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ORIGINAL RESEARCH

Cardiovascular Risk for Patients With and Without Schizophrenia, Schizoaffective Disorder, or Bipolar Disorder

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BACKGROUND: To compare estimated 10-year and 30-year cardiovascular risk in primary care patients with and without serious mental illness (SMI; bipolar disorder, schizophrenia, or schizoaffective disorder).

METHODS AND RESULTS: All patients aged 18 to 75 years with a primary care visit in January 2016 to September 2018 were included and were grouped into those with and without SMI using diagnosis codes. Ten-year cardiovascular risk was estimated using atherosclerotic cardiovascular disease scores for patients aged 40 to 75 years without cardiovascular disease; 30-year cardiovascular risk was estimated using Framingham risk scores for patients aged 18 to 59 years without cardiovascular disease. Demographic, vital sign, medication, diagnosis, and health insurance data were collected from the electronic health record by a clinical decision support system. Descriptive statistics examined unadjusted differences, while general linear models examined differences for continuous variables and logistic regression models for categorical variables. Models were then adjusted for age, sex, race, ethnicity, and insurance type. A total of 11 333 patients with SMI and 579 924 patients without SMI were included. After covariate adjustment, 10-year cardiovascular risk was significantly higher in patients with SMI (mean, 9.44%; 95% CI, 9.29%–9.60%) compared with patients without SMI (mean, 7.99%; 95% CI, 7.97–8.02). Similarly, 30-year cardiovascular risk was significantly higher in those with SMI (25% of patients with SMI in the highest-risk group compared with 11% of patients without SMI; $P<0.001$). The individual cardiovascular risk factors contributing most to increased risk for those with SMI were elevated body mass index and smoking. Among SMI subtypes, patients with bipolar disorder had the highest 10-year cardiovascular risk, while patients with schizoaffective disorder had the highest 30-year cardiovascular risk.

CONCLUSIONS: The significantly increased cardiovascular risk associated with SMI is evident even in young adults. This suggests the importance of addressing uncontrolled major cardiovascular risk factors in those with SMI at as early an age as possible.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02451670.

Key Words: bipolar disorder ■ cardiovascular ■ risk factors ■ schizophrenia ■ serious mental illness

Cardiovascular disease is the leading cause of death for people with serious mental illness (SMI; bipolar disorder, schizophrenia, or schizoaffective disorder).[1] On average, people with SMI die 10 to 20 years earlier than the general population.[2] Cardiovascular risk prediction models such as the American College of Cardiology/American Heart Association cardiovascular disease (CVD) pooled 10-year risk equations were developed for the general adult population aged 40 to 75 years on the basis of age, race, sex, blood pressure (BP), BP medication status, diabetes status, smoking status, and lipoprotein levels. For those aged 20 to 59 years, the Framingham 30-year CVD risk equations can be used to estimate risk. Both of these equations predict likelihood

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CLINICAL PERSPECTIVE

What Is New?

- Adults of all ages with serious mental illness—bipolar disorder, schizophrenia, or schizoaffective disorder—had significantly increased cardiovascular risk compared with their peers.

What Are the Clinical Implications?

- It is important to address uncontrolled major cardiovascular risk factors in those with serious mental illness at as early an age as possible to reduce morbidity and mortality in this population.

Nonstandard Abbreviations and Acronyms

DBP	diastolic blood pressure
NIMH	National Institute of Mental Health
SBP	systolic blood pressure
SMI	serious mental illness

of a nonfatal myocardial infarction or stroke or cardiovascular death. Although these equations are known to be imperfect, they provide a standardized metric that can be used to assess the contributions of major uncontrolled cardiovascular risk factors to overall cardiovascular risk in those with and without SMI.

A handful of studies have examined cardiovascular risk estimates in those with and without SMI, but most have used control populations from separate studies or general population estimates.[3–5] This approach is suboptimal, as there can be underlying and unaccounted-for differences in such factors as race and ethnicity, socioeconomic status, or geographic representation between cohorts. As part of a cluster-randomized trial aimed at reducing cardiovascular risk in patients with SMI, we collected baseline cardiovascular risk estimates for patients with and without SMI from the same clinic populations, allowing for adjustment for baseline differences in age, sex, race, ethnicity, and insurance coverage.[6] These analyses are the focus of this article.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. This study was approved by the HealthPartners Institutional Review Board, and a waiver of informed consent was granted.

Study Design and Settings

Two health care delivery organizations (HealthPartners and Park Nicollet) in Minnesota and Wisconsin participated in a larger trial of clinical decision support in primary care clinics to reduce cardiovascular risk in patients with SMI.[7] Study enrollment occurred between January 20, 2016, and September 19, 2018.

Enrollment and Eligibility

Encounter data were collected for every patient who made a visit to a randomized primary care clinic during the study enrollment period. To be included in this study, patients had to have an index visit, defined as the first visit at a randomized primary care clinic during the enrollment period for which patients met the following criteria at the time of the index visit: (1) age 18 to 75 years; (2) no evidence of pregnancy; (3) no active cancer diagnosis; and (4) not residing in a nursing home or receiving palliative care (see Figure for participant flow).

To be included in the SMI group, patients had to have ≥2 outpatient diagnostic codes or ≥1 inpatient codes for SMI documented in the electronic health record (EHR) in the 2 years before the index date. SMI was defined as having bipolar disorder (*International Classification of Diseases, Ninth Revision* [*ICD-9*] codes of 296.00–296.89, 301.11; *International Classification of Diseases, Tenth Revision* [*ICD-10*] codes of F30.1–F31.9), schizophrenia (*ICD-9* codes of 295.0–295.6, 295.8–295.9, 297.1, 297.3, 298.8, 298.9, 301.22; *ICD-10* codes of F20.0–F24, F28–F29), or schizoaffective disorder (*ICD-9* code of 295.6; *ICD-10* codes of F25.0–F25.9). Patients with codes that crossed subcategories of SMI (schizophrenia+schizoaffective disorder, bipolar disorder+schizoaffective disorder, bipolar disorder+schizophrenia) were considered to have schizoaffective disorder. Patients who had only 1 outpatient SMI code were excluded from analyses. Patients who did not have any SMI codes were included in the non-SMI group. Patients who requested to be excluded from research studies were omitted from analyses.

Measures

Cardiovascular Risk

Total cardiovascular risk was calculated using 2 different equations. For patients aged 40 to 75 years without CVD, 10-year cardiovascular risk was estimated using the atherosclerotic cardiovascular disease (ASCVD) risk score.[6] This score theoretically ranges from 0 to 100 and corresponds to the percent likelihood of having a myocardial infarction, stroke, or cardiovascular death in the next 10 years. Patients with diagnosed ASCVD were excluded from

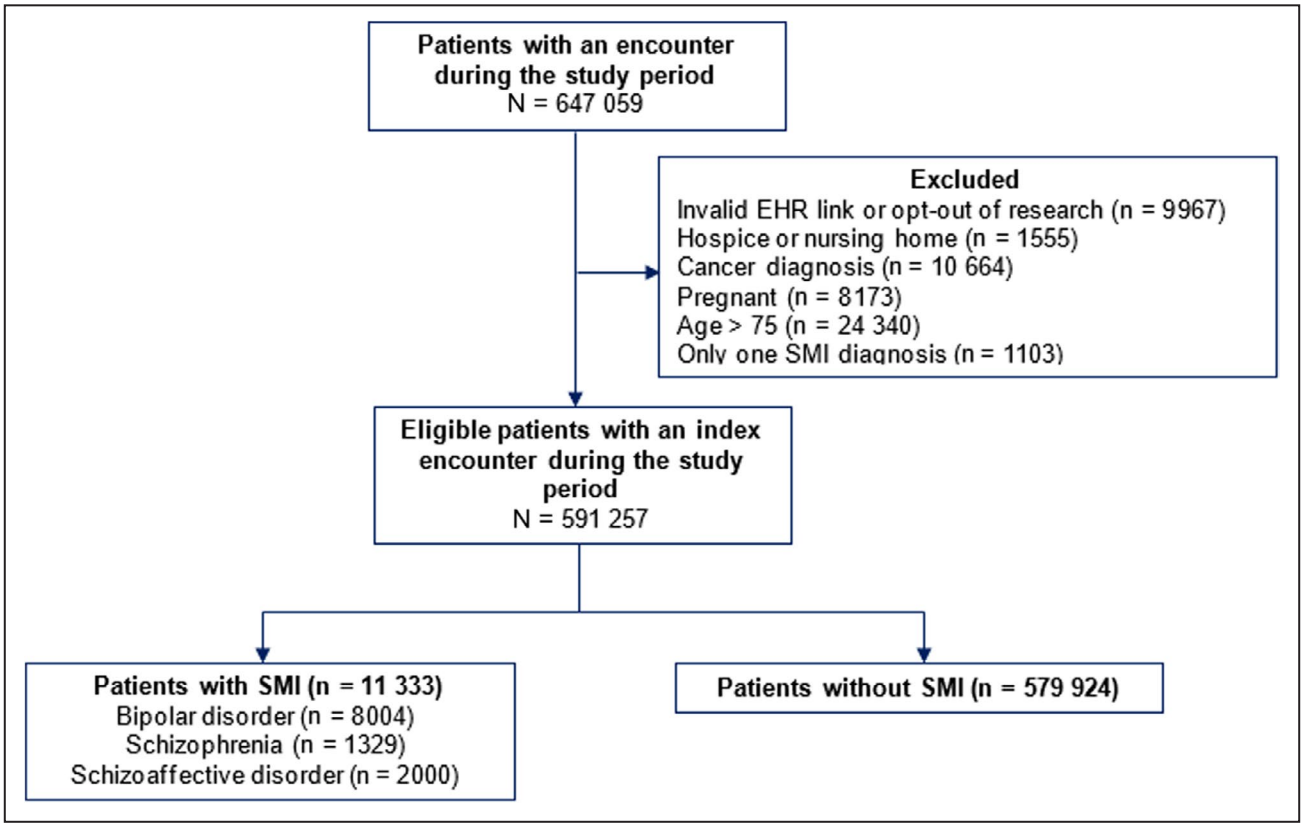

Figure. Study participant flow.
EHR indicates electronic health record; and SMI, serious mental illness.

analyses of total cardiovascular risk. For patients aged 18 to 59 without CVD, 30-year (lifetime) risk was estimated using the Framingham risk score.[8] Patients were categorized into one of five 30-year risk groups based on risk factors (BP, lipids, diabetes status, and smoking status): *all optimal risk factors* (BP <120/80 mm Hg, total cholesterol<180 mg/dL, nonsmoker, without diabetes), *≥1 not optimal risk factor* (systolic BP [SBP] 120–139 mm Hg, diastolic BP [DBP] 80–89 mm Hg, total cholesterol 180–199 mg/dL, nonsmoker, without diabetes), *≥1 elevated risk factor* (total cholesterol 200–239 mg/dL, SBP 140–159 mm Hg, DBP 90–99 mm Hg, nonsmoker, without diabetes), *1 major risk factor* (total cholesterol ≥240 mg/dL, SBP ≥160 mm Hg, DBP ≥100 mm Hg, smoker, or with diabetes), or *≥2 major risk factors*.

Six major modifiable cardiovascular risk factors (in addition to age, race, and sex) were captured by the clinical decision support system: blood pressure (SBP and DBP), lipids (total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, and statin use), glycemic control as measured by glycosylated hemoglobin, weight (body mass index as kg/m^2 [BMI]), smoking status, and aspirin use. For glycosylated hemoglobin and lipids, the most recent test in the past 5 years was used for analyses. Appropriateness of aspirin use was considered for patients with coronary heart disease according to US Preventive Services Task Force recommendations.[9] Treatment with an antihypertensive medication was also used in the 10-year American College of Cardiology/American Heart Association CVD risk equations.

Diagnoses

Diagnoses for coronary heart disease, CVD, hypertension, and diabetes were defined as having ≥2 outpatient diagnostic codes or ≥1 inpatient codes documented in the EHR in the 2 years before the index date. Coronary heart disease was identified with *ICD-9* codes of 410 to 414.9 and 429.2, and *ICD-10* codes of I20-I25.9. ASCVD was identified using *ICD-9* codes of 430 to 432.9, 433 to 434.91, 435, 435.8 to 435.9, 436, 440 to 440.4, and 445 to 445.89, and *ICD-10* codes of I63.02 to I63.9, I65 to I67.82, I70.0 to I70.92, and I74 to I74.9. Hypertension was identified via *ICD-9* codes of 401 to 405.9 and *ICD-10* codes of I10 to 15.9. Diabetes was identified using *ICD-9* codes of 250 to 250.93, 357.2, 362.01 to 362.07, and 366.41, and *ICD-10* codes of E10 to E11.9.

Table 1. Patients With and Without SMI: Demographics, Total Cardiovascular Risk, and Individual Modifiable Cardiovascular Risk Factors

Patient characteristic	Patients With SMI n=11 333				Patients Without SMI n=579 924				*P* value
	n	%	Mean	SD	n	%	Mean	SD	
Age, y			44.8	14.1			45.3	15.7	<0.0001
Age, y, categorical									<0.0001
18–34	3177	28.0			173 939	30.0			
35–49	3639	32.1			155 391	26.8			
50–64	3482	30.7			175 061	30.2			
65+	1035	9.1			75 533	13.0			
Sex, female	6550	57.8			313 345	54.0			<0.0001
Race									<0.0001
White	8808	77.7			446 603	77.0			
Black	1543	13.6			53 735	9.3			
Asian	335	3.0			32 621	5.6			
Native American/Alaska Native	91	0.8			1753	0.3			
Native Hawaiian/Pacific Islander	16	0.1			745	0.1			
Multiple	101	0.9			2342	0.4			
Other	89	0.8			7721	1.3			
Unknown	350	3.1			34 404	5.9			
Ethnicity									<0.0001
Hispanic	309	2.7			18400	3.2			
Non-Hispanic	9689	85.5			437 042	75.4			
Unknown	1335	11.8			124 481	21.5			
Insurance type									<0.0001
Self-pay/uninsured	215	1.9			13 307	2.3			
Medicare only	1209	10.7			49 154	8.5			
Medicaid only	3027	26.7			68 594	11.8			
Commercial only	2552	22.5			348 319	60.1			
Other only	78	0.7			5924	1.0			
Medicare+Medicaid	1970	17.4			6593	1.1			
Medicare+Commercial	345	3.0			17 774	3.1			
≥2 insurances	1937	17.1			70 259	12.1			
10-year ASCVD risk*			8.0	8.4			7.9	8.4	0.58
10-year ASCVD risk, categorical*									<0.0001
<5%	2503	48.0			120 890	49.8			
5%–9.9%	1292	24.8			53 506	22.1			
10%–14.9%	647	12.4			29 253	12.1			
15%–19.9%	322	6.2			17 040	7.0			
≥20%	454	8.7			22 002	9.1			
30-year lifetime risk†									<0.0001
All optimal risk factors	612	9.8			30 840	14.2			
≥1 not optimal risk factors	894	14.4			54 465	25.1			
≥1 elevated risk factors	231	3.7			19 393	8.9			
1 major risk factor	2844	45.8			85 887	39.6			
≥2 major risk factors	1636	26.3			26 536	12.2			
CHD	337	3.0			15 114	2.6			0.0152

(*Continued*)

Table 1. Continued

Patient characteristic	Patients With SMI n=11 333				Patients Without SMI n=579 924				*P* value
	n	%	Mean	SD	n	%	Mean	SD	
CVD	520	4.6			21 164	3.7			<0.0001
BP									
Hypertension	1684	14.9			76 314	13.2			<0.0001
High BP at visit (≥140/90 mm Hg)	1889	16.7			101 489	17.5			0.0213
SBP			121.4	16.4			123.6	16.7	<0.0001
DBP			77.1	11.5			76.7	11.3	0.0017
Cholesterol									
Total cholesterol			183.0	42.1			188.1	39.1	<0.0001
LDL (statin only)			94.2	36.7			98.9	35.0	<0.0001
LDL (nonstatin only)			109.5	32.4			115.6	31.6	<0.0001
HDL			48.3	15.8			52.3	16.5	<0.0001
Triglycerides			153.3	118.2			128.0	93.2	<0.0001
Statin use	2478	21.9			91 532	15.8			<0.0001
Glucose									
Diabetes	1553	13.7			37805	6.5			<0.0001
A_{1c} (Diabetes only)[c]			7.3	1.8			7.4	1.6	0.0019
A_{1c} (non DM only)[§]			5.6	0.8			5.7	0.7	0.0022
A_{1c} (DM only), categorical[‡]									<0.0001
<7.0	803	54.6			17 325	47.9			
7.0–7.9	319	21.7			9379	30.0			
8.0–8.9	126	8.6			4125	11.4			
≥9	222	15.1			5031	13.9			
Weight									
BMI			31.1	7.8			28.8	6.7	<0.0001
BMI, categorical									<0.0001
<18.5, underweight	117	1.2			6354	1.3			
18.5–24.9, normal	2075	21.1			146 034	30.0			
25–29.9, overweight	2779	28.2			161 544	33.2			
30–34.9, obese I	2282	23.2			96479	19.8			
35–39.9, obese II	1378	14.0			45 042	9.3			
≥40, obese III	1227	12.5			31 720	6.5			
Smoking status									<0.0001
Current smoker	4099	36.2			70 375	12.1			
Former smoker	3065	27.0			123 316	21.3			
Nonsmoker	4169	36.8			386 174	66.6			
Appropriate aspirin use[‖]	295	87.5			13 699	90.6			0.05

A1c indicates glycosylated hemoglobin; ASCVD, 10-year atherosclerotic cardiovascular disease risk; BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SMI, serious mental illness; and SBP, systolic blood pressure.

*ASCVD risk is calculated only for patients aged 40–75 years without known CVD (n=247 909).

†Thirty-year lifetime risk of CVD is calculated only for patients aged 18–59 years without known CVD (n=233 308).

‡Calculated for patients with diabetes who have available A_{1c} tests within the past 5 years (n=37 600).

§Calculated for patients without diabetes who have available A_{1c} tests within the past 5 years (n=33 055).

‖Aspirin use was calculated only for individuals with known CHD (n=15 451).

Data Sources

Much of the data collection was done by the clinical decision support tool itself, which harvested EHR data for each web service call, including vitals, medications, diagnoses, and orders. Data not routinely collected by the clinical decision support, such as race and ethnicity or insurance status, were harvested from the EHR data repository.

Statistical Analysis

Descriptive statistics were calculated to examine unadjusted differences in demographic characteristics (age, sex, race, ethnicity, health insurance coverage) and cardiovascular risk factors between patients with and without diagnosed SMI and among patients with different SMI diagnoses (bipolar disorder, schizophrenia disorder, and schizoaffective disorder). General linear models were used to examine differences among the groups for continuous variables (eg, 10-year cardiovascular risk), and χ^2 analyses were used to examine differences among categorical variables (eg, smoking status). Because of significant differences among groups in demographic characteristics, models were then adjusted for age, sex, race, ethnicity, and insurance coverage to predict differences in overall and individual cardiovascular risk factors. General linear models were used for continuous dependent variables (eg, 10-year ASCVD risk, BMI, SBP, DBP, and lipids). For categorical dependent variables, 3 types of logistic regression were used: (1) binary (for dichotomous outcomes, such as presence or absence of a diagnosis; (2) ordinal (for ranked categorical outcomes, such as 30-year lifetime risk or categorized versions of 10-year ASCVD risk, glycosylated hemoglobin, and BMI); and (3) multinomial (for categorical outcomes in the absence of an ordered list, including smoking status). In sensitivity analyses, we stratified models by age to determine the pattern of age differences between patients with and without SMI on 10-year and 30-year cardiovascular risk.

RESULTS

A total of 647 059 patients had primary care visits at a randomized primary care clinic during the study period (January 20, 2016, to September 19, 2018; Table 1, Figure). After applying study eligibility criteria, 591 257 patients were retained for analyses. Of note, 1103 patients were excluded from analyses because they had only 1 outpatient diagnosis of SMI. In the final sample, 11 333 patients (1.9%) were included in the SMI group. The majority of patients with SMI were diagnosed with bipolar disorder (n=8004; 70.6% of those with SMI), followed by schizoaffective disorder (n=2000; 17.6%) and schizophrenia (n=1329; 11.7%). On average, patients with SMI were younger and more likely to be women; to self-identify as Black, Native American/Alaskan Native, or of multiple races; and to be insured by Medicaid or Medicare than their counterparts.

Differences in Baseline Cardiovascular Risk Between Patients With and Without SMI

Unadjusted estimates suggested overall 10-year cardiovascular risk was not significantly different between patients with (mean, 8.0; SD, 8.4) and without SMI (mean, 7.9; SD, 8.4; Table 1). However, 30-year cardiovascular risk was significantly higher for patients with SMI in unadjusted estimates, with a greater proportion of patients with SMI having ≥1 major uncontrolled cardiovascular risk factor than patients without SMI. A greater proportion of patients with SMI were diagnosed with CVD (4.6% versus 3.7%; $P<0.0001$), coronary heart disease (3.0% versus 2.6%; $P=0.015$) or hypertension (14.9% versus 13.2%; $P<0.0001$). Patients with SMI were twice as likely to be diagnosed with diabetes, yet they were more likely to have a glycosylated hemoglobin <7.0% than patients without SMI. Patients with SMI generally had lower BP and cholesterol than patients without SMI, but these differences were small. Patients with SMI had significantly higher triglycerides and statin use than patients without SMI. There were no differences in appropriate aspirin use.

Patients with SMI had rates of elevated BMI and smoking. BMI was significantly higher in patients with SMI (mean, 31.1; SD, 7.8) compared with patients without SMI (mean, 28.8; SD, 6.7). Further, compared with patients without SMI, patients with SMI were more likely to have BMIs ≥30 (49.7% versus 35.6%; $P<0.0001$) and nearly twice the rate of obesity class III (BMI ≥40 kg/m^2). Patients with SMI were 3 times more likely to be current smokers (36.2%) than those without SMI (12.1%).

After adjusting for age, race, ethnicity, sex, and insurance coverage, many of the differences between patients with and without SMI remained the same or increased (Table 2, Table S1). Notably, estimated 10-year cardiovascular risk in those aged 40 to 75 years was significantly higher in patients with SMI than those without SMI (mean, 7.92; 95% CI, 7.90–7.95; $P<0.0001$) Similarly, for those aged 18 to 59 years, having a diagnosis of SMI was associated with 1.92 greater odds (95% CI, 1.82–2.01; $P<0.0001$) of being in a higher-risk group compared with patients without SMI.

Differences in Baseline Cardiovascular Risk Among Patients With Different SMI Diagnoses

Patients within the SMI group were then compared by specific SMI diagnosis: bipolar disorder, schizophrenia disorder, or schizoaffective disorder (see Table 3 for unadjusted estimates and Table 4 and Table S2 for adjusted estimates). Patients with bipolar disorder were younger and more likely to be women and White compared with patients with schizophrenia or schizoaffective disorder. In unadjusted estimates, patients with schizophrenia had the highest 10-year cardiovascular risk, and patients with bipolar disorder had the lowest risk. However, after adjusting for

Table 2. Patients With and Without SMI: Adjusted Estimates of Total Cardiovascular Risk and Individual Modifiable Cardiovascular Risk Factors

	Patients With SMI n=11 333				Patients Without SMI n=579 924				
			95% CI				95% CI		
Cardiovascular risk	Mean	PP	LL	UL	Mean	PP	LL	UL	*P* value
10-year ASCVD risk*	8.31		8.15	8.46	7.92		7.90	7.95	<0.0001
10-year ASCVD risk*, categorical									<0.0001
<5%		39.6	38.1	41.1		49.3	49.0	49.6	
5%–9.9%		45.9	44.4	47.4		40.5	40.2	40.8	
10%–14.9%		10.8	10.0	11.6		7.7	7.6	7.9	
15%–19.9%		2.5	2.3	2.8		1.7	1.7	1.8	
≥20%		1.2	1.1	1.3		0.8	0.8	0.8	
30-year lifetime risk†									<0.0001
All optimal risk factors		6.9	6.6	7.2		12.4	12.3	12.6	
≥1 not optimal risk factors		17.7	17.3	18.0		26.0	25.8	26.1	
≥ 1 elevated risk factors		8.0	7.1	8.9		9.7	9.4	9.9	
1 major risk factor		48.6	47.6	49.7		41.2	41.0	41.4	
≥2 major risk factors		18.8	18.1	19.6		10.8	10.7	10.9	
CHD		0.8	0.7	0.9		0.7	0.6	0.7	0.004
CVD		1.4	1.2	1.6		1.2	1.1	1.2	<0.0001
Blood pressure									
Hypertension		10.0	9.4	10.4		8.1	8.0	8.1	<0.0001
High BP at visit (≥140/90 mm Hg)		16.1	15.4	16.8		16.0	15.9	16.1	0.73
SBP	122.2		121.9	122.5	123.6		123.6	123.6	<0.0001
DBP	77.8		77.6	78.0	76.7		76.7	76.7	<0.0001
Cholesterol									
Total cholesterol	188.8		188.0	189.7	188.8		188.7	189.0	0.98
LDL (statin only)	92.3		90.9	93.8	99.0		98.7	99.2	<0.0001
LDL (nonstatin only)	114.7		113.9	115.5	115.8		115.7	116.0	0.007
HDL	49.5		49.1	49.8	52.0		51.9	52.0	<0.0001
Triglycerides	151.8		149.7	153.9	129.0		128.7	129.4	<0.0001
Statin use		12.8	12.3	13.5		7.4	7.3	7.5	<0.0001
Glucose									
Diabetes		7.6%	7.2%	8.0%		3.7%	3.6%	3.7%	<0.0001
A_{1c} (diabetes only)‡	7.14		7.05	7.22	7.41		7.39	7.42	<0.0001
A_{1c} (non-diabetes only)§	5.52		5.50	5.55	5.58		5.57	5.58	<0.0001
A1c (diabetes only), categorical‡									<0.0001
<7.0		55.4	52.9	57.9		48.3	47.8	48.8	
7.0–7.9		24.3	21.8	26.8		26.4	25.9	26.9	
8.0–8.9		9.6	7.9	11.2		11.5	11.1	12.0	
≥9		10.7	9.7	11.7		13.8	13.4	14.1	
Weight									
BMI	30.8		30.6	30.9	28.8		28.8	28.9	<0.0001
BMI, categorical									<0.0001
<18.5, underweight		0.7	0.6	0.7		1.2	1.2	1.2	
18.5–24.9, normal		19.3	19.2	19.3		29.8	29.6	29.9	
25–29.9, overweight		31.4	30.8	31.9		34.5	34.4	34.7	
30–34.9, obese I		24.8	23.9	25.6		19.6	19.5	19.8	

(*Continued*)

Table 2. Continued

Cardiovascular risk	Patients With SMI n=11 333				Patients Without SMI n=579 924				*P* value
	Mean	PP	95% CI		Mean	PP	95% CI		
			LL	UL			LL	UL	
35–39.9, obese II		13.5	12.8	14.1		8.8	8.7	8.9	
≥40, obese III		10.5	10.1	10.8		6.1	6.0	6.2	
Smoking status									<0.0001
Current smoker		27.6	26.8	28.4		11.6	11.6	11.7	
Former smoker		27.9	27.0	28.8		19.7	19.6	19.8	
Nonsmoker		44.5	43.5	45.5		68.7	68.5	68.8	
Appropriate aspirin use‖		90.4	87.2	93.0		91.1	90.6	91.5	0.69

Models adjusted for age, sex, race, ethnicity, and insurance coverage. A1c indicates glycosylated hemoglobin; ASCVD, 10-year atherosclerotic cardiovascular disease risk; BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein; LL, lower 95% confidence limit; PP, predicted probability (proportion); SBP, systolic blood pressure; SMI, serious mental illness; and UL, upper 95% confidence limit.

*ASCVD risk is calculated only for patients aged 40–75 years without known CVD (n=247 909).

†Thirty-year lifetime risk of CVD is calculated only for patients aged 18–59 without known CVD (n=233 308).

‡Calculated for patients with DM who have available A_{1c} tests within the past 5 years (n=37 600).

§Calculated for patients without DM who have available A_{1c} tests within the past 5 years (n=33 055).

‖Aspirin use was calculated only for individuals with known CHD (n=15 451).

demographics, patients aged 40 to 75 years with bipolar disorder had significantly greater 10-year cardiovascular risk than patients with schizophrenia or schizoaffective disorder. In contrast, after adjusting for demographics, patients aged 18 to 59 years with schizoaffective disorder had 30-year cardiovascular risk that was significantly higher than in patients with schizophrenia or bipolar disorder.

Sensitivity Analyses

To determine which covariate(s) contributed the most to cardiovascular risk differences between groups, models predicting differences for patients with and without SMI on 10-year cardiovascular risk and 30-year cardiovascular risk were run separately for each covariate. For both models, adjusting for sex or race and ethnicity alone had little impact on estimates. For example, for 10-year cardiovascular risk, adjusting for race and ethnicity slightly decreased cardiovascular risk estimates and adjusting for sex slightly increased cardiovascular risk estimates for patients with SMI. In contrast, adjusting for age greatly increased estimated 10-year cardiovascular risk (predicted mean, 9.30; 95% CI, 9.13–9.48) and adjusting for insurance type greatly decreased estimated 10-year cardiovascular risk (predicted mean, 6.11; 95% CI, 5.9–6.3).

To further understand the impact of age on cardiovascular risk, models predicting differences in 10-year cardiovascular risk and 30-year cardiovascular risk for patients with and without SMI were stratified by age (Table 5). For both the 10-year and 30-year cardiovascular risk measures, the differences in cardiovascular risk were greatest at younger ages, suggesting a clinically significant increased cardiovascular risk in young adult patients with SMI compared with young adult patients without SMI. The differences in 10-year cardiovascular risk between SMI and non-SMI patients were attenuated at older ages.

DISCUSSION

In this cross-sectional study of 11 333 people with SMI, patients with SMI had greater cardiovascular risk at younger ages than those without SMI. Patients with SMI who were aged 40 to 75 years without known CVD had a significantly elevated mean 10-year cardiovascular risk of 8.31, compared with 7.95 in those without SMI, after adjustment for age, sex, race, ethnicity, and insurance type. This difference in risk diminished with age. This observation might be related to increased treatment and control of cardiovascular risk factors in older patients with SMI. Alternatively, it may reflect survival bias, with patients with SMI dying at younger ages than those without SMI. For 30-year risk, calculated for those aged 18 to 59 years without known CVD, significantly more patients with SMI were in the highest tier of risk (≥ 2 major risk factors) compared with those without SMI (18.8% versus 10.8%; $P<0.0001$). This elevated 30-year risk in patients with SMI may be related to elevated rates of smoking and obesity in young adults with SMI, as well as delayed recognition or management of elevated cardiovascular risk factors in this population. Regardless, these data support the growing body of evidence that early identification and management of major cardiovascular risk factors in young adults with SMI is indicated and could

Table 3. Patients With SMI: Demographics, Total Cardiovascular Risk and Individual Modifiable Cardiovascular Risk Factors

Patient characteristic	Patients with bipolar disorder n=8004				Patients with schizophrenia disorder n=1329				Patients with schizoaffective disorder n=2000				*P* value
	n	%	Mean	SD	n	%	Mean	SD	n	%	Mean	SD	
Age, y			43.7*,†	14.1			47.8	14.5			47.1	13.5	<0.0001
Age, y, categorical													
18–34	2439*,†	30.5			308†	23.2			430	21.5			<0.0001
35–49	2673	33.4			346	26.0			620	31.0			
50–64	2212	27.6			506	38.1			764	38.2			
65+	680	8.5			1169	12.7			186	9.3			
Sex, female	5091*,†	63.6			450†	33.9			1009	50.5			<0.0001
Race													<0.0001
White	6585*,†	82.3			830†	62.5			1393	69.7			
Black	827	10.3			317	23.9			399	20.0			
Asian	139	1.7			107	8.1			89	4.5			
Native American/Alaska Native	65	0.8			11	0.8			15	0.8			
Native Hawaiian/Pacific Islander	10	0.1			3	0.2			3	0.2			
Multiple	72	0.9			6	0.5			23	1.2			
Other	58	0.7			11	0.8			20	1.0			
Unknown	248	3.1			44	3.3			58	2.9			
Ethnicity													<0.0001
Hispanic	216*,†	2.7			26†	2.0			67	3.4			
Non-Hispanic	6852	85.6			1097	82.5			1740	87.0			
Unknown	936	11.7			206	15.5			193	9.6			
Insurance type													<0.0001
Self-pay/uninsured	167*,†	2.1			22	1.7			26	1.3			
Medicare only	779	9.7			176	13.2			254	12.7			
Medicaid only	2150	26.9			354	26.7			523	26.2			
Commercial only	2297	28.7			97	7.3			158	7.9			
Other only	61	0.8			8	0.6			9	0.5			
Medicare+Medicaid	845	10.6			477	35.9			648	32.4			
Medicare+Commercial	249	3.1			31	2.3			65	3.3			
2 or more insurances	1456	18.2			164	12.3			317	15.9			
10-year ASCVD risk‡			7.4*,†	8.4			10.1†	9.0			8.5	7.9	<0.0001

(*Continued*)

Table 3. Continued

Patient characteristic	Patients with bipolar disorder n=8004				Patients with schizophrenia disorder n=1329				Patients with schizoaffective disorder n=2000				*P* value
	n	%	Mean	SD	n	%	Mean	SD	n	%	Mean	SD	
10-year ASCVD risk[‡], categorical													<0.0001
<5%	1793[*,†]	52.6			244[†]	34.4			466	42.4			
5%–9.9%	788	23.1			202	28.5			302	27.5			
10%–14.9%	377	11.1			112	15.8			158	14.4			
15%–19.9%	181	5.3			66	9.3			75	6.8			
≥20%	271	8.0			85	12.0			98	8.9			
30-year lifetime risk[§]													<0.0001
All optimal risk factors	448[*,†]	10.5			77[†]	10.7			87	7.1			
≥ 1 not optimal risk factors	674	15.8			86	11.9			134	11.0			
≥ 1 elevated risk factors	149	3.5%			35	4.8%			47	3.9%			
1 major risk factor	1989	46.5			320	44.3			535	43.9			
≥ 2 major risk factors	1014	23.7			205	28.4			417	34.2			
CHD	224	2.8			38	2.9			75	3.8			0.08
CVD	342[†]	4.3			64	4.8			114	5.7			0.02
Blood pressure (BP)													
Hypertension	1117[*,†]	14.0			233	17.5			334	16.7			0.0001
High BP at visit (≥140/90 mm Hg)	1369	17.1			221	16.6			299	15.0			0.07
SBP			118.3	14.2			118.6	13.8			118.1	13.6	0.84
DBP			76.4	11.0			75.6	10.7			76.9	11.1	0.19
Cholesterol													
Total cholesterol			178.2	37.1			175.2	38.1			177.4	39.3	0.45
LDL (statin only)			97.8[*,†]	38.0			88.4	33.6			89.5	34.6	<0.0001
LDL (nonstatin only)			110.4[*,†]	32.1			106.1	33.4			107.9	33.1	0.0014
HDL			48.1[*,†]	15.7			41.8	11.9			44.0	13.6	<0.0001
Triglycerides			143.0[†]	128.9			149.1	100.5			161.6	145.2	.02
Statin use	1486[*,†]	18.6			395	29.7			597	29.9			<0.0001
Glucose													
Diabetes	892[*,†]	11.1			239[†]	18.0			422	21.1			<0.0001
A_{1c} (DM only)[‖]			7.4	1.8			7.1	1.7			7.2	1.7	0.08

(*Continued*)

Table 3. Continued

Patient characteristic	Patients with bipolar disorder n=8004				Patients with schizophrenia disorder n=1329				Patients with schizoaffective disorder n=2000				*P* value
	n	%	Mean	SD	n	%	Mean	SD	n	%	Mean	SD	
A1c (non-diabetes only)[#]			5.6	0.9			5.6	0.7			5.6	0.8	0.75
A_{1c} (diabetes only), categorical[‖]													0.14
<7.0	437	52.2			141	59.8			225	56.7			
7.0–7.9	185	22.1			52	22.0			82	20.7			
8.0–8.9	78	9.3			20	8.5			28	7.1			
≥9	137	16.4			23	9.8			62	15.6			
Weight													
BMI			30.7*,†	8.2			30.0†	7.4			32.3	8.3	<0.0001
BMI, categorical													<0.0001
<18.5, underweight	81†	1.2			18†	1.6			18	1.0			
18.5–24.9, normal	1536	22.1			250	21.8			289	16.5			
25–29.9, overweight	1977	28.4			361	31.4			441	25.1			
30–34.9, obese I	1569	22.6			260	22.6			453	25.8			
35–39.9, obese II	944	13.6			145	12.6			289	16.5			
≥40, obese III	847	12.2			115	10.0			265	15.1			
Smoking status													<0.0001
Current smoker	2702*,†	33.8			549†	41.3			848	42.4			
Former smoker	2272	28.4			292	22.0			501	25.1			
Nonsmoker	3030	37.9			488	36.7			651	32.6			
Appropriate aspirin use**	190	84.8			70	93.3			35	92.1			0.10

A1c indicates glycosylated hemoglobin; ASCVD,10-year atherosclerotic cardiovascular disease risk; BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; and SMI, serious mental illness.

*Significantly different from schizophrenia ($P<0.05$).

†Significantly different from schizoaffective disorder ($P<0.05$).

‡ASCVD risk is calculated only for patients aged 40–75 years without CVD (n=5218).

§Thirty-year lifetime risk of CVD is calculated only for patients aged 18–59 years without CVD (n=6217).

‖Calculated for patients with diabetes who have available A_{1c} tests within the past 5 years (n=1470).

#Calculated for patients without diabetes who have available A_{1c} tests within the past 5 years (n=812).

**Aspirin use was calculated only for individuals with known CHD (n=337).

Table 4. Patients With SMI at Baseline: Adjusted Estimates of Total Cardiovascular Risk and Individual Modifiable Cardiovascular Risk Factors

Cardiovascular risk	Patients with bipolar disorder n=8004				Patients With schizophrenia disorder n=1329				Patients with schizoaffective disorder N=2000				*P* value
	M	PP	LL	UL	M	PP	LL	UL	M	PP	LL	UL	
10-year ASCVD risk[‡]	8.24*,†		8.03	8.47	7.22		6.28	7.71	7.76		7.37	8.14	0.0008
10-year ASCVD risk,[‡] categorical													0.0008
<5%		45.7*	43.6	47.8		53.6†	49.5	57.5		45.2	42.0	48.5	
5%–9.9%		38.9	36.8	41.0		34.7	30.7	38.7		39.1	35.9	42.4	
10%–14.9%		10.3	9.0	11.6		7.9	6.2	9.7		10.5	8.6		
15%–19.9%		2.9	2.3	3.5		2.2	1.5	2.8		3.0	2.2	3.7	
≥20%		2.2	1.9	2.5		1.6	1.3	2.0		2.2	1.9	2.7	
30-year lifetime risk[§]													0.0002
All optimal risk factors		8.5*,†	7.8	9.3		10.3†	9.0	11.9		7.4	6.6	8.4	
≥1 not optimal risk factors		14.0	13.2	14.7		16.1	14.6	17.6		12.6	11.6	13.5	
≥1 elevated risk factors		3.8	2.6	5.0		4.2	1.4	7.1		3.5	1.7	5.4	
1 major risk factor		49.1	47.8	50.4		48.5	45.4	51.6		49.0	47.0	51.1	
≥2 major risk factors		24.6	23.4	25.9		20.8	18.5	23.4		27.5	25.3	29.8	
CHD		1.4*	1.2	1.8		0.8†	0.6	1.2		1.4	1.0	1.9	0.018
CVD		2.4*	2.1	2.9		1.6†	1.2	2.2		2.3	1.8	2.9	0.027
BP													
Hypertension		11.9	11.0	12.8		10.3	8.9	12.0		10.9	9.6	12.3	0.14
High BP at visit (≥140/90 mm Hg)		17.1*,†	16.1	18.2		13.2	11.4	15.1		13.1	11.6	14.7	<0.0001
SBP	122.1*,†		121.8	122.5	118.8†		117.9	119.7	120.1		119.3	120.7	<0.0001
DBP	77.5*,†		77.3	77.7	75.2†		74.6	75.9	76.4		75.9	77.0	<0.0001
Cholesterol													
Total cholesterol	185.0*,†		183.9	186.2	177.7		175.0	180.3	180.1		178.0	182.2	<0.0001
LDL (statin only)	97.3*,†		95.9	99.3	90.3		86.4	94.1	89.7		86.7	92.8	<0.0001
LDL (nonstatin only)	110.0		109.0	111.1	106.8		104.2	109.4	108.7		106.7	110.7	0.071
HDL	49.2*,†		48.8	49.6	47.2		46.2	48.1	46.1		45.4	46.9	<0.0001
Triglycerides	152.4†		149.1	155.6	144.1†		136.5	151.8	159.3		153.4	165.3	0.006
Statin use		14.5†	13.5	15.5		15.8†	13.9	17.9		19.0	17.2	20.9	<0.0001
Glucose													
Diabetes		9.5†	8.8	10.3		9.6†	8.2	11.2		13.4	12.0	15.1	<0.0001
A_{1c} (diabetes only)[‖]	7.32		7.20	7.44	7.17		6.94	7.41	7.20		7.02	7.38	0.40
A_{1c} (non-diabetes only)[#]	5.51		5.48	5.54	5.45		5.39	5.52	5.49		5.44	5.55	0.36

(*Continued*)

Table 4. Continued

Cardiovascular risk	Patients with bipolar disorder n=8004				Patients With schizophrenia disorder n=1329				Patients with schizoaffective disorder N=2000				*P* value
	M	PP	LL	UL	M	PP	LL	UL	M	PP	LL	UL	
A_{1c} (diabetes only), categorical‖													0.166
<7.0		52.3	48.9	55.8		59.1	52.4	65.4		55.9	51.1	60.7	
7.0–7.9		23.1	19.6	26.5		21.0	14.5	27.6		22.1	17.2	26.9	
8.0–8.9		9.2	6.4	12.0		7.7	3.3	12.1		8.4	4.8	12.0	
≥9		15.4	13.4	17.8		12.2	9.4	15.6		13.6	11.2	16.5	
Weight													
BMI	31.0*,†		30.9	31.2	30.3†		29.8	30.8	32.0		31.6	32.4	<0.0001
BMI, categorical													<0.0001
<18.5, underweight		1.2*,†	1.0	1.4		1.4†	1.1	1.7		0.9	0.8	1.1	
18.5–24.9, normal		21.1	20.2	22.0		23.6	23.3	23.9		17.3	17.1	17.5	
25–29.9, overweight		28.7	27.8	29.7		29.7	27.6	31.8		26.5	25.1	27.9	
30–34.9, obese I		23.4	22.2	24.6		22.4	19.7	25.1		24.6	22.4	26.7	
35–39.9, obese II		13.7	12.8	14.7		12.5	10.5	14.5		15.9	14.0	17.8	
≥40, obese III		11.9	11.2	12.6		10.4	9.3	11.6		14.8	13.6	16.0	
Smoking status													<0.0001
Current smoker		34.3*,†	33.0	35.6		36.3†	33.4	39.1		38.6	36.2	40.9	
Former smoker		28.6%	27.3%	30.0%		22.6%	20.1%	25.1%		25.4%	23.3%	27.5%	
Nonsmoker		37.2	35.9	38.4		41.1	38.2	44.1		36.0	33.8	38.3	
Appropriate aspirin use**,††		91.2†	0.1	100		95.3	0.2	100		97.7	0.5	100	0.048

Models adjusted for age, sex, race, and ethnicity. A1c indicates glycosylated hemoglobin; ASCVD, 10-year atherosclerotic cardiovascular disease risk; BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PP, predicted probability (percent); SBP, ystolic blood pressure; and SMI, serious mental illness.

*Significantly different from schizophrenia ($P<0.05$).

†Significantly different from schizoaffective disorder ($P<0.05$).

‡ASCVD risk is calculated only for patients aged 40–75 years without CVD ($n=5218$).

§Thirty-year lifetime risk of CVD is calculated only for patients aged 18–59 years without CVD (n=6217).

‖Calculated for patients with diabetes who have available A_{1c} tests within the past 5 years (n=1470).

#Calculated for patients without diabetes who have available A_{1c} tests within the past 5 years (n=812).

**Aspirin use was only calculated for individuals with known CHD (n=337).

††Separation occurred with this model, which inflated the confidence limits.

Table 5. Cardiovascular Risk for Patients With SMI and Without SMI, Stratified by Age

Cardiovascular risk	β	LL	UL	*P* value
10-year ASCVD risk*				
Age 40–49 y, n=64 240	1.46	1.30	1.62	<0.0001
Age 50–59 y, n=86 425	1.70	1.46	1.93	<0.0001
Age 60–69 y, n=74 355	0.76	0.31	1.20	0.0008
Age 70–75 y, n=22 889	−0.04	−1.26	1.18	0.95
	OR	**LL**	**UL**	***P* value**
30-year lifetime risk*				
Age 18–29 y, n=24 960	2.98	2.64	3.37	<0.0001
Age 30–39 y, n=46 559	3.20	2.92	3.52	<0.0001
Age 40–49 y, n=65 281	2.89	2.62	3.13	<0.0001
Age 50–59 y, n=86 508	0.45	0.41	0.48	<0.0001

β indicates unstandardized regression coefficient; LL, 95% lower confidence limit; OR, odds ratio; SMI, serious mental illness; and UL; 95% upper confidence limit.

*10-year ASCVD risk and 30-year lifetime risk are calculated only for patients without CVD.

have a substantive impact on subsequent adverse cardiovascular outcomes in this group of young adults.[10]

Estimated 10-year cardiovascular risk in unadjusted models was highest for patients with schizophrenia, followed by schizoaffective disorder and bipolar disorder. However, because patients with bipolar disorder were younger, more likely to be women, and more likely to be White, adjustment for age, sex, race, and ethnicity resulted in 10-year cardiovascular risk estimates that were more similar across SMI subgroups. The adjusted mean estimated 10-year cardiovascular risk for patients with SMI of 8.31 is similar to those reported in previous studies.[3,11–13] Of note, inclusion of patients with mental health diagnoses other than SMI in the "patients without SMI" group may make our estimates of elevated cardiovascular risk for "patients with SMI" conservative.

To our knowledge, this is the first study examining estimated 30-year (lifetime) cardiovascular risk in a large outpatient sample of patients with SMI, and the differences in 30-year risk between patients with and without SMI are striking, with considerably higher 30-year risk for patients with SMI in both unadjusted and adjusted models. As noted above, in adjusted models, 18.8% of those with SMI were at the highest level of 30-year risk (ie, ≥2 major risk factors) compared with only 10.8% of those without SMI. Among those with SMI, nearly 3 times as many patients with schizoaffective disorder were at the highest level of 30-year risk compared with those without SMI (27.5%; 95% CI, 25.3%–29.8%), while the rates of patients with bipolar disorder (24.6%; 95% CI, 23.4%–25.9%) and schizophrenia (20.8%; 95% CI, 18.5%–23.4%) with this highest level of risk were about twice that of patients without SMI. Given evidence that people with SMI die significantly earlier than their peers,[2] increased time spent in better midlife cardiovascular health has significant benefits for cardiovascular outcomes later in life for the general population,[14] and interventions to address cardiovascular risk for patients with SMI are maximally beneficial when initiated at younger ages,[10] we strongly encourage health care systems and clinicians to use 30-year/lifetime estimated cardiovascular risk to identify at-risk patients with SMI who are aged <40 years for early intervention. The more widely used 10-year cardiovascular risk equations are not valid until age 40 years, and delayed clinical recognition and control of cardiovascular risk factors for many years may be a major factor driving excess mortality in those with SMI. Of note, Osborn and colleagues have developed and tested 10-year cardiovascular risk prediction models meant to be specific to people with SMI, and we look forward to studies validating and implementing these models.[15] However, we think our findings stress the importance of also using 30-year risk models in this highly at-risk SMI population.

Many previous studies of cardiovascular risk for people with SMI have included only inpatients with SMI, cohorts that tend to have more severe SMI and more medical comorbidities than outpatients with SMI, or included patients with major depression in their definition of SMI.[16] This study, in contrast, includes a large sample of community-dwelling US outpatients with SMI (defined as having bipolar disorder, schizophrenia, or schizoaffective disorder but not unipolar depression). Accordingly, our findings are likely more representative of cardiovascular risk in community populations with bipolar disorder or psychosis. These estimates of cardiovascular risk are still significantly higher than the general population.

Additionally, there are few studies that estimate cardiovascular risk in people both with and without SMI in the same study sample. Several studies, for example, compare cardiovascular risk in people with SMI in their sample to a National Health and Nutrition Examination

study sample.[3–5] Such comparisons are potentially more fraught with volunteer and other bias and challenges in adjustment for sample characteristics; our study sample includes people with and without SMI cared for in the same outpatient care setting. However, despite inclusion of a large sample of people with SMI and without SMI insured by Medicaid or Medicare in additional to commercial insurance, we acknowledge that the patients receiving care in an integrated health care system may be relatively healthier than those seeking care in other settings, such as safety net clinics. The likely effect of this would be to make our estimates of cardiovascular risk associated with SMI more conservative.

By examination of the absolute differences in proportions of people with and without SMI not at goal for individual cardiovascular risk factors, the risk factors contributing most to increased cardiovascular risk for those with SMI were elevated BMI and smoking. In unadjusted estimates, nearly 80% of patients with SMI had a BMI >24.9 compared with 69% of patients without SMI, with 50% of patients with SMI meeting criteria for obesity (BMI ≥30) compared with 36% of patients without SMI (Table 1). This prevalence of obesity in patients with SMI is in line with other studies[17–20] that have reported rates generally ranging from 40% to 55%. Patients with schizoaffective disorder in our study had the highest mean BMI, at 32.3, and the highest percentage of patients with a BMI ≥40 at 15%. Of patients with SMI, 36% were current smokers compared with 12% of patients without SMI. Of note, this smoking prevalence for patients with SMI is lower than most previously reported rates (ranging from 49% to 68%)[15,19,20] and may reflect increasing access to smoking cessation strategies for those with SMI in our study population.[21,22] This is admittedly speculation, however, as we did not collect data on smoking cessation medication use in this study.

Regarding other individual cardiovascular risk factors, patients with SMI had double the rate of diagnosed diabetes than did patients without SMI (13.7% versus 6.5%; $P<0.0001$). These rates are similar to those reported in other studies[19,23,24] but lower than found in a large outpatient primary care sample in England, where 18.9% of patients with schizophrenia and 13.5% of patients with bipolar disorder were reported to have diabetes.[19,20] Patients with SMI had statistically but not clinically meaningfully lower total cholesterol compared with those without SMI, but clinically meaningful higher triglyceride levels (151.8 versus 129.0; $P<0.0001$), which would be consistent with metabolic changes associated with increased rates of obesity and diabetes. Notably, patients with SMI were more likely to be prescribed a statin than were those without SMI (12.8% versus 7.4%; $P<0.0001$). Overall, 10% of patients with SMI were diagnosed with hypertension. Estimates of hypertension for people with SMI have varied widely in other studies, with reported prevalence ranging from 19% to 61%.[16,19,20]

This study focuses on the contribution of conventional major cardiovascular risk factors to overall cardiovascular risk for people with SMI. Our data are consistent with previous studies that found inferior preventative cardiovascular care and decreased or delayed treatment when cardiovascular risk is identified in those with SMI.[25–28] However, it is widely recognized that a number of other factors, including increased alcohol use, lower physical activity, poorer socioeconomic status, and suboptimal diet, also contribute to the observed excess burden of CVD in SMI patients.[29] Additionally, there is evidence of overlap between genetic risk for SMI and risk for hypertension, cardiac dysrhythmia, nonrheumatic heart disease, and type 1 diabetes.[30] Moreover, many medications used to treat SMI may increase cardiovascular risk, largely through cardiometabolic side effects.[31]

We have already mentioned that a potential limitation of this study is its conduct in an integrated health care system, which may limit its generalizability to other settings. Other potential limitations include those inherent in observational studies, including possible classification bias related to SMI status when using EHR data and measured and unmeasured confounders that may affect findings. Additionally, we did not have data on some social determinants of health, such as relationship status, exercise, institutionalization, income, or education, all of which are significant predictors of cardiovascular health. We also did not take use of medications into account. Nonetheless, we submit that the benefits of understanding baseline cardiovascular risk in a large outpatient sample of patients with and without SMI using rich and reasonably complete EHR data outweigh these potential limitations.

In conclusion, patients with SMI have elevated 10-year and 30-year CV risk compared with patients without SMI. Given the shortened life span of people with SMI, and the considerable contribution of CV disease to earlier mortality, the data support more thorough screening and effective management of major cardiovascular risk factors for patients with SMI starting at a younger age, especially in those aged <40 years. Use of 30-year cardiovascular risk estimates to help guide decisions about cardiovascular risk factor management and prevention in young adults with SMI may be important to decreasing rates of cardiovascular morbidity and mortality.

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Supplemental Material

Tables S1–S2

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SUPPLEMENTAL MATERIAL

Table S1: Adjusted differences in total CV risk and individual modifiable CV risk factors between patients with and without SMI

			95% CI		
Cardiovascular Risk	***OR***	***β***	***LL***	***UL***	***p***
10-year ASCVD risk*		0.38	0.23	0.54	<.0001
10-year ASCVD risk*, categorical	1.48		1.39	1.58	<.0001
30-year Lifetime risk†	1.92		1.82	2.01	<.0001
CHD	1.19		1.06	1.36	.004
CVD	1.23		1.12	1.36	<.0001
Blood Pressure					
HTN	1.26		1.19	1.33	<.0001
High BP at visit (≥140/90 mmHg)	1.01		0.96	1.06	.73
SBP		-1.43	-1.73	-1.14	<.0001
DBP		1.07	0.86	1.28	<.0001
Cholesterol					
Total cholesterol		0.01	-0.86	0.88	.98
LDL (statin only)		-6.65	-8.12	-5.17	<.0001
LDL (non-statin only)		-1.14	-1.97	-0.31	.007
HDL		-2.51	-2.86	-2.17	<.0001
Triglycerides		22.78	20.65	24.92	<.0001
Statin use	1.85		1.75	1.95	<.0001
Glucose					
DM	2.16		2.03	2.29	<.0001
A1c (DM only)‡		-0.27	-0.35	-0.18	<.0001
A1c (non DM only)§		-0.05	-0.08	-0.03	<.0001
A1c (DM only), categorical‡	0.75		0.68	0.83	<.0001
Weight					
BMI		1.94	1.81	2.08	<.0001
BMI, categorical	1.80		1.74	1.87	<.0001
Smoking status					<.0001
Current smoker	3.66		3.50	3.84	
Former smoker	2.18		2.08	2.29	
Nonsmoker	REF				
Appropriate aspirin use‖	0.93		0.66	1.31	.69

Note. Models adjusted for age, sex, race, ethnicity and insurance coverage.

ASCVD = 10-year atherosclerotic cardiovascular disease risk; BMI = Body mass index; CHD = Coronary Heart Disease; 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; REF = Reference group; SBP = Systolic blood pressure; UL = Upper 95% Confidence Limit

*ASCVD risk is only calculated for patients age 40-75 without known CVD (*n* = 247909)

†30 year lifetime risk of cardiovascular disease is only calculated for patients ages 18-59 without known CVD (*n* = 233308)

‡Calculated for patients with DM who have available A1c tests within the last 5 years (*n* = 37600)

§Calculated for patients without DM who have available A1c tests within the last 5 years (*n* = 33055)

‖Aspirin use was only calculated for individuals with known CHD (*n* = 15451)

Table S2: Adjusted differences in total CV risk and individual modifiable CV risk factors among people with SMI

Cardiovascular Risk	Schizophrenia				Schizoaffective				*p*
	OR	***β***	***LL***	***UL***	***OR***	***β***	***LL***	***UL***	
10-year ASCVD risk‡		-1.02	-1.58	-0.47		-0.49	-0.95	-0.04	. 0008
10-year ASCVD risk,‡ categorical	0.73		0.61	0.87	1.02		0.88	1.18	. 0008
30-year Lifetime risk§	0.81		0.69	0.95	1.16		1.02	1.32	. 0002
CHD	0.59		0.40	0.86	0.97		0.73	1.29	. 018
CVD	0.67		0.50	0.90	.0.96		0.75	1.21	. 027
Blood Pressure									
HTN	0.85		0.71	1.02	0.90		0.78	1.05	. 14
High BP at visit (≥140/90 mmHg)	0.74		0.62	0.87	0.73		0.63	0.84	<.0001
SBP		-3.35	-4.33	-2.37		-2.13	-2.94	-1.32	<.0001
DBP		-2.26	-2.97	-1.55		-1.07	-1.65	-0.48	<.0001
Cholesterol									
Total cholesterol		-7.37	-10.3	-4.39		-4.95	-7.38	-2.53	<.0001
LDL (statin only)		-7.04	-11.51	-2.58		-7.59	-11.30	-3.87	<.0001
LDL (non-statin only)		-3.24	-6.09	-0.38		-1.36	-3.66	0.93	.071
HDL		-2.05	-3.11	-0.99		-3.10	-3.97	-2.24	<.0001
Triglycerides		-8.23	-16.70	0.25		6.95	0.07	13.83	.006
Statin use	1.11		0.95	1.30	1.38		1.21	1.57	<.0001
Glucose									
DM	1.01		0.85	1.21	1.48		1.28	1.70	<.0001
A1c (DM only)‖		-0.15	-0.42	0.12		-0.12	-0.34	0.09	.40
A1c (non DM only)#		-0.05	-0.13	0.02		-0.02	-0.08	0.05	.36
A1c (DM only), categorical‖	0.76		0.56	1.03	0.86		0.68	1.10	.166
Weight									
BMI		-0.73	-1.25	-0.22		0.98	0.56	1.40	<.0001
BMI, categorical	0.86		0.76	0.97	1.29		1.17	1.42	<.0001
Smoking status									<.0001
Current smoker	0.96		0.83	1.11	1.16		1.02	1.31	
Former smoker	0.72		0.61	0.85	0.92		0.80	1.05	
Nonsmoker	REF				REF				
Appropriate aspirin use** ††	1.96		0.53	7.27	4.12		1.27	13.32	.048

Note. Models adjusted for age, sex, race, ethnicity, and insurance coverage. ASCVD = 10-year atherosclerotic cardiovascular disease risk; B = unstandardized regression coefficient; BMI = Body mass index; CHD = Coronary Heart Disease; CVD = Cardiovascular Disease; DBP = Diastolic blood pressure; DM = Diabetes Mellitus; HDL = high density lipoprotein; HTN = Hypertension; LDL = low density lipoprotein; OR = Odds Ratio; SBP = Systolic blood pressure

* Significantly different from schizophrenia ($p < .05$)

† Significantly different from schizoaffective disorder ($p < .05$)

‡ ASCVD risk is only calculated for patients age 40-75 without CVD (*n* = 5218)

§ 30 year lifetime risk of CVD is only calculated for patients ages 18-59 without CVD (*n* = 6217)

‖ Calculated for patients with DM who have available A1c tests within the last 5 years (*n* = 1470)

Calculated for patients without DM who have available A1c tests within the last 5 years (*n* = 812)

** Aspirin use was only calculated for individuals with known CHD (*n* = 337)

†† Separation occurred with this model, which inflated the confidence limits