Published in final edited form as:
J Am Pharm Assoc (2003). 2014 ; 54(4): 374–382. doi:10.1331/JAPhA.2014.13195.

Prescription Medication Burden in Patients with Newly-Diagnosed Diabetes: A SUrveillance, PREvention, and ManagEment of Diabetes Mellitus (SUPREME-DM) Study

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Abstract

Objective—To understand the burden of medication use for newly-diagnosed diabetes patients both before and after diabetes diagnosis, and to identify subpopulations of newly-diagnosed diabetes patients who face a relatively high drug burden.

Design—Retrospective cohort.

Setting—Eleven U.S. integrated health systems.

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The authors have no conflicts of interest or competing financial interests to report.

Presented previously at the EDM Forum Stakeholder Symposium, Baltimore, Maryland, June 22, 2013; and the European Association for the Study of Diabetes Annual Meeting, Barcelona, Spain, September 24, 2013.

Patients—196,654 insured adults aged ≥20 diagnosed with newly-diagnosed diabetes from 1/1/2005 – 12/31/2009.

Main Outcome Measure—Number of unique therapeutic classes of drugs dispensed in the 12 months prior to, and 12 months post, the diagnosis of diabetes in 5 categories: overall, antihypertensive, antihyperlipidemic, mental health, and antihyperglycemic (post-period only).

Results—The mean number of drug classes used by newly-diagnosed diabetes patients is high before diagnosis (5.0), and increases significantly afterwards (6.6, $p<.001$). Eighty-one percent of this increase is due to antihyperglycemic initiation and increased use of medications to control hypertension and lipid levels. Multivariate analyses showed that overall drug burden after diabetes diagnosis was higher in female, older, white, and obese patients, as well as among those with higher A1cs and comorbidity levels ($p<.001$ for all comparisons). The overall number of drug classes used by newly-diagnosed diabetes patients after diagnosis decreased slightly between 2005 and 2009 ($p<.001$).

Conclusions—Diabetes patients face significant drug burden to control diabetes and other comorbidities, and our data indicate an increased focus on cardiovascular disease risk factor control after diabetes diagnosis. However, total drug burden may be slightly decreasing over time. This information can be valuable to pharmacists working with newly-diagnosed diabetes patients to address their increasing drug regimen complexity.

Keywords

diabetes; medication burden; surveillance

NTRODUCTION

Over 25 million Americans have diabetes mellitus (1), a disease associated with significant medical and financial burden to individuals and to society at large (1–4). The use of prescription drugs to control blood glucose and treat comorbid conditions in individuals with diabetes is a major component of diabetes care, and may contribute substantially to the costs for this disease (5). While a number of studies have examined the use of antihyperglycemic medications in diabetes patients (6–8), very few also examine drug burden overall, or assess the use of specific therapeutic categories used to treat hypertension, depression, or other common co-occurring conditions (9–10). Most studies of drug burden in diabetes patients are focused specifically on the elderly (8–11), examine non-U.S. populations (8–10), or rely on self-reported data (5,8,12). There is very little data based on electronic health record (EHR) information that quantifies overall drug burden in a diverse, representative sample of diabetes patients nationally, or examines whether drug burden is changing over time. Additionally, almost no studies examine the patient characteristics that predict prescription drug burden across a variety of drug use categories. Understanding the burden of prescription drug use in newly-diagnosed diabetes patients can help us inform clinical and pharmaceutical practice for this large, growing, and vulnerable population (4).

The purpose of this study is to use longitudinal EHR data to examine prescription drug burden immediately before and after the diagnosis of diabetes; to determine patient-level

correlates of drug burden; and to examine if drug burden is changing over time within a nationally-based sample of newly-diagnosed diabetes patients.

METHODS

Study Setting and Population

This retrospective cohort was drawn from the membership of The SUrveillance PREvention and ManagEment of Diabetes Mellitus (SUPREME-DM) study health systems between January 1, 2005 and December 31, 2009. SUPREME-DM combines patient demographic, health care utilization, diagnosis, procedure, medication, and laboratory data from EHR and other clinical and administrative databases of 11 integrated U.S. health care systems. Because the SUPREME-DM distributed database (known as the DataLink) represents a defined population with of over one million patients with diabetes, it provides an exceptionally robust, geographically distributed research resource (13). SUPREME-DM includes HealthPartners (Minnesota), Group Health (Washington), Henry Ford Health System (Michigan), Marshfield Clinic (Wisconsin), Geisinger Health System (Pennsylvania), and Kaiser Permanente regions in Colorado (KPCO), Northern California (KPNC), Southern California (KPSC), Hawaii (KPHI), Georgia (KPGA), and Northwest (Oregon and Washington, KPNW). Members in these health plans receive their insurance through group plans, self-pay, Medicare, and Medicaid.

For the current study, patients were identified using the SUPREME-DM DataLink, and included if they were age 20 or older and met either diagnosis or laboratory criteria for new-onset diabetes mellitus. The diagnosis was established by: at least one inpatient or two outpatient diagnoses of diabetes (ICD-9-CM 250.xx, 357.2, 366.41, 362.01–362.07) on separate dates no more than two years apart; or fasting plasma glucose ≥ 126 mg/dl, random plasma glucose ≥ 200 mg/dl, HbA1c ≥ 6.5%, or 2-hour 75g oral glucose tolerance test (OGTT) ≥ 200 mg/dl not obtained during pregnancy. With the exception of the OGTT, at least two abnormal ambulatory tests were required. Patients with an antihyperglycemic dispensed in the two years prior, or who had any diagnosis or laboratory values indicating diabetes in the two years prior, were excluded from this incident cohort. Patients were required to have health plan membership and pharmacy benefits for at least two years prior to the diagnosis of diabetes, and one year post-diagnosis, in order to ensure that lapses in insurance coverage did not impact our calculation of medication burden.

Calculating Medication Burden

We used number of unique therapeutic drug classes of medications dispensed as our measure of medication burden; this serves as a conservative estimate of drug burden consistent with other diabetes-specific studies in this area (6), and avoids the counting of switching to another medication within a therapeutic class as additional medication burden. Prescription dispensings of drug classes were categorized using the American Hospital Formulary Services (AHFS) classification system (14). We defined unique drug classes using the first 6 digits of the AHFS Classification Code. We excluded drug products not intended to be used for chronic conditions, specifically: antihistamine drugs, anti-infective agents, diagnostic agents, disinfectants, local anesthetics, devices, pharmaceutical aides,

serums, toxoids, and vaccines (corresponding to AHFS Class Numbers 4:00, 8:00, 36:00, 38:00, 72:00, 80:00, 94:00, and 96:00). We then calculated the overall unique number of drug classes dispensed in the 12 months pre- and 12 months post-diabetes diagnosis, and also calculated the unique number of dispensed therapeutic classes of antihypertensives; antihyperlipidemics; and mental health medications such as antidepressants and anti-anxiety medications. The number of therapeutic subclasses within the antihyperglycemics class was calculated for the 12 month period post diabetes diagnosis.

Statistical Analysis

A Wilcoxon signed-rank test was used to examine the differences in the number of drug classes in the pre- and post-12 month periods. Multivariate nonlinear regression models with Poisson distribution were used to examine the relationship of the number of unique therapeutic classes dispensed in the 12 months post-diabetes diagnosis with baseline patient clinical and demographic characteristics. For the models predicting overall drug burden and mental health drug burden, multivariate nonlinear regression models with negative binomial distribution were used to address overdispersion in the dependent variables (15). Models adjusted for age; gender; race/ethnicity; presence of key comorbidities (chronic kidney disease stage 3 or 4, hyperlipidemia, depression, hypertension, end-stage renal disease); A1c; body mass index (BMI) categorized as ‘underweight’ (<18.5), ‘normal’ (18.5–24.9), ‘overweight’ (>24.9–29.9) ‘obese level 1’ (>29.9–34.5), ‘obese level 2’ (>34.5–39.9), or ‘obese level 3’ (>39.9), and year of the new diabetes diagnosis. Site was included as a fixed effect in all analyses. Separate categories were created for missing covariates, race/ethnicity, A1c, and BMI, and were included in the multivariate regressions. Adjusted rate ratios (i.e. ratio of number of drug classes per year) were calculated by exponentiating the coefficients from multivariate models.

All data analyses were performed with STATA version 12. This study was approved by the KPCO Institutional Review Board (IRB) and each participating site either ceded oversight to the KPCO IRB or received approval from their local site IRB.

RESULTS

We identified 196,654 patients with newly-diagnosed diabetes between 2005 and 2009 (Table 1). The mean patient age was 58.6 (SD=13.3), 47.6% were female, and 47.1% were white.

The mean number of therapeutic drug classes dispensed to newly-diagnosed diabetes patients in the 12 months prior to the diagnosis of diabetes was 5.0; this increased to 6.6 therapeutic classes in the 12 months post-diabetes diagnosis ($p<.001$) (Table 2). In the twelve months following diagnosis of diabetes, a mean of 0.60 antihyperglycemic therapeutic classes were dispensed to patients. Across the cohort, 54.9% used no antihyperglycemics, 31.9% used one antihyperglycemic, 11.5% used two antihyperglycemics, and 1.7% used three or more antihyperglycemics (data not shown). Antihypertensive use increased from 1.24 to 1.54 therapeutic classes between the pre- and post-period; antihyperlipidemia drug use increased from 0.39 to 0.75 therapeutic classes on average ($p<.001$ for all pre-post comparisons). The mean number of mental health drug

therapeutic classes increased more modestly, from 0.35 classes in the pre-diabetes period to 0.39 in the post-period. Fifty-eight percent of the mental health drugs dispensed in the post-period were antidepressants (data not shown.)

Overall medication burden in the 12 months after the diagnosis of diabetes was significantly higher in women (RR=1.13 compared to men, p<.001), obese patients (RR=1.12 in patients with BMI 40 and above vs. normal weight patients, p<.001), and those with A1c >=7.5% compared with A1c<6.5% (p<.001) (Table 3a). Non-hispanic White patients had higher drug burden than patients of most other race/ethnicities (p<.001), with the overall drug use of Non-hispanic White and Black patients being similar (p<.0.2). Drug burden was higher in patients ages 70–79 (RR=1.05, p<.001) and ages 80–89 (RR=1.07, p<.001) compared with patients ages 60–69.

A1c level at the time of diagnosis was the strongest predictor of the number of antihyperglycemic drug classes after diabetes diagnosis, with patients with an A1c >=9.0% having the highest use of anti-diabetes medications (RR=5.21 compared to patients with A1c<6.5%, p<.001) (Table 3b). Unlike with overall drug burden, antihyperglycemic drug burden increased slightly between 2005 and 2009 (p<.001). Predictors of antihypertensive and antihyperlipidemic burden were similar to those of overall drug burden (Table 3c); however, use of these drugs was lower in women than in men (p<.001). The use of mental health medications in the period post-diabetes diagnosis (Table 3c) was highest in patients with lower A1cs, and higher in women compared to men (RR=1.48, p<.001).

DISCUSSION

This study is one of the first to use EHR data to examine the overall use of prescription medications to treat diabetes and co-morbid conditions in a large national, longitudinal cohort of patients with newly-diagnosed diabetes. We found that the mean number of drug classes used by newly-diagnosed diabetes patients is already high before diagnosis (5.0 therapeutic classes), and increases substantially afterwards (to 6.6 therapeutic classes). A total of 1.25 mean therapeutic classes, or 81% of the increase, was due to anti-hyperglycemic initiation and new antihypertensive and antihyperlipidemic drug use. This increased use of cardiovascular disease (CVD) risk factor medications suggests that the diagnosis of diabetes was accompanied by increased attention to CVD risk factor control, which would be an appropriate and expected clinical response to the onset of this disease. Considering the significantly increased risk of CVD in patients with diabetes, and the effectiveness of CVD risk factor control medications to reduce this risk (16–23), our findings reflect a strong and appropriate clinical response to encourage CVD prevention in these high risk patients.

While the use of medications for CVD risk factor management increased significantly after diabetes diagnosis, the use of medications for mental health conditions increased only marginally after diabetes diagnosis. Approximately 60% of the mental health medications dispensed in this study were for antidepressants, and many studies have found that depression is correlated with diabetes (21–23) and with poor diabetes outcomes (24–30). While it was beyond the scope of our study to assess whether patients with depression or

other mental illnesses were receiving appropriate treatment either before or after diabetes onset, our results suggest the diagnosis of diabetes may present an opportunity to diagnose and treat co-occurring depression and potentially other mental health conditions as well.

The use of medications to help patients manage their diabetes and comorbidities is a key component of care for this disease. However, it is important to note that polypharmacy in patients with diabetes may be associated with an increase in both contraindicated medication use and the occurrence of potential side effects. (9, 31–32). A pharmacist's priority is helping patients make the best use of their medicine. Our finding that newly-diagnosed diabetes patients are managing a high and increasing average number of medication classes in the period following diagnosis suggests that pharmacists, physicians, nurses, and other clinicians, as well as health care systems, should be sensitive to the impact of this potential burden on patients. Responses should include increased monitoring of patients with high drug burden, and counseling from pharmacists on how to deal with additional diabetes and CVD regimen complexity (33–34). When a patient presents with a first-ever prescription for an antihyperglycemic medication, this prescription can serve as an alert for pharmacists and other members of the care team to assess overall medication burden, and to initiate medication regimen review and counseling.

Our study found that while prescription drug burden was high in newly-diagnosed diabetes patients for relevant comorbidities, it appeared to be slightly decreasing in the period between 2005 and 2009 even as antihyperglycemic use was increasing. There has been almost no surveillance over time of trends in overall levels of drug burden in diabetes patients, and the research that has been published has focused on self-reported insulin use (12). One recent study of temporal trends in diabetes medication initiation was limited to patients who received an oral antihyperglycemic and analyzed just 3 years of data (6). Our study uses EHR data across a national group of health plans to demonstrate that the overall use of medications among patients with newly-diagnosed diabetes is holding steady, and perhaps slightly decreasing, over time. This may be related to increasing screening for diabetes, resulting in earlier diagnosis and less need for aggressive initial therapy due to lower baseline glucose levels. It may also be due to clinician attempts to be sensitive to the risks of overall drug burden, and efforts to appropriately streamline drug regimens. This information may be useful to pharmacists and policy-makers seeking to understand care patterns and drug regimens for diabetes patients over time.

Our study is one of the first to look at the association of overall drug burden with patient characteristics in a wide cross-section of adult diabetes patients. Our study found that women and older patients with new-onset diabetes have a higher level of overall drug burden compared with men and younger patients respectively. As in prior studies examining potential disparities in the use of prescription medications in diabetes patients (35–36), our study found small but consistent differences in the overall use of prescription medications across racial/ethnic categories. We found lower rates of overall prescription drug burden and mental health drug use between Non-hispanic Whites and Blacks and Hispanics, but higher levels of use of diabetes and CVD risk factor medications in the 12 months post-diabetes diagnosis in Blacks and Hispanics compared to Non-Hispanic Whites. The higher use of CVD risk factor medications may reflect acknowledgement of higher risk of CVD and its

complications in Blacks and Hispanics in particular (37–38), while signaling potential continued disparities in prescription drug access even within insured populations with similar access to care.

Limitations to this study include the inability to distinguish between clinicians not prescribing medication versus patients not filling an ordered prescription, since the SUPREME-DM sites did not incorporate prescription orders into a standardized format within their EHRs. It is possible that more medications were ordered for patients in the periods pre- and post-diagnosis of diabetes than are reflected in the prescription dispensing data. However, previous work suggests that the no-fill rate for diabetes patients is fairly low in the health systems studied (39–40). We were not able to distinguish between Type 1 and Type 2 diabetes within the SUPREME-DM population. In addition, the findings of a study of the insured population in the SUPREME-DM systems may not generalize to the newly identified diabetes population in all healthcare systems or to the uninsured, although members of these health plans are diverse and receive their insurance through Medicare and Medicaid as well as through commercial plans. However, as the SUPREME-DM systems exemplify care models recommended by recent legislation such as meaningful use of EHR data and integrated care, our results likely provide a timely surveillance benchmark for the use of prescription drug therapies in newly-diagnosed diabetes patients in the U.S. (41–43). Finally, we chose to measure medication burden as the number of unique therapeutic classes dispensed to patients, as opposed to the unique number of medications dispensed. While our use of unique number of therapeutic classes served as a conservative estimate of drug burden consistent with prior studies in this area, the use of individual medications dispensed is another accepted approach that may have slightly increased the level of drug burden observed in our study.

Conclusions

Diabetes patients face significant drug burden to control diabetes and other comorbidities. Our data suggests a reassuring and appropriate increased focus on CVD risk factor control by pharmacists, other clinicians, and patients after diabetes diagnosis within this high risk population. However, total drug burden may be slightly decreasing over time. This information may be useful to pharmacists, physicians, nurses, and other clinicians, as well as policy-makers, seeking to understand care patterns and drug regimens for diabetes patients over time. This information can also be a valuable tool for guiding pharmacy practice for diabetes patients in the era of health care reform.

Acknowledgments

This project was supported by grant number R01HS019859 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality. AHRQ had no role in the design, conduct, or reporting of this work. Dr. Schmittdiel received additional support from the NIDDK-funded Health Delivery Systems Center for Diabetes Translational Research (1P30 DK92924)

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Table 1

Newly-Diagnosed Diabetes Patient Characteristics

	N	%
No. of Patients	196,654	100
Year of Diabetes Incidence (Cohort Entry)		
2005	43,024	21.9
2006	40,567	20.6
2007	39,838	20.3
2008	36,587	18.6
2009	36,638	18.6
Female	93,539	47.6
Mean Age (St dev)	58.61 (13.30)	
Age Categories		
20–29	2,351	1.2
30–39	12,045	6.1
40–49	35,051	17.8
50–59	57,328	29.1
60–69	46,886	23.8
70–79	29,764	15.1
80–89	11,975	6.1
90+	1,254	0.6
Race/Ethnicity		
White	92,657	47.1
Black	20,332	10.3
Native Hawaiian/Pacific Islander	1,415	0.7
American Indian/Alaska Native	530	0.3
Multiple Race	3,588	1.8
Hispanic	37,076	18.9
Asian	22,046	11.2
Unknown	19,010	9.7
Hypertension Diagnosis in 2 yrs Prior to Cohort Entry	101,468	51.6
Hyperlipidemia Diagnosis in 2 yrs Prior to Cohort Entry	65,862	33.5
Depression Diagnosis in 2 yrs Prior to Cohort Entry	18,072	9.2
Renal Disease (Stage 3, 4) in 2 yrs Prior to Cohort Entry	6,096	3.1
End Stage Renal Disease in 2 yrs Prior to Cohort Entry	1,203	0.6
A1c Closest to Cohort Entry (2 year lookback)		
Missing	61,856	31.4
<6.5	44,155	22.5
6.5–6.9	33,310	16.9
7.0–7.4	16,549	8.4

	N	%
7.5–7.9	7,474	3.8
8.0–8.4	5,180	2.6
8.5–8.9	3,563	1.8
9.0+	24,567	12.5
Mean A1c (Closest to cohort entry, 2yr lookback) (Stdev)	7.49 (2.02)	
Mean BMI (Stdev)	32.69 (7.89)	

Table 2

Mean Number of Drug Classes in the Year Before and the Year After Diabetes **Diagnosis**

Variable	Year Before Diabetes Incidence Mean (StDev)	Year After Diabetes Incidence Mean (StDev)	Difference Mean (StDev)	Ho: Means are Equal P-Value
Number of Diabetes Drug Classes	n/a	0.60 (0.76)	**0.60 (0.76)**	n/a
Number of Antihypertensive Drug Classes	1.24 (1.28)	1.54 (1.28)	0.30 (0.87)	<.0001
Number of Lipid-lowering Drug Classes	0.39 (0.58)	0.74 (0.62)	0.35 (0.58)	<.0001
Number of Mental Health Drug Classes	0.35 (0.68)	0.39 (0.71)	0.04 (0.53)	<.0001
Overall Number of Drug Classes	4.98 (4.05)	6.63 (4.14)	1.65 (3.18)	<.0001

Table 3a

Estimated Rate Ratios of Overall Number of Drug Classes in the Year Following Diabetes **Diagnosis**

Independent Variables	RR	95% CI	*p*
Year of Cohort Entry (ref: 2005)			
2006	0.96	0.95–0.97	<.001
2007	0.92	0.91–0.92	<.001
2008	0.90	0.89–0.90	<.001
2009	0.89	0.88–0.90	<.001
Female	1.13	1.12–1.13	<.001
Age (ref: 60–69)			
20–29	0.78	0.76–0.80	<.001
30–39	0.81	0.80–0.82	<.001
40–49	0.88	0.87–0.88	<.001
50–59	0.94	0.94–0.95	<.001
70–79	1.05	1.04–1.06	<.001
80–89	1.07	1.06–1.08	<.001
90+	1.02	0.99–1.05	0.265
Race/Ethnicity (ref: White)			
Hispanic	0.91	0.90–0.92	<.001
Unknown	0.79	0.78–0.79	<.001
Black	0.99	0.99–1.00	0.203
Hawaiian/Pacific Islander	0.91	0.88–0.94	<.001
Asian	0.86	0.85–0.87	<.001
Native American	0.98	0.94–1.03	0.527
More than 1 Race	0.96	0.95–0.98	<.001
A1c Closest & Prior to Cohort Entry (ref: <6.5%)			
6.5–6.9%	0.94	0.93–0.94	<.001
7.0–7.4%	0.98	0.97–0.99	<.001
7.5–7.9%	1.03	1.02–1.05	<.001
8.0–8.4%	1.03	1.02–1.05	<.001
8.5–8.9%	1.05	1.03–1.08	<.001
>=9.0%	1.07	1.06–1.08	<.001
Missing	1.05	1.04–1.06	<.001
History of Depression	1.38	1.37–1.39	<.001
History of Hypertension	1.30	1.29–1.31	<.001
History of Hyperlipidemia	1.13	1.12–1.14	<.001
History of Chronic Renal Disease (Stage 3, 4)	1.25	1.23–1.26	<.001
History of End Stage Renal Disease	1.39	1.35–1.43	<.001
Body Mass Index (ref: Normal)			
Missing	0.94	0.93–0.95	<.001
Underweight (<**18.5**)	1.05	1.01–1.10	0.010
Overweight (>**24.9**–**29.9**)	0.99	0.98–0.99	0.035

Independent Variables	RR	95% CI	*p*
Obese Level 1(**>29.9**–**34.5**)	1.01	1.00–1.02	0.020
Obese Level 2 (**>34.5**–**39.9**)	1.05	1.04–1.06	<.001
Obese Level 3(**>39.9**)	1.12	1.11–1.14	<.001

Notes: (1) RR = Rate Ratio, CI = Confidence Interval, (2) model includes site fixed effects, (3) n=196,654

Table 3b

Estimated Rate Ratios of Number of **Diabetes Drug Classes in the Year Following Diabetes Diagnosis**

Independent Variables	RR	95% CI	*p*
Year of Cohort Entry (ref: 2005)			
2006	1.03	1.01–1.05	0.001
2007	1.03	1.01–1.05	0.010
2008	1.05	1.02–1.07	<.001
2009	1.07	1.05–1.09	<.001
Female	1.01	0.99–1.02	0.098
Age (ref: 60–69)			
20–29	1.39	1.33–1.45	<.001
30–39	1.31	1.27–1.34	<.001
40–49	1.25	1.22–1.27	<.001
50–59	1.17	1.15–1.18	<.001
70–79	0.78	0.76–0.80	<.001
80–89	0.59	0.57–0.62	<.001
90+	0.44	0.39–0.50	<.001
Race/Ethnicity (ref: White)			
Hispanic	1.04	1.02–1.05	<.001
Unknown	0.99	0.97–1.01	0.303
Black	1.07	1.05–1.09	<.001
Hawaiian/Pacific Islander	1.08	1.01–1.16	0.023
Asian	0.95	0.93–0.97	<.001
Native American	1.12	1.01–1.23	0.029
More than 1 Race	0.99	0.95–1.04	0.639
A1c Closest & Prior to Cohort Entry (ref: <6.5%)			
6.5–6.9%	1.21	1.18–1.25	<.001
7.0–7.4%	2.34	2.27–2.41	<.001
7.5–7.9%	3.28	3.18–3.39	<.001
8.0–8.4%	3.77	3.64–3.91	<.001
8.5–8.9%	4.15	4.00–4.31	<.001
>=9.0%	5.21	5.08–5.33	<.001
Missing	2.74	2.68–2.80	<.001
History of Depression	1.06	1.04–1.09	<.001
History of Hypertension	0.97	0.96–0.98	<.001
History of Hyperlipidemia	0.90	0.89–0.92	<.001
History of Chronic Renal Disease (Stage 3, 4)	0.82	0.79–0.87	<.001
History of End Stage Renal Disease	0.53	0.47–0.59	<.001
Body Mass Index (ref: Normal)			
Missing	0.94	0.92–0.97	<.001
Underweight (**<18.5**)	0.97	0.87–1.09	0.388
Overweight (**>24.9**–**29.9**)	1.01	0.98–1.03	0.572

Independent Variables	RR	95% CI	*p*
Obese Level 1(**>29.9**–**34.5**)	1.01	0.99–1.04	0.283
Obese Level 2(**>34.5**–**39.9**)	1.05	1.02–1.08	0.001
Obese Level 3(**>39.9**)	1.10	1.07–1.13	0.033

Notes: (1) RR = Rate Ratio, CI = Confidence Interval, (2) model includes site fixed effects, (3) n=196,654

Table 3c

Estimated Rate Ratios of **Number of Antihypertensive, Lipid-Lowering, and Mental Health Drug Classes in the Year Following Diabetes Diagnosis**

	Number of Antihypertensive Drug Classes			Number of Lipid-Lowering Drug Classes			Number of Mental Health Drug Classes		
Independent Variables	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
Year of Cohort Entry (ref: 2005)									
2006	0.95	0.94–0.96	<.001	1.03	1.01–1.05	0.001	0.96	0.93–0.98	<.001
2007	0.89	0.88–0.90	<.001	1.00	0.98–1.02	0.834	0.90	0.88–0.92	<.001
2008	0.86	0.85–0.88	<.001	0.97	0.95–0.98	<.001	0.85	0.83–0.87	<.001
2009	0.84	0.83–0.86	<.001	0.98	0.96–0.99	0.020	0.84	0.82–0.86	<.001
Female	0.96	0.95–0.97	<.001	0.95	0.94–0.96	<.001	1.48	1.46–1.51	<.001
Age (ref: 60–69)									
20–29	0.44	0.42–0.46	<.001	0.45	0.42–0.49	<.001	1.00	0.93–1.08	0.932
30–39	0.55	0.53–0.56	<.001	0.69	0.67–0.71	<.001	0.99	0.95–1.03	0.509
40–49	0.71	0.71–0.72	<.001	0.87	0.86–0.89	<.001	1.09	1.06–1.11	<.001
50–59	0.86	0.85–0.87	<.001	0.97	0.95–0.98	<.001	1.07	1.05–1.09	<.001
70–79	1.09	1.08–1.10	<.001	0.96	0.94–0.97	<.001	0.96	0.94–0.99	0.001
80–89	1.12	1.10–1.13	<.001	0.82	0.80–0.84	<.001	0.95	0.92–0.98	0.002
90+	1.06	1.02–1.10	0.007	0.63	0.59–0.69	<.001	0.94	0.86–1.02	0.110
Race/Ethnicity (ref: White)									
Hispanic	0.91	0.91–0.92	<.001	0.94	0.92–0.95	<.001	0.77	0.75–0.79	<.001
Unknown	0.91	0.89–0.92	<.001	0.93	0.91–0.95	<.001	0.65	0.63–0.67	<.001
Black	1.09	1.07–1.10	<.001	0.89	0.88–0.91	<.001	0.79	0.77–0.81	<.001
Hawaiian/Pacific Islander	0.99	0.94–1.04	0.613	1.03	0.97–1.10	0.307	0.47	0.42–0.54	<.001
Asian	0.98	0.97–0.99	0.008	0.98	0.97–1.00	0.101	0.52	0.51–0.54	<.001
Native American	0.93	0.86–1.00	0.050	1.02	0.93–1.13	0.644	0.98	0.86–1.12	0.765
More than 1 Race	1.03	1.00–1.06	0.042	0.99	0.95–1.03	0.557	0.77	0.72–0.81	<.001
A1c Closest & Prior to Cohort Entry (ref: <6.5%)									
6.5–6.9%	0.97	0.96–0.98	<.001	0.99	0.98–1.01	0.396	0.87	0.85–0.89	<.001
7.0–7.4%	1.00	0.99–1.02	0.738	1.09	1.07–1.11	<.001	0.84	0.81–0.86	<.001
7.5–7.9%	1.05	1.03–1.07	<.001	1.14	1.12–1.18	<.001	0.81	0.77–0.84	<.001

	Number of Antihypertensive Drug Classes			Number of Lipid-Lowering Drug Classes			Number of Mental Health Drug Classes		
Independent Variables	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
8.0–8.4%	1.06	1.04–1.09	<.001	1.16	1.12–1.20	<.001	0.81	0.77–0.85	<.001
8.5–8.9%	1.07	1.03–1.10	<.001	1.19	1.14–1.24	<.001	0.82	0.77–0.87	<.001
>=9.0%	1.06	1.05–1.08	<.001	1.25	1.23–1.28	<.001	0.70	0.68–0.72	<.001
Missing	1.01	0.99–1.02	0.187	1.02	1.01–1.04	0.004	0.95	0.94–0.97	<.001
History of Depression	0.97	0.96–0.99	<.001	0.98	0.96–0.99	0.038	3.59	3.53–3.65	<.001
History of Hypertension	2.19	2.17–2.20	<.001	1.00	0.99–1.02	0.561	1.20	1.18–1.22	<.001
History of Hyperlipidemia	1.02	1.01–1.03	<.001	1.71	1.69–1.73	<.001	1.09	1.08–1.11	<.001
History of Chronic Renal Disease (Stage 3, 4)	1.22	1.20–1.24	<.001	1.04	1.01–1.07	0.008	1.18	1.14–1.23	<.001
History of End Stage Renal Disease	1.14	1.10–1.19	<.001	0.81	0.76–0.87	<.001	1.36	1.27–1.46	<.001
Body Mass Index (ref: Normal)									
Missing	1.10	1.07–1.11	<.001	1.03	1.00–1.05	0.028	0.84	0.82–0.87	<.001
Underweight (**<18.5**)	0.91	0.85–0.96	0.001	0.74	0.67–0.82	<.001	1.11	1.01–1.23	0.032
Overweight (**>24.9–29.9**)	1.09	1.08–1.11	<.001	1.09	1.07–1.11	<.001	0.90	0.87–0.92	<.001
Obese Level1(**>29.9–34.5**)	1.16	1.14–1.18	<.001	1.11	1.08–1.13	<.001	0.89	0.86–0.91	<.001
Obese Level2(**>34.5–39.9**)	1.23	1.21–1.25	<.001	1.09	1.06–1.11	<.001	0.89	0.86–0.92	<.001
Obese Level3(**>39.9**)	1.35	1.32–1.37	<.001	1.03	1.00–1.06	0.028	0.92	0.89–0.95	<.001

Notes: (1) RR = Rate Ratio, CI = Confidence Interval, (2) model includes site fixed effects, (3) n=196,654

‡Includes patients with baseline data available for every listed characteristic and patients for whom data for one or more of the following baseline characteristics were missing and therefore imputed: Glycosylated hemoglobin, smoking, race, and/or serum creatinine