activity cancer prevention guidelines and cancer outcomes: a systematic review. Cancer Epidemiol Biomarkers Prev 2016;25(7):1018–28.