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30-year Cardiovascular Disease Risk for Young Adults with Serious Mental Illness

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Abstract

Objective: To estimate 30-year CVD risk and modifiable risk factors in young adults with serious mental illness (SMI) versus those without, and assess variations in CVD risk by race, ethnicity, and sex.

Method: In this cross-sectional study, we estimated and compared the Framingham 30-year CVD risk score and individual modifiable CVD risk factors in young adult (20-39 years) primary care patients with and without SMI at two US healthcare systems (January 2016-Septemeber 2018). Interaction terms assessed whether the SMI-risk association differed across demographic groups.

Results: Covariate-adjusted 30-year CVD risk was significantly higher for those with (n=4228) versus those without (n=155,363) SMI (RR 1.28, 95% CI [1.26, 1.30]). Patients with SMI had higher rates of hypertension (OR 2.02 [1.7, 2.39]), diabetes (OR 3.14 [2.59, 3.82]), obesity (OR 1.93 [1.8, 2.07]), and smoking (OR 4.94 [4.6, 5.36]). The increased 30-year CVD risk associated with SMI varied significantly by race and sex: there was an 8% higher risk in Black compared to White patients (RR 1.08, [1.04, 1.12]) and a 9% lower risk in men compared to women (RR 0.91 [0.88, 0.94]).

Conclusions: Young adults with SMI are at increased 30-year risk of CVD, and further disparities exist for Black individuals and women.

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Keywords

schizophrenia; schizoaffective disorder; bipolar disorder; cardiometabolic disorders; health disparities

1.0 Introduction

Schizophrenia spectrum and bipolar disorders are serious mental illnesses (SMI) with a typical age of onset in late adolescence or early adulthood. Individuals with SMI face striking health disparities including premature mortality of up to 10-20 years [1]. Cardiovascular disease (CVD) is the leading driver of early mortality, with high rates of modifiable CVD risk factors, including obesity, smoking, diabetes, and hypercholesteremia [2-4]. Although increased CVD risk has been well-established for individuals with SMI, most studies have focused on risk in middle aged and older samples [5] who may have different risk profiles than young adults. Intervention trials aimed at reducing overall CVD risk or individual risk factors have shown promise but have also largely targeted middle aged patients [6-11], with few conducted in younger samples when early interventions could substantially reduce long term risk [12, 13]. Due to the early age of onset of SMI and the rapid accumulation of CVD risk factors after psychotropic treatment initiation [14-16], long-term CVD risk prediction is essential from the beginning of the illness to guide early intervention strategies for modifiable risk factors to reduce the burden of premature morbidity and mortality later in life.

Estimates of 30-year or lifetime CVD risk provide the most accurate prediction of long-term risk [17-19]. Only one prior study has characterized the Framingham 30-year CVD risk estimates in young adults with SMI, finding 30-year CVD risk to be twice as high in those recently diagnosed with bipolar disorder compared to healthy controls in a Danish sample. However absolute 30-year CVD risk scores were low in both groups [20]. Another previous report found that in adults with and without SMI, the largest differential lifetime CVD risk occurred in those under 40 years old [21]. The Framingham 30-year CVD risk scores and modifiable risk factors contributing to this increased risk in young adults with SMI remain to be elucidated.

As the burden of CVD risk factors is increasing among young adults in the US, especially for Black and Hispanic individuals [22], understanding risk factors for young adults with SMI is critical to inform prevention and intervention strategies for this at-risk population. Previous research was constrained by small sample sizes and lack of comparison groups that allow for adjustment of important patient characteristics. Additionally, CVD risk estimates for those with SMI reported by sociodemographic characteristics such as race, ethnicity, and sex have been scarce, largely limited to older patients with SMI, and results have been mixed [23, 24]. The combined effect of sociodemographic characteristics and SMI on 30 year-CVD risk has not been explored in young adults and could further inform intervention strategies.

We aimed to characterize continuous 30-year CVD risk and specific modifiable risk factors in a large sample of young adults aged 20-39 years with and without schizophrenia spectrum

and bipolar disorders. Second, we explored differences in 30-year CVD risk by race, ethnicity, sex, and age to identify specific high-risk subgroups.

2.0 Methods

2.1 Study Design and Settings

Two large healthcare delivery organizations in Minnesota and Wisconsin, HealthPartners and Park Nicollet, participated in a larger trial of clinical decision support in primary care clinics aimed at reducing CVD risk for patients with SMI aged 18-75 years [11, 25]. The clinical decision support system is a web-based tool embedded within the electronic health record. The tool collects clinical data to generate evidenced based, patient specific treatment recommendations for addressing modifiable CVD risk factors, including blood pressure, lipids, glycated hemoglobin (HbA1c), smoking status, and body mass index (BMI). Study enrollment occurred between January 20, 2016 and September 19, 2018. The present study used data from index (baseline) visits for all patients who visited a randomized primary care clinic during the enrollment period of the randomized controlled trial. This study was approved by the HealthPartners Institutional Review Board, and a waiver of consent was granted.

2.2 Enrollment and Eligibility

Patients were included in the present study if they met the following criteria at the index visit: 1) aged 20 to 39 years, 2) not pregnant, 3) no active cancer, and 4) not residing in a nursing home. Patients younger than 20 years old were excluded because the 30-year CVD risk score used in this study has not been validated in those under 20 years old [17]. Patients were included in the SMI group if they had ≥2 outpatient or ≥1 inpatient diagnostic codes for SMI documented in the electronic health record (EHR; which included medical and mental health encounters) in the 2 years prior to index. Qualifying SMI diagnoses included bipolar disorder, schizophrenia, and schizoaffective disorder (see Supplemental Table S1 for International Classification of Disease (ICD) codes). Patients with ICD codes that crossed subcategories (i.e., bipolar disorder+schizophrenia) were assigned a diagnosis of schizoaffective disorder. Patients with schizophrenia or schizoaffective diagnoses were combined in the schizophrenia spectrum disorders group. Patients were included in the non-SMI group if they did not have any codes for SMI, depression, or anxiety.

2.3 Data Sources

Data were primarily collected via the clinical decision support tool, which recorded EHR data at each index visit, including age, race, sex, vital signs, diagnoses, and lab values. Ethnicity and insurance status were collected from the EHR data repository.

2.4 Measures

2.4.1 Estimated cardiovascular risk and cardiovascular risk factors.—

Thirty-year CVD risk was estimated using a sex-specific multivariable algorithm, the Framingham 30-year risk score [17]. Recent evidence supports use of the Framingham 30-year risk models as the preferred method to identify at-risk adults under 40 years old [18, 19]. This score provides a continuous estimate of risk of a CVD event, which may be more clinically

useful than categorical lifetime risk scores [18]. The full 30-year CVD risk score estimates the risk of both hard CVD events (coronary death, myocardial infarction, or stroke), and coronary insufficiency, angina pectoris, transient ischemic attack, intermittent claudication, or congestive heart failure occurring in the next 30 years. This score utilizes eight individual risk factors including age, sex, body mass index, systolic blood pressure, diabetes mellitus, antihypertensive prescription, and current smoking status. As antihypertensive medication orders were not available in the clinical decision system data for this secondary analysis, we used a hypertension diagnosis as a proxy for antihypertensive prescription. To assess the impact of this proxy measure, we also calculated the 30-year risk scores without the proxy (i.e., all patients coded “no” for antihypertensive treatment). Previous research suggests that most patients (approximately 85%) who are aware of their hypertension diagnosis are treated [26], with similarly high rates of concordance between hypertension diagnosis and treatment in the health system used in this study [27, 28]. We report results using the proxy measure, and in sensitivity analysis found no difference in the results when the proxy measure was excluded from the 30-year risk score calculations.

The clinical decision support system captured modifiable cardiovascular risk factors: blood pressure, lipids (total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, and statin use), HbA1c, weight (BMI), and smoking status. Blood pressure and weight were captured at the index encounter. Patients were considered to be treated with a statin if they had an active prescription for a statin at the index visit. For the remaining risk factors, the most recent value in the last 5 years was used for analyses.

2.4.2 Cardiometabolic Diagnoses.—

Diagnoses for coronary heart disease, CVD, hypertension, and diabetes were defined as having ≥2 outpatient or ≥1 inpatient codes documented in the EHR in the 2 years before the index date (see Supplemental Table S2 for included ICD codes).

2.5 Statistical Analysis

Descriptive statistics were used to characterize unadjusted differences in demographics, CVD risk factors, and estimated 30-year CVD risk among patients with and without SMI and by SMI subtype. Chi-square analyses were used to assess the significance of unadjusted group differences in categorical variables, and general linear models for continuous variables with approximately normal distributions. Models were then adjusted for baseline demographics, including age, sex, race, ethnicity, and insurance status. For adjusted models with categorical dependent variables, binary, ordinal, or multinomial logistic regression models were used as appropriate. Generalized Poisson regression models estimated unadjusted and covariate-adjusted group differences in 30-year CVD risk. Interaction terms between demographic categories and SMI status were added to these models to estimate associations between SMI and 30-year CVD risk within demographic groups, and to assess whether the SMI-risk association was differential across demographic groups. As the data used in this study were collected as part of usual care, an absent value for a laboratory test was assumed to indicate that the test was not performed or collected, rather than performed but not entered in the EHR or missed by the clinical decision support

system. Chi-square tests were used to assess differential patterns of absent data. Absent data were not imputed and listwise deletion was used in regression analyses.

3.0 Results

A total of 997 individuals with a schizophrenia spectrum disorder, 3231 with bipolar disorder and 155,363 without SMI were included in the analysis (see Supplementary Figure S1 for participant flow diagram). Patients with SMI were slightly older and were more likely to be female, to self-identify as Black, Native-American or with multiple races, and to be insured by Medicaid (Table 1). Compared to patients with bipolar disorder, patients with schizophrenia spectrum disorders were more likely to be male, to identify as Black, and to be insured by Medicaid. Patients without SMI were more likely to have absent data for lipids and BMI (Supplemental Table S3). As BMI is included in the 30-year CVD risk equation, patients without SMI were also more likely to have absent 30-year risk scores compared to those with SMI (18.4% vs. 12.3% absent).

3.1 Unadjusted differences in estimated 30-year CVD risk and modifiable CVD risk factors

3.1.1 SMI compared to non-SMI.—Patients with SMI had significantly higher estimated 30-year CVD risk scores (mean 15.3%, SD 12.2%) compared to those without SMI (mean 10.8%, SD 9%, $p < 0.001$)) (Table 1). Regarding individual CVD risk factors, patients with SMI had higher rates of obesity (BMI ≥30) (47.1% vs. 28%), smoking (42.2% vs. 12.7%), hypertension (4.7 vs 1.8%) and diabetes (4% vs. 0.8%) than those without SMI. Patients with SMI were more likely to be treated with a statin (4.1% vs. 0.9%) and had higher triglycerides and HDL cholesterol, but not total cholesterol.

3.1.2 Specific SMI diagnoses.—CVD risk was generally higher in the schizophrenia spectrum group compared to the bipolar disorder group (Table 1). For example, mean estimated 30-year cardiovascular risk was 18.6% (SD 13.9%) for patients with schizophrenia spectrum disorder compared to 14.3% (SD 11.5%) for patients with bipolar disorder. Schizophrenia spectrum disorder patients had higher rates of hypertension (5.7% vs 4.4%), diabetes (6.7% vs. 3.1%), obesity (53.0% vs 45.3%), and smoking (49.7% vs 39.9%) compared to patients with bipolar disorder.

3.2 Adjusted differences in estimated 30-year CVD risk and modifiable risk factors

3.2.1 SMI compared to non-SMI.—After adjusting for age, race, ethnicity, sex, and insurance type, differences in CVD risk profiles between patients with and without SMI persisted (Table 2).

Patients with SMI had an adjusted 30-year CVD risk score of 12.0% (95% CI = 11.8, 12.2%) compared to 9.3% (95% CI = 9.3, 9.4%) for patients without SMI, resulting in a 28% higher relative risk (95% CI = 1.26, 1.30) (Table 3).

Patients with SMI had greater odds of being diagnosed with hypertension (adjusted prevalence 2.3% vs. 1.1%; OR 2.02 [95% CI = 1.7, 2.39]) and diabetes (1.4% vs 0.5%; OR 3.14 [95% CI = 2.59, 3.82]) compared to patients without SMI. There were no significant differences in A1c values for those with diabetes.

There were no differences in total cholesterol between patients with and without SMI; however, patients with SMI had lower HDL and higher triglycerides than patients without SMI (HDL: b = −4.5 [95% CI = −5.06, −3.93]; triglycerides: b = 35.06 [95% CI = 31.24, 38.93]).

High rates of obesity and smoking persisted for those with SMI in the adjusted models. The adjusted mean BMI for those with SMI was 30.7 (95% CI = 30.5, 30.9) compared to 27.6 95% CI = 27.6, 27.7) in those without SMI. Patients with SMI were more likely to have obesity (BMI ≥30) (42.3% vs. 27.5%, OR 1.93 [95% CI = 1.8, 2.07]) and were nearly five times more likely to be current smokers (OR 4.94 [95% CI = 4.6, 5.36]).

3.2.2 Specific SMI diagnoses.—As with unadjusted comparisons, patients with schizophrenia spectrum diagnosis continued to have higher CVD risk profiles than those with bipolar disorder (Table 3). Schizophrenia spectrum disorder was associated with a 31% higher CVD risk (95% CI = 1.28, 1.35), and bipolar disorder with a 27% higher CVD risk (95% CI = 1.25, 1.29), compared to those without SMI.

3.3 Adjusted estimated 30-year CVD risk among patient subgroups

We next examined whether the increased risk associated with having SMI varied across demographic subgroups, including race, ethnicity, sex, and age (Table 4).

3.3.1 Race.—The interaction between SMI diagnosis and race was assessed for groups with sufficient sample sizes, including Asian, Black, multiple races, and White. Within each race category, patients with SMI had greater estimated 30-year CVD risk than those without SMI. Specifically, 30-year CVD risk was increased for patients with SMI by 27% (95% CI = 1.18, 1.38) for Asian patients, 36% (95% CI = 1.32, 1.41) for Black patients, 39% (95% CI = 1.21, 1.60) for patients who identified with multiple races, and 26% (95% CI = 1.24, 1.29) for White patients.

The omnibus interaction between SMI status and race on 30-year CVD risk was significant (p=0.001). The association between SMI and 30-year CVD risk was 8% higher for Black relative to White patients (RR = 1.08 [95% CI = 1.04, 1.12]). No differential relationship between SMI and 30-year CVD risk was found among patients who self-identified as Asian or with multiple races.

3.3.2 Ethnicity.—Patients with SMI of both Hispanic and non-Hispanic ethnicity had higher 30-year CVD risk compared to patients of the same ethnicity without SMI (Hispanic: RR 1.27 [95% CI = 1.18, 1.38]; non-Hispanic RR 1.29 [95% CI = 1.27, 1.32]). The relationship between SMI and 30-year CVD risk was sufficiently smaller (RR 1.21 [95% CI = 1.16, 1.26]) among patients with unknown ethnicity that the comparison to non-Hispanic patients was statistically significant (RR 0.93, [95% CI = 0.89, 0.98]) as was the omnibus interaction (p<0.01).

3.3.3 Sex.—Both women and men with SMI had higher 30-year CVD risk compared to women and men without SMI, respectively (women: RR 1.35 [95% CI = 1.32, 1.38], men RR 1.23 [95% CI = 1.21, 1.26]). The increased risk associated with having SMI varied by

sex, with a 9% lower association between SMI and 30-year CVD risk among men relative to women (RR 0.91 [95% CI = 0.88, 0.94], p<0.001).

3.3.4 Age group.—Patients with SMI in both the 20-29 and 30-39-year age groups had higher 30-year CVD risk compared to patients without SMI in each respective age group. Although 30-39-year-old patients with SMI had a 30-year CVD risk of 18.6% [95% CI = 18.2, 19.1] compared to 7.6% [95% CI = 7.4, 7.9] for 20-29-year-old patients, the increased risk associated with SMI did not vary by age group.

4.0 Discussion

In this cross-sectional study comparing 4,228 young adults with SMI to 155,363 without, the estimated 30-year risk of a cardiovascular event was 28% higher for patients with SMI, and patients with SMI had higher rates of modifiable CVD risk factors. The increased 30-year CVD risk was more pronounced for Black individuals and women with SMI, highlighting possible intersectional health disparities. This is the largest study of CVD risk specifically focused on young adults with SMI and one of only a few to characterize long-term CVD risk in this population. While 30-year risk estimates are more accurate in young adults than the more commonly used 10-year profiles [19], even these estimates may underestimate the true long-term risk associated with SMI because they were not developed in SMI populations [29, 30]. Our results underscore the need for more effective strategies to prevent and manage CVD starting at younger ages for these patients.

High rates of obesity and smoking drove the increased 30-year CVD risk in our sample of young adults with SMI. In fully adjusted models, obesity rates were 42.3% for patients with SMI compared to 27.5% for those without. These rates are similar to those in middle aged and older samples of patients with SMI, yet substantially higher than typically found in recently diagnosed patients [31]. Previous research points to a trajectory of substantial initial weight gain following SMI diagnosis and psychotropic medication initiation, followed by gradual gain over the next 10-20 years [15, 32]. Accordingly, this could be a driver of the large difference in estimated 30-year CVD risk that we observed between those with SMI aged 20-29 (7.7%) compared to 30-39 years (18.1%). Patients with SMI also had significantly higher rates of diabetes (4% vs. 0.8%) and hypertension (4.7% vs. 1.8%). Although elevated, these rates are lower than in samples of older patients with SMI, where rates of diabetes may exceed 15% [33, 34]. As early weight gain predicts longer-term risk for obesity for patients with SMI [32, 35], prevention of weight gain in the first years of SMI treatment could have significant impacts on long-term health trajectories, including diabetes prevention. These results emphasize the importance of obesity prevention strategies for patients with SMI, including behavioral interventions [13], use of lower metabolic-risk antipsychotic medications [36, 37], and early initiation of adjunctive medications that may attenuate antipsychotic induced weight gain [38, 39]. Additionally, smoking is likely the largest driver of early mortality for patients with SMI [40], yet safe and effective evidenced-based smoking cessation treatments are grossly underutilized in this population [41].

We observed significant variation in the 30-year CVD risk associated with having SMI across race and sex subgroups. The increased risk associated with SMI was 8% higher

for Black compared to White patients. Although 30-year CVD risk was similar among Black and White patients without SMI in our sample, there is well-established evidence of the impact of structural racism on CVD risk for Black Americans [42, 43]. Additionally, individuals with SMI experience marginalization, social disadvantage, discrimination, and stigma, all of which are related to poorer health [44, 45]. Our results add to the small literature suggesting a possible “double jeopardy” for CVD risk for Black individuals living with SMI [44]. A review of US studies with small sample sizes suggested that Black individuals with SMI were at higher risk for obesity and diabetes [23]. One study found no difference in 10-year CVD risk between Black and White patients with SMI [46]. Our findings extend recent reports of increasing CVD risk factors for young adults in the US which disproportionately affect Black individuals [22], suggesting that Black individuals with SMI may be a particularly high-risk subgroup requiring targeted interventions.

Additionally, we found that SMI is associated with higher 30-year CVD risk to a greater degree for women than men. Sex and gender disparities in CVD risk have been established in the general population [47], with a growing literature suggesting that middle aged and older women with SMI may have higher relative risk of CVD incidence and risk factors compared to men [48-54]. Several potential drivers of sex and gender disparities in CVD risk for those with SMI could exist, including sex-hormone irregularities [55], higher rates of anxiety, depression, and early life traumatic experiences in women compared to men with SMI [56-58], and the additive impacts of socioeconomic disadvantage experienced by women [47].

Our results highlight the need to initiate CVD screening and intervention early for patients with SMI. Behavioral, pharmacological, and clinical decision support interventions have shown promising initial results in lowering total CVD risk and specific risk factors for those with SMI [6, 11, 13, 39], with some evidence suggesting these interventions may be most effective for younger adults [11, 38]. Yet few studies focused on CVD risk reduction have specifically targeted young adults with SMI [13], and evidence suggests young adults may have unique preferences, motivations, and barriers to engaging in health promotion interventions [59-62]. There is an urgent need for effective interventions tailored to young adults with SMI [63] to capitalize on a potential critical window for prevention and early intervention of cardiovascular disease [64].

4.1 Limitations

Our study has several potential limitations. Our sample consisted of patients receiving care in a large integrated healthcare system in the Midwest, with a large number insured with commercial insurance, which may limit generalizability to other clinical settings, geographic regions, and to patients with SMI with limited primary care access. Together, the effect of these limitations could be an underestimation of 30-year CVD risk in young adults with SMI. Absent lab values for lipids, especially for those without SMI, limited the sample size for comparisons on these measures. Similarly, those without SMI were more likely to have absent data for BMI, which is a variable in the 30-year risk equation. Patients with SMI may have routine lipid and weight monitoring if prescribed psychotropic medications, regardless of risk for dyslipidemia or obesity. Conversely, those without SMI undergoing

lipid and weight monitoring may have poorer cardiometabolic health than patients without SMI who did not have these measures collected, resulting in a higher risk non-SMI sample in this comparison. Therefore, our results potentially underestimate the difference in these risk factors and 30-year risk between those with and without SMI. We used hypertension diagnosis as a proxy for antihypertensive medication orders in the risk models, however as previously noted, evidence suggests that most patients (approximately 85%) who are aware of their hypertension diagnosis are treated [26], and the clinics in this study have high rates of concordance between hypertension diagnosis and treatment [27, 28]. Our sensitivity analysis also indicated that using diagnosis as a proxy for antihypertensive medications did not change the results, likely because rates of hypertension were low in both groups. Finally, we were unable to perform subgroup analyses for some racial groups due to small sample size.

5.0 Conclusions

We found a clinically and statistically significant 28% higher 30-year risk of having a cardiovascular event for young adults with SMI compared to those without SMI. The disparity in 30-year CVD risk associated with having SMI was even higher for Black individuals and women. Early and effective strategies for prevention and management of major CVD risk factors – especially smoking and elevated body mass index – are critically needed for young adults with SMI to reduce health disparities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Young adults with serious mental illness (SMI) are at elevated 30-year risk of cardiovascular disease (CVD)
- Young adults with SMI are almost 2x as likely to have obesity and 5x as likely to be smokers compared to those without SMI
- These disparities in 30-year CVD risk for young adults with SMI are even more pronounced in Black individuals and women
- CVD risk factors must be addressed as early as possible for young adults with SMI to reduce later morbidity and mortality

Table 1.

Demographics, 30-year Cardiovascular Risk, and Individual Modifiable Cardiovascular Risk Factors between Patients with and Without SMI

Patient characteristic	Bipolar Disorder				Schizophrenia Spectrum				SMI				No SMI				
	n = 3231 (2.0%)				*n* = 997 (0.6%)				*n* = 4228 (2.7%)				*n* = 155,363 (97.4%)				
	n	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***p* (SMI vs. No-SMI)**
Age			30.6	5.4			30.7	5.4			30.6	5.4			29.7	5.6	<.0001
Age, categorical																	<.0001
20-29	1335	41.3%			400	40.1%			1735	41.0%			75094	48.3%			
30-39	1896	58.7%			597	59.9%			2493	59.0%			80269	51.7%			
Female	2084	64.5%			359	36.0%			2443	57.8%			79186	51.0%			<.0001
Race																	<.0001
Asian	69	2.1%			75	7.5%			144	3.4%			12818	8.3%			
Black	396	12.3%			280	28.1%			676	16.0%			21387	13.8%			
Native American/Alaska Native	21	0.7%			11	1.1%			32	0.8%			462	0.3%			
Multiple	39	1.2%			16	1.6%			55	1.3%			971	0.6%			
Other	27	0.8%			10	1.0%			37	0.9%			3690	2.4%			
Unknown	125	3.9%			28	2.8%			153	3.6%			14174	9.1%			
White	2554	79.1%			577	57.9%			3131	74.1%			101861	65.6%			
Ethnicity																	<.0001
Hispanic	119	3.7%			32	3.2%			151	3.6%			6757	4.4%			
Non-Hispanic	2705	83.7%			841	84.4%			3546	83.9%			106807	68.8%			
Unknown	407	12.6%			124	12.4%			531	12.6%			41799	26.9%			
Insurance Type																	<.0001
Self-pay/Uninsured	87	2.7%			17	1.7%			104	2.5%			4944	3.1%			
Medicare Only	54	1.7%			46	4.6%			100	2.4%			167	62.6%			
Medicaid Only	1154	35.7%			405	40.6%			1559	36.9%			25770	16.6%			
Commercial Only	1026	31.8%			95	9.5%			1121	26.5%			104776	67.4%			

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Patient characteristic	Bipolar Disorder				Schizophrenia Spectrum				SMI				No SMI				
	n = 3231 (2.0%)				*n* = 997 (0.6%)				*n* = 4228 (2.7%)				*n* = 155,363 (97.4%)				
	n	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***p* (SMI vs. No-SMI)**
Other Only	27	0.8%			5	0.5%			32	0.8%			2242	1.4%			
Medicare + Medicaid	241	7.5%			250	25.1%			491	11.6%			703	0.5%			
Medicare + Commercial	16	0.5%			13	1.3%			29	0.7%			77	0.1%			
2 or more insurances	626	19.0%			166	16.7%			792	18.7%			16684	10.7%			
30-year risk[a] (n=130,276)	2818		14.3	11.5	868		18.6	13.9	3686		15.3	12.2	126590		10.8	9.0	<.0001
CVD	20	0.6%			3	0.3%			23	0.5%			204	0.1%			<.0001
Blood Pressure																	
HTN	142	4.4%			57	5.7%			199	4.7%			2773	1.8%			
SBP (n = 159546)			118.3	14.1			118.4	13.5			118.3	13.9			119.3	14.4	<.0001
DBP (n = 159548)			76.4	10.9			76.6	10.8			76.4	10.9			75.3	10.9	<.0001
Cholesterol																	
Total cholesterol (n = 43061)			178.2	37.1			175.9	38.2			177.6	37.4			177	35.2	0.47
LDL (statin only) (n = 1323)			102.1	39.4			94.6	31.5			98.4	35.8			118.3	46.8	<.0001
LDL (non-statin only) (n = 37768)			103.7	30.1			104.3	33.9			103.9	31.1			105.3	30.2	0.04
HDL (n = 43107)			48.4	15.7			42.9	12.7			46.8	15.2			50.4	14.6	<.0001
Triglycerides (n = 37904)			140	109			155.3	122.1			144.3	113.1			114	92.3	<.0001
Statin use	94	2.9%			80	8.0%			174	4.1%			1462	0.9%			<.0001
Glucose																	
DM	101	3.1%			67	6.7%			168	4.0%			1290	0.8%			<.0001
A1c (DM only)[b] (n=1330)			7.9	2.2			7.5	2.1			7.72	2.2			8.1	2.3	0.06
Weight																	
BMI (n=130532)			30.7	8.3			31.5	7.9			30.89	8.2			27.6	6.5	<.0001
BMI, categorical (n=130532)																	<.0001
<18.5, underweight	41	1.4%			11	1.3%			52	1.4%			2282	1.8%			
18.5-24.9, Normal	748	26.4%			181	20.8%			929	25.0%			48578	38.3%			

Patient characteristic	Bipolar Disorder				Schizophrenia Spectrum				SMI				No SMI				
	n = 3231 (2.0%)				*n* = 997 (0.6%)				*n* = 4228 (2.7%)				*n* = 155,363 (97.4%)				
	n	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***p* (SMI vs. No-SMI)**
25-29.9, Overweight	766	27.0%			218	25.0%			984	26.5%			40533	32.0%			
30-34.9, Obese I	545	19.2%			214	24.6%			759	20.5%			19909	15.7%			
35-39.9, Obese II	350	12.3%			129	14.8%			479	12.9%			8963	7.1%			
≥40, Obese III	389	13.7%			118	13.6%			507	13.7%			6557	5.2%			
Smoking status (n = 159573)[f]																	<.0001
Current smoker	1288	39.9%			498	49.7%			1783	42.2%			19721	12.7%			
Former smoker	768	23.8%			173	17.4%			941	22.3%			18498	11.9%			
Nonsmoker	1175	36.4%			329	33.0%			1504	35.6%			117126	75.4%			

Note. 30-year risk = Framingham 30-year cardiovascular disease risk score; BMI = body mass index; CVD = cardiovascular disease; DBP = diastolic blood pressure; DM = diabetes mellitus; HDL = high density lipoprotein; HTN = hypertension; LDL = low density lipoprotein; LL = lower 95% confidence limit; M = predicted mean; P% = predicted percent; SBP = systolic blood pressure; UL = upper 95% confidence limit

[a]30-year cardiovascular disease risk score only calculated for those without known CVD and with recorded age, sex, body mass index, systolic blood pressure, diabetes mellitus, hypertension status, and current smoking status (n = 130,276)

[b]Calculated for patients with DM who have available A1c tests within the last 5 years (n = 1,330)

Table 2.

Adjusted Estimates of 30-year Cardiovascular Risk and Individual Modifiable Cardiovascular Risk Factors between Patients with and Without SMI

Patient characteristic	Bipolar Disorder				Schizophrenia Spectrum				SMI				No SMI			
	n = 3231 (2.0%)				*n* = 997 (0.6%)				*n* = 4228 (2.7%)				*n* = 155,363 (97.4%)			
	P%	*M*	*95% LL*	*95% UL*	*P%*	*M*	*95% LL*	*95% UL*	*P%*	*M*	*95% LL*	*95% UL*	*PP*	*M*	*95% LL*	*95% UL*
30-year risk[a] (n=130,276)		11.9	11.7	12.1		12.3	11.9	12.6		12.0	11.8	12.2		9.3	9.3	9.4
Blood Pressure																
HTN	2.4%		2.0%	2.9%	2.0%		1.5%	2.7%	2.3%		1.9%	2.7%	1.1%		1.1%	1.2%
SBP (n = 159546)		120.1	119.6	120.5		118.3	117.5	119.2		119.7	119.3	120.1		119.3	119.2	119.4
DBP (n = 159548)		76.7	76.3	77.0		76.1	75.5	76.8		76.6	76.2	76.9		75.3	75.2	75.3
Cholesterol																
Total cholesterol (n = 43061)		179.8	178.1	181.5		176.8	174.2	179.4		179.0	177.6	180.4		177.2	176.8	177.5
LDL (statin only) (n = 1323)		103.9	93.7	114.1		93.5	82.3	103.8		98.7	91.5	106.0		118.2	115.6	120.8
LDL (non-statin only) (n = 37768)		106.5	104.3	105.4		104.3	101.9	106.7		105.9	104.6	107.2		105.4	105.0	105.7
HDL (n = 43107)		46.2	45.6	46.9		44.5	43.4	45.5		45.7	45.2	46.3		50.2	50.1	50.4
Triglycerides (n = 37904)		146.8	142.4	151.2		155.6	148.6	162.6		149.3	145.6	153.1		114.2	113.2	115.2
Statin use	1.2%		0.9%	1.5%	1.6%		1.2%	2.2%	1.3%		1.1%	1.6%	0.5%		0.4%	0.5%
Glucose																
DM	1.3%		1.1%	1.7%	1.6%		1.2%	2.1%	1.4%		1.2%	1.7%	0.5%		0.4%	0.5%
A1c (DM only)[b] (n=1330)		8.1	7.6	8.6		7.4	6.8	8.0		7.8	7.4	8.2		8.1	7.9	8.2
Weight																
BMI		30.5	30.3	30.8		31.1	30.7	31.6		30.7	30.5	30.9		27.6	27.6	27.7
BMI, categorical																
<18.5, underweight	0.9%		0.8%	1.0%	0.8%		0.7%	0.9%	0.9%		0.8%	0.9%	1.7%		1.6%	1.8%
18.5-24.9, Normal	24.9%		23.6%	26.2%	23.5%		23.4%	23.6%	24.5%		23.3%	25.6%	38.3%		38.2%	38.3%
25-29.9, Overweight	32.7%		31.4%	33.9%	32.2%		29.9%	34.5%	32.5%		31.3%	33.6%	32.9%		32.6%	33.2%
30-34.9, Obese I	21.4%		19.8%	23.1%	22.0%		19.0%	25.1%	21.6%		20.1%	23.1%	15.5%		15.2%	15.7%
35-39.9, Obese II	11.2%		10.1%	12.3%	11.8%		9.7%	13.9%	11.4%		10.4%	12.4%	6.8%		6.6%	6.9%
≥40, Obese III	9.0%		8.4%	9.6%	9.6%		8.6%	10.8%	9.2%		8.7%	9.8%	4.8%		4.8%	5.0%

Patient characteristic	Bipolar Disorder				Schizophrenia Spectrum				SMI				No SMI			
	n = 3231 (2.0%)				*n* = 997 (0.6%)				*n* = 4228 (2.7%)				*n* = 155,363 (97.4%)			
	P%	*M*	*95% LL*	*95% UL*	*P%*	*M*	*95% LL*	*95% UL*	*P%*	*M*	*95% LL*	*95% UL*	*PP*	*M*	*95% LL*	*95% UL*
BMI, binary																
>= 30, obese	41.4%		39.6%	43.3%	45.4%		41.9%	49.0%	42.3%		40.6%	44.0%	27.5%		27.3%	27.8%
Smoking status																
Current smoker	33.4%		31.7%	35.1%	34.2%		31.1%	37.2%	33.6%		32.1%	35.1%	11.9%		11.7%	12.1%
Former smoker	23.2%		21.7%	24.8%	19.7%		16.9%	22.5%	22.6%		21.2%	24.0%	11.0%		10.8%	11.1%
Nonsmoker	43.3%		41.5%	45.2%	46.1%		42.6%	45.2%	43.9%		42.2%	45.5%	77.1%		76.9%	77.4%

Note. 30-year risk = Framingham 30-year cardiovascular disease risk score; BMI = body mass index; CVD = cardiovascular disease; DBP = diastolic blood pressure; DM = diabetes mellitus; HDL = high density lipoprotein; HTN = hypertension; LDL = low density lipoprotein; LL = lower 95% confidence limit; M = predicted mean; P% = predicted percent; SBP = systolic blood pressure; UL = upper 95% confidence limit

[a]30-year cardiovascular disease risk score only calculated for those without known CVD and with recorded age, sex, body mass index, systolic blood pressure, diabetes mellitus, hypertension status, and current smoking status (n = 130,276)

[b]Calculated for patients with DM who have available A1c tests within the last 5 years (n = 1,330)

Table 3.

Adjusted Models Predicting Estimated 30-year Cardiovascular Risk and Individual Modifiable Cardiovascular Risk Factors between Patients with and Without SMI

Patient characteristic	SMI vs. No SMI					Bipolar Disorder vs. No SMI					Schizophrenia Spectrum vs. No SMI				
	OR	*b*	*95% LL*	*95% UL*	*p*	*OR*	*b*	*95% LL*	*95% UL*	*p*	*OR*	*b*	*95% LL*	*95% UL*	*p*
30-year risk[a] (Risk Ratio)	1.28		1.26	1.30	<.0001	1.27		1.25	1.29	<.0001	1.31		1.28	1.35	<.0001
CVD	1.78		1.08	2.95	0.025	2.24		1.34	3.72	0.002	0.65		0.20	2.17	0.48
Blood Pressure															
HTN	2.02		1.70	2.39	<.0001	2.11		1.75	2.54	<.0001	1.77		1.30	2.40	0.0003
SBP		0.37	−0.05	0.79	0.09		0.75	0.27	1.22	0.002		−0.99	−1.84	−0.13	0.024
DBP		1.28	0.94	1.62	<.0001		1.39	1.02	1.78	<.0001		0.88	0.19	1.57	0.012
Cholesterol															
Total cholesterol		1.82	0.40	3.24	0.012		2.66	1.01	4.33	0.002		−0.35	−2.97	2.27	0.79
LDL (statin only)		−19.46	−27.19	−11.74	<.0001		−14.28	−24.87	−3.69	0.008		−24.64	−35.22	−14.05	<.0001
LDL (non-statin only)		0.54	−0.74	1.82	0.41		1.13	−0.36	2.61	0.14		−1.04	−3.45	1.37	0.40
HDL		−4.50	−5.06	−3.93	<.0001		−4.01	−4.67	−3.35	<.0001		−5.76	−6.81	−4.72	<.0001
Triglycerides		35.08	31.24	38.93	<.0001		32.60	28.06	37.07	<.0001		41.38	34.34	48.42	<.0001
Statin use	2.90		2.38	3.53	<.0001	2.58		2.05	3.26	<.0001	3.64		2.72	4.89	<.0001
Glucose															
DM	3.14		2.59	3.82	<.0001	2.99		2.39	3.74	<.0001	3.50		2.59	4.73	<.0001
A1c (DM only)[b]		−0.29	−0.67	0.10	0.15		0.00	−0.49	0.50	0.99		−0.69	−1.25	−0.11	0.02
Weight															
BMI		3.03	2.82	3.24	<.0001		2.89	2.65	3.13	<.0001		3.49	3.06	3.92	<.0001
BMI, categorical	1.96		1.82	2.09	<.0001	1.91		1.79	2.05	<.0001	2.07		1.82	2.34	
BMI, binary	1.93		1.80	2.07	<.0001	1.86		1.72	2.01	<.0001	2.19		1.90	2.53	<.0001
Smoking status															<.0001
Current smoker	4.97		4.60	5.36	<.0001	5.00		4.59	5.45	<.0001	4.80		4.13	5.59	<.0001
Former smoker	3.62		3.31	3.96	<.0001	3.77		3.43	4.16	<.0001	3.00		2.47	3.67	<.0001
Nonsmoker	REF					REF					REF				

Note. 30-year risk = Framingham 30-year cardiovascular disease risk score; BMI = body mass index; CVD = cardiovascular disease; DBP = diastolic blood pressure; DM = diabetes mellitus; HDL = high density lipoprotein; HTN = hypertension; LDL = low density lipoprotein; LL = lower 95% confidence limit; M = predicted mean; P% = predicted percent; SBP = systolic blood pressure; UL = upper 95% confidence limit

[a]30-year cardiovascular disease risk score only calculated for those without known CVD and with recorded age, sex, body mass index, systolic blood pressure, diabetes mellitus, hypertension status, and current smoking status (n = 130,276)

[b]Calculated for patients with DM who have available A1c tests within the last 5 years (n = 1,330)

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Table 4.

Adjusted Estimated 30-year Cardiovascular Risk by Patient Subgroups and Interaction Between SMI Status and Subgroup

	SMI	No-SMI	Adjusted Risk Ratio for 30-year CVD risk score (SMI vs. No-SMI)		Adjusted Risk Ratio for 30-year CVD risk score (subgroup vs. reference)	
	Adjusted Mean (95% CI)	**Adjusted Mean (95% CI)**	**RR (95% CI)**	**p**	**RR (95% CI)**	**p**
Overall	12.0 (11.8 – 12.2)	9.3 (9.3 – 9.4)	1.28 (1.26 – 1.30)	<0.001		
RACE *						
Asian	11.0 (10.2 – 11.9)	8.6 (8.6 – 8.7)	1.27 (1.18 – 1.38)	<0.001	1.01 (0.93 – 1.09)	0.84
Black	12.7 (12.3 – 13.2)	9.4 (9.3 – 9.4)	1.36 (1.32 – 1.41)	<0.001	**1.08 (1.04 – 1.12)**	**<0.001**
Multiple	13.0 (11.4 – 14.9)	9.3 (9.0 – 9.7)	1.39 (1.21 – 1.60)	<0.001	1.10 (0.96 – 1.27)	0.17
White	11.9 (11.7 – 12.1)	9.4 (9.4 – 9.5)	1.26 (1.24 – 1.29)	<0.001	Reference	
ETHNICITY **						
Hispanic	12.4 (11.5 – 13.4)	9.8 (9.6 – 9.9)	1.27 (1.18 – 1.38)	<0.001	0.99 (0.91 – 1.07)	0.71
non-Hispanic	12.1 (11.9 – 12.3)	9.3 (9.3 – 9.4)	1.29 (1.27 – 1.32)	<0.001	Reference	
Unknown	11.2 (10.8 – 11.7)	9.3 (9.2 – 9.4)	1.21 (1.16 – 1.26)	<0.001	0.93 (0.89 - 0.98)	**0.002**
SEX ***						
Women	9.2 (9.0 – 9.4)	6.8 (6.8 – 6.8)	1.35 (1.32 – 1.38)	<0.001	Reference	
Men	16.0 (15.7 – 16.3)	13.0 (13.0 – 13.1)	1.23 (1.21 – 1.26)	<0.001	**0.91 (0.88 – 0.94)**	**<0.001**
AGE GROUP						
20-29	7.7 (7.5 – 7.9)	6.0 (6.0 – 6.0)	1.28 (1.25 – 1.32)	<0.001	1.00 (0.97 – 1.03)	0.98
30-39	18.1 (17.8 – 18.4)	14.1 (14.0 – 14.1)	1.28 (1.26 – 1.30)	<0.001	Reference	

Note. *Race x SMI interaction, p = 0.001

** Hispanic x SMI interaction p < 0.01

*** Sex x SMI interaction, p < 0.001

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