Comparing the downstream costs and healthcare utilization associated with the use of low-dose computed tomography (LDCT) in lung cancer screening in patients with and without alzheimer's disease and related dementias (ADRD)

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Abstract

Objective: This study aims to compare the downstream costs and healthcare utilization associated with using low-dose computed tomography (LDCT) for lung cancer screening in patients with and without Alzheimer's disease and related dementias (ADRD).

Methods: Based on data from IBM MarketScan Commercial Claims Databases (2014–2018), we have identified four study cohorts: ADRD and non-ADRD patients who went through LDCT screening; ADRD and non-ADRD patients without LDCT screening. Annually healthcare utilization and cost were grouped into outpatient, inpatient, and pharmacy. We used difference-in-differences (DID) models to estimate the downstream healthcare utilization and cost associated with LDCT screening in both ADRD and non-ADRD population. We used a difference-in-difference-in-differences (DDD) model to explore whether LDCT screening was associated with higher downstream cost and healthcare utilization in ADRD population than non-ADRD population.

Result: Compared to individuals without LDCT screening, LDCT screening was associated with increased outpatient visits (2.1, 95% CI 0.7, 3.4) and outpatient cost ($2301.0, 95% CI 296.2, 4305.8) in the ADRD population and increased outpatient visits (0.6, 95% CI 0.1, 1.1) in the non-ADRD population within 1 year after screening. Compared with the non-ADRD population,

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LDCT screening was found to be associated with an additional 1.5 (95% CI 0.2, 2.8) outpatient visits, 0.7 (95% CI 0.1, 1.3) days of inpatient stays, and $4,960.4 (95% CI 532.7, 9388.0) in overall healthcare costs within 1-year after LDCT in the ADRD population (all p < .5).

Conclusion: The downstream cost and healthcare utilization associated with LDCT screening were found to be higher in the ADRD population compared to the average population.

Keywords

Lung cancer screening; low-dose computed tomography; Alzheimer's disease and related dementias; healthcare utilization; expenditures

Introduction

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer-related death worldwide[1]. In the United States (US), 228,820 new lung cancer cases and 135,720 lung cancer-related deaths were estimated for 2020, accounting for 22.4% of all cancer deaths[2]. Lung cancer is deadly when diagnosed at an advanced stage, where the 5-year relative survival rate dropped substantially from 59.0% for localized cases to 5.8% for metastasized cases[2]. Finding an effective screening strategy for the early detection of lung cancer is thus critical as it allows timely cancer treatments at an early stage and offers a better chance of prolonging the life expectancy. In 2011, results from the National Lung Screening Trial (NLST) revealed that screening for lung cancer using low-dose computed tomography (LDCT) had superior clinical efficacy compared to screening using traditional radiography by reducing lung cancer mortality rate by 20%[3]. Based on findings from the NLST, professional societies including the US Preventive Services Task Force (USPSTF)[4], the National Comprehensive Cancer Network (NCCN)[5], and the American Cancer Society (ACS)[6], published guidelines and recommended annual screening with LDCT in populations at a higher risk for lung cancer. On 5 February 2015, The Centers for Medicare & Medicaid Services (CMS) issued the decision memo for lung cancer screening with LDCT, added the annual screening for LDCT as a preventive service benefit for the eligible populations[7].

Although lung cancer screening using LDCT was proven to be effective in the randomized controlled trials, several concerns have been raised by researchers and policymakers. Firstly, within 3 years of the annual screening in NLST, 96.4% of the positive results were false positives, which account for 24.2% of the total number of screening tests[3]. False-positive tests induced a substantial burden on patients as follow-up confirmatory imaging tests and invasive procedures were required after an LDCT positive result. A secondary analysis of the NLST data showed that invasive procedures after a false positive result contributed to 8.5–9.8% of the LDCT screening-related complications (e.g. acute respiratory failure, anaphylaxis, hemorrhage, etc.)[8]. Secondly, the NLST was conducted in controlled settings that involved relevant specialist services and a defined nodule management algorithm. Furthermore, the NLST participants might be relatively healthier compared to the overall lung cancer patient population[9]. As a consequence, the false-positive rates and the associated complication risks may be amplified when an LDCT-based lung cancer screening program is implemented in the real-world setting[10]. A study using national representative claims data had shown that the complication rate was approximately twice as that reported in

the NLST[11]. Thirdly, patients with serious comorbid conditions may experience more complications from lung cancer screening with LDCT, and benefit less from the screening due to the competing risks of death[12]. In light of these concerns, most published lung cancer screening guidelines recommended that individuals with health problems that substantially limit life expectancy or the ability or willingness to have curative lung surgery consider opting out of lung cancer screening using LDCT[4,13].

Alzheimer's disease and related dementias (ADRD) represent a significant public health challenge globally. It is the sixth leading cause of death in the US, and approximately 5.5 million Americans are living with ADRD[14,15]. The prevalence of ADRD is projected to reach 13.8 million by 2050, with direct medical costs rising from $236 million to $1 trillion[16,17]. Patients with ADRD suffer from cognitive decline, behavioral and psychiatric disorders, and declines in functional status[18]. Consequently, the ADRD patients are more vulnerable to complications related to downstream invasive procedures following lung cancer screening, and thus more likely to experience harm from LDCT and require more healthcare resources than the general population. Besides, the ADRD population has decreased life expectancy, which could reduce the cumulative benefits of LDCT screening over a lifetime window. Further, ADRD patients may experience symptoms caused by overdiagnosis due to lung cancer screening[19]. Therefore, it remained unclear whether the benefit from lung cancer screening outweights the potential harm in ADRD patients. Due to the potential burden for patients and the healthcare system caused by cancer screening, many caregivers feel hesitant about conducting screening for these patients[20]. Further evidence for decision-making is needed for the ADRD patients who are eligible for lung cancer screening. This study aims to compare the downstream costs and healthcare utilization associated with the use of LDCT in lung cancer screening in patients with and without ADRD.

Methods

Data sources and study population

We extracted claims records from the 2014–2018 IBM MarketScan Commercial Claims databases[21]. The Marketscan data contain information on outpatient visits, inpatient enrollments and stays, drug prescriptions, and plan enrollment of a multi-million sample of employees, dependents, and retirees mainly covered by large employer-sponsored health plans in the US. The Marketscan Medicare Supplemental Database is also included in the study, which contains a subset of claims records from beneficiaries receiving Medicare supplemental insurance paid by employers[21,22].

We adopted a difference-in-difference-in-difference (DDD) design to examine the incremental healthcare utilization and expenditure associated with LDCT screening of the ADRD population compared to the non-ADRD population. To execute the DDD design, we identified four study cohorts: (1) patients with established ADRD who underwent the LDCT screening (group 1) during the enrollment period, which is defined as between 5 February 2015 and 31 December 2017; (2) patients with established ADRD but did not receive LDCT screening during the enrollment period (group 2); (3) patients without ADRD and underwent LDCT screening during the enrollment period (group 3); and (4) patients without ADRD

and did not receive LDCT screening during the enrollment period (group 4). The LDCT was identified using Healthcare Common Procedure Coding System (HCPCS) code G0297, which became available on 5 February 2015. We defined the index date as the date of receiving the LDCT. The year (12 months) before the index date was defined as the baseline period, while the year (12 months) after the index date was defined as the post period. For those who did not receive LDCT (i.e. group 2 and group 4), a random date was assigned as the index date. We restricted our study sample to patients aged 55 to 77 at baseline, which corresponded with the lung cancer screening eligibility criteria published by CMS [7]. We required the patients to have a 12-month continuous enrollment before and after the index date to capture the annual healthcare utilization and expenditure. In addition, patients were required to have no diagnostic records of lung cancer during the baseline period and post period.

Outcomes and covariates

We included both healthcare utilization and healthcare expenditure measures as outcomes. The healthcare utilization categories included the frequency of outpatient visits, the number of days stayed in the hospital, and the number of drug prescriptions fulfilled. Healthcare expenditure was similarly grouped into outpatient, inpatient, and pharmacy expenditures. The expenditures referred to the gross payments to providers, which were the summation of out-of-pocket costs and the amount paid by health plans. We calculated the total healthcare utilization and expenditure as a summation of the three sub-categories. In order to model the change of the outcomes associated with LDCT screening, both the healthcare utilization and expenditure were aggregated annually before and after the index date.

The primary predictors included ADRD status, LDCT status, and the interaction term between them. ADRD status was defined as a binary variable according to whether the patients had ADRD (group 1 and group 2: yes vs. group 3 and group 4: no). Similarly, LDCT status was defined as a binary variable whether according to whether the patients received LDCT screening (group1 and group 3: yes vs. group 2 and group 4: no).

The covariates included age, gender, US region, and comorbidity conditions. Age was stratified as 55–64 and 65–77 years old. US region was categorized as northeast, north-central, south, west, and unknown. Comorbidity conditions were indicated using the Charlson comorbidity index (CCI) score. The index score was a summation of weighted scores of 17 comorbidities constructed from the 12-month claims data[23]. CCI at baseline period and post period were calculated respectively.

Statistical analysis

We summarized the values of the covariates at baseline period for each identified study cohort for descriptive purposes, and performed Wilcoxon rank-sum tests to examine the differences in those variables across cohorts.

We applied a 1:10 multi-group nearest neighbor propensity score matching algorithm to match the patients in group 1 (ADRD patients who received LDCT) with the other three groups. Age, gender, region, and CCI at the baseline period were used to estimate the propensity scores using logistic regression.

A difference-in-differences (DID) model was used to estimate the LDCT incurred healthcare utilization and cost in the ADRD and non-ARDR populations. We regressed the pre-post change (from the baseline period to the post period) in outcomes on the pre-post change in the covariates on the matched sample. The primary predictor was the LDCT screening status. We also controlled for baseline age, gender, change of CCI, and region in the DID model.

Next, we applied a DDD model to assess the incremental cost and healthcare utilizations associated with LDCT screening for the ADRD population (group1 vs. group2) compared to the non-ADRD population (group3 vs. group4). To apply the DDD model, we regressed the annual change in the outcomes on three primary predictors: ADRD status, change of LDCT screening status, and an interaction term between the two (variable of interest). In this model, we controlled for the same covariates used in the DID model. All analyses were performed using SAS version 9.4 (SAS Institute Inc).

Results

Patient characteristics

We presented the baseline characteristics of the study cohorts in Table 1. We identified 619 ADRD patients who received LDCT screening between 2015 and 2017 (group 1), and 332,133 ADRD patients without LDCT screening (group 2). ADRD patients who had an LDCT screening were significantly younger than those who did not (62.2 vs. 66.3 years, p < .0001). There were more males in the ADRD LDCT cohort (54.0%), but more females in the ADRD non-LDCT cohort (53.9%, p < .0001). Compared to ADRD non-LDCT group, the mean CCI score in the ADRD with LDCT group was slightly higher (2.6 vs. 2.4, p = .0005). Patients from those two groups were approximately uniformly distributed in each region (Northeast: 28.8% vs. 26.2%, North Central: 27.1% vs. 25.3%, South: 35.4%, West: 8.6% vs. 8.4%, Unknown: 0.2% vs. 0.1%, p = .04).

Among the non-ADRD population, 12,747 individuals received LDCT screening and 7,797,547 did not. Individuals in the non-ADRD with LDCT screening group (group3) were one year younger (60.3 vs. 61.3 years, p < .0001) than the non-ADRD non-LDCT group (group 4), and both groups had a dominant percentage of individuals from the 55–64 age group (90.0% vs. 79.1%, p < .0001) compared with the 65–74 age group. Among the non-ADRD population, the LDCT group had a higher proportion of females (52.6% vs. 46.5%, p < .0001) than the non-LDCT group, and the average CCI scores of the LDCT group were higher than the non-LDCT group (1.4 vs. 0.9, p < .0001).

Healthcare utilization and expenditure

Figure 1 shows the 1-year healthcare utilization and expenditure before and after the index date for each study cohort. The annual number of outpatient visits were estimated to be 24.4, 25.0, 16.0, 12.1 for groups 1–4 at baseline, and these numbers increased to 27.9. 27.4, 17.5, 12.7, respectively. The annual outpatient expenditures were estimated to be $13,700.6, $14,069.73, $6,581.4, $5,389.6 for groups 1–4 at baseline, and $16,925.8, $16,713.7, $8,358.7, $6,101.8 in the post period after LDCT screening, correspondingly. The average

number of days spend in hospital were estimated to be 0.57,1.94, 0.29, and 0.27 for groups 1–4 at baseline, which generated $2,727.4, $9,760.0, $2,170.2, $2,015.4 expenditures, respectively. The average number of hospitals stay days after the index date of groups 1–4 increased to 1.37, 2.42, 0.49, and 0.31, and the 1-year inpatient expenditures were increased to $5,930.3, $12,404.4, $3,386.3, $2,329.6, correspondingly. The number of days of supply of prescribed medications in 1-year were estimated to be 1328.7, 1573.4, 1155.3, 858.1 for group 1–4 at baseline, and this amount increased to 1394.7, 1663.8, 1260.2, 904.2, respectively. The annual pharmacy expenditures were estimated to be $3,676.8, $4,971.8, $3,465.4, $2,466.3 for groups 1–4 at baseline, and $4,357.1, $5,436.9, $4,009.0, $2,683.7 at post period after LDCT screening, correspondingly. The total expenditures of group 1–4 increased from $20,104.7 to $27,213.1, $28,801.5 to $34,555.0, $12,216.9 to $15,754.0, $9,871.3 to $11,115.2 respectively.

Results from the DID and DDD models

We summarized results from the DID models in Panel 1 of Table 2. The DID models estimated the LDCT incurred annual healthcare utilization and expenditure among ADRD and non-ADRD populations, separately. In the ADRD population, LDCT screening was found to be associated with additional 2.1 outpatient visits ($p = .002$), additional $2853.6 outpatient expenditure ($p = .02$) and additional overall expenditure by a marginal amount ($5310.8 with $p = .06$), when compared with cohort without LDCT screening. We did not find a statistically significant association between LDCT screening and days of inpatient stays, days' supply of prescribed medicines, inpatient expenditure, and pharmacy expenditure. In the non-ADRD population, LDCT screening was found to be associated with additional 0.6 outpatients' visits ($p = .01$) and 61.4 additional days supplies of prescribed medication ($p = .001$). We did not find a statistically significant association between LDCT screening and an increase in the healthcare expenditure.

We summarized the result from the DDD model in Panel 2 of Table 2. The DDD model estimated the incremental cost and healthcare utilization incurred by LDCT in the ADRD population compared with the non-ADRD population. The LDCT screening in the ADRD population was associated with an additional 1.5 outpatient visits ($p = .02$), 0.7 stays ($p = .02$) in the hospital and 83.2 days decreasing in medication supplies ($p = .046$) yearly, when compared with performing LDCT screening in the non-ADRD population. For healthcare expenditure, we found additional $1684.4 outpatient expenditures ($p = .12$), additional $3,157.4 inpatient expenditures ($p = .08$) and additional $118.5 medication expenditures ($p = .8$) associated with LDCT screening in the ADRD population compared with the non-ADRD population; however, none of the single expenditure items were found to be statistically significant. Collectively, LDCT screening in the ADRD population was found to be associated with an additional $4960.4 overall healthcare expenditure compared with the non-ADRD population ($p = .03$).

Discussion

This study estimated the downstream cost and healthcare utilization associated with the use of LDCT in lung cancer screening in the non-ADRD and ADRD population.

Because the downstream healthcare utilization and expenditures are mostly contributed from confirmation tests and complications induced by invasive procedures, we assumed that the LDCT screening would have a larger impact on outpatient visits and inpatient stays, but less likely to impact prescribed medications. In general, the results from our models are as expected. We show that LDCT screening is associated with more outpatient visits in both ADRD and non-ADRD populations, and the increase in ADRD group is greater (2.1 vs. 0.6). Besides, there is a significant increment of outpatient expenditure ($2301.0) associated with LDCT screening among the ADRD population. Although not statistically significant, we also show that the use of LDCT is associated with additional 0.7 days of hospitalization in the ADRD population and 0.06 days of hospitalization in the non-ADRD population, which generated additional $2853.6 and $309.0 inpatient cost correspondingly. Overall, we show that lung cancer screening with LDCT is associated with a $5310.8 annual cost in the ADRD population and $1032.5 in the non-ADRD population.

Although LDCT was found to be associated with additional healthcare utilization and expenditures in both the ADRD and non-ADRD populations, the magnitude of such increments is greater in the ADRD population. Our presumption was that patients with ADRD suffer from cognitive decline, behavioral and psychiatric disorders, and declines in functional status, thus were more vulnerable to LDCT-related complications and more likely to require more healthcare resources. Our study results have found supporting evidence for this argument. When compared with the non-ADRD population, LDCT screening was found to incur additional outpatient visits and inpatient stays. In addition, the annual healthcare cost incurred by LDCT screening in the ADRD population was $4960.4 higher than in the non-ADRD population. One thing that need to be mentioned here is that the false positive rates of LDCT observed in the European NELSON study (1.2%)[24] was much lower than observed in the NLST from the US (24.2%), suggesting our estimation may not be generalizable to the Europe population.

An economic evaluation on the NLST found that LDCT screening incurred an additional annual cost of $1631 among the non-ADRD population[25], which is comparable to our estimation on the non-ADRD population who underwent LDCT (i.e. $1032). The cost associated with LDCT screening can vary substantially depending on factors such as the proficiency of the physicians, the level of clinical infrastructure, and the health status of the patients may influence the quality of the screening and subsequent procedures. All of these factors may influence the related healthcare utilization and cost[26]. Huo and colleagues have reported that the estimated complication rate of invasive procedures in real-world settings was approximately twice as high as that reported in the NLST, and the incremental cost could be more than $50,000 for those who experienced major complications[11]. In summary, our study showed consistent evidence that LDCT screening could cause additional healthcare expenditures, and the ADRD population was more greatly influence. Overall, our study provided important evidence that ADRD could potentially be an important factor that escalates the health and economic burden associated with LDCT screening.

Lung cancer screening using LDCT has been shown to be beneficial in reducing lung cancer-related mortality. Although our study indicates an increased downstream cost and healthcare utilization associated with LDCT screening, which provides indirect evidence

for worse health outcomes after LDCT screening, whether LDCT screening should be recommended for the ADRD population stays inconclusive. Further studies focusing on the benefit and harm trade-offs of LDCT screening among the ADRD population are warranted.

This study has several limitations. First, smoking status is unavailable in the MarketScan data. As a result, we were unable to accurately identify patients eligible for lung cancer screening using LDCT following the CMS guideline[7]. As a result, instead of the LDCT-eligible population, we used the general population to serve as the comparison group to evaluate the LDCT incurred cost. However, our comparison group might introduce bias because the normal population can be different from the LDCT-eligible population in healthcare cost and utilization. We have applied DID and DDD models to reduce this bias by borrowing analytical strength from self-control and panel design, however, a proportion of the residual bias might still persists Second, although we included Medicare supplemental database in our study, the major data source was from commercial health plans. Thus, the study population was younger than the general ADRD population. The vast majority of ADRD patient is over 75 years old, however, the mean age of our ADRD groups are below 70 years old. Third, the claims data does not contain detailed information on the severity of ADRD. Thus, the estimated incremental cost and health utility associated with LDCT in ADRD population are more generalizable to patients with an average level of ADRD severity in this population.

The downstream cost and healthcare utilization associated with LDCT screening were found to be higher in the ADRD population than the normal population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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(a) Total expenditure

■ 1-year before index date

■ 1-year after index date

Group1: ADRD[a] group with LDCT[b] scans

Group2: ADRD group without LDCT scans

Group3: Non-ADRD group with LDCT scans

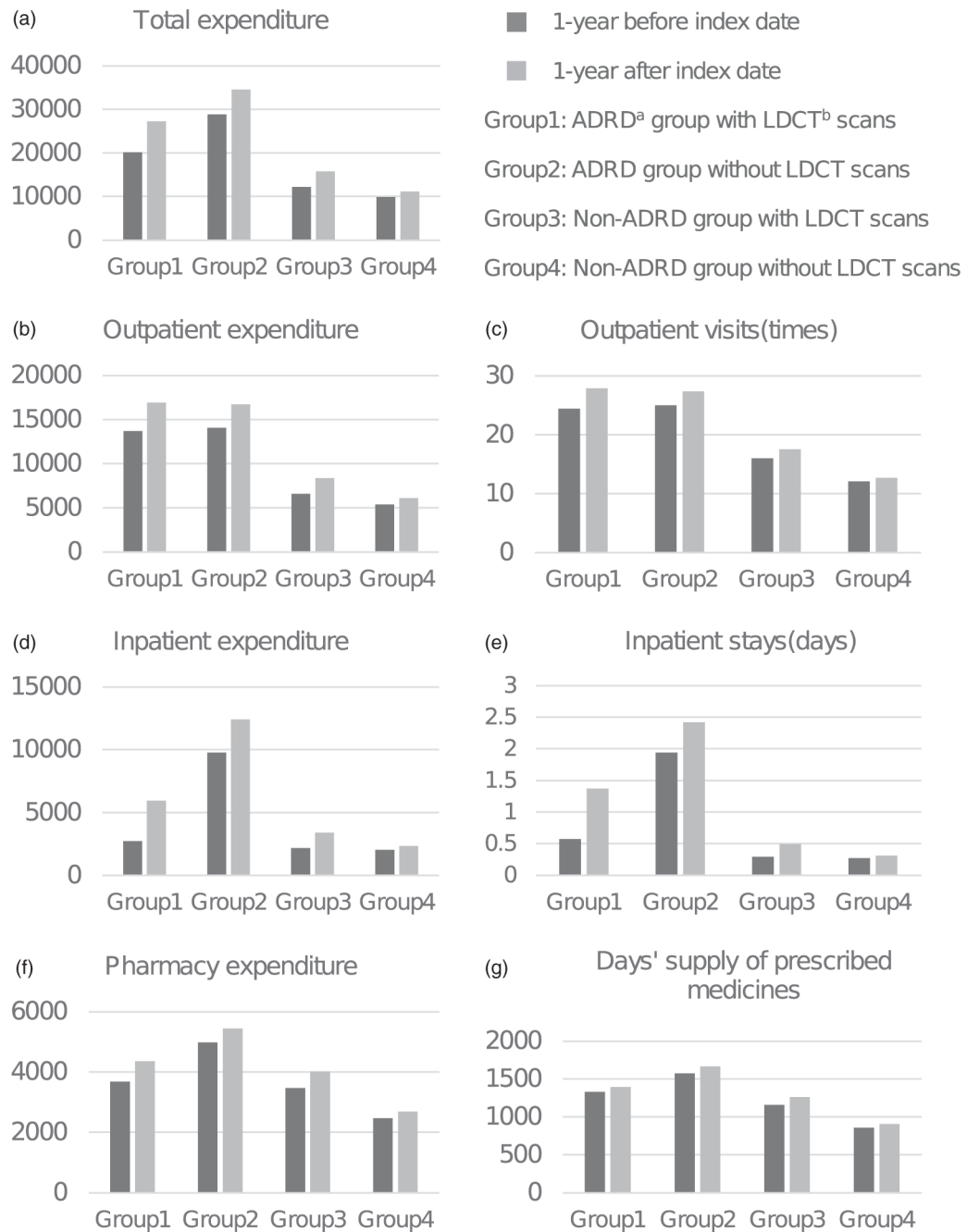Group4: Non-ADRD group without LDCT scans

Figure 1.

Healthcare expenditure and utilization 1-year before and after the LDCT screening. 1-year outcomes before and after the index date of the four groups. Respectively, (a) Sum of outpatient, inpatient and pharmacy expenditure. (b) Outpatient expenditure. (c) Times of outpatient visits. (d) Inpatient expenditure. (e) Total days of inpatient stays. (f) Pharmacy expenditure. (g) Total days' supply of prescribed medicines. [a]Alzheimer's disease and related dementias. [b] Low-dose computed tomography.

Table 1.

Baseline characteristics of the four study cohorts.

Characteristic	ADRD[a] population			Non-ADRD population		
	LDCT[b] No. (%)	No LDCT No. (%)	p-Value	LDCT No. (%)	No LDCT No. (%)	p-Value
Sample size	619	332,133		12,747	7,797,547	
Age, Mean (SE)	62.2(0.2)	66.3(0.01)	<.0001	60.3(0.04)	61.3(0.002)	<.0001
Age group						
55–64	466(75.3)	143,707(44.7)	<.0001	11,467(90.0)	6,165,602(79.1)	<.0001
65–77	153(24.7)	177,526(55.3)		1280(10.0)	1,631,945(20.9)	
Gender			<.0001			<.0001
Male	334(54.0)	148,090(46.1)		6710(52.6)	3,627,746(46.5)	
Female	285(46.0)	173,143(53.9)		6037(47.4)	4,169,801(53.5)	
Region			.04			<.0001
Northeast	178(28.8)	84,175(26.2)		3588(28.1)	1,669,287(21.4)	
North central	168(27.1)	81,251(25.3)		3540(27.8)	1,772,147(22.7)	
South	219(35.4)	125,162(39.0)		4574(35.9)	3,257,340(41.8)	
West	53(8.6)	30,293(9.4)		1030(8.1)	1,088,192(14.0)	
Unknown	1(0.2)	3552(0.1)		12(0.1)	10581(0.1)	
CCI[c], mean (SE)	2.6(0.1)	2.4(0.004)	.0005	1.4(0.002)	0.9(0.0006)	<.0001

[a] ADRD: Alzheimer's Disease and Related Dementias.

[b] LDCT: low-dose computed tomography.

[c] CCI: Charlson comorbidity index.

Table 2.

Full model results of matched samples.

Outcomes		Difference-in-differences model result [b]				Difference-in-difference-in-differences model result [c]	
		ADRD[a] group		Non-ADRD group			
		Estimates	p-Value	Estimates	p-Value	Estimates	p-Value
Healthcare Utilization	Frequency of outpatient visits	2.1 (0.7, 3.4)	.002	0.6 (0.1, 1.1)	.01	1.5 (0.2, 2.8)	.03
	Days of inpatient stays	0.7 (−0.2, 1.5)	.13	0.06 (−0.06, 0.2)	.3	0.7 (0.1, 1.3)	.02
	Days' supply of prescribed medicines	−25 (−77.2, 27.1)	.3	61.4 (23.7, 99.1)	.001	−83.2 (−164.9, −1.4)	.046
Healthcare Expenditure	Outpatient	2301.0 (296.2, 4305.8)	.02	607.8 (−245.3, 1460.9)	.2	1684.4 (−454.2, 3823.0)	.12
	Inpatient	2853.6 (−1861.9, 7569.1)	.2	309 (−497.2, 1115.3)	.4	3157.4 (−356.4, 6671.3)	.08
	Pharmacy	156.2 (−947.9, 1260.3)	.8	115.6 (−360.9, 592.2)	.6	118.5 (−1069.9, 1307.0)	.8
	Total	5310.8 (−177.7, 10,799.3)	.06	1032.5 (−245.3, 2310.2)	.11	4960.4 (532.7, 9388.0)	.03

95% confidence intervals were reported in brackets.

[a] Alzheimer's disease and related dementias.

[b] Difference-in-differences model result estimating the downstream healthcare utilization and expenditure related to low-dose computed tomography scan in ADRD and non-ADRD population respectively.

[c] Difference-in-difference-in-differences model result estimating the excessive downstream healthcare utilization and expenditure related with low-dose computed tomography scan among ADRD population.