Overtreatment and Deintensification of Diabetic Therapy among Medicare Beneficiaries

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BACKGROUND: Deintensification of diabetic therapy is often clinically appropriate for older adults, because the benefit of aggressive diabetes treatment declines with age, while the risks increase.

OBJECTIVE: We examined rates of overtreatment and deintensification of therapy for older adults with diabetes, and whether these rates differed by medical, demographic, and socioeconomic characteristics.

DESIGN, SUBJECTS, AND MAIN MEASURES: We analyzed Medicare claims data from 10 states, linked to outpatient laboratory values to identify patients potentially overtreated for diabetes (HbA1c < 6.5% with fills for any diabetes medications beyond metformin, 1/1/2011–6/30/2011). We examined characteristics associated with deintensification for potentially overtreated diabetic patients. We used multinomial logistic regression to examine whether patient characteristics associated with overtreatment of diabetes differed from those associated with undertreatment (i.e. HbA1c > 9.0%).

KEY RESULTS: Of 78,792 Medicare recipients with diabetes, 8560 (10.9%) were potentially overtreated. Overtreatment of diabetes was more common among those who were over 75 years of age and enrolled in Medicaid ($p < 0.001$), and was less common among Hispanics ($p = 0.009$). Therapy was deintensified for 14% of overtreated diabetics. Appropriate deintensification of diabetic therapy was more common for patients with six or more chronic conditions, more outpatient visits, or living in urban areas; deintensification was less common for those over age 75. Only 6.9% of Medicare recipients with diabetes were potentially undertreated. Variables associated with overtreatment of diabetes differed from those associated with undertreatment.

CONCLUSIONS: Medicare recipients are more frequently overtreated than undertreated for diabetes. Medicare recipients who are overtreated for diabetes rarely have their regimens deintensified.

KEY WORDS: Medicare; beneficiary; diabetes; potential overtreatment; deintensification.

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INTRODUCTION

Treating diabetes requires balancing the risks of long-term harm from undertreatment with the short-term and long-term harm from potential overtreatment. At times, deintensification of therapy—removing treatments that were previously recommended¹—is appropriate. The Choosing Wisely campaign, which has been promoted in multiple countries,^{2–4} focuses on reducing overtreatment. The American Geriatrics Society (AGS) specifically states that medications other than metformin should be avoided when an older patient's hemoglobin A1c is less than 7.5%, because the risks of hypoglycemia are increased and the potential benefits of treatment are decreased for older adults with diabetes.^{5, 6} The National Institute for Health and Care Excellence (NICE) in the United Kingdom offers a similar recommendation,⁷ as randomized trials have shown that the benefits of aggressive glycemic control begin only after at least 8 years of treatment,^{8–11} yet the harms of aggressive glycemic control—hypoglycemia, cardiovascular events, cognitive impairment, fractures, and death—can happen at any time.^{12–16} Several studies have reported that a significant proportion of adults with diabetes are potentially overtreated.^{17–23} A United States (US) Veterans Health Administration study found that only a small minority of overtreated diabetic patients received medication deintensification, causing unnecessary exposure to potentially harmful treatments.¹⁹

Prior work has identified a number of disparities in control of diabetes and its complications.^{24–28} However, most attention has focused on undertreatment of diabetes, and investigation of patient characteristics associated with overtreatment of diabetes²⁰ or severe hypoglycemia²¹ has been limited. Therefore, we examined rates of overtreatment and deintensification of therapy for Medicare beneficiaries, and whether there were any disparities in these rates by race/ethnicity, dual eligibility, age, sex,

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rurality, or multimorbidity. To put these overtreatment findings into context, we compared the rates and patient characteristics associated with overtreatment and undertreatment of diabetes in the same cohort of patients.

METHODS

Data Source

We used Medicare claims from fee-for-service beneficiaries in 10 eastern US states (NY, NJ, MD, DE, VA, NC, SC, GA, FL, AL) from a data linkage project that has been described previously.²⁹ We accessed the data through the Centers for Medicare & Medicaid Services Chronic Conditions Data Warehouse (CCW) Virtual Research Data Center. The data included Medicare Part D files, carrier Standard Analytic Files, Chronic Conditions Data Warehouse (CCW) summary files, and the corresponding denominator files from 2010 to 2011. The Medicare Part D files contain brand and generic prescription drug names, strength, days' supply, quantity dispensed, and service date. The carrier files contain noninstitutional provider claims for services covered under Medicare Part B, including International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes, place of service, Current Procedural Terminology codes, and dates of service. Medicare claims for laboratory services were linked to actual outpatient laboratory values processed by a national laboratory vendor in 2011 for Medicare beneficiaries. The CCW summary file provides flags for 27 chronic diseases based on diagnoses in Parts A and B Medicare claims from 1999 onward.³⁰ Denominator files include patient demographic characteristics, birth and death dates, and information about program eligibility and enrollment.

Study Cohort

We included older adults who met all the following criteria: enrolled in Medicare Parts A, B, and D between January 1, 2010, and December 30, 2011; had a diagnosis of diabetes in the CCW summary file in the 2 years before June 30, 2010; had at least one HbA1c lab result available between January 1, 2011, and June 30, 2011, and were 65 years or older at this HbA1c date; and were alive on December 31, 2011 (eFigure 1). If multiple HbA1c lab results existed for a patient, the first HbA1c lab was selected for analysis, and defined as the index date.

Medications

Diabetes medications were identified in the Medicare Part D files by searching, from 120 days before to 180 days after the index date, generic drug names for the following classes of medications: insulin, biguanides, sulfonylureas, thiazolidinediones, meglitinides, GLP-1 agonists, amylin analogs, DPP-4 inhibitors, and alpha-glycosidase inhibitors (see Appendix Table 5 for details). For patients on combination medications, we counted each component as a separate medication. Daily dose was calculated using medication strength, days' supply, and quantity dispensed¹⁹ for all oral agents.

Outcomes

Patients were classified as potentially overtreated for diabetes if they had an index HbA1c value of less than 6.5% during the period from January through June 2011 and had filled any diabetes medications other than metformin in a pre-index medication regimen during the months leading up to this index HbA1c value. We chose this HbA1c threshold because it was substantially lower than the Choosing Wisely and AGS⁵ recommendations to avoid medications other than metformin when HbA1c values were less than 7.5%,³¹ and lower than the American Diabetes Association's guidelines for glucose control for patients with diabetes.³² Patients were classified as potentially undertreated if their index HbA1c was greater than 9.0%, regardless of medication status, consistent with Healthcare Effectiveness Data and Information Set (HEDIS) measures since 1999.³³ All others were classified as having acceptable treatment of their diabetes.

We defined medication deintensification among potentially overtreated older adults using a previously published method.¹⁹ Briefly, older adults on oral agents were defined as having had their regimens deintensified if they had medication fills with a lower dose than the index dose in the 1 to 180 days after the index date, or no refills of previously prescribed medications in the 22 to 180 days after the index date (see eFigure 1 in Sussman¹⁹ for an illustration). The index dose was defined as the medication dosage in the months leading up to the index HbA1c value used to define overtreatment, undertreatment, or neither. Medications filled in the 1–21 days after the date of the index dose were ignored for defining deintensification. We did this to account for blood draws or other visit-related work that occurs after the visit. Since HbA1c measurements are rarely repeated in under 3 months, this is unlikely to create any biases. Following prior work,¹⁹ older adults on insulin, pramlintide, or exenatide were defined as having deintensification if there were no medication refills in the 22 to 180 days after the index date. As the focus of this study was overtreatment and deintensification of therapy, we did not examine intensification of therapy for undertreated older adults, as many previous studies have examined this question.³⁴

Study Variables

Covariates of interest obtained from the Medicare denominator files included baseline patient demographic characteristics, specifically age (65–70, 71–75, 76+), race/ethnicity (non-Hispanic white, Hispanic, non-Hispanic black, other),²³ Medicaid dual eligibility, indication for Medicare eligibility (age vs. disability), gender, and urban location.^{35, 36} We derived urban location from rural-urban commuting area codes based on ZIP Code of residence. The number of chronic conditions (0–1, 2–3, 4–5, 6+) was constructed from the CCW chronic disease flags at end of year for 18 conditions (see Appendix Table 6 for details). From carrier physician claims, we obtained the number of outpatient visits for evaluation and management (E&M) visits in 2010 based on Healthcare Common Procedure Coding System codes 992.xx, 993.xx, and 994.xx.

Statistical Analysis

The associations between diabetes overtreatment and covariates of interest were summarized using means and standard deviations for continuous variables and frequencies with percentages for categorical variables. We compared rates of overtreatment to undertreatment and adequate treatment by groups, using χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. To assess the association between patient characteristics and three-level treatment outcome, we used a multinomial logistic regression with the reference category as adequate treatment that adjusted for age, race/ethnicity, Medicaid dual eligibility, indication for Medicare eligibility (age vs. disability), gender, multimorbidity, number of outpatient visits, and urban location (Table 1).^{35, 36} To account for multiple comparisons, we report 99% confidence intervals and used a two-tailed $\alpha = 0.01$ to establish the statistical significance of tests for all analyses.

Among potentially overtreated individuals, we examined variables associated with treatment deintensification using means and standard deviations for continuous variables and frequencies with percentages for categorical variables. To test for differences between those who did and did not receive deintensification of treatment, we used χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. We then examined whether deintensification differed based on race/ethnicity, dual eligibility, older age, sex, rurality (urban/

rural), or multimorbidity, using multivariable logistic regression. Results are presented in both tabular and graphical form. The institutional review board of the Duke University Health System approved the study, and analyses were performed using SAS version 9.4 software (SAS Institute Inc., Cary, NC, USA).

RESULTS

We identified 78,972 older adults who had been diagnosed with diabetes and met the inclusion criteria (Appendix figure 1), of whom 10.8% ($n = 8560$) were potentially overtreated and 6.9% ($n = 5487$) were potentially undertreated for diabetes. Overtreatment was more prevalent than undertreatment in all subgroups examined except those with one or fewer comorbidity (Table 2). Rates of overtreatment were highest among those who were dual eligible for Medicaid (13.4%) and those over 75 years of age (12.1%), and ranged from 11.1% for non-Hispanic blacks to 9.6% for those of “other” race/ethnicity.

After adjustment, overtreatment remained more likely for those dually enrolled in Medicaid and those over 75 years of age, while overtreatment was less likely for Hispanic beneficiaries and those in urban areas (Table 2). The variables associated with overtreatment of diabetes differed considerably from those associated with undertreatment (Table 2).

Table 1 Characteristics of Medicare Patients with Diabetes Who Are Potentially Overtreated Compared to Others with Diabetes ($n = 78,792$)*

	Potentially overtreated (HgbA1c $\leq 6.5\%$) ($n = 8560$)	Potentially undertreated (HgbA1c $> 9.0\%$) ($n = 5487$)	Appropriately treated (HgbA1c 6.5–9.0%) ($n = 64,925$)
Age, mean (SD)	75.9 (7.0)	73.4 (6.1)	75.2 (6.7)
Age group			
65–70	2321 (27.1%)	2193 (40.0%)	19,394 (29.9%)
71–75	2186 (25.5%)	1625 (29.6%)	17,786 (27.4%)
76+	4053 (47.3%)	1669 (30.4%)	27,745 (42.7%)
Gender			
Female	5036 (58.8%)	3040 (55.4%)	38,175 (58.8%)
Male	3524 (41.2%)	2447 (44.6%)	26,750 (41.2%)
Race/ethnicity			
Hispanic	449 (5.2%)	428 (7.8%)	3329 (5.1%)
Non-Hispanic white	6492 (75.8%)	3579 (65.2%)	49,792 (76.7%)
Non-Hispanic black	1368 (16.0%)	1311 (23.9%)	9602 (14.8%)
Other	251 (2.9%)	169 (3.1%)	2202 (3.4%)
Medicaid-enrolled			
No	6708 (78.4%)	4147 (75.6%)	54,278 (83.6%)
Yes	1852 (21.6%)	1340 (24.4%)	10,647 (16.4%)
Geographic location			
Rural	2172 (25.4%)	1506 (27.4%)	15,526 (23.9%)
Urban	6388 (74.6%)	3981 (72.6%)	49,399 (76.1%)
Chronic conditions			
0–1	482 (5.6%)	501 (9.1%)	3866 (6.0%)
2–3	2460 (28.7%)	1609 (29.3%)	20,446 (31.5%)
4–5	2888 (33.7%)	1731 (31.5%)	21,881 (33.7%)
6+	2730 (31.9%)	1646 (30.0%)	18,732 (28.9%)
Outpatient visits in 2010 (mean, SD)	12.0 (9.0)	11.1 (8.7)	11.7 (8.9)
Baseline HbA1c (mean, SD)	6.1 (0.3)	10.4 (1.3)	6.9 (0.8)
Diabetes mellitus treatment			
Insulin	748 (8.7%)	1326 (24.2%)	4716 (7.3%)
Sulfonylurea	5042 (58.9%)	1926 (35.1%)	14,581 (22.5%)
Metformin	3292 (38.5%)	1660 (30.3%)	21,556 (33.2%)
Thiazolidinediones	2124 (24.8%)	360 (6.6%)	4052 (6.2%)
Other oral medications	1489 (17.4%)	536 (9.8%)	4340 (6.7%)
No pharmacotherapy	0 (0.0%)	1790 (32.6%)	30,914 (47.6%)

*All between-column comparisons, statistically significant at $p < 0.001$

Table 2 Variables Associated with Potential Overtreatment Compared to Undertreatment of Diabetes ($n = 78,792$)*

	Potentially overtreated		Potentially undertreated	
	Unadjusted %	Adjusted* OR (99% CI)	Unadjusted %	Adjusted* OR (99% CI)
Age group				
65–70	9.7	Reference	9.2	Reference
71–75	10.1	1.02 (0.94, 1.11)	7.5	0.81 (0.74, 0.88)
76+	12.1	1.19 (1.10, 1.28)	5.0	0.53 (0.49, 0.58)
Female	10.9	Reference	6.6	Reference
Male	10.8	1.06 (1.00, 1.13)	7.5	1.21 (1.12, 1.30)
Non-Hispanic white	10.8	Reference	6.0	Reference
Hispanic	10.7	0.87 (0.75, 1.00)	10.2	1.54 (1.32, 1.79)
Non-Hispanic black	11.1	1.02 (0.93, 1.11)	10.7	1.74 (1.58, 1.91)
Other race/ethnicity	9.6	0.81 (0.68, 0.96)	6.4	0.93 (0.75, 1.16)
Not Medicaid-enrolled	10.3	Reference	6.4	Reference
Medicaid-enrolled	13.4	1.43 (1.32, 1.55)	9.7	1.46 (1.33, 1.60)
Rural	11.3	Reference	7.8	Reference
Urban	10.7	0.94 (0.88, 1.01)	6.7	0.86 (0.79, 0.94)
Chronic Conditions				
0–1	9.9	Reference	10.3	Reference
2–3	10.0	0.96 (0.84, 1.10)	6.6	0.63 (0.55, 0.72)
4–5	10.9	1.03 (0.90, 1.18)	6.5	0.67 (0.58, 0.78)
6+	11.8	1.08 (0.94, 1.25)	7.1	0.80 (0.69, 0.94)
Outpatient visits in 2010 (increments of 5)	–	1.00 (0.98, 1.02)	–	0.97 (0.95, 1.00)

*Multinomial logistic regression with the reference outcome “appropriately treated diabetes” that adjusted for all variables shown in table

Of the 8560 older adults who were potentially overtreated (Table 3), 13.9% ($n = 1187$ of 8560) received treatment deintensification within 180 days following the index HbA1c. Rates of deintensification were highest for adults aged 65–70 (15.1%) and Hispanic patients (Table 4). Treatment deintensification increased with the number of chronic conditions.

In adjusted analysis, deintensification of diabetes therapy was more likely for those with 6 or more chronic conditions (adj. OR = 1.57, 99% confidence interval [CI]: 1.13–2.16), in urban areas (adj. OR = 1.17, 99% CI: 1.01–1.36) or with more outpatient visits (adj. OR = 1.04, 99% CI: 1.00–1.08). Deintensification was less likely for those over 75 years of age (adj. OR = 0.78, 99% CI: 0.67–0.90).

DISCUSSION

We found that overtreatment was more common than undertreatment of diabetes for Medicare beneficiaries in 2011. Among those overtreated, only about 14% received treatment deintensification, which is lower than rates of deintensification reported in prior studies of veterans in 2012¹⁹ and privately insured individuals in 2013.²¹ As the AGS began recommending less aggressive treatment of diabetes in 2013, current rates of overtreatment may be somewhat lower than what we report here.

We found that overtreatment of diabetes for Medicare patients was associated with age over 75 and Hispanic race/ethnicity, which is consistent with prior studies of overtreatment of diabetes.^{20, 21} Interestingly, older adults dually enrolled in Medicaid and Medicare were both more likely to be overtreated and more likely to be undertreated for diabetes than individuals without dual enrollment, possibly because this

is a very heterogeneous group with highly variable diabetes control and a greater diversity of comorbid conditions. Future work is needed to determine whether there are distinct subgroups of dual-eligible individuals with diabetes who might benefit from specific approaches to diabetes management.

Table 3 Deintensification of Medication Regimens for Potentially Overtreated Medicare Beneficiaries with Diabetes, by Demographic Characteristics

	Deintensified ($N = 1187$)	Not deintensified ($N = 7373$)	P- value
Age, mean (SD)	75.6 (7.0)	76.0 (7.0)	0.11
Age group			0.079
65–70	351 (29.6%)	1970 (26.7%)	
71–75	305 (25.7%)	1881 (25.5%)	
76+	531 (44.7%)	3522 (47.8%)	
Gender			0.63
Female	706 (59.5%)	4330 (58.7%)	
Male	481 (40.5%)	3043 (41.3%)	
Ethnicity			0.46
Hispanic	68 (5.7%)	381 (5.2%)	
Non-Hispanic white	913 (76.9%)	5579 (75.7%)	
Non-Hispanic black	174 (14.7%)	1194 (16.2%)	
Other	32 (2.7%)	219 (3.0%)	
Medicaid-enrolled			0.23
No	946 (79.7%)	5762 (78.2%)	
Yes	241 (20.3%)	1611 (21.8%)	
Geographic location			0.006
Rural	263 (22.2%)	1909 (25.9%)	
Urban	924 (77.8%)	5464 (74.1%)	
Chronic conditions			<.0001
0–1	52 (4.4%)	430 (5.8%)	
2–3	300 (25.3%)	2160 (29.3%)	
4–5	377 (31.8%)	2511 (34.1%)	
6+	458 (38.6%)	2272 (30.8%)	
Outpatient visits in 2010, mean (SD)	13.2 (9.4)	11.8 (8.9)	<.0001

Table 4 Logistic Regression of Deintensification of Diabetes Medications among Potentially Overtreated Older Adults

	Unadjusted %	Adjusted OR (99% CI)	P- value
Age group			
65–70	15.1	Reference	
71–75	14.0	0.87 (0.74, 1.03)	0.109
76+	13.1	0.78 (0.67, 0.90)	0.001
Female	14.0	Reference	
Male	13.6	0.93 (0.82, 1.08)	0.301
Non-Hispanic white	14.1	Reference	
Hispanic	15.1	1.05 (0.79, 1.39)	0.738
Non-Hispanic black	12.7	0.93 (0.78, 1.11)	0.425
Other race/ethnicity	12.7	0.91 (0.62, 1.34)	0.649
Not Medicaid-enrolled	14.1	Reference	
Medicaid-enrolled	13.0	0.89 (0.75, 1.05)	0.159
Rural	12.1	Reference	
Urban	14.5	1.17 (1.01, 1.36)	0.039
Chronic conditions			
0–1	10.8	Reference	
2–3	12.2	1.13 (0.82, 1.54)	0.458
4–5	13.1	1.20 (0.87, 1.63)	0.263
6+	16.8	1.57 (1.13, 2.16)	0.007
Outpatient visits in 2010 (increments of 5)	—	1.04 (1.00, 1.08)	0.048

We found deintensification of diabetes therapy to be more common for Medicare beneficiaries with six or more chronic conditions, more outpatient visits, or living in urban areas, and less likely for those over age 75. It is troubling that the oldest Medicare beneficiaries were more likely to be overtreated and less likely to have their medication regimens deintensified, because these older adults are least likely to benefit from tight glycemic control and most likely to be harmed. It is encouraging that those with multiple chronic conditions were more likely to receive deintensification, because they often have complex medication regimens, and prior studies have shown that risk for hypoglycemia increases with age, comorbidity burden, and polypharmacy.¹³

Despite the relative lack of patient characteristics associated with overtreatment and deintensification, we found substantial disparities in potential undertreatment of diabetes among Medicare beneficiaries, consistent with previous findings.^{24–28} These disparities have long plagued American healthcare. This is the first study to examine overtreatment and deintensification in a Medicare population and to examine rates of potential overtreatment and undertreatment in the same cohort. Nonetheless, several limitations must be acknowledged. First, we were unable to separately examine age-eligible and disability-eligible older adults, since all adults were 65 years of age or older. Second, we stratified older adults by demographic characteristics and comorbidity burden, but did not stratify them by health status defined by activities of daily living¹⁸ or by life expectancy¹⁹ as in prior work. Similarly, we did not examine subgroup differences via interaction terms, which would merit consideration in future work with larger samples. Third, the reasons for a lack of deintensification among those potentially overtreated for diabetes are unknown. It is possible that clinicians did not recommend a change in regimen, and it is also possible that deintensification was recommended but patients preferred to remain on their existing regimen. Fourth, glycemic control

was based upon a single cross-sectional measurement in 2011, so it is unknown whether older adults' control was stable or changing prior to the index value we studied. Fifth, the results may not generalize to older adults outside of these 10 eastern states or those enrolled in Medicare Advantage. Finally, we were not able to examine whether potential overtreatment or lack of deintensification was associated with clinically relevant adverse outcomes.

Optimizing glucose control is clinically difficult, but it is a public health imperative. Major trials have shown that aggressive diabetes control has both significant benefits for younger, healthy patients and substantial risks for older patients and those with comorbidities.^{8–11} Recent clinical practice guidelines acknowledge that these risks must be addressed for older adults in particular.^{5, 7, 37} However, this guidance was not universal in 2011. Therefore, our findings on the prevalence of overtreatment of Medicare beneficiaries in 2011 may in part reflect the fact that clinicians had not adapted to recent clinical guidelines for diabetes management that relaxed glycemic control targets for older adults with multiple chronic conditions, limited life expectancy, diabetic complications, or functional impairment.⁵ Future studies should examine whether rates of overtreatment and deintensification of diabetes regimens have changed over the last 6 years, and whether the disparities observed here have narrowed.

The management of diabetes in the presence of comorbidities must also be carefully considered, because comorbidity may alter medication choices. Guidelines from the American Diabetes Association have long recommended less intensive treatment for people with “important comorbidities,” and modeling studies have long shown that factors in addition to HbA1c should influence the overall net benefit of intensive treatment.³⁸ However, this study and other work in different settings and countries has shown that comorbidity has a minimal impact on diabetes treatment intensity as measured by the A1c achieved. Additional work is needed to understand whether deintensification of diabetic therapy affects older adults differently depending on their number of comorbid conditions, because so little is yet known in this emerging area of research and clinical practice.

For decades, diabetes guidelines and performance measures have focused only on reducing the undertreatment of diabetes. Even now, while guidelines mention more relaxed HbA1c targets for appropriate patients, there are no algorithms for deintensifying treatments. The focus on undertreatment has resulted in dramatic improvements in glycemic control, on average, but has apparently also encouraged overtreatment. In the current era, effective treatment of diabetes requires a major shift in approach toward greater personalization of treatment based on individual potential risk and benefit. Our study points the way for identifying not only those patients who may benefit from more intensive treatment, but also those who may need deintensification. By focusing at both the overtreatment and undertreatment ends of the diabetes quality spectrum, we can best begin to truly improve the quality of diabetes care, ensuring that patients get needed care while avoiding unnecessary potential harm.

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Compliance with Ethical Standards:

Conflict of Interest: Dr. Maciejewski has received institutional grants from the VA HSR&D, the Agency for Healthcare Research and Quality, the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Cancer Institute, and an institutional contract from the Centers for Medicare & Medicaid Services; and reports ownership of Amgen stock due to his spouse's employment. Dr. Maciejewski received honoraria for speaking at a workshop held at the University of Alabama-Birmingham. Dr. Sussman has received research support from VA HSR&D in the form of a career development award. Dr. Curtis has received research support from the Agency for Healthcare Research and Quality, the Patient-Centered Outcomes Research Institute, Boston Scientific, Bristol-Myers Squibb, GE Healthcare, GlaxoSmithKline, Johnson & Johnson, Medtronic, Merck, and Novartis. Dr. Kerr has received research support from VA HSR&D to examine deintensification of medical services. All other authors declare that they have no conflict of interest.

APPENDIX

Figure 1 CONSORT figure for development of study cohort.

Table 5 Therapeutic Classes of Diabetes Medication Examined

Drug class	Examples of medications included
Insulin	<ul style="list-style-type: none"> • Insulin glargine • Insulin aspart • Insulin (human)
Biguanides	<ul style="list-style-type: none"> • Metformin
Sulfonylureas	<ul style="list-style-type: none"> • Chlorpropamide • Glimepiride • Glipizide • Glyburide • Tolazamide • Tolbutamide
Thiazolidinediones	<ul style="list-style-type: none"> • Rosiglitazone • Pioglitazone
Meglitinides	<ul style="list-style-type: none"> • Nateglinide • Repaglinide
GLP-1 agonists	<ul style="list-style-type: none"> • Exenatide • Liraglutide
Amylin analogs	<ul style="list-style-type: none"> • Pramlintide
DPP-4 inhibitors	<ul style="list-style-type: none"> • Sitagliptin • Saxagliptin • Linagliptin
Alpha-glycosidase inhibitors	<ul style="list-style-type: none"> • Acarbose • Miglitol
Combination oral antidiabetic agents	<ul style="list-style-type: none"> • Metformin and sulfonamides • Metformin and pioglitazone • Metformin and sitagliptin

Table 6 Eighteen Chronic Conditions Constructed from Chronic Conditions Warehouse Data

Acquired hypothyroidism	Atrial fibrillation
Anemia	Asthma
Benign prostatic hyperplasia	Cancer (as a combination of indicators for breast, colorectal, prostate, lung, and endometrial cancer)
Chronic kidney disease	Chronic obstructive pulmonary disease (COPD)
Alzheimer's disease, dementia, and related disorders (ADRD)	Depression
Diabetes mellitus	Heart failure
Hyperlipidemia	Hypertension
Ischemic heart disease	Osteoporosis
Rheumatoid arthritis/osteoarthritis	Stroke

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