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The disproportionate burden of Alzheimer's Disease and related dementias (ADRD) in diverse older adults diagnosed with cancer

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Abstract

Introduction.—Older adults living with Alzheimer's disease and related dementias (ADRD) who are then diagnosed with cancer are an understudied population. While the role of cognitive impairment during and after cancer treatment have been well-studied, less is understood about patients who are living with ADRD and then develop cancer. The purpose of this study is to contribute evidence about our understanding of this vulnerable population.

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Author Contributions. Please see our attached form as well.

All authors contributed and have approved the final manuscript.

Study concepts MKS, PG, WD, JDM, AAM

Study design MKS, PG, WD, JDM, AAM

Data acquisition MKS, VN, JDM

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Declaration of Competing Interests.

Nothing to declare.

Materials and Methods.—This was a retrospective cohort study of a linked, representative family of databases of cancer registries and Medicare administrative claims that make up the SEER-Medicare database. Older adults ages 68 and older with a first primary cancer type: breast, cervical, colorectal, lung, oral, or prostate were eligible for inclusion (N=337 932). Prevalence estimates of ADRD across cancer types and a 5% non-cancer comparison sample were compared by patient factors.

Results.—The overall prevalence of patients who had an ADRD diagnosis anytime in the three years prior to their cancer diagnosis was 5.6%. Patients with ADRD were more likely to be female, older (over age 75), a racial/ethnic minority, single, with multiple chronic conditions, and a tumor diagnosed early (stage I) or were unstaged. Black patients with colorectal and oral cancer had the highest and second highest prevalence of ADRD compared to White patients (13.46% vs 7.95% and 12.64% vs 7.82% respectively, p<.0001). We observed the highest prevalence of ADRD among Black patients for breast (11.85%), cervical (11.98%), lung (8.41%), prostate (4.83), and the 5% sample (9.50%, p>.0001).

Discussion.—The higher prevalence of ADRD among Black and Latine older adults with cancer not only aligns with the trend observed in our non-cancer comparison sample, but also, these findings demonstrate the compounded risk experienced by minoritized older adults over the life course. The greater than expected prevalence of patients with ADRD who go on to develop cancer demonstrates better assessment of cognition is urgently needed. Accurate identification of these vulnerable populations is critical to improve assessment, care coordination, and address inequities in screening and treatment planning.

1. Introduction

Older adults with cancer are an increasingly racially and ethnically diverse population that face disproportionate challenges as they navigate diagnosis and treatment. While older adults represent 60% of patients diagnosed with cancer, approximately 23% are from minoritized populations[1] and will account for 73% of survivors by 2040.[2–4] A growing proportion of older adults diagnosed with cancer will do so while living with another increasingly common condition -- Alzheimer's disease or a related dementia (ADRD). Overall, in the U.S., an estimated 10.3% of older adults are living with ADRD.[5,6] The added burden experienced by older adults living with Alzheimer's disease and related dementias (ADRD) who are then diagnosed with cancer are an understudied and growing population. The evidence related to the role of ADRD in cancer is mixed, with some studies suggesting an inverse relationship related to dementia and cognitive impairment and lower cancer risk. Evidence also suggests prevalence estimates vary widely; one study estimates a range of <1% to nearly 50%, and much of the research is focused on ADRD that presents after initiating cancer therapy, thus making it challenging to compare to patients living with ADRD who are then diagnosed with cancer.[7,8]

Black and Latine populations shoulder a greater burden of both cancer and ADRD than White populations (1.5 and 2-fold greater odds of ADRD, respectively, compared with White populations),[5,6,9] due to existing structural discrimination and disparities in access to care. The compounded burden of these inequities over the life course contribute to not only a disproportionate share of disease but also a lower likelihood of quality cancer care.[10–12]

Taking into account how the burden of social and health disparities compound over the life course, poor quality patient-provider communication and impaired decision-making are just some of the additional considerations that physicians must take into account and that demand significant coordination. Given that age alone is not a sufficient proxy for ADRD, an understanding of the prevalence of ADRD among cancer survivors is necessary to better understand the unique needs and degree of support needed as people diagnosed with cancer navigate treatment decisions and ongoing care.

There is strong evidence that clinicians continue to rely heavily on chronological age to make treatment recommendations, resulting in under- and over-treatment in older adults.[13–15] Accounting for additional age-related risk factors such as functional status could result in better indication of tolerance for the intensity of some cancer therapies.[16] In 2018, the American Society of Clinical Oncology (ASCO) recommended that oncologists consider age-related risk factors beyond chronological age in treatment decision-making. The domains the expert panel recommended included assessment of cognition among several other evidence-based domains.[17,18] Several evidence-based tools to evaluate frailty and other age-related risk factors exist to this end. However, utilization of such tools, in particular those that assess cognitive impairment, has been incremental and not systemically employed in oncology.[19] This represents a critical gap given the growing estimates of older adults diagnosed with cancer who are living with varying degrees of cognitive impairment (CI). One study estimated 15–30% of patients who were diagnosed with cancer in a clinical setting demonstrated cognitive impairment ranging from moderate CI to ADRD.[20] However, the literature suggests ADRD is underestimated in most cancer research datasets, including administrative claims data.[13,14,20,21] Oncologists must take into account the differential disease burden of comorbid dementia that can prevent receipt of guideline concordant care.[13,22,23] These include a lower likelihood of receiving curative intent treatment, a lower likelihood of receiving chemotherapy, radiation, or surgery and higher overall mortality compared to patients with cancer only.[24]

Recent studies have attempted to use administrative claims data and international classification of diseases (ICD) codes to assess ADRD prevalence in older adult patient populations (e.g., Medicare). One approach for classifying ADRD in the NCI SEER-Medicare database has been to use the Charlson Comorbidity Index (CCI) modified for administrative claims data with the Klabunde and Deyo adaptations,[25–27] though this approach has shown consistent underestimation of ADRD.[28–34] A more recent study by Taylor et al. using claims codes drawn from clinical records published an approach that more accurately estimate ADRD in claims data and is the algorithm used for classifying ADRD by the Centers for Medicare and Medicaid (CMS) research Chronic Conditions Warehouse (CCW). The goal of the present analysis is to assess the prevalence of ADRD among patients diagnosed with cancer applying a validated algorithm. Understanding the prevalence of dementia in patients that are then diagnosed with cancer is critical for oncologists, researchers, hospital leaders, and other stakeholders to ensure appropriate resources are allocated for cancer treatment planning that is tailored to older adults. This will help to ensure screening for dementia is done in new patients with cancer during treatment planning and that treatment is adapted where appropriate.

2. Sample & Methods

2.1 Data

In the present observational retrospective cohort of older adults diagnosed with cancer, we assessed the prevalence of ADRD in patients with one of six cancer types using the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) cancer registries linked to Medicare administrative claims for study years 2003–2014 (N=337,932). The SEER-Medicare database is a part of a family of linked databases that allow us to model population-representative estimates of prevalence and utilization for most of the United States. SEER is a program of NCI, and is a population-based source that integrates 22 geographically distributed registries to collect detailed tumor data. These data are then linked to Medicare claims information for each case linked to beneficiaries over age 65, including provider procedures, costs, and diagnoses. We also included estimates of non-cancer ADRD populations using the 5% Medicare sample provided by NCI to compare population-based estimates for the same period to understand whether the burden of ADRD among patients with cancer were different than a 5% random sample of Medicare patients without cancer. We extracted data on tumor and patient characteristics from the SEER-Medicare data for patients with breast, cervical, colorectal, head and neck (oropharyngeal), lung, and prostate tumors. We matched these patients with their available fee-for-service (FFS) Medicare claims for the study years available. We included a non-cancer equivalent comparison group available from the same source, a 5% non-cancer sample (ADRD only), and report the prevalence of ADRD for comparison. The same data management approach was utilized for the 5% non-cancer sample to identify ADRD Medicare beneficiaries since none would have a history of cancer at the time of extraction. [35–38] *Inclusion Criteria*. We had a unique age inclusion for our sample, including older adults (age ≥68) with a first diagnosis of cancer and continuous coverage of both Medicare parts A and B for a minimum of 36 months before their cancer diagnosis. This was intentional to ensure we could extract a dementia diagnosis during this look-back period with confidence, based on the best algorithm currently available that is used by the Chronic Conditions Warehouse (CCW, Centers for Medicaid and Medicare Services) to identify dementia in claims data; normally only a one year look period is utilized to calculate comorbidities in claims.[30–34,39] These data were used with permission from the National Cancer Institute Data Use Agreement (DUA) and approval of the UC San Diego IRB Human Research Protections Program.

2.2 Primary Outcome of Interest

For the primary comparator of ADRD, we extracted a group of ICD-9 codes to develop a yes/no flag for ADRD with a three-year look-back period based on a previously validated algorithm currently in use by the CCW.[29,35,36]

2.3 Independent Variables

Additional independent variables used to describe the cohort included available racial and ethnic categories, age, sex, marital status, geography, chronic conditions status, and tumor stage. We developed a combined racial and ethnic category to avoid double counting any non-Hispanic White populations by classifying race and ethnicity as: Asian, Black, Hispanic/Latine, Other (2 or more races or multiple-races), and White (reference group).

Only male or female sex at diagnosis were available in the present analysis. Age cut-offs included the three-year look-back period for identifying ADRD patients, so we categorized patient age at diagnosis into three categories to study variation in older age cohorts (under age 75; 75 to 85 years; 85 years and over). Marital status was classified as divorced, married, other, or single. Patient geographic location was classified as either metropolitan/urban or rural location. Chronic conditions status was classified based on the number of diagnoses, if a patient had one or fewer versus two or more. We based this classification on the definition of multiple chronic conditions, which is defined as two or more.[2] We did not include ADRD or cancer status in our estimate. Tumor staging was coded to reflect variation by cancer type. Early-stage tumors were classified as stage I or II. Stage III and IV tumors were combined into a single group as late-stage. Finally, tumors that were classified as Stage 0 or 8 were to reference prostate cancer staging guidelines. Given the evidence of the higher prevalence of unstaged tumors among patients living with ADRD, we included unstaged tumors for cancer types.[7,8,38]

2.4 Statistical Analysis

Descriptive statistics were calculated for all factors (Table 1). We assessed differences in the prevalence of ADRD and additional factors of interest by cancer site using a chi-square test (Table 2). Any cell with a value below n=11 is suppressed in compliance with NCI SEER-Medicare data use agreement, and are presented as a combined categories or an asterisk to ensure compliance with the minimum cell size suppression standards of our DUA. All data were managed, and analyses conducted, using SAS 9.4 (Cary, N.C).

3. RESULTS

3.1. Sample Characteristics/Prevalence by Dementia Status

The overall prevalence of patients whose ADRD was diagnosed anytime within three years of their cancer diagnosis was 5.6% (See Appendix for combined table). Patients with ADRD were more likely to be female, older (over age 75), a racial/ethnic minority, single, with multiple chronic conditions, and a tumor diagnosed at an early (stage I) or a tumor that is deemed unstaged.

Table 1 details the sample characteristics of patients with cancer across primary tumor site: breast, cervical, head and neck (oropharyngeal), colorectal, lung, and prostate or a 5% control sample of patients without cancer. While our sample was primarily comprised of white patients with cancer, among minoritized patients, we observed the highest prevalence of cancer among Black patients across all cancer types and the 5% sample compared with White patients with cancer. Asian patients followed as the second largest group for the same types with the exception of breast cancer. The oldest adults (85+) represented the smallest proportions of patients with cancer. ADRD prevalence by cancer type ranged from ~8.5% for patients diagnosed with cervical or colorectal cancer to 2.6% for patients with prostate cancer, the prevalence of ADRD for the 5% non-cancer sample was 6.4%. Table 2 further compares patient and tumor characteristics by ADRD prevalence.

The prevalence of ADRD by tumor type across risk factors (ADRD-negative patients with cancer are not presented in the tables due to space but can be found in the SUPP FILE) are presented in Table 2, the final column also contains the prevalence of ADRD in the 5% non-cancer sample. The prevalence of ADRD is significantly higher among Black and Latine patients (vs White) across any cancer type in our sample including the 5% sample. Black patients with colorectal and oral cancer had the highest and second highest prevalence of ADRD compared to White patients (13.46% vs 7.95% and 12.64% vs 7.82% respectively, p<.001). We observed the highest prevalence of ADRD among Black patients for breast (11.85%), cervical (11.98%), lung (8.41%), prostate (4.83), and the 5% sample (9.50%, p>.0001), see Figure 1. Latine patients had the highest prevalence of ADRD among patients with oral cancer compared to White patients (12.67%, p<.0001). Latine older adults had the second-highest prevalence on these cancer types: breast (10.65%), colorectal (10.02%), lung (6.96%), prostate (4.63%), and the 5% sample (6.88%). A significantly higher prevalence of ADRD was observed among Asian patients diagnosed with cervical cancer compared to White or Latine patients in our sample (11.11% vs 7.56%, p<.001).

Additionally, we observed significant differences in the prevalence of ADRD by patient age, with the highest prevalence among patients over 85 years old across all cancer types and the 5% sample. We observed a similar pattern in sex with a significantly higher prevalence of ADRD observed among female patients with all cancer types except for breast cancer, which was higher among men (7.43% vs 6.39%). Finally, a significantly higher prevalence of ADRD was observed among patients with multiple chronic conditions or multi-morbidity across all cancer types and the 5% sample compared to patients with one or fewer chronic conditions. The prevalence of ADRD differed significantly in urban areas for patients with colorectal, lung, and prostate cancer, and the 5% sample (p<.001). Conversely, for cancer types where ADRD prevalence was greater in rural areas, the difference observed was not significant.

4. DISCUSSION

The present analysis demonstrates the disproportionate burden of ADRD in older adults with cancer in racial/ethnic subgroups. Further, the ADRD prevalence estimates reported in this study are higher than those currently reported in the cancer literature, emphasizing the fact that the method used to assess this condition, particularly in claims, matters and efforts to improve our approach are valuable. These findings confirm consistent underreporting of ADRD in large claims databases.[31,33–35,40] These efforts, in conjunction with improving our ability to link these data to clinical assessments and medical records, will be vital going forward for better validation in particular, as we are able to collect high-quality records that include appropriate frequencies of minoritized populations. Further, we demonstrated a higher prevalence of ADRD among Black and Latine older adults, a finding that was consistent across every cancer site examined. This is an additional burden on minoritized groups who are already less likely to get recommended care and experience additional barriers to high-quality cancer care. We observed age differences in the prevalence of ADRD across all cancer types among the oldest adults, defined as age 85 and older. These higher than previously reported estimates underscore the need to use claims data for population-

level estimates while also developing algorithms that inform this work using clinical data for improved accuracy.

There is a substantial body of evidence supporting the need for improved accuracy in assessing a patient's ability to actively participate in treatment planning and to what extent they may need additional supports. The lack of information regarding patients at higher risk of ADRD may contribute to concerns regarding under- and over-treatment of older adults with cancer. Our findings suggest a disproportionate burden of ADRD across cancer types and racial/ethnic groups, which likely puts these patients at higher risk of under- or over-treatment. These risks include not only toxicity for older adults that cannot tolerate their treatment dose, but also the potential for under-treatment of highly functional older adults who are given lower dose therapy when, perhaps, their functional age would have permitted more intense therapy. Assessments that can be run against billing and other data types could facilitate the early identification of patients, however, our sample underscores the need for more diverse data to address the issues of representation that is a problem in most large real-world-data (RWD) datasets used in healthcare analyses today. Further, understanding patients at higher risk could lead to earlier screening of these patients. It is important to emphasize that other communication barriers, such as language barriers, magnify these challenges, making it less likely that these patients receive recommended care. These data are especially useful in the context of caring for the growing population of diverse older adults, 75% of whom experience an adverse event during cancer treatment.[41,42]

Limitations

While the algorithm we employed to identify ADRD was a more accurate classifier than prior studies, there remain significant limitations to this approach. Mild cognitive impairment, a potential indicator of early dementia, was not included in the extraction given the documented poor performance of this administrative code in previous studies.[32,40] Thus, we identified only confirmed cases of diagnosed ADRD given the longer 'look-back' period. This was helpful in ensuring the accuracy of our estimates, but likely resulted in more conservative estimates of burden. Further, the CCW algorithm is based off a single primary study which was poorly powered for racially and ethnically diverse patients,[29,38,39] meaning that in spite of statistically significant variation in race and ethnicity, our estimates may also be conservative. This particular finding warrants critical research in classifying ADRD in diverse populations and data.

Conclusion

Improving our population-based understanding of cognitive status in older adults as well as for individual patients preparing for cancer treatment garners additional benefits for patients, including better patient-provider communication and improved treatment outcomes. Additional research in the area of ADRD and cancer including exploring the role of ADRD on time to treatment, curative and surgical treatment decisions, and survival is needed. This work is necessary for improving diversity of population-based estimates of ADRD in patients being diagnosed with cancer. It is clear that assessing cognition in minoritized older

adults diagnosed with cancer with evidence-based tools like geriatric assessment can help ensure guideline concordant care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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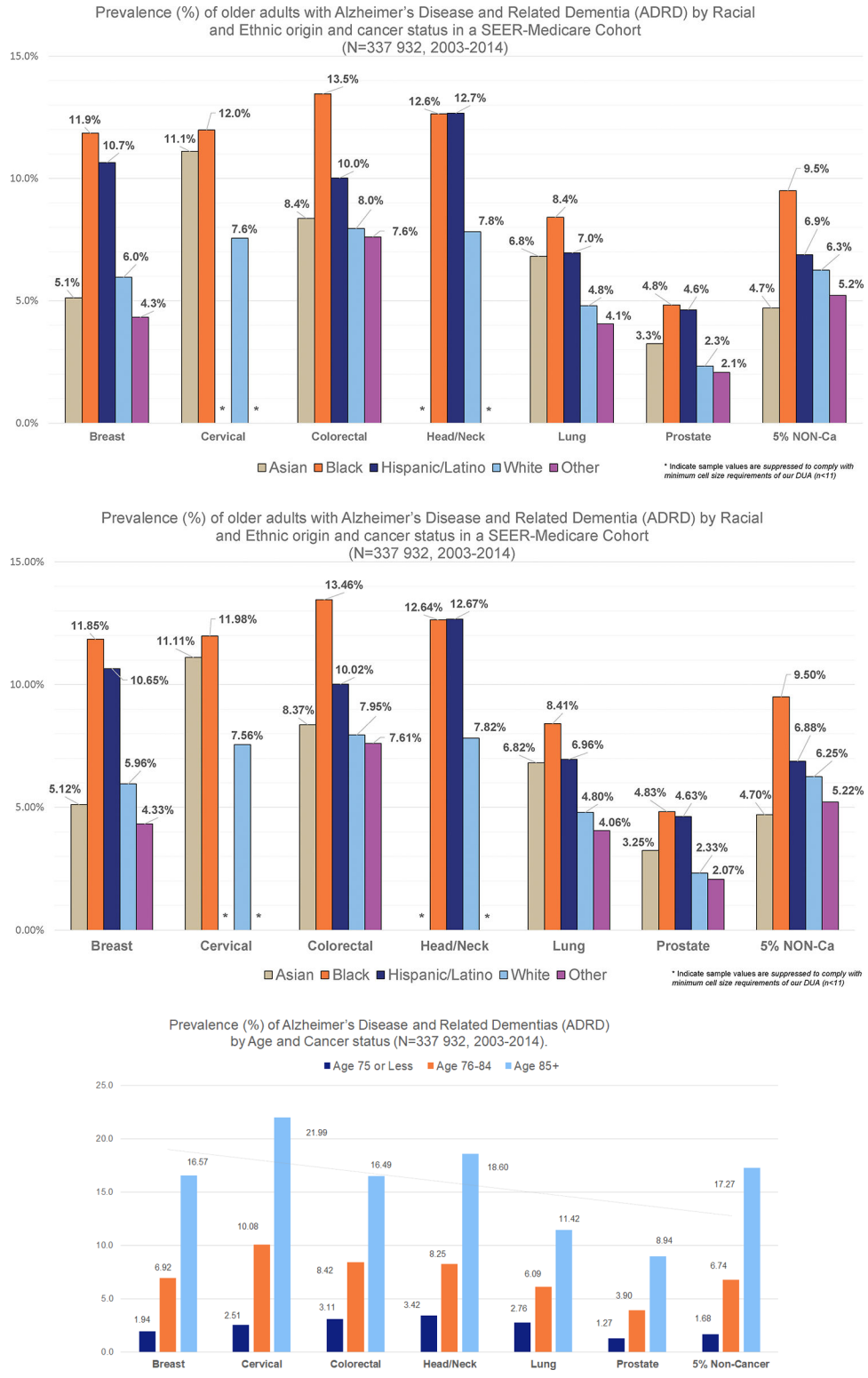

Fig. 1.

Prevalence of Alzheimer's Disease and Related Dementias (ADRD) among Older Adults with Cancer in an NCI SEER-Medicare cohort (N = 337,932, 2004–2013). *one decimal place*. *two decimal places.

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Table 1.

Population characteristics of patients in a SEER-Medicare linked cohort 2004–2013 (N=337 932) and 5% non-cancer comparison sample.

Cancer Site and 5%	Breast		Cervical		Colorectal		Head/Neck		Lung		Prostate		5% Non-Cancer	
	70888		1930		69444		10882		105689		79099		204 348	
	N	col%	N	col%	N	col%	N	col%	N	col%	N	col%	N	col%
ADRD														
Yes	4536	6.40	163	8.45	5877	8.46	871	8.00	5454	5.16	2088	2.64	13126	6.42
No	66352	93.60	1767	91.55	63567	91.54	10011	92.00	100235	94.84	77011	97.36	191222	93.58
Race/Ethnicity														
Asian	1464	2.07	117	6.06	2234	3.22	312	2.87	3343	3.16	1814	2.29	5725	2.80
Black	5274	7.44	334	17.31	6016	8.66	633	5.82	8467	8.01	8276	10.46	14161	6.93
Hispanic/Latino	742	1.05	78	4.04	1008	1.45	150	1.38	1236	1.17	1232	1.56	3706	1.81
Other	1523	2.15	65	3.37	1695	2.44	235	2.16	2141	2.03	2266	2.86	4676	2.29
White	61885	87.30	1336	69.22	58491	84.23	9552	87.78	90502	85.63	65511	82.82	176080	86.17
Age														
75 years or less	29319	41.36	875	45.34	22651	32.62	4595	42.23	46700	44.19	46057	58.23	86356	42.26
76 to 84 years	30264	42.69	764	39.59	31499	45.36	4400	40.43	48258	45.66	28780	36.38	82612	40.43
85 years +	11305	15.95	291	15.08	15294	22.02	1887	17.34	10731	10.15	4262	5.39	35380	17.31
Sex														
Male	713	1.01			30607	44.07	6562	60.30	53924	51.02	79099	100	75 552	36.97
Female	70175	98.99	1930	100	38837	55.93	4320	39.70	51765	48.98			128796	63.03
Geography														
Urban	59014	83.25	1578	81.76	56951	82.01	8772	80.61	86536	81.88	65252	82.49	128908	63.08
Rural	11874	16.75	352	18.24	12493	17.99	2110	19.39	19153	18.12	13847	17.51	75440	36.92
Marital Status														
Divorced	5174	7.30	232	12.03	4556	6.56	931	8.56	9561	9.05	3992	5.05		
Married	28680	40.47	528	27.37	21419	45.26	5181	47.66	51868	49.10	53453	67.61		
Other	31571	44.55	942	48.83	27482	39.59	3785	34.82	36095	34.17	16361	20.69		
Single	5438	7.67	227	11.77	5962	8.59	974	8.96	8120	7.69	5255	6.65		
Comorbidities (*Excluding Dementia*)														

Cancer Site and 5%	Breast		Cervical		Colorectal		Head/Neck		Lung		Prostate		5% Non-Cancer	
	70888		1930		69444		10882		105689		79099		204 348	
	N	col%	N	col%	N	col%	N	col%	N	col%	N	col%	N	col%
1 or less comorbidities	49099	69.26	1276	66.11	41970	60.44	6490	59.64	54591	51.65	57475	72.66	166563	81.51
2 or more	21789	30.74	654	33.89	27474	39.56	4392	40.36	51098	48.35	21624	27.34	37785	18.49
Tumor Stage														
Stage I	46440	65.51	449	23.26	27794	40.02	3436	32.75	18625	17.62				
Stage II	17409	24.56	960	49.74	24117	34.73	4836	46.10	24566	23.24				
Stage III or IV	5617	7.92	382	19.79	14133	20.35	1551	14.78	58882	55.71	4730	5.98		
Unstaged	1422	2.01	139	7.2	3400	4.90	668	6.37	3616	3.42	1135	1.43		
Stage 0 or 8											73232	92.58		

Cells with an asterisk (*) are suppressed to comply with minimum cell size requirements of our DUA (n<11); Cells that are shaded are not applicable, e.g. there is no tumor information in the non-cancer sample. Col%=column percent is being reported (vs. row percent)

Table 2.

Prevalence of pre-existing ADRD among patients with cancer in a SEER-Medicare Cohort 2004–2013 (N=337932) and ADRD in a comparable non-cancer 5% sample (N=13126). Only ADRD prevalence (Row %) presented, cancer-only data are available in the supplemental file.

Cancer Site*(ADRD)*	Breast*(ADRD)*		Cervical*(ADRD)*		Colorectal*(ADRD)*		Head/Neck*(ADRD)*		Lung*(ADRD)*		Prostate*(ADRD)*		5% Non-Cancer Sample*(ADRD)*	
	N=4536		N=163		N=5877		N=871		N=5454		N=2088		N=13126	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Race/Ethnicity														
Asian	75	5.12	13	11.11	187	8.37	*	*	228	6.82	59	3.25	269	4.70
Black	625	11.85	40	11.98	810	13.46	80	12.64	712	8.41	400	4.83	1346	9.50
Hispanic / Latino	79	10.65	*	*	101	10.02	19	12.67	86	6.96	57	4.63	255	6.88
Other	66	4.33	*	*	129	7.61	*	*	87	4.06	47	2.07	244	5.22
White	3691	5.96	101	7.56	4650	7.95	747	7.82	4341	4.80	1525	2.33	11012	6.25
p-value	***<.001***		***0.016***		***<.001***		***<.001***		***<.001***		***<.001***		***<.001***	
Age														
Under 75yrs	568	1.94	22	2.51	704	3.11	157	3.42	1289	2.76	585	1.27	1447	1.68
75 to 85yrs	2095	6.92	77	10.08	2651	8.42	363	8.25	2939	6.09	1122	3.9	5570	6.74
Over 85yrs	1873	16.57	64	21.99	2522	16.49	351	18.60	1226	11.42	381	8.94	6109	17.27
p-value	***<.001***		***<.001***		***<.001***		***<.001***		***<.001***		***<.001***		***<.001***	
Sex														
Male	53	7.43			2076	6.78	419	6.39	2494	4.63	2088	2.64	3639	4.82
Female	4483	6.39	163	8.45	3801	9.79	452	10.46	2960	5.72			9487	7.37
p-value	*0.257*		-		***<.001***		***<.001***		***<.001***		-		***<.001***	
Geography														
Urban	3822	6.48	132	8.37	4982	8.75	710	8.09	4702	5.43	1773	2.72	12713	9.86
Rural	714	6.01	31	8.81	895	7.16	161	7.63	752	3.93	315	2.27	413	0.55
p-value	*0.060*		*0.788*		***<.001***		*0.481*		***<.001***		***<.001***		***<.001***	
Marital Status														
Divorced	348	6.73	17	7.33	383	8.41	81	8.70	503	5.26	111	2.78		
Married	943	3.29	23	4.36	1784	5.68	268	5.17	2050	3.95	1098	2.05		
Other	2825	8.95	102	10.83	3073	11.18	434	11.47	2351	6.51	657	4.02		

Cancer Site*(ADRD)*	Breast*(ADRD)*		Cervical*(ADRD)*		Colorectal*(ADRD)*		Head/Neck*(ADRD)*		Lung*(ADRD)*		Prostate*(ADRD)*		5% Non-Cancer Sample*(ADRD)*	
	N=4536		N=163		N=5877		N=871		N=5454		N=2088		N=13126	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Single	419	7.71	21	9.25	635	10.65	88	9.03	548	6.75	222	4.22		
p-value	***<.001***		***<.001***		***<.001***		***<.001***		***<.001***		***<.001***			
Comorbidities (*Excluding Dementia*)														
1 or fewer	1969	4.01	58	4.55	2104	5.01	295	4.55	1558	2.85	962	1.67	7769	4.66
2 or more	2567	11.78	105	16.06	3773	13.73	576	13.11	3896	7.62	1126	5.21	5357	14.18
p-value	***<.001***		***<.001***		***<.001***		***<.001***		***<.001***		***<.001***		***<.001***	
Tumor Stage														
Stage I	2457	5.29	36	8.02	2361	8.49	249	7.25	1045	5.61				
Stage II	1346	7.73	84	8.75	1774	7.36	377	7.80	1154	4.70				
Stage III or IV	419	7.46	21	5.50	950	6.72	108	6.96	2928	4.97	201	4.25		
Unstaged	314	22.08	22	15.83	792	23.29	112	16.77	327	9.04	60	5.29		
Stage 0 or 8											1827	87.50		
p-value	***<.001***		***0.003***		***<.001***		***<.001***		***<.001***		***<.001***			

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