Achievement of Adequate Glycemic Control in Patients With Type 2 Diabetes and Comorbid Mental Health Conditions Treated in a Primary Care Setting

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ABSTRACT

Objective. This study investigated the association between the presence of a mental health condition (MHC) diagnosis and glycemic control in patients with type 2 diabetes in a primary care clinic network.

Methods. This retrospective cross-sectional study compared adequate glycemic control (A1C <8.0%) in patients with type 2 diabetes with and without any MHC, as well as by MHC subtypes of depression or anxiety, bipolar or schizophrenia disorders, and substance use disorder.

Results. Of 3,025 patients with type 2 diabetes, 721 (24%) had a diagnosis for one or more MHC. The majority (54.9%) were <65 years of age, female (54.9%), and Caucasian (74.5%). Mean A1C was statistically lower in the MHC cohort at 7.14 ± 1.66% compared to 7.38 ± 1.73% in the group without any MHC (P = 0.001). Furthermore, those with an MHC were more likely to attain adequate glycemic control than those without an MHC (odds ratio 1.27, 95% CI 1.01–1.59). Among patients with MHCs, similar rates of adequate glycemic control were seen between those with depression or anxiety and those with other MHCs. However, fewer patients with substance use disorder had adequate glycemic control compared to those without this condition (66.7 vs. 80.10%, P = 0.004).

Conclusion. Patients with diabetes and MHCs had slightly better glycemic control than those without any MHC. However, the presence of substance use disorder may present more barriers to adequate glycemic control. Additional research is needed to identify barriers unique to each MHC to optimize diabetes management in this population.

Type 2 diabetes is a chronic medical condition affecting ~29.3 million Americans (1). This is a progressive disease state requiring substantial self-management skills to maintain adequate glycemic control to avoid poor outcomes. Unfortunately, there are numerous barriers to successful self-management, including disease and treatment knowledge, access to care, attitudes, nonadherence, and comorbid conditions (2). Patients with mental health conditions (MHCs) are particularly vulnerable to these barriers and thus are likely to exhibit poor self-management (2).

MHCs encompass a spectrum of disorders, including bipolar disorder, schizophrenia, psychosis, depression, anxiety, and substance use disorder, which are not always mutually exclusive. A subcategory of MHCs, referred to as "serious mental illness," is also distinguished from the overall class of MHCs and includes mental, behavioral, or emotional disorders that lead to functional impairment that seriously interferes with or limits major life activities (3). Although

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there is no consensus about which mental illnesses are considered serious and that determination differs across studies, this category generally includes at least schizophrenia, psychosis, and bipolar disease, with other diagnoses included based on the specific population evaluated (4–7).

Data regarding the effect of MHCs on diabetes control outcomes are difficult to assess and compare, in part because of the complexity of diagnoses and classifications. Although limited, previous research (4,8) has shown that patients with serious mental illness are at a higher risk for premature mortality than the general population. For example, patients with schizophrenia are 3.6 times more likely to suffer premature death from cardiovascular complications and 4.2 times more likely to suffer premature death from diabetes complications than the general population (9). Premature mortality in this population has been attributed to the prevalence of nonadherence, economic disadvantage, poor glycemic control, smoking, obesity, and limited physical activity (9,10). Additionally, patients with serious mental illness are often prescribed atypical antipsychotic medications, which through adverse metabolic effects further increase their risk for poor cardiovascular and diabetes outcomes (11–13).

Contrary to the earlier findings, other studies (14,15) have found that patients with diabetes and a serious mental illness may have better glucose control than those without a comorbid serious mental illness. Specifically, one cross-sectional study (15) found that patients with type 2 diabetes and bipolar disorder, depression, or schizophrenia had significantly better glycemic control than patients without one of these comorbid serious mental illnesses. The authors associate this finding with increased contact with health care providers. A follow-up longitudinal study (14) in these patients further validated previous findings but also noted that both groups of patients had suboptimal glycemic control.

Data are conflicting regarding the effect of comorbid depression and anxiety on glycemic control in patients with type 2 diabetes (14–20), and data on patients with diabetes and a substance use disorder are very limited. One study (20) suggests that depression increases mortality 1.5-fold in patients with diabetes. Additionally, two studies (16,18) have demonstrated poorer glycemic control in patients with type 2 diabetes and comorbid depression. Conversely, anxiety diagnoses and anxiety scores in patients with serious mental illness and type 2 diabetes have not been shown to have significant effects on glycemic control (16,17). The previous studies had small sample sizes and limited generalizability of findings, which may partially explain why existing data are inconclusive about the association between depression and anxiety and glycemic control. Furthermore, there is a lack of data exploring the effect of substance use disorders on glycemic control. This is an important subgroup of patients to consider because they generally receive a lower quality of diabetes care, have poorer adherence to antidiabetic agents, and suffer higher rates of adverse diabetes outcomes compared to patients with other MHCs (5,6,21).

The limited data and lack of consensus on the relationship between MHCs and diabetes control hinder the effectiveness of clinicians who strive to manage the care of patients with diabetes who have the added complexity of comorbid MHCs. Although patients with MHCs are more likely to face access and self-management barriers, there is heterogeneity in terms of how such conditions affect patient functioning, both within and across conditions (6,22). Thus, we hypothesized that the presence of any MHC would be associated with worse diabetes control and serious mental illness and substance use disorders would be associated with worse diabetes control relative to other MHCs.

Objective

The objective of this study was to investigate the association between the diagnosis of an MHC (bipolar disorder, depression, anxiety, psychotic disorder, or substance use disorder) and glycemic control in patients with type 2 diabetes treated by providers in a network of 10 community-based primary care clinics. Glycemic control in patients diagnosed with an MHC was compared to that of patients without an MHC. Additionally, the subset of patients diagnosed with an MHC was stratified by diagnosis of severe mental illness versus depression and/or anxiety only and separately by substance use disorders.

This study contributes to the existing body of evidence by exploring, through examination of medical record data, the associations between specific MHCs, including substance use disorder, and glycemic control in a cohort of patients with diabetes treated in a large network of community clinics. We expect that the findings will aid clinicians in managing their patients with diabetes and comorbid mental illness.

Design and Methods

We conducted a historical cross-sectional analysis of patients with type 2 diabetes treated by primary care providers at the University of Utah Community Clinics (UUCCs) between 2010 and 2012. The UUCCs include 10 health centers that provide primary and select specialty care to patients in the communities they serve. The UUCC patient population is relatively diverse in terms of race, ethnicity, and socioeconomic status, and although owned by the University, most UUCCs are not academic teaching sites.

Data

This study used data from the University of Utah Health Care System Electronic Data Warehouse. This database contains electronic

medical records (EMRs), including diagnoses codes, treatment, and laboratory test data, as well as patient billing data for 1.4 million patients dating back to 1990. The data used for this study were de-identified.

Population

Included patients had documented type 2 diabetes and two or more UUCC visits with a health care provider, nurse, or pharmacist or a documented order between 2010 and 2012. The first and last visit or order were required to be at least 13 months apart. Patients were considered to have type 2 diabetes based on the presence of at least one International Classification of Disease, 9th Revision, Clinical Modification (ICD-9), code for type 2 diabetes (250.X0 or 250.X2) recorded in the EMR or a medication order for any antidiabetic agent (online appendix Table S1). Included patients also had at least one A1C value during the study period that was recorded 365 days or more after the first activity date during the observation period. Exclusion criteria included a diagnosis code for type 1 diabetes, polycystic ovary syndrome, or gestational diabetes in the absence of a diagnosis code for type 2 diabetes.

Exposure

Diagnosis of an MHC was the primary exposure of interest and was identified based on the presence of at least one ICD-9 diagnosis code for depression, anxiety, schizophrenia, bipolar spectrum disorder, substance use disorder, or other psychotic disorder (online appendix Table S2). Within the primary care clinics, diagnoses may be entered in a patient's medical record based on the following: *1*) patient report of symptoms and primary care physician diagnosis, often using a standardized questionnaire; *2*) diagnosis of an MHC by a specialist in a different clinic within the same hospital system (e.g., psychiatry specialty clinic); or *3*) diagnosis by an outside provider, typically confirmed by outside medical records. Patients with a medication history significant for common MHCs were not considered to have an MHC unless they had a documented diagnosis because many of these agents are also used for other indications. Patients with an MHC were further stratified by diagnoses of a serious mental illness versus depression and/or anxiety without other MHCs. For the purpose of this study, mental health diagnoses other than depression and anxiety (bipolar spectrum disorder, psychotic disorder, schizophrenia, and substance use disorder) were categorized into the serious mental illness category. We then separately stratified the mental health cohort by diagnosis for substance use disorder.

Outcome Variable of Interest

The primary outcome of interest was glycemic control. The A1C value used for this outcome was the first A1C recorded after 1 year of documented clinical activity during the 2010–2012 study period. The secondary outcome was the proportion of patients with adequate glycemic control (A1C <8.0%). We used 8.0% as the threshold instead of 7.0% based on clinician input that, although an A1C <7.0% would be the ideal diabetes treatment target for most study patients (23), providers often set a higher individual target of <8.0% while stabilizing MHCs because uncontrolled MHCs can interfere with diabetes self-management (24). Stratification by substance abuse disorder was also considered a secondary outcome analysis.

Covariates

Patient demographic, clinical, and treatment characteristics were also identified during the year before the glycemic control evaluation date to describe the study cohort and control for confounding. Demographic variables included age and sex. Diabetes-specific variables included microvascular complications (i.e., neuropathy, retinopathy, and nephropathy), macrovascular complications (i.e., cardiovascular disease, myocardial infarction, and cerebrovascular events), and antidiabetic agents prescribed before the evaluation date by drug class and number of classes. Additional clinical characteristics included BMI, systolic and diastolic blood pressure, triglycerides, LDL cholesterol, HDL cholesterol, and overall comorbidity measured by the Charlson Comorbidity Index (25).

Statistical Analysis

Descriptive statistics were used to identify differences between patients with or without an MHC and by categories of MHCs using the χ^2 test or Fisher's exact test for categorical values and independent *t* tests for continuous variables. Multivariable linear regression analysis was conducted in the overall cohort to identify the association between having an MHC and A1C; a multivariable logistic regression model was used to identify the likelihood of patients having an A1C <8.0% in the overall cohort. Statistical analyses were performed using RStudio version 0.99.489 (RStudio, Inc., Boston, Mass.) and Stata version 12 (StataCorp, College Station, Tex). A preliminary power analysis on the primary outcome within the MHC cohort indicated that a study including 410 patients with a diagnosis for depression or anxiety alone and 205 patients with a serious mental illness would have 90% power to detect a 0.5% absolute difference in A1C. The protocol for this study was reviewed and approved by the University of Utah institutional review board.

Results

Patient Characteristics

This study identified 9,810 patients with type 2 diabetes treated at a UUCC between 2010 and 2012. Of these, 3,025 patients had a sufficient duration of clinical activity and an A1C value at least 365 days after their first EMR activity date in the observation period for assessing glycemic control. Of this cohort, 721 patients had a diagnosis for at least one MHC. The mean age of the population was

62.2 ± 13.5 years, more than half (54.9%) were female, and a majority (74.5%) were Caucasian. The overall mean A1C value was 7.32 ± 1.72%, and 76.1% of the cohort had an A1C <8.0% (Table 1).

The MHC cohort included significantly more women (62.1 vs. 51.3%, P <0.001) and was significantly younger (58.6 vs. 63.3 years, P <0.001) than the group without MHCs (Table 1). Patients with MHCs had a higher prevalence of microvascular complications (31.1 vs. 24.6%, P = 0.001). The most prevalent MHCs were anxiety (62.4%), depression (38.7%), and substance use disorders (13.7%). Sulfonylureas were prescribed less often in patients with MHCs (25.7 vs. 31.7%, P = 0.002).

Severe mental illness was diagnosed in 252 patients with MHCs (Table 2). The severe mental illness

TABLE 1. Baseline Characteristics of Patients With Type 2 Diabetes by Diagnosis of an MHC

	Overall (*n* = 3,025)	Without MHC (*n* = 2,304)	With MHC (*n* = 721)	*P*
Age (years; mean [SD])	62.2 (13.5)	63.3 (13.2)	58.6 (13.6)	<0.001
Sex, male (*n* [%])	1,394 (46.1)	1,121 (48.7)	273 (37.9)	<0.001
Race (*n* [%])				0.002
Caucasian	2,255 (74.5)	1,686 (73.2)	569 (78.9)	
African American	62 (2.0)	44 (1.9)	18 (2.5)	
Other	708 (23.5)	574 (24.9)	134 (18.6)	
Baseline BMI (kg/m^2; mean [SD])	34.23 (8.22)	34.11 (8.22)	34.59 (8.25)	0.474
Charlson Comorbidity Index (*n* [%])				0.012
0	249 (8.2)	179 (7.8)	70 (9.7)	
1	784 (25.9)	583 (25.3)	201 (27.9)	
2	594 (19.6)	480 (20.8)	114 (15.8)	
≥3	1,062 (46.3)	1,062 (46.1)	336 (46.6)	
Diabetes complications (*n* [%])				
Macrovascular	736 (24.3)	544 (23.6)	192 (26.6)	0.110
Microvascular	795 (26.3)	571 (24.7)	224 (31.1)	0.001
MHCs (*n* [%])				NA
Depression	279 (9.2)	0 (0)	279 (38.7)	
Anxiety	450 (14.9)	0 (0)	450 (62.4)	
Bipolar disorder	84 (2.8)	0 (0)	84 (11.7)	
Psychosis	41 (1.4)	0 (0)	41 (5.7)	
Schizophrenia	52 (1.7)	0 (0)	52 (7.2)	
Substance use disorder	99 (3.3)	0 (0)	99 (13.7)	
Psychotic disorder	36 (1.2)	0 (0)	36 (5.0)	
Diabetes medication drug classes used (*n* [%])				
Metformin	1,823 (60.3)	1,397 (60.6)	436 (59.1)	0.485
Sulfonylurea	916 (30.3)	731 (31.7)	185 (25.7)	0.002
Thiazolidinedione	233 (7.7)	192 (8.3)	41 (5.7)	0.025
Insulin	729 (24.1)	559 (24.3)	170 (23.6)	0.745
Dipeptidyl peptidase-4 inhibitor	123 (4.1)	99 (4.3)	24 (3.3)	0.298
Glucagon-like peptide 1 receptor agonists	30 (1.0)	23 (1.0)	7 (1.0)	1.0
Other diabetes medications*	18 (0.6)	12 (0.5)	6 (0.8)	0.502
Antidiabetic drug classes used pre-evaluation date (*n* [%])				0.126

TABLE CONTINUED ON P. 281 →

TABLE 1. Baseline Characteristics of Patients With Type 2 Diabetes by Diagnosis of an MHC, ***continued from p. 280***

	Overall (*n* = 3,025)	Without MHC (*n* = 2,304)	With MHC (*n* = 721)	*P*
0	703 (23.2)	518 (22.5)	185 (25.7)	
1–2	1,969 (65.1)	1,507 (65.4)	462 (64.1)	
>3	353 (11.7)	279 (12.1)	74 (11.2)	
Central nervous system drug classes used (*n* [%])				<0.001
Antidepressant	984 (32.5)	520 (22.6)	464 (64.6)	
Anxiolytics	334 (11.0)	107 (4.6)	227 (31.5)	
Antipsychotics	145 (4.8)	42 (1.8)	103 (14.3)	
Analgesic	1,098 (36.3)	733 (31.8)	365 (50.6)	
Anticonvulsants	661 (21.9)	360 (15.6)	301 (41.7)	
Hypnotics	312 (10.3)	188 (8.2)	124 (17.2)	
Other psychiatric/neurological drugs	482 (15.9)	294 (12.8)	188 (26.1)	

**Other diabetes medications include α-glucosidase inhibitors, amylin analogs, and meglitinide analogs.*

TABLE 2. Baseline Characteristics of Patients With Type 2 Diabetes and MHCs, Stratified by Serious Mental Illness and Substance Use Disorder

	Depression/ Anxiety (*n* = 469)	Serious Mental Illness (*n* = 252)	*P*	No Substance Use Disorder (*n* = 622)	Substance Use Disorder (*n* = 99)	*P*
Age (years; mean [SD])	60.4 (13.7)	55.4 (12.7)	<0.001	59.4 (13.8)	53.8 (10.9)	<0.001
Sex, male (*n* [%])	144 (30.7)	129 (51.2)	0.007	212 (34.1)	82 (82.8)	<0.001
Race (*n* [%])			0.143			0.384
Caucasian	367 (78.3)	202 (80.2)		493 (79.3)	76 (76.8)	
African American	7 (1.5)	11 (4.4)		13 (2.1)	5 (5.1)	
Other	95 (20.2)	39 (15.4)		116 (18.6)	18 (18.1)	
Baseline BMI (kg/m^2; mean [SD])	34.44 (8.32)	34.86 (8.13)	0.205	34.8 (8.47)	33.35 (6.71)	0.689
Charlson Comorbidity Index (*n* [%])			0.940			0.233
0	45 (9.6)	25 (9.9)		59 (9.5)	11 (11.1)	
1	129 (27.5)	72 (28.6)		178 (29.0)	23 (23.2)	
2	77 (16.4)	37 (14.7)		103 (16.6)	11 (11.1)	
≥3	218 (46.5)	118 (46.8)		282 (45.1)	54 (54.6)	
Diabetes complications (*n* [%])						
Macrovascular	111 (23.7)	81 (32.1)	0.018	164 (26.4)	28 (28.3)	0.781
Microvascular	138 (29.4)	86 (34.1)	0.224	190 (30.5)	34 (34.3)	0.521

TABLE CONTINUED ON P. 282 →

TABLE 2. Baseline Characteristics of Patients With Type 2 Diabetes and MHCs, Stratified by Serious Mental Illness and Substance Use Disorder, *continued from p. 281*

MHCs (*n* [%])						
Depression	216 (46.1)	63 (25)	<0.001	245 (39.4)	34 (34.3)	0.397
Anxiety	352 (75.1)	98 (38.9)	<0.001	397 (63.8)	53 (53.5)	0.064
Bipolar disorder	0 (0)	84 (33.3)	<0.001	63 (10.1)	21 (21.2)	0.002
Psychosis	0 (0)	41 (16.3)	<0.001	37 (5.9)	4 (4.0)	0.598
Schizophrenia	0 (0)	52 (20.6)	<0.001	44 (7.1)	8 (8.1)	0.880
Substance use disorder	0 (0)	99 (39.3)	<0.001	0 (0)	99 (100.0)	<0.001
Psychotic disorder	0 (0)	36 (14.3)	<0.001	26 (4.2)	10 (10.1)	0.024
Diabetes medications used (*n* [%])						
Metformin	282 (60.1)	144 (57.1)	0.485	372 (59.8)	54 (54.5)	0.379
Sulfonylurea	121 (25.8)	64 (25.4)	0.977	168 (27.0)	17 (17.2)	0.050
Thiazolidinedione	26 (5.5)	15 (6.0)	0.954	34 (5.5)	7 (7.1)	0.684
Insulin	106 (22.6)	64 (25.4)	0.453	139 (22.3)	31 (31.3)	0.068
Dipeptidyl peptidase-4 inhibitor	14 (3.0)	10 (4.0)	0.628	23 (3.7)	1 (1.0)	0.279
Glucagon-like peptide 1 receptor agonist	2 (0.4)	5 (2.0)	0.102	4 (0.6)	3 (3.0)	0.089
Other diabetes medications*	3 (0.6)	3 (1.2)	0.729	6 (1.0)	0 (0.0)	
Antidiabetic drug classes used pre-evaluation date (*n* [%])			0.124			0.989
0	115 (24.5)	70 (27.8)		159 (25.6)	26 (26.3)	
1–2	312 (66.6)	150 (59.5)		399 (64.1)	63 (63.6)	
>3	42 (8.9)	32 (12.7)		64 (10.3)	10 (10.1)	
Central nervous system drug classes used (*n* [%])						
Antidepressant	330 (70.4)	134 (53.2)	<0.001	408 (65.6)	56 (56.6)	0.103
Anxiolytics	172 (36.7)	55 (21.8)	<0.001	201 (32.3)	26 (26.3)	0.277
Antipsychotics	22 (4.7)	81 (32.1)	<0.001	80 (12.9)	23 (23.2)	0.010
Analgesic	232 (49.5)	133 (52.8)	0.441	305 (49.0)	60 (60.6)	0.042
Anticonvulsants	178 (38.0)	123 (48.8)	0.006	253 (40.7)	48 (48.5)	0.176
Hypnotics	84 (17.9)	40 (15.9)	0.557	106 (17.0)	18 (18.2)	0.892
Other psychiatric/ neurological drugs	107 (22.8)	81 (32.1)	0.009	150 (24.1)	38 (38.4)	0.004

**Other diabetes medications include α-glucosidase inhibitors, amylin analogs, and meglitinide analogs.*

cohort included significantly more men (51.2 vs. 30.7%, P = 0.007) and was younger (55.4 vs. 60.4 years, P <0.001) than the cohort with depression and/or anxiety alone. Macrovascular complications were significantly more prevalent in patients diagnosed with severe mental illness (32.1 vs. 23.7%, P = 0.018). Clinical characteristics and prescribed antidiabetic medications were similar between the groups. Antidepressants and anxiolytics were more frequently prescribed for patients with depression and/or anxiety alone. More patients with severe mental illness received antipsychotics (32.1 vs. 4.7%, P <0.001), other psychiatric/neurological drugs (32.1 vs. 22.8%, P = 0.009), and anticonvulsants (48.8 vs. 38.0%, P = 0.006).

Substance use disorder was present in 99 patients with MHCs (14%), of which 82.8% were male and the mean age was 53.8 ± 10.9 years versus 34.1% male and age 59.4 ± 13.8 years for patients without a substance use disorder diagnosis (Table 2). The prevalence of bipolar disorder and

TABLE 3. Glycemic Control Stratified by MHC

	Without MHC (*n* = 2,304)	With MHC (*n* = 721)	*P*	Depression/ Anxiety (*n* = 469)	Serious Mental Illness (*n* = 252)	*P*	Without Substance Abuse (*n* = 622)	With Substance Abuse (*n* = 99)	*P*
Baseline A1C (%; mean [SD])	7.38 (1.73)	7.14 (1.66)	0.001	7.08 (1.55)	7.25 (1.85)	0.188	7.05 (1.56)	7.69 (2.15)	<0.001
Baseline A1C (*n* [%])			0.138			0.287			0.004
<8.0%	1,738 (75.4)	564 (78.2)		373 (79.5)	191 (75.8)		498 (80.1)	66 (66.7)	
>8.0%	566 (24.6)	157 (21.8)		96 (20.5)	61 (24.0)		124 (19.9)	33 (33.3)	

psychotic disorders was significantly higher in those with a substance use disorder. Patients with substance use disorder were more often prescribed antipsychotics (23.2 vs. 12.9%, P = 0.01) and analgesics (60.6 vs. 49.0%, P = 0.04) than those without a substance use disorder diagnosis.

Glycemic Control in Patients With and Without MHCs

The study found that A1C was statistically significantly lower in patients with any MHC than those with no recorded MHC. Mean A1C was 7.14 ± 1.66% in the MHC cohort versus 7.38 ± 1.73% in the cohort without MHCs, a difference of 0.24% (P = 0.001). The proportion of patients with adequate glycemic control (A1C <8.0%) was similar between groups (78.2 and 75.4% for those with and without MHCs, respectively, P = 0.138) (Table 3). Results were similar in the multivariate linear regression analysis, with a diagnosis of an MHC associated with a 0.25% lower A1C relative to no MHC diagnosis (correlation coefficient –0.25, 95% CI –0.38 to –0.11, P <0.001) (Table 4). In the multivariable logistic regression analysis, patients with an MHC were 1.27 times more likely to have an A1C <8.0% than those without an MHC (odds ratio [OR] 1.27, 95% CI 1.01–1.59, P = 0.041) (Table 5). Both regression models controlled for age, sex, comorbidities, and baseline diabetes medication use.

When stratifying by MHC categories in the subset of patients with any MHC, glycemic control was found to be similar between patients with depression and/or anxiety alone and those with a serious mental illness. Patients with depression and/or anxiety only had a mean A1C of 7.08 ± 1.55%, and 79.5% had an A1C <8.0%. In the severe mental illness group, the mean A1C was 7.25 ± 1.85%, and 75.8% attained an A1C <8.0% (P = 0.188 and 0.287, respectively). Restratification of patients with MHCs by the presence of substance use disorder revealed that the group of patients with a substance use disorder had a higher mean A1C (7.69 ± 2.15% vs. 7.05 ± 1.56%, P <0.001) and a lower proportion of patients with adequate glycemic control than patients without a substance use disorder (66.7 vs. 80.1%, P = 0.004).

Discussion

This large, cross-sectional study of patients with diabetes treated in a network of community-based primary care clinics found that patients with any MHC had a lower mean A1C than patients with diabetes but no MHC diagnoses (7.14 vs. 7.38%, P = 0.001; correlation coefficient –0.25, 95% CI –0.38 to –0.11, P <0.001), and a higher likelihood of attaining an A1C <8.0% (OR 1.27, P = 0.041). Within the subset of patients with an MHC, we found no difference in unadjusted mean A1C or attainment of an A1C <8.0% when patients with an MHC were stratified by the presence of a serious mental illness versus depression and/or anxiety alone.

This study contributes new insight into the diabetes control of patients with substance use disorders and found that patients with a substance use disorder had worse diabetes control than those without a substance use disorder diagnosis (mean A1C 7.69 and 66.7% with an A1C <8.0% vs. mean A1C 7.05 and 80.1% with an A1C <8.0%, P ≤0.004 for each). This finding is noteworthy because data are limited regarding diabetes control and substance use disorders. We identified one previous study that examined diabetes complications in Medicaid or Medicare patients with behavioral disorders (5). Although this study found that patients with a drug or alcohol use disorder had a higher likelihood of experiencing several adverse diabetes outcomes compared to patients without substance abuse, it did not assess glycemic control. There is a national movement to increase screening for substance use disorders within primary care (26). Our findings suggest that this may be particularly import-

TABLE 4. Multivariable Linear Regression Analysis for Association Between A1C and MHC Diagnosis

	Correlation Coefficient	95% CI	*P**
MHC diagnosis	–0.246	–0.379 to –0.112	**<0.001**
Age (years)	–0.020	–0.025 to –0.016	**<0.001**
Sex (female vs. male)	0.256	0.144–0.369	**<0.001**
Comorbidities			
Hypertension	–0.158	–0.287 to –0.028	**0.017**
Dyslipidemia	–0.074	–0.215 to 0.068	0.307
Chronic kidney disease	–0.306	–0.522 to –0.090	**0.005**
Retinopathy	0.497	0.154–0.841	**0.005**
Neuropathy	–0.111	–0.254 to 0.031	0.126
Cardiovascular disease	–0.156	–0.415 to 0.103	0.239
Stroke	–0.105	–0.474 to 0.263	0.575
Myocardial infarction	0.077	–0.365 to 0.520	0.732
Diabetes medication use			
Metformin	0.009	–0.111 to 0.128	0.888
Sulfonylurea	0.631	0.504–0.757	**<0.001**
Thiazolidinedione	–0.028	–0.239 to 0.184	0.798
Insulin	1.342	1.209–1.476	**<0.001**
Dipeptidyl peptidase-4 inhibitor	0.033	–0.251 to 0.316	0.822
Glucagon-like peptide 1 receptor agonist	–0.087	–0.651 to 0.478	0.764
Constant	8.168	7.867–8.470	**<0.001**

** Bold type indicates statistical significance.*

ant in the context of patients with poor diabetes control.

This study also found that patients with a diagnosed MHC were more likely to achieve adequate glycemic control (A1C <8.0%) than those without an MHC. Others studies (14–19) have not consistently identified differences in diabetes control for individuals with and without depression or anxiety. This finding could be partially explained by differences in depression management; patients who have well-managed depression are more likely to have improved glycemic control (27), and our study population had regular access to health care services. However, we were unable to examine differences in depression management in this population. It is also possible that not all individuals with symptoms of anxiety or depression have this documented in their medical records, which could bias our findings towards the null hypothesis.

Our study found that patients with a serious mental illness had better diabetes control than those with depression and/or anxiety but without a serious mental illness. This finding is somewhat counterintuitive given the barriers to health care that patients with serious mental illness often face, as well as the use of second-generation antipsychotics in this cohort (12,16,28). However, this finding is consistent with other studies, including findings by Brown et al. (14) and Dixon et al. (15). The same challenges faced by individuals with serious mental illness may also lead to more intensive diabetes monitoring and treatment by providers, enhanced diabetes management through caregiver support, and connections with primary care practices that have the training, experience, and resources to manage serious mental illness (29). Other studies reporting an association between depression and poor glycemic control have been conducted in different populations (16,18). One study, conducted in a population of veterans (18) found a small but statistically significant difference in the mean A1C of veterans with and without depression (0.13%, P = 0.008). Another study examining the effect of comorbid anxiety disorders on glycemic control found no association between anxiety and glycemic control but reported an association between the presence of depressive symptoms and total diabetes control as measured by A1C (16). Despite this finding, mean A1C was similar between the study groups (serious mental illness with anxiety and with greater depressive symptoms 7.92% vs. serious mental illness without anxiety and with lesser depressive symptoms 8.11%, P = 0.857), leaving the association between depression and glycemic control unclear.

It should be noted that we included substance use disorders in our definition of serious mental illness. There is no uniform definition of which mental health diagnoses should be included in this definition, and substance use disorders are inconsistently included in other studies. In a post-hoc analysis, we removed patients with substance abuse but without other serious mental illness diagnoses from the definition of serious mental illness, and this did not change the study conclusions, with a mean A1C of 7.12 ± 1.70% in patients with serious mental illness and 7.08 ± 1.55% in patients with depression and/or anxiety (P = 0.84). Furthermore, we combined depression and anxiety diagnoses into one category for comparison, which may mask the effect of depression on glycemic control in patients who do not have another serious mental illness.

TABLE 5. Multivariable Logistic Regression Analysis for Association Between A1C and MHC Diagnosis

	OR	95% CI	*P**
MHC diagnosis	1.268	1.010–1.593	**0.041**
Age (years)	1.038	1.030–1.047	**<0.001**
Sex (female vs. male)	0.722	0.598–0.871	**0.001**
Comorbidities			
Hypertension	1.056	0.853–1.307	0.618
Dyslipidemia	1.036	0.821–1.306	0.767
Chronic kidney disease	1.459	1.003–2.121	**0.048**
Retinopathy	0.444	0.266–0.739	**0.002**
Neuropathy	1.267	0.992–1.617	0.058
Cardiovascular disease	1.320	0.819–2.126	0.254
Stroke	1.068	0.527–2.162	0.856
Myocardial infarction	0.782	0.375–1.628	0.510
Diabetes medication use			
Metformin	1.025	0.836–1.256	0.812
Sulfonylurea	0.414	0.337–0.508	**<0.001**
Thiazolidinedione	0.946	0.672–1.333	0.753
Insulin	0.158	0.128–0.193	**<0.001**
Dipeptidyl peptidase-4 inhibitor	0.869	0.553–1.366	0.543
Glucagon-like peptide 1 receptor agonist	1.221	0.553–2.694	0.621

**Bold type indicates statistical significance.*

We therefore conducted a post-hoc analysis of patients with serious mental illness or with depression but not a serious mental illness and found no difference in A1C or likelihood of attaining an A1C <8.0% between these groups.

This study has several strengths. First, to our knowledge, this is the largest cross-sectional study describing the effect of MHCs, including substance use disorders, on glycemic control in patients managed in a network of primary care clinics. Results from previously conducted studies (14,15) may have been confounded by variation in diabetes management because patients were recruited from various settings. In addition, our study examines the overlap of substance use disorders with both depression and anxiety, as well as other serious mental illnesses ,and examines its association with barriers to achieving adequate glycemic control. This is a unique contribution suggesting the possibility that previous inconsistencies in the literature examining relationships between MHCs and glycemic control could have been related to methodological differences in examining substance use disorders.

With regard to study limitations, our cross-sectional design does not support inferences of causality. Our population included patients with documented clinic activity on multiple days, which may have excluded some patients with poorer glycemic control.

Generalizability may be limited because the study population was drawn from community-based primary care clinics in Utah. Although diabetes control in our study population is similar to national estimates (30,31) (mean A1C 7.4 vs. 7.2% and 75.4 vs. 77.9% of patients achieving an A1C <8.0%, respectively), the majority of our study patients were Caucasian and <65 years of age. In our study, 23.8% of patients had an MHC diagnosis, which is somewhat higher than the national estimate of 18.1% (32). However, the proportion of patients with an MHC in Utah overall is 22% (33), and the prevalence of depression and anxiety is higher in patients with diabetes. Thus, the higher prevalence of MHC diagnoses was expected.

Finally, our study is limited by reliance on diagnoses having been entered into the EMR to identify patients for inclusion or to determine exposure. This is a commonly noted concern with EMR-based studies (34). A systematic review of studies using EMR data suggests the highest sensitivity for prescribing data and for conditions with clear diagnostic criteria (35), both of which were used in this study. However, diagnostic codes may have been entered incorrectly or added before the diagnosis was confirmed. Because we only had access to de-identified data, we were not able to validate diabetes and MHC diagnoses in the EMR problem list, which may have indicated diagnostic uncertainty or changes in conditions over time.

It will be important for future research to examine factors that influence diabetes self-management, adherence to lifestyle recommendations and medications, and diabetes screening in patients treated with atypical antipsychotics, all of which likely vary between comparison groups. In addition, attention to recording specific diagnoses and treatment within patients' medical records may help providers better understand the morbidity and mortality risks facing their patients with diabetes. Finally, incorporating screening tools to identify patients with diabetes who also have substance use disorder may better serve this population in primary care. Ongoing research is investigating these questions with an aim of providing additional insight for health care providers managing

patients with diabetes and comorbid MHCs.

In conclusion, our results show that patients with MHCs achieve rates of adequate glycemic control similar to those without MHCs. Despite these findings, different MHCs may pose unique challenges to achieving adequate glycemic control. Physicians should recognize that patients with substance abuse disorder may be more vulnerable to poorer glycemic control and adverse diabetes outcomes. Thus, barriers to achieving adequate glycemic control that are specific to various MHCs should be identified and addressed. These efforts will be supported by ongoing research into barriers to and facilitators of glycemic control for patients with MHCs.

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Duality of Interest

No potential conflicts of interest relevant to this article were reported.

Author Contributions

K.B. researched data and wrote the manuscript. K.F. contributed to the discussion and reviewed and edited the manuscript. L.G. researched data, contributed to the discussion, and reviewed and edited the manuscript. K.G. contributed to the discussion and reviewed and edited the manuscript. C.M.-M. researched data, contributed to the discussion, and wrote, reviewed, and edited the manuscript. C.M.-M. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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