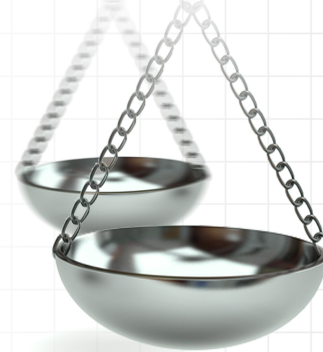




The impact of dementia on antidiabetic drug use in Medicare beneficiaries with diabetes: findings post-Medicare part D

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Aim: The objectives of the study were to measure the utilization rates of antidiabetic drugs in diabetic patients with dementia and to assess the impact of dementia on antidiabetic drug use. **Materials & methods:** This study was a pooled cross-sectional study of the Medicare Current Beneficiaries Survey from 2006 to 2010. **Results & conclusion:** Lower utilizations of biguanides, DPP-4 inhibitors and thiazolidinediones were observed in dementia patients. The likelihood of using antidiabetic drugs was about 30% (odds ratio: 0.69; 95% CI: 0.56–0.84) lower in dementia patients and 40% (odds ratio: 0.61; 95% CI: 0.44–0.84) lower in patients with Alzheimer's disease. Healthcare providers should be aware of underuse of antidiabetic drugs in patients with dementia.

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Keywords: Alzheimer's disease • antidiabetic drugs • dementia • Medicare • vascular dementia

Diabetes and dementia are two prevalent chronic conditions in the elderly population. For the US population aged 65 years or older, 25.9% (11.2 million) had diabetes (diagnosed or undiagnosed) in 2012 [1]. Alzheimer's disease and vascular dementia are two common types of dementia. In 2002, among individuals aged 71 years or older in USA, the prevalence of dementia, Alzheimer's disease and vascular dementia were 13.9, 9.7 and 2.4%, respectively. [2] Diabetes is found to be associated with significantly increased risks of dementia, Alzheimer's disease and vascular dementia [3–5].

Diabetes self-management (e.g., blood glucose testing, meal planning, exercising and medication) is important in controlling blood glucose levels and in preventing potential risks of diabetes complications. Unfortunately, however, diabetes conditions are often poorly managed, particularly among diabetic patients with dementia due to poor adherence. The literature documents that under

use of antidiabetic drugs and poor adherence is a major challenge for patients with diabetes. How to ensure that patients with diabetes take oral antidiabetic medications as prescribed is a major challenge for healthcare givers. Factors associated with under use of these drugs include, but not limited to certain demographics or economic status, cost burden, comorbidities or medications. Diabetic patients with a concomitant dementia may be unable to properly manage their diabetes conditions (e.g., forget or have difficulties in taking antidiabetic drugs) and thus may have difficulty in reaching their goal in managing diabetes.

In addition, certain oral antidiabetic drugs and insulins can slow cognitive decline in patients with dementia [6,7]. Compelling experimental and clinical evidences suggested that Alzheimer's disease and diabetes are closely related [8,9]. Both diseases are pathologically featured in insulin resistance. Therefore, antidiabetic drugs may halt the

Z Kevin Lu^{*1}, Minghui Li¹, Karen McGee¹, Cynthia M Phillips¹, Jing Yuan¹ & S Scott Sutton¹

¹Department of Clinical Pharmacy & Outcomes Sciences, South Carolina College of Pharmacy, University of South Carolina, 715 Sumter Street, Columbia, SC 29208, USA

*Author for correspondence:

Tel.: +1 803 777 2653

Fax: +1 803 777 2820

luk@sccp.sc.edu

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disease process of dementia. Several completed and ongoing clinical trials investigate the efficacy and safety profiles of different antidiabetic drugs in treating dementia and its subtypes (Alzheimer's disease and vascular dementia) [10].

Given the current poor managements of diabetes, and the potential benefit of proper use of antidiabetic drugs among diabetic patients with dementia, it is critical to understand the utilization patterns of antidiabetic drugs among diabetic patients with dementia, particularly in the elderly population. In addition, understanding the potential impact of dementia on antidiabetic drug use will inform stakeholders (e.g., patients, caregivers, healthcare providers and policy makers) so better strategies should be used to manage diabetes among those with a concomitant dementia and the subtypes. Unfortunately, the majority of the published studies have been focusing on antidiabetic drugs and the associated risk of dementia. No existing studies, however, have specifically examined how antidiabetic drugs are used among diabetic patients with concomitant dementia and its subtypes and how dementia may impact antidiabetic drug use among patients with diabetes. This is important because the findings may help guide the stakeholders when managing diabetes with concomitant dementia in clinical practice, which is currently lacking in the literature.

The objectives of the study were to measure the utilization rates of overall and different classes of antidiabetic drugs among elderly Medicare diabetics with a concomitant dementia and to assess the impact of dementia and its subtypes on overall and different classes of antidiabetic drug use. We hypothesize that compared with diabetics without dementia; those with dementia are less likely to use antidiabetic drugs.

Material & methods

Data source

This study used data from the Medicare Current Beneficiaries Survey (MCBS). The MCBS is a longitudinal survey conducted by the Centers for Medicare and Medicaid Services to measure expenditures and sources of payment for healthcare services used by Medicare beneficiaries. Participants of the MCBS are followed up to 4 years. When survey participants are not available or physically or mentally unable to respond to the MCBS by themselves, they can name proxy respondents to answer survey questions on their behalf. Proxy responses are very common in dementia patients.

Comprehensive information on health services use, healthcare expenditures, health insurance coverage and socioeconomic and demographic characteristics of Medicare beneficiaries are collected in the MCBS. In

addition to information self- or proxy-reported, Medicare part A and B claims for survey respondents are linked to the MCBS. By keeping medical bill records and/or medication containers, prescribed medicine events are reported by survey or proxy respondents. Medicare part D went into effect in 2006. Since then, Medicare part D utilization information was added to prescribed medicine events in the MCBS. When a prescribed medicine event is reported in the survey and found in Medicare part D claims, they will be combined as one record.

Study population

Participants of the MCBS from 2006 to 2010 comprised the population of the study. In the study, we included survey participants if they were 65 years of age or older and had been diagnosed with diabetes. We excluded survey participants if they were institutionalized during the time of the interview or were eligible for Medicare because of end-stage renal disease.

Measurement

Information regarding the overall and different classes of antidiabetic drugs was measured based on prescribed medicine events. Users of antidiabetic drugs in a given year were defined as having at least one prescribed medicine event with any antidiabetic drug during that year. Antidiabetic drugs were classified into eight categories in the study: alpha-glucosidase inhibitors, biguanides, DPP-4 inhibitors, GLP-1 receptor agonists, insulins, meglitinides, sulfonylureas and thiazolidinediones. Due to the low utilization, other classes of antidiabetic drugs (e.g., bile acid sequestrants, dopamine-2 agonists, sodium-glucose cotransporter-2 inhibitors and amylin mimetics) were not included in the study. Definitions of users of different classes of antidiabetic drugs were similar to users of overall antidiabetic drugs. Since in a given year a diabetic patient may use more than one class of antidiabetic drugs, the classification of antidiabetic drugs was not mutually exclusive in the study.

Based on the Chronic Condition Data Warehouse algorithms along with the relevant The International Classification of Diseases, Ninth Revision, Clinical Modification codes from Medicare part A and B claims, we identified Medicare beneficiaries who had been diagnosed with diabetes, dementia, Alzheimer's disease or vascular dementia. Characteristics of the study population, including age, gender, race, education, marital status, income level, residence status, census region, BMI and smoking status were reported by survey or proxy respondents. Based on Medicare part A and B claims, we also calculated a modified Charlson comorbidity index (CCI) excluding diabetes and dementia to adjust for possible comorbidity confounding.

Statistical analysis

This study was a pooled cross-sectional study from 2006 to 2010. Since each survey respondent might be interviewed in multiple years, the unit of analysis of the study is person-year. Survey sampling weights were used in the analysis to get national estimates of elderly Medicare beneficiaries with diabetes.

Rao–Scott Chi-square tests, to deal with the complex survey design, were performed to compare characteristics of Medicare beneficiaries with and without dementia and its subtypes. Three weighted logistic regression models (model 1, model 2 and model 3) were conducted in the study to identify predictors of antidiabetic drug use. Dependent variables (antidiabetic drug use) and covariates (used to control for confounding) were the same in all three models. To estimate the impact of dementia and its subtypes on antidiabetic drug use, main independent variables were different in three models. Dementia, Alzheimer's disease and vascular dementia served as main independent variables in model 1, model 2 and model 3, respectively. We further performed subgroup analyses to evaluate the impact of dementia and its subtypes on different classes of antidiabetic drug use. For each class of antidiabetic drugs, three weighted logistic regression models were performed. Results for certain classes of antidiabetic drugs with very low utilization rates were not reported.

Institutional Review Board approval was obtained for this study. SAS software (version 9.4; Statistical Analysis Systems, NC, USA) was used to perform all statistical analyses.

Results

The study identified 8539 person-years observations for elderly Medicare beneficiaries with diabetes. Among them, 683 (6.3% weighted percentage), 296 (2.5%) and 59 (0.5%) had been diagnosed with dementia, Alzheimer's disease and vascular dementia, respectively. In addition, 22 had been diagnosed with both Alzheimer's disease and vascular dementia. Some characteristics of Medicare beneficiaries differed statistically significantly ($p < 0.05$) between individuals with and without dementia and its subtypes. Compared with elderly Medicare beneficiaries without dementia, dementia patients were more likely to be 75 years of age or older, be non-Hispanic black, have less than high school education, be widowed, have income equal or less than US\$20,000 per year, live in other census regions (e.g., Puerto Rico), be underweight (BMI: <18.5) or normal weight (BMI: 18.5 – 24.9), be a nonsmoker or have one or more comorbidities in addition to dementia (Table 1). Similar types of differences were observed when elderly Medicare beneficiaries with and without subtypes of dementia were compared.

Utilization rates of overall and some classes of antidiabetic drugs were significantly different between elderly Medicare beneficiaries with and without concomitant dementia or Alzheimer's disease (Table 1). About half (51.5%) of dementia patients used antidiabetic drugs; while about three fifths (59.4%) of individuals without dementia used antidiabetic drugs ($p = 0.002$). Similarly, patients with Alzheimer's disease had lower utilization of antidiabetic drugs (47.8%), compared with those without Alzheimer's disease (59.2%; $p = 0.003$). For different classes of antidiabetic drugs, lower utilizations of biguanides ($p < 0.001$), DPP-4 inhibitors ($p = 0.024$) and thiazolidinediones ($p = 0.002$) were observed in dementia patients. Patients with Alzheimer's disease had lower utilization of biguanides, compared with individuals without Alzheimer's disease ($p < 0.001$). Overall and different classes of antidiabetic drug utilizations between individuals with and without vascular dementia were similar.

After controlling for demographic and socioeconomic characteristics of elderly Medicare beneficiaries, dementia patients were about 30% (odds ratio [OR]: 0.69; 95% CI: 0.56–0.84) less likely to take antidiabetic drugs compared with individuals without dementia (Table 2). The likelihood of taking antidiabetic drugs was about 40% (OR: 0.61; 95% CI: 0.44–0.84) lower in patients with Alzheimer's disease compared with individuals without Alzheimer's disease. The probability of taking antidiabetic drugs was not significantly different between individuals with and without vascular dementia. (OR: 0.59; 95% CI: 0.33–1.04) Other predictors of lower utilizations of antidiabetic drugs were younger age, higher level of education and lower BMI.

Same demographic and socioeconomic characteristics were controlled in the subgroup analyses. Compared with individual without dementia, dementia patients were about 40% (OR: 0.62; 95% CI: 0.49–0.79), 20% (OR: 0.78; 95% CI: 0.63–0.96) and 30% (OR: 0.70; 95% CI: 0.53–0.94) less likely to take biguanides, sulfonylureas and thiazolidinediones, respectively (Table 3). The likelihood of using DPP-4 inhibitors, insulins and meglitinides was similar between individuals with and without dementia. The probability to take biguanides and sulfonylureas were about 40% (OR: 0.59; 95% CI: 0.41–0.84) and 30% (OR: 0.69; 95% CI: 0.50–0.97) lower in patients with Alzheimer's disease, compared with individuals without Alzheimer's disease. The likelihood of using DPP-4 inhibitors, insulins, meglitinides and thiazolidinediones was similar between individuals with and without Alzheimer's disease. Utilization rates of biguanides, insulins, sulfonylureas and thiazolidinediones were not significantly different between individuals with and without vascular dementia.

Table 1. Characteristics of Medicare beneficiaries with diabetes, 2006–2010 (n = 8539).

Characteristics		Dementia		Alzheimer's disease			Vascular dementia			
		No, n = 7856 (%)	Yes, n = 683 (%)	p-value	No, n = 8243 (%)	Yes, n = 296 (%)	p-value	No, n = 8480 (%)	Yes, n = 59 (%)	p-value
Age (years):				<0.001			<0.001			<0.001
– 65–74	55.1	21.0		53.7	18.3		52.8	26.0		
– 75–84	34.5	45.6		35.0	45.9		35.3	34.3		
– 85+	10.4	33.4		11.3	35.8		11.9	39.7		
Gender:				0.054			0.101			0.294
– Male	47.0	41.7		46.8	40.7		46.6	54.3		
– Female	53.0	58.3		53.2	59.3		53.4	45.7		
Race:				0.028			0.008			0.039
– Non-Hispanic white	75.0	70.0		74.9	66.3		74.7	71.5		
– Non-Hispanic black	10.8	16.0		11.0	18.3		11.1	21.9		
– Hispanic	8.2	8.1		8.1	9.5		8.2	1.7		
– Other	6.0	6.0		6.0	5.9		6.0	4.8		
Education:				<0.001			0.000			0.080
– Less than high school	27.4	41.5		28.0	41.9		28.3	45.8		
– High school graduate	29.7	25.9		29.6	23.4		29.4	23.0		
– Some college	21.6	16.9		21.3	20.7		21.3	17.8		
– College graduate	21.3	15.7		21.2	14.0		21.0	13.5		
Marital status:				<0.001			<0.001			0.118
– Married	55.5	39.3		54.7	42.5		54.5	36.7		
– Widowed	29.4	47.8		30.1	49.6		30.6	44.1		
– Single	15.0	12.9		15.1	7.8		14.9	19.1		
Income (US\$):				<0.001			<0.001			0.003
– <10,000 per year	12.8	23.2		13.3	21.0		13.5	28.7		
– 10,001–20,000 per year	26.1	31.6		26.3	32.0		26.5	31.1		
– 20,001–40,000 per year	35.6	30.0		35.2	34.5		35.2	31.6		
– ≥40,000 per year	25.5	15.2		25.1	12.6		24.8	8.5		
Residence:				0.732			0.453			0.610
– Nonmetropolitan	26.3	25.6		26.3	24.1		26.2	30.1		
– Metropolitan	73.7	74.4		73.7	75.9		73.8	69.9		

CI: Chadson comorbidity index; NA: Not available

CCI: Charlson comorbidity index; NA: Not available.

Table 2. Predictors of antidiabetic drug use.

Variables	Model 1		Model 2		Model 3	
	OR	95% CI:	OR	95% CI:	OR	95% CI:
Dementia:						
– No	Ref					
– Yes	0.69	0.56–0.84				
Alzheimer’s disease:						
– No			Ref			
– Yes			0.61	0.44–0.84		
Vascular dementia:						
– No					Ref	
– Yes					0.59	0.33–1.04
Age (years):						
– 65–74	Ref		Ref		Ref	
– 75–84	1.77	1.55–2.01	1.76	1.54–2.00	1.74	1.52–1.98
– 85+	1.33	1.10–1.61	1.30	1.08–1.58	1.27	1.05–1.53
Gender:						
– Male	1.09	0.95–1.25	1.09	0.95–1.25	1.09	0.95–1.25
– Female	Ref		Ref		Ref	
Race:						
– Non-Hispanic white	Ref		Ref		Ref	
– Non-Hispanic black	0.97	0.79–1.20	0.98	0.80–1.20	0.97	0.79–1.19
– Hispanic	1.14	0.85–1.52	1.14	0.86–1.53	1.15	0.86–1.53
– Other	1.08	0.80–1.46	1.09	0.80–1.47	1.08	0.80–1.47
Education:						
– Less than high school	Ref		Ref		Ref	
– High school graduate	0.75	0.62–0.92	0.75	0.62–0.92	0.76	0.62–0.93
– Some college	0.67	0.55–0.81	0.67	0.55–0.82	0.67	0.55–0.82
– College graduate	0.67	0.54–0.84	0.68	0.54–0.85	0.68	0.54–0.85
Marital status:						
– Married	Ref		Ref		Ref	
– Widowed	1.17	1.00–1.38	1.17	1.00–1.37	1.17	1.00–1.37
– Single	1.22	0.99–1.51	1.21	0.98–1.50	1.22	0.99–1.51
Income (US\$):						
– <10,000 per year	Ref		Ref		Ref	
– 10,001–20,000 per year	0.84	0.67–1.05	0.84	0.67–1.06	0.85	0.68–1.06
– 20,001–40,000 per year	0.89	0.69–1.14	0.90	0.70–1.15	0.90	0.70–1.16
– ≥40,000 per year	0.91	0.67–1.25	0.92	0.67–1.25	0.92	0.68–1.26
The ref group represents the row in the variable column.						
Model 1: use dementia (yes [Y]/no [N]) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.						
Model 2: use Alzheimer’s disease (Y/N) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.						
Model 3: use vascular dementia (Y/N) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.						
CCI: Charlson comorbidity index; OR: Odds ratio; Ref: Reference.						

Table 2. Predictors of antidiabetic drug use (cont.).

Variables	Model 1		Model 2		Model 3	
	OR	95% CI:	OR	95% CI:	OR	95% CI:
Residence:						
– Nonmetropolitan	1.16	0.99–1.36	1.16	0.99–1.36	1.16	0.99–1.36
– Metropolitan	Ref		Ref		Ref	
Census region:						
– Northeast	Ref		Ref		Ref	
– Midwest	1.14	0.90–1.46	1.14	0.89–1.45	1.14	0.90–1.46
– South	1.26	1.05–1.51	1.26	1.05–1.50	1.26	1.05–1.50
– West	1.03	0.78–1.37	1.03	0.78–1.35	1.03	0.78–1.35
– Other	0.82	0.50–1.32	0.83	0.50–1.37	0.76	0.48–1.23
BMI:						
– Underweight (<18.5)	0.58	0.36–0.93	0.57	0.35–0.92	0.57	0.36–0.92
– Normal (18.5–24.9)	Ref		Ref		Ref	
– Overweight (25–29.9)	1.37	1.16–1.62	1.38	1.16–1.63	1.39	1.17–1.64
– Obese (≥30)	1.76	1.49–2.07	1.77	1.50–2.09	1.79	1.52–2.11
Smoking:						
– No	Ref		Ref		Ref	
– Former	1.04	0.89–1.21	1.04	0.89–1.21	1.04	0.89–1.21
– Current	0.98	0.79–1.22	0.99	0.80–1.22	0.99	0.80–1.23
CCI:						
– 0	Ref		Ref		Ref	
– 1	0.90	0.76–1.07	0.89	0.75–1.06	0.90	0.75–1.07
– 2+	1.02	0.83–1.25	1.01	0.82–1.25	1.02	0.83–1.25

The ref group represents the row in the variable column.

Model 1: use dementia (yes [Y]/no [N]) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.

Model 2: use Alzheimer's disease (Y/N) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.

Model 3: use vascular dementia (Y/N) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.

CCI: Charlson comorbidity index; OR: Odds ratio; Ref: Reference.

Discussion

This study provided national estimates on the prevalence of overall and different classes of antidiabetic drug use among elderly Medicare beneficiaries with diabetes. Overall, the prevalence of antidiabetic drug class utilization did not change much as compared with Margolis *et al.*'s report among diabetic Medicare beneficiaries [11]. However, this study further provided national estimates on the prevalence of overall and different classes of antidiabetic drug utilizations among diabetic patients with dementia and its subtypes. Among diabetic patients without dementia or its subtypes, biguanides were the most frequently used class of antidiabetic drugs; while sulfonylureas ranked as the second. Utilization patterns of biguanides and sulfo-

nylureas were consistent among diabetic patients with vascular dementia. However, among diabetic patients with dementia or Alzheimer's disease, the utilization patterns were reversed, where sulfonylureas ranked as the first and biguanides ranked as the second most frequently used class of antidiabetic drugs. Healthcare providers should be aware of the special utilization patterns of biguanides and sulfonylureas among diabetic patients with dementia or Alzheimer's disease and modify prescription patterns when appropriate.

Dementia poses a significant challenge on the self-management in diabetes. Because of dementia, diabetic patients may have problems when communicating with healthcare providers and forget to fill prescriptions. Furthermore, diabetic patients with

Table 3. Predictors of different classes of antidiabetic drug use.						
Classes	Model 1		Model 2		Model 3	
	OR	95% CI:	OR	95% CI:	OR	95% CI:
Alpha-glucosidase inhibitors	–	–	–	–	–	–
Biguanides	0.62	0.49–0.79	0.59	0.41–0.84	0.90	0.50–1.63
DPP-4 inhibitors	0.61	0.34–1.09	0.54	0.21–1.37	–	–
GLP-1 receptor agonists	–	–	–	–	–	–
Insulins	1.20	0.92–1.57	1.04	0.70–1.55	0.99	0.42–2.33
Meglitinides	1.02	0.59–1.77	1.31	0.60–2.87	–	–
Sulfonylureas	0.78	0.63–0.96	0.69	0.50–0.97	0.54	0.26–1.14
Thiazolidinediones	0.70	0.53–0.94	0.87	0.56–1.35	0.60	0.22–1.65
Model 1: use dementia (yes [Y]/no [N]) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and Charlson comorbidity index (CCI).						
Model 2: Use Alzheimer’s disease (Y/N) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.						
Model 3: Use vascular dementia (Y/N) as the main independent variable and controlled for age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI.						
OR: Odds ratio.						

dementia may be unable to interpret blood glucose test results. Hence, they cannot adjust antidiabetic drug doses when necessary. In addition, dementia patients may forget to take antidiabetic drugs as prescribed. All of these may contribute to the lower utilizations of overall antidiabetic drugs, biguanides, sulfonylureas and thiazolidinediones among diabetic patients with dementia or Alzheimer’s disease observed in the study. Insulin use was not associated with dementia or Alzheimer’s disease in the study. The administration of insulins requires visual and motor skills. Diabetic patients with dementia may be unable to inject insulins properly by themselves and need caregivers for help. With the involvement of caregivers, having dementia or Alzheimer’s disease should have minimal impact on insulins use.

Antidiabetic drugs can slow the progression of Alzheimer’s disease and improve cognitive functions through different mechanisms [6,7]. Biguanides were found to play a neuroprotective role in preventing against apoptotic cell death in primary cortical neurons [12]. Sulfonylureas could inhibit mammalian target of rapamycin, which played a role in developing diabetes and Alzheimer’s disease [13]. Thiazolidinediones had been shown to reduce soluble amyloid beta oligomers, which caused synapse deterioration underlying memory loss in Alzheimer’s disease [14]. However, this study found that patients with dementia or Alzheimer’s disease were less likely to use antidiabetic drugs, biguanides, sulfonylureas and thiazolidinediones. Healthcare providers should be aware of the

low utilizations of antidiabetic drugs among diabetic patients with dementia or Alzheimer’s disease and prescribe appropriate antidiabetic drugs to them if not contraindicated or tolerated. Strategies are warranted to address the underuse of antidiabetic drugs among Medicare diabetics with a concomitant dementia.

This study is the first of its kind to provide national estimates on the prevalence of overall and different classes of antidiabetic drug utilizations among diabetic patients with dementia, and to assess the impact of dementia and its subtypes on overall and different classes of antidiabetic drug use. Several factors should be considered when interpreting the data. First, disease/conditions were identified based on Medicare claims only. Dementia is frequently undiagnosed and not properly coded in the reimbursement systems [15–17]. The study might underestimate the number of dementia patients. Second, this study was unable to measure the disease severity, which may influence antidiabetic drug use. Third, because of small sample sizes, the impact of dementia and its subtypes on alpha-glucosidase inhibitors and GLP-1 receptor agonists use were unmeasurable. Similarly, the association between vascular dementia and the use of DPP-4 inhibitors and meglitinides were not assessed due to the low prevalence of vascular dementia. Fourth, characteristics of diabetic patients with and without dementia and its subtypes were statistically significant different. Whether they were clinically or epidemiologically different were unknown. Fifth, this study might be subject to endogeneity problems, however, as

noted in Table 3, we did control for a large number of confounding factors, including age, gender, race, education, marital status, income, residence, census region, BMI, smoking and CCI. These variables combined should be adequate and the endogeneity problem should be minimal. Finally, due to the cross-sectional design, the study was unable to establish a causal relationship between dementia and antidiabetic drug use. Also, the duration of diabetes and dementia could not be measured in the study.

Despite of the limitations listed above, the findings of the study, which were based on real-world, nationally representative data, provide important information to patients, healthcare givers and/or policy makers in future clinical practice. First, special attention by healthcare providers or family care givers should be given to elderly diabetics with dementia, particularly those with Alzheimer's disease, as they are more likely to under use diabetes medications compared with their counter parts. Strategies such as intensive family care givers, memory aids, reminders, mutual goal setting or incentives and/or reinforcements in future clinical practice may be considered.

Second, certain types of antidiabetic drugs may be significantly under used by diabetics with dementia. These drugs include biguanides, sulfonylureas and thiazolidinediones. Strategies such as education sessions may be helpful by emphasizing the importance of being adherent to these drugs. Third, similar strategies may also be needed for patients with predictive characteristics (e.g., educational status, lower BMI).

Conclusion

In conclusion, about half of elderly diabetic Medicare beneficiaries with dementia used antidiabetic drugs from 2006 to 2010. Patients with dementia were about 30% less likely to use antidiabetic drugs. Sulfonylureas were the most frequently used class of antidiabetic drugs in diabetic patients with dementia. Given the benefits of antidiabetic drugs in treating demen-

tia, healthcare providers should prescribe antidiabetic drugs in diabetic patients with dementia when appropriate. Strategies that focus on how to improve antidiabetic drug use among the elderly diabetics with a concomitant dementia are warranted.

Future perspective

The literature documents that patients with diabetes have a higher risk of developing dementia. Our study showed that diabetic patients with developed dementia significantly underuse antidiabetic drugs compared with their counterparts without dementia. Specifically, patients with dementia were about 30% less likely to use antidiabetic drugs, and thus posing a serious challenge for diabetes management among Medicare population. Healthcare providers should be aware of the potentially significant underuse of biguanides, sulfonylureas and thiazolidinediones when prescribing these drugs. Future studies on the impact of improved use of antidiabetics on outcomes of diabetic patients with comorbid dementia are warranted.

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Executive summary

- Diabetes and dementia are pathologically related. Use of antidiabetic drugs has potential benefits for patients with a comorbid dementia.
- A comorbid dementia poses a significant challenge to diabetes management.
- Diabetic patients with a comorbid dementia (e.g., Alzheimer's disease) are less likely to use antidiabetic drugs.
- Sulfonylureas were the most frequently used class of antidiabetic drugs in diabetic patients with dementia.
- Diabetic patients with dementia were less likely to use biguanides, sulfonylureas and thiazolidinediones.
- Diabetic patients with Alzheimer's disease were less likely to use biguanides and sulfonylureas.
- Healthcare providers should be aware of the potentially significant underuse of biguanides, sulfonylureas and thiazolidinediones when prescribing these drugs.
- Strategies that focus on how to improve antidiabetic drug use among the elderly diabetics with a comorbid dementia are warranted.

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