Cardiovascular Disease in Individuals with Severe Mental Illness

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Abstract

Individuals with severe mental illness (SMI) exhibit significant social and functional impairments, interfering with normal daily living. These individuals exhibit heightened cardio-metabolic vulnerability and often face disparities in access and quality of care. Individuals with SMI are less likely to be screened for cardiovascular (CV) risk factors and are less likely to receive guideline-directed treatment once these risk factors have been identified, suggesting systemic bias. This thesis aims to explore the bidirectional association between SMI and cardiovascular disease (CVD), focusing on primary prevention strategies and overcoming access barriers to quality care.

The aim of our Cardio-Psychiatry clinic was to improve access to preventative services in this highly vulnerable population. Patients were referred from outpatient psychiatry clinics to a newly created Cardio-Psychiatry clinic for CV risk screening and treatment. We found newly diagnosed CV risk factors in over 50% of participants. Interestingly, the majority of these individuals were followed by a primary care practionner. These findings accentuate the increased cardiometabolic risk among individuals with SMI and also highlight the care disparity in this population. Proactive identification of CV risk factors, CV risk determination, and initiation/follow-up of appropriate therapy is crucial in optimizing patient outcomes in individuals with SMI.

A systematic review of American and European professional cardiology and psychiatry society guidelines exposed gaps in care recommendations for CV care in psychiatric patients and psychiatric care in CV patients. Less than 40% of CV guidelines included psychiatric considerations compared to 77% of psychiatric guidelines having CV recommendations. While comprehensive data regarding the cardiometabolic vulnerability of individuals with SMI is available, the lack of expert guidance on the management of CV disease in this population is

concerning. Our findings support further professional society recommendations on the managing of CV conditions in SMI and SMI considerations in CV care.

Cardio-Psychiatry is an emerging field of healthcare delivery that will require a substantial level of multidisciplinary collaboration to effect change and improve outcomes for this at-risk population. There is a need for future clinical and research efforts to facilitate the development of effective interdisciplinary care models.

Résumé

Les personnes souffrant d'une maladie mentale grave présentent d'importantes déficiences sociales et fonctionnelles qui les empêchent de mener une vie quotidienne normale. Non seulement ces personnes présentent une vulnérabilité cardio-métabolique importante, mais elles sont également confrontées à des inégalités en matière d'accès et de qualité des soins. Les personnes atteintes de maladies mentales graves sont moins fréquemment examinées pour les facteurs de risque cardiovasculaire (CV) et reçoivent moins souvent un traitement conforme aux recommandations, ce qui suggère une forme de bias systémique. Cette thèse vise à explorer l'association réciproque entre les maladies mentales graves et les maladies cardiovasculaires, en se concentrant sur les stratégies de prévention primaire et sur les obstacles à l'accès à des soins de qualité.

L'objectif de notre clinique de cardio-psychiatrie était d'améliorer l'accès aux services de prévention dans cette population très vulnérable. Les patients ont été orientés des cliniques psychiatriques externes vers une clinique cardio-psychiatrique nouvellement créée pour le dépistage et le traitement des risques CV. Nous avons trouvé des facteurs de risque CV nouvellement diagnostiqués chez plus de 50 % des participants. Il est intéressant de noter que la majorité de ces personnes étaient suivies par un médecin de première ligne. Ces résultats soulignent le risque cardiométabolique accru chez les personnes atteintes de SMI et mettent également en évidence la disparité des soins au sein de cette population. L'identification proactive des facteurs de risque cardiovasculaire, la détermination du risque cardiovasculaire et l'instauration/le suivi d'un traitement approprié sont essentiels pour optimiser les résultats des patients atteints de maladies mentales graves.

Une analyse systématique des recommandations des sociétés professionnelles américaines et européennes de cardiologie et de psychiatrie a mis en évidence les lacunes des recommandations

de soins pour les soins CV chez les patients psychiatriques et les soins psychiatriques chez les patients CV. Moins de 40 % des guides sur les soins cardiovasculaires incluaient des considérations psychiatriques, alors que 77 % des guides sur les soins psychiatriques contenaient des recommandations sur les soins cardiovasculaires. Bien que l'on dispose de données complètes sur la vulnérabilité cardiométabolique des personnes atteintes de troubles mentaux graves, l'absence de recommandations d'experts sur la prise en charge des maladies cardiovasculaires au sein de cette population est préoccupante. Nos résultats soutiennent le développement de recommandations de sociétés professionnelles sur la gestion des maladies cardiovasculaires chez les personnes souffrant de troubles mentaux et sur les considérations liées aux troubles mentaux dans les soins cardiovasculaires.

La cardio-psychiatrie est un domaine émergent qui nécessitera un niveau de collaboration multidisciplinaire important afin d'apporter des changements et d'améliorer les traitements pour cette population à risque. Des efforts cliniques et expérimentaux sont nécessaires pour faciliter le développement de modèles de soins interdisciplinaires efficaces.

Contributions of Authors

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Thesis candidate. Performed literature review. Wrote informed consent documents, CV risk assessment data collection form, and other study related documents. Co-developed study design and methodology for studies. Obtained clinical data and assisted in data analysis. Wrote initial and revised manuscripts for the quality improvement study and the systematic review of guidelines study. Presented findings to Master's Thesis Committee, McGill University's High Value Healthcare Symposium, Maurice McGregor Cardiovascular Research Day, and the Canadian Cardiovascular Society's Vascular conference. Wrote thesis document.

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Abbreviations

BD-I:	Bipolar I Disorder
BMI:	Body Mass Index
CHANGE:	Clinical Antipsychotic Trials of Intervention Effectiveness
CHD:	Coronary Heart Disease
CV:	Cardiovascular
CVD:	Cardiovascular Disease
FRS:	Framingham Risk Score
HCP:	Health Care Provider
HPA:	Hypothalamic-Pituitary-Adrenal
MDD:	Major Depressive Disorder
MI:	Myocardial Infarction
PCP:	Primary Care Physician
PRIMROSE:	PRedIction and Management of cardiovascular Risk in peOple with SEvere mental illnesses
QI:	Quality Improvement
QT:	QT interval (related to heart rate variability)
SES:	Socio-Economic Status
SMI:	Severe Mental Illness

Introduction

Severe mental illness (SMI) is defined as a subset of psychiatric disorders, in which mental, behavioural, and emotional limitations result in serious functional impairment.[1] Individuals with SMI, such as schizophrenia, schizoaffective disorder, and bipolar I disorder, exhibit major biopsychosocial impairments, many of which directly interfere with their daily living.[2] According to the National Institute of Mental Health, SMI has been shown to affect approximately 5.5% of American adults, with prevalence higher among females (7.0%) than males (4.0%).[1] SMI prevalence is highest in young adults ages 18-25 (11.4%) and in individuals of American Indian/American Native ethnicities (9.3%), suggesting potential systemic barriers.[1] Individuals with SMI have an average mortality rate that is 2 to 3 times higher compared to the general population, resulting in a 10- to 25-year shortened life expectancy.[3-6] A large-scale meta-analysis by Correll *et al.* found that physical diseases, such as cardiovascular (CV) diseases (CVD), are the main contributor to the increased mortality rate in this population.[7] Individuals with SMI exhibit a 78% greater risk of developing CVD, and an 85% higher risk of death from CVD compared to the general population.[7] According to a recent review of international evidence, the prevalence of CVD and cardiac comorbidities is twice as high in the SMI-population.[8] Approximately 25% of individuals with schizophrenia, and 33% of individuals with bipolar disorder die from CVD.[9] A clear relationship between CVD and SMI has been established, with CVD-related mortality increasing in magnitude over last decades.[10, 11] Such findings highlight the high vulnerability of the SMI population, and the need for further efforts to reduce CV risk and disease in this high-risk population. In this review, we will explore the association between SMI and CVD, focusing on primary prevention strategies and overcoming access barriers to quality care.

1.0 Literature Review

1.1 Severe Mental Illness

1.1.1 Schizophrenia/Schizoaffective Disorder:

Schizophrenia is a debilitating, long-term psychiatric disorder characterized by abnormalities in cognition and conduct.[12] 1% of Americans have schizophrenia, with a prevalence four times higher in men than in women.[13] Schizoaffective disorder is defined as the presence of mood episodes in concurrence with the classical symptoms of schizophrenia (delusions, hallucinations, disorganized speech and behaviour).[12]

The intensity, duration, and frequency of symptoms often result in major functional impairments. Schizophrenia spectrum disorders are associated with elevated rates of CV associated morbidity and mortality.[14] People with schizophrenia have a mortality ratio of 3.2, compared to the general population, which accounts for a reduced life expectancy of 15 to 20 years.[10, 14] The cause of excess CV mortality in patients with schizophrenia is largely attributable to modifiable lifestyle behaviours.[10, 14, 15] People with schizophrenia are more likely to smoke, maintain a high-fat diet, and lack physical activity.[14-17] The negative symptoms characteristic of schizophrenia spectrum disorders such as withdrawal, lack of motivation, and self-efficacy make the creation and implementation of healthy habits challenging.[14] Individuals with schizophrenia spectrum disorders report more than double the rates of somatic comorbidities such as diabetes, dyslipidemia, metabolic syndrome, obesity and hypertension.[18] African American and Hispanic women with schizophrenia appear to have the highest susceptibility for these metabolic disorders.[19, 20] The effects of these cardiac comorbidities have also been shown to compound more rapidly in schizophrenia patients, in part due to the use of antipsychotics.[9] Second-generation antipsychotics have been shown to cause major metabolic disturbances, resulting in

hyperglycemia, hyperlipidemia, and weight gain, further exacerbating metabolic conditions.[9] Moreover, antipsychotics in schizophrenia patients have also been linked with reduced left ventricular ejection fraction, ventricular arrhythmias and sudden cardiac death.[9] Finally, as schizophrenia has been associated with reduced education, lower socio-economic-status (SES) and poor health literacy, treatment adherence and navigation of the healthcare system are challenging.[11, 21, 22] The high levels of discrimination and stigma faced by this population also contribute to medical mistrust, worsening CV outcome.[23]

1.1.2 Bipolar Disorder

Bipolar disorders (BD) are a class of psychiatric disorders characterized by chronic, relapsing oscillations between states of mania, hypomania and depression.[24] Bipolar I disorder (BD-I), formerly known as manic-depression disorder, is a subset of BD, and is considered to be the most severe form due to the intensity of manic symptoms.[11, 25] Bipolar spectrum disorders have a lifetime prevalence of 2.2%, with 70% of individuals experiencing symptoms by 25 years of age.[24] As BD-I clinical manifestations overlap with other psychiatric disorders, diagnosis is often delayed. Consequently, the management of medical comorbidities is also delayed, worsening prognosis.

CVD, mainly circulatory events, are the leading cause of morbidity, and premature mortality in patients with BD-I, accounting for 35-40% of deaths.[26] Individuals with BD-I experience significant impairment in their ability to function effectively. Similar to schizophrenia, CV risk behaviours such as smoking, immobility, and poor nutrition are highly prevalent.[27] People with BD-I report elevated rates of obesity, diabetes, and metabolic syndrome, doubling the risk for CVD-related death.[26] Hypertension is especially prevalent in BD-1 patients as a result of

antidepressant use.[28] Lithium, valproic acid, and antipsychotics also contribute to increased CV risk through impaired insulin metabolism, promoting adiposity and weight gain.[11, 29] Individuals with BD-1 are uniquely more susceptible to CV risk due to the direct consequences of hypomania and depressive episodes.[30] These negative symptoms are strongly associated with substance use, social isolation, and medication nonadherence, all of which worsen prognosis.[27]

1.1.3 Major depressive disorder

Major depression disorder (MDD) is a highly prevalent mood disorder, predicted to be the number one contributor to the global burden of disease by 2030.[31] The annual and lifetime prevalence of MDD in Americans is 10.4% and 20.6% respectively, with prevalence higher in women than in men.[32] In MDD, biological, genetic, and environmental factors cause abnormalities in neurotransmitters. Imbalances in serotonin, norepinephrine and dopamine result in anhedonia, appetite changes, sleep disturbances, and in severe cases, suicidal ideations.[31] Individuals with MDD have a reduced life expectancy of 14 years in men and 10 years in women.[33] Compared to the general population, individuals with MDD exhibit a 2- to 4-fold increase in cardiac mortality, with rates twice as elevated in urban areas than in rural areas.[34, 35]

MDD and CVD have been shown to be related through several pathways, many of which are reciprocal. The direct effects of the disorder cause sympathetic nervous system hyperactivity, dysregulation of immune mechanisms and coagulation abnormalities, all of which contribute to increased CV risk. [36] As in other SMIs, people with MDD exhibit major CV behavioural risk factors (smoking, inactivity, poor nutrition).[37] Depressed patients report higher nicotine dependence and are less likely to be successful in smoking cessation.[37] Engaging in only five minutes vigorous intensity activity per day, over 65% of people with MDD do not meet the

recommendations for physical activity.[38] As a result, obesity, diabetes and metabolic syndrome are highly prevalent. Treatment with antidepressants is associated with elevated risks of diabetes, hypertension, and hyperlipidemia.[39] Individuals of African American ethnicity not only report more severe and untreated MDD, they are also more susceptible to metabolic disturbances, magnifying their CV risk.[40] Poor social skills, inadequate coping mechanisms and social isolation are further behavioural factors that compound CV risk in patients with MDD. While the direction of causality has not been fully elucidated, poor social support networks are associated with a two- to three-fold increase in coronary heart disease incidence over time.[37]

1. 2 Shared Pathophysiology between Cardiovascular Disease and Severe Mental Illness

Growing evidence suggests a shared etiology between CVD and mental disorders, particularly with MDD. Studies using perfusion imaging have shown that 30-70% of patients develop worsening acute myocardial ischemia in response to psychological distress.[41, 42] As this form of stress-induced ischemia does not manifest as typical cardiac chest pain, it is often missed, increasing the risk of recurrent CVD and morality.[42] Similarly, the American Heart Association has recognized depression in post-MI patients as an independent risk factor for worsening CV prognosis.[43] The American Heart Association also recognized BD and MDD in youth to be moderate-risk conditions that predispose young adults to accelerated atherosclerosis and early CHD.[3, 11] Conversely, the occurrence of acute coronary events may serve as a catalyst for developing mental illness.[3] The prevalence of major depression is three times more common in patients who have experienced acute coronary syndromes when compared to the general population.[44-46]

The bidirectional link between SMI and CVD exists through biological, behavioural, and genetic pathways, often creating a pathogenic cycle.[3, 42] Biological mechanisms are associated with autonomic nervous system dysfunction, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, oxidative stress and lipid abnormalities.[3] For instance, psychiatric conditions often cause hyperactivation of the HPA axis and sympathetic nervous system, resulting in elevated circulating levels of cortisol and catecholamines.[3] These mediators are associated with metabolic abnormalities, inflammation, endothelial dysfunction, and platelet reactivity, all of which promote the development of atherosclerosis.[3] Additionally, autonomic dysfunction associated with SMI causes decreased heart-rate-variability, increased variability in the QT interval, systemic vascular resistance, and hypertension, all of which worsen CV prognosis.[3, 11] Behavioural mechanisms are associated with the traditional, modifiable CV risk factors, such as smoking, inadequate physical activity, poor nutrition, obesity, obstructive sleep apnea, and poor medication adherence.[3] Up to 80% of people with schizophrenia are smokers.[17] Individuals with SMI spend approximately eight of their waking hours engaging in sedentary behaviours.[16] SMI is associated with more than double the rates of the major cardiac risk factors such as diabetes, dyslipidemia, metabolic syndrome and hypertension.[16, 18, 47] Genetic mechanisms linking SMI and CVD are complex and remain unknown.[3] Current evidence has suggested shared genetic correlations between cardiometabolic diseases, SMI and CVD.[3] However, further research is needed.

1.3 Primary Prevention of Cardiovascular Disease

Evaluating the risk for CV events, as well as identifying the presence of CVD risk factors, is foundational in guiding primary prevention strategies and optimizing patient outcomes.[9] The 10-year and 30-year Framingham Risk Scores (FRS) are validated assessment tools, used in the

general population, to quantify CV risk. These tools stratify individuals who are at high risk of developing coronary heart disease, cerebrovascular events, peripheral vascular disease, or heart failure within the next 10 and 30 years, with the goal of implementing early preventative treatment.[11, 48] These CVD risk calculators are based on traditional risk factors such as age, sex, smoking status, blood lipid profile, as well as the presence of comorbidities such as hypertension and diabetes mellites.[9, 11] However, these conventional tools have been developed without particular consideration of the SMI population, and therefore do not consider SMI-related factors.[49] Consequently, they have been shown to inadequately quantify CV risk in this population, resulting in suboptimal screening, monitoring and treatment.[9]

Given the significant cardio-metabolic vulnerability of individuals with SMI, adequate CV risk determination is essential for the implementation of tailored primary prevention strategies. Osborn *et al.,* developed and validated the PRIMROSE (PRedIction and Management of cardiovascular Risk in peOple with SEvere mental illnesses) body mass index (BMI), and the PRIMROSE lipid scores.[49] These CV risk prediction models incorporate SMI-related factors such as SMI diagnosis, use of psychotropic/antidepressant medication, history of heavy alcohol intake, BMI, all of which impact CV risk.[49] Consequently, both models have been shown to estimate the 10-year risk of a first CV event in the SMI population with greater accuracy than the 10-year FRS.[9, 11] As individuals with SMI are often reluctant to provide blood samples, the PRIMROSE BMI model is especially useful considering it does not rely on laboratory values.[49] This tool is easy to implement in the clinical setting and is associated with improved patient outcome and cost-effective care.[50] In other words, applying a 10% threshold for the initiation of statin therapy has been shown to reduce the occurrence of CV events, while yielding higher cost-savings among individuals with SMI at high CV risk.[11, 50]

The PRIMROSE prediction models, as well as the conventional CVD risk calculators do not consider lifestyle habits when determining CV risk. Omission of such consideration is a significant limitation, as lifestyle behaviours are closely related to CV health, especially in SMI. It is crucial for clinicians to be vigilant when using prediction models to guide treatment measures.[11]

1.4 Disparities in Cardiovascular Care

Disparities in access and quality of CV care in individuals with SMI are well documented.[51-53] These health disparities are significant contributors to the increased morbidity and mortality seen in people with SMI. The National Ambulatory Medical Care Survey reported that individuals with SMI receive preventative screening services during only 11% of the visits with their psychiatrists.[53, 54] Not only are these individuals less likely to be screened for CVD risk factors, they are also less likely to receive guideline-directed treatment once these risk factors have been identified.[51, 52] Following coronary events, individuals with SMI undergo invasive coronary interventions 50% less often compared to the general population.[51] The lack of appropriate CVD screening, monitoring and treatment measures in this population is concerning and presents an opportunity to improve care in this high-risk population.

Ethnic and racial differences in the SMI population have also been associated with disparities in access to holistic care.[55] African-Americans (62.3%) and Hispanics (58.6%) are less likely to receive mental health and primary health care services than White (68.6%) people.[1, 11, 19] This group has also reported higher rates of somatic comorbidities such as obesity, diabetes and metabolic syndrome.[19] An integrative literature review of 40 articles reported a potential double burden of cardio-metabolic risk among African-American and Hispanic individuals with SMI.[19]

Factors such as low SES/health literacy, medical mistrust and lack of culturally appropriate care contribute to poor access and quality care in racial/ethnic subgroups with SMI.[19] Given the pronounced cardio-metabolic vulnerability of African-American and Hispanic individuals with SMI, and their lack of representation in research studies, there is a dire need for culturally adapted health promotion interventions.[56]

Provider, patient and system-related factors, acting independently and in conjunction, play a large role in the disparities of care faced by the SMI population.[57] On a provider-level, a large psycho-somatic divide in clinicians' approach prevails. Mental health clinicians often lack knowledge on medical issues and may be uncomfortable with the management of somatic comorbidities.[57] Conversely, primary healthcare providers are unaware of the clinical needs that accompany an SMI diagnosis (i.e., frequency of cardio-metabolic screening when on antipsychotics) and may lack the soft skills needed to collaborate with this population effectively.[57, 58] Moreover, a negative attitude of general practitioners towards patients with SMI may result in poor communication, delays in diagnostic procedures/treatment, and disregard of patient's preferences.[9] Patient-related factors, such as low self-efficacy, poor medication adherence, and high appointment non-attendance rates are challenges faced when working the SMI population, all of which contribute to reduced quality of care.[59, 60] Additionally, the direct effects of mental illness often impair patients' capacity to serve as self-advocates, resulting in sustained health access inequalities.[57] Systemic factors contributing to disparities in care include care fragmentation, lack of interdisciplinary coordination, and stigmatization.[57]

1.5 Strategies to Improve Cardiovascular Health

The elevated CV morbidity and mortality in people with SMI is predominantly attributed to modifiable factors, both on a patient-level and on a provider-level. Nevertheless, there are many opportunities for the implementation of strategies to reduce the burden of CV disease in this population.

On a patient-level, modifiable factors increasing CV risk involve unhealthy lifestyle habits. Behavioural interventions reduce CV risk through lifestyle modifications, such as increasing physical activity, improving dietary habits, and facilitating smoking cessation. Smoking cessation interventions appear to be the most impactful in CV risk reduction.[61, 62] However, other behavioural studies report inconsistent findings.[63-65] This may be due to the difficulty of engaging the SMI population in the application of consistent behavioural modifications. Behavioural interventions have shown to be most successful when they include high intensity, coordinated interventions.[11, 65] Additionally, actively involving patients with SMI and their families in the decision-making process is essential in improving adherence to lifestyle modifications.[11] Refraining from paternalistic approaches, and utilizing empowering techniques such as motivational interviewing may also improve behavioural outcomes.[11]

While individuals with SMI should be given the same respect for patient autonomy, certain aspects of mental illness should elicit healthcare providers to integrate additional considerations and actions.[11] For instance, given the high cardio-metabolic burden in people with SMI, increased CV risk screening, especially in vulnerable ethnic minorities, is paramount. Tools such as the Positive Cardiometabolic Health algorithm encourage vigilant CV screening, as well as prompt treatment when appropriate.[66] Screening for depression following acute CV events should be routinely performed. Moreover, as psychopharmacology has been associated with increased CV

morbidity and mortality, up-to-date prescribing practices aimed towards risk reduction are crucial. Emerging evidence encourages the prophylactic use of antidiabetic agents in patients using atypical antipsychotic therapies, even in the absence of baseline dysglycemia or other risk factors.[67] Prescribing simplified treatment regimens such daily doses or polypills could also contribute to increased medication adherence.[11] Text message reminders, phone calls and electronic pill counters can be effective supportive strategies to increase medication adherence in this population.[11, 68]

There is a dire need for interdisciplinary collaboration between mental health and CV health professionals to optimize patient outcomes. The digitalization of medical records could facilitate referrals and communication between disciplines.[11] Additionally, this could encourage the implementation of electronic health record decision support tools, especially in primary care clinics.[69] Finally, as the traditional medical approach has shown to be suboptimal when caring for individuals with SMI, efforts toward developing a more inclusive approach is primordial. Recovery-oriented care, which is based on principles of autonomy, empowerment and shared-decision making, has been highlighted as more effective in accounting for the complex, multifaceted nature of treatment engagement in people with SMI.[60]

2.0 Study Objectives

Considering the elevated cardio-metabolic vulnerability of people with SMI, and associated disparities in access and quality of care, this thesis aims to expose and palliate the gap in care between cardiology and psychiatry.

2.1 First Objective:

To evaluate the feasibility of the implementation of a nurse-driven Cardio-Psychiatry clinic for CV primary prevention in individuals with SMI.

2.2 Second Objective

To review CV and psychiatric recommendations in American and European professional society guidelines and statements over the past decade.

Manuscript 1: Implementation of a cardio-psychiatry clinic for cardiovascular primary prevention in individuals with severe mental illness

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Abstract:

Background: Individuals with severe mental illness (SMI), such as schizophrenia, schizoaffective disorder, and bipolar disorder, have twice the risk for cardiovascular disease compared to the general population. Disparity in cardiovascular care access has been reported for people with SMI. Our objective was to create a Cardio-Psychiatry clinic for cardiovascular risk assessment and initiation of evidence-based treatment in people with SMI.

Methods: Patients were referred from outpatient psychiatry clinics to a newly created Cardio-Psychiatry clinic at a tertiary care hospital in Montreal, Canada between November 2022 and July 2023. Patients were eligible if they had SMI and no known cardiovascular disease. Pre-existing and newly identified cardiovascular risk factors were recorded. The 10-year Framingham Risk Score was calculated. If indicated, treatment was initiated for cardiovascular risk factors per evidence-based guidelines.

Results: Twenty-three participants were evaluated at the Cardio-Psychiatry clinic (age 52.6±10.8 years; 30% female). The most common SMI was schizophrenia (65%). The mean Framingham Risk Score was 13.8%±8.1. The most prevalent known cardiovascular risk factors were smoking (61%) and obesity (74%). Over half of participants (N=13; 57%) had new cardiovascular risk factors identified and pharmacological treatment initiated: metabolic syndrome and dyslipidemia (N=7), hypertension (N=7), and diabetes (N=2).

Conclusion: The new clinic represents a collaborative effort between cardiology and psychiatry. Our study demonstrated the importance of cardiovascular screening and treatment initiation in a

highly vulnerable population. Larger scale studies are needed to address the lack of access to quality cardiovascular care in individuals with SMI.

Introduction:

Severe mental illness (SMI) is a subset of psychiatric disorders in which mental, behavioural, and emotional limitations result in serious functional impairment.[1] Individuals with SMI, such as schizophrenia, schizoaffective disorder, and bipolar I disorder, exhibit major biopsychosocial impairments, many of which directly interfere with their daily living.[2] SMI affects 5.5% of American adults, with a higher prevalence among females (7.0%) than males (4.0%).[1] People with SMI have a 78% greater risk of developing cardiovascular disease (CVD) and an 85% higher risk of death from CVD, as compared to the general population.[7] The burden of excess CVD contributes greatly to a 10- to 25-year reduced life expectancy in people with SMI.[3-6] In addition, cardiovascular (CV) mortality in SMI has been increasing over the past decades.[10]

The increased risk for CVD is caused by interconnected pathophysiological, pharmacological, behavioural, and genetic factors.[3] Disparities in access and quality of CV care have also been shown to increase CV related morbidity and mortality in the SMI population.[51-53] Patient-related factors, such as low self-efficacy, poor medication adherence, and high appointment non-attendance rates are challenges faced when working the SMI population, all of which contribute to worsening outcomes.[59, 60] As the traditional medical approach has shown to be suboptimal when caring for individuals with SMI, new approaches that take into consideration patient-related factors are urgently needed to address CVD in SMI. Recovery-oriented care, which is based on principles of autonomy, empowerment and shared-decision making, has been highlighted as more effective in accounting for the complex, multifaceted nature of treatment engagement in people with SMI.[60]

Given the high CV risk factor burden in people with SMI, the disparity in access and quality of care, there is a strong need to screen for CV risk factors and initiate and monitor guideline-

directed therapies. Moreover, these primary prevention strategies should be tailored to the SMI population in order to optimize outcomes. The objective of this project is to evaluate the feasibility of the implementation of a Cardio-Psychiatry clinic for CV primary prevention in individuals with SMI.

Methods:

Design, Participants and Setting

A quality improvement (QI) project was conducted at the Jewish General Hospital (JGH), a tertiary care academic centre in Montreal, Canada, between November 2022 and July 2023. Eligible patients were initially referred from the Institute of Community and Family Psychiatry's Continuing Care Clinic, a hospital-affiliated outpatient psychiatry clinic that manages adults with SMI using a multidisciplinary, longitudinal approach. The Cardio-Psychiatry clinic was led by a cardiologist with expertise in primary prevention and a nurse. The clinic was based in the ambulatory cardiology department of the JGH.

Patients who met the following inclusion criteria were eligible for referral: (1) age ≥ 30 years old, (2) diagnosis of schizophrenia, schizoaffective disorder, or bipolar I disorder, and (3) no known CV disease (history of coronary artery disease, cerebrovascular disease, or peripheral vascular disease). The lower age limit cut off was chosen as the Framingham 10-year risk score is validated in populations ≥ 30 years old. Exclusion criteria were (1) psychiatric instability, as judged by treating psychiatry team, and (2) participant unwilling to undergo CV prevention screening. Eligibility was assessed by the referring healthcare professional (HCP) and validated by the research team upon referral. This study was conducted as a QI project and was approved by the institutional QI department. Research ethics approval was waived for this study.

From November 2022 to February 2023, participants were recruited in-person from the Institute of Community and Family Psychiatry's Continuing Care Clinic. The referring HCP initiated contact between the patient and the Cardio-Psychiatry team. Informed verbal consent for participation was obtained by a member of the Cardio-Psychiatry team at the outpatient psychiatry center. An appointment for a CV risk assessment visit at the Cardio-Psychiatry clinic was offered within the following two weeks, in order to maximize patient motivation. During this initial encounter at the outpatient psychiatry center, a nurse from the Cardio-Psychiatry clinic obtained a blood sample for a baseline complete blood count, electrolytes, creatinine, lipid profile, hemoglobin A1c, blood glucose levels, liver enzymes, and creatine kinase.

In February 2023, two additional university-based outpatient psychiatry centers started to refer participants to the Cardio-Psychiatry clinic. Participants were referred by the treating HCP by email to the Cardio-Psychiatry clinic. A member of the Cardio-Psychiatry clinic contacted the participant by phone and scheduled an appointment for CV risk assessment within 2 weeks. Blood tests were taken at the initial in-person visit.

Risk Factor Screening and Treatment

At the initial visit to the Cardio-Psychiatry clinic, a nurse performed a focused CV history and physical examination. The CV risk assessment followed the Canadian Cardiovascular Society's recommendations for primary prevention.[70] Weight, height, and body-mass index (BMI) were recorded. In accordance with the Canadian Hypertension guidelines, blood pressure using a BpTRU machine was obtained (BpTRU™ Medical Devices, Coquitlam, BC).[71] History of known CV risk factors was defined by self-report, or through the prescription of a medication to treat the condition (i.e., statin for dyslipidemia). Family history of premature CV disease was defined by the Canadian Cardiovascular Society's dyslipidemia guideline.[70] New diagnoses of dyslipidemia

were made if the patient exhibited a "statin-indicated condition" or if they met the criteria for "consider initiation pharmacotherapy" as defined by the Canadian Cardiovascular Society's dyslipidemia guidelines.[70] In accordance was Diabetes Canada, diabetes mellitus was diagnosed based on fasting plasma glucose ≥7.0 mmol/L, random plasma glucose ≥11.0 mmol/L, HbA1c ≥6.5%, or plasma glucose ≥ 11.0 mmol/L two hours post-oral 75 gram oral tolerance test.[72] Metabolic syndrome was diagnosed based on the presence of at least three of the five risk factors: elevated waist circumference, dyslipidemia (i.e. elevated triglycerides and decreased high-density lipoprotein (HDL) cholesterol), elevated blood pressure, and elevated fasting glucose.[72] Smoking status and alcohol intake were assessed through patient self-report.

The 10-year and 30-year Framingham Risk Scores (FRS) are validated assessment tools, used in the general population, to quantify CV risk. These tools stratify individuals who are at high risk of developing coronary heart disease, cerebrovascular events, peripheral vascular disease, or heart failure within the next 10 and 30 years, with the goal of implementing early preventative treatment.[11, 48] 10-year and 30-year Framingham CV risk scores were calculated for each participant.[70] The PRedIction and Management of cardiovascular Risk in peOple with SEvere mental illnesses (PRIMROSE) body mass index (BMI) and lipids score were calculated for all participants. The PRIMROSE BMI and lipid prediction models are tools that have been specifically designed and validated for people with SMI.[49] The EQ-5D-5L was used to assess patient-reported health status.[73] Screening for obstructive sleep apnea (OSA) was performed using the STOP-Bang questionnaire.[74]

Newly identified or poorly managed CV risk factors were identified and treated with evidence-based recommendations.[70-72] Consultation with a cardiologist was offered and follow-up appointments were scheduled as needed (i.e., hypertension diagnostic criteria). Participants

stratified as intermediate risk using the STOP-bang questionnaire were referred for further investigative studies for OSA. When appropriate, patients were also referred to smoking cessation programs and other allied HCP.

The CV risk assessment report was shared and explained to the participant in layperson terms. Tailored education and counselling (i.e., lifestyle counselling, medication adherence, available resources) on evidence-based methods to improve CV risk was provided. The CV risk assessment report was also shared to the referring psychiatrist and the participant's primary care physician (PCP). Participants were encouraged to maintain their efforts towards CV primary prevention with their PCP following this QI project. In patients without a PCP, information on how to obtain one was provided. Follow-up visits were provided at the Cardio-Psychiatry clinic for the duration of the study for participants requiring monitoring or medication adjustment.

Data Collection

The psychiatric diagnosis and list of current medications was obtained from the referring HCP. The following data was collected from the participant: age, sex, ethnicity, presence/absence of a primary care physician, last CV investigations (if any), weight, height, blood pressure recording, physical examination findings, and other CV risk factors (i.e., obstructive sleep apnea, smoking status, alcohol intake). Newly identified CV risk factors, or previous poorly managed ones, were recorded at the initial visit (i.e., blood pressure, lipid levels, HbA1c). The following validated assessment tools were administered: 10-year & 30-year FRS score, PRIMROSE BMI & lipids scores, EQ-5D-5L and the STOP-bang questionnaire. FRS scores of >30% were recorded as 30%. The study met the institution's ethical guidelines for protection of human subjects concerning their safety and privacy.

Measures

The feasibility of the implementation of the Cardio-Psychiatry clinic for CV primary prevention in individuals with SMI was assessed by the enrollment rate. Enrollment rate was defined as the number of patients who attended the CV risk assessment visit divided by the total number of appropriate patients referred/approached. According to the Canadian Cardiovascular Society guidelines, 10-year FRS is recommended to guide therapy and should be repeated when there is an expected change in risk status.[70]

Data analysis

Continuous data are presented as mean with standard deviation and categorical data are presented as frequencies and percentages.

Results:

There were 41 participants who were referred to the Cardio-Psychiatry clinic for a CV risk assessment (Figure 1). 13 (40%) participants were recruited in-person during the first 13 weeks of recruitment. Additional referral centers were initiated at weeks 14 and 30, generating 28 referrals collectively (Figure 2). Of these, four (14%) were excluded due to the presence of an inappropriate SMI diagnosis, and five (18%) refused to participate when contacted by the research team. Of participants agreeing to participate, 9 were excluded due to scheduling challenges (i.e., unable to contact the patient to schedule/reschedule the initial visit). Approximately one-third of patients (N=8; 34%) did not attend their scheduled CV risk assessment visit and required multiple rescheduling efforts.

There were 23 participants who attended the initial CV risk assessment visit (enrollment rate of 62%). The mean age of participants attending the initial visit was 52.6 ± 10.8 years old and

30% were female (Table 1). Over one-third of participants (N=9; 39%) were from a racial or ethnic minority group. 17 (74%) participants were followed by a PCP. The most common SMI was schizophrenia (65%), followed by bipolar I disorder (17%). The majority of patients were being treated with second-generation antipsychotics (SGA) (N=21; 91%), while only two were taking first-generation antipsychotics (FGA) (9%), and 5 (22%) were a receiving a combination of both SGA and FGA. Obesity (74%) was the most prevalent known CV risk factor, as evidenced by a mean BMI of 35.7 ± 8.10, followed by smoking (61%). The mean 10-year and 30-year FRS were 13.8% ± 8.1 and 37.6% ± 13.2. The mean PRIMROSE BMI and lipid scores were 3.0% ± 3.0 and 2.4% ± 2.7, respectively.

Over half (N=13; 57%) of participants had new CV risk factors identified and had pharmacological treatment initiated: hypertension (N=7), metabolic syndrome and dyslipidemia (N=7), and diabetes (N=2; Figure 3). Smoking cessation resources were accepted by 50% of smokers (Table 2). Diet and exercise recommendations were accepted by 78% of participants. Referrals for further OsA investigation were accepted by only 6% of participants who were offered.

Discussion:

The goal of our project was to evaluate the feasibility of the implementation of the Cardio-Psychiatry clinic to improve CV risk in this highly vulnerable population. Various recruitment strategies (i.e., in person, multicenter referrals) resulted in more than half of the referred participants attending the initial visit. An intermediate or high 10-year FRS was found in more than half of the participants. Moreover, approximately half of the participants had newly diagnosed CV risk factors and pharmacological treatment initiated. We hypothesized that the implementation

of a Cardio-Psychiatry clinic would enable individuals with SMI to gain access to CV primary prevention services.

Growing evidence suggests a shared etiology between CVD and mental disorders, through common biological and behavioural pathophysiologic pathways.[42] Biological mechanisms are associated with autonomic nervous system dysfunction, hypothalamic-pituitary-adrenal axis dysregulation, systemic inflammation, oxidative stress and lipid abnormalities.[3] Behavioural mechanisms are associated with the traditional, modifiable CV risk factors, such as smoking, inadequate physical activity, poor nutrition, obesity, as well as poor medication and OSA treatment adherence.[3] Up to 80% of people with schizophrenia are smokers.[17] Individuals with SMI have shown to spend approximately eight of their waking hours engaging in sedentary behaviours.[16] As a result, SMI is associated with more than twice the rates of diabetes, dyslipidemia, metabolic syndrome and hypertension as compared to the general population.[16, 18, 47] On the other hand, acute coronary events and chronic CVD disease have been shown to exacerbate depressive symptoms, or even trigger the onset of mental illness.[42]

The prevalence of CVD and cardiac comorbidities in the SMI population is elevated. Lifestyle factors, such as smoking, poor nutrition and physical inactivity, are key contributors to the increased cardio-metabolic vulnerability of people with SMI.[14] We found that obesity was present in nearly 75% of participants, which is more than the prevalence reported in other studies (ranging between 45-55%).[75-77] Smoking was highly prevalent in our population with the majority of participants (61%) reporting a positive history of smoking, which is in line with previous research.[39, 49, 77] Interventions aimed towards lifestyle modification, especially smoking cessation initiatives, could have a significant impact in reducing CV risk in people with SMI.[61, 62] Baker et al. conducted a two arm randomized control trial exploring the efficacy of nicotine replacement

therapy, in addition to a telephone or in-person smoking cessation intervention.[78] One quarter of participants reduced smoking by more than 50% and both groups showed a reduction in 10-year FRS at the 3-year follow-up.[78] On the other hand, a feasibility study comparing a specialized smoking cessation intervention to usual care showed no between groups differences.[62] Given the inconsistency of findings, there is a dire need for further research on specialized health promotion interventions.[56]

Evaluating the risk for CV events, as well as identifying the presence of CVD risk factors, is foundational in guiding primary prevention strategies and optimizing patient outcomes.[9] We found that the mean 10-year FRS was more elevated than in other studies of SMI patients (ranging from 4.2% to 6.3% in females and 7.0% to 10.2% in males),[18, 79] highlighting the increased risk for CVD in individuals with SMI, especially males.[30] On the other hand, no participants were identified as intermediate or high risk using the PRIMROSE BMI and lipid prediction models. These tools have been shown to predict CV risk in the SMI population with greater accuracy as they consider SMI-related factors such as SMI diagnosis, use of antipsychotics/antidepressants, and history of heavy alcohol intake, all of which impact CV risk.[9, 49] The underestimation of CV risk using the PRIMROSE BMI and lipids scores has also been reported in other studies, prompting the need for further investigation on the design of these prediction models.[80]

The lack of appropriate CVD screening, monitoring and treatment measures in the SMI population is concerning and presents an opportunity to improve care. The Cardio-Psychiatry clinic represents a collaborative effort to improve access to preventative screening in this vulnerable population. More than half of participants were diagnosed with new CV risk factors and had pharmacological treatment initiated. This included many participants that were followed by a PCP, accentuating the relevance of our findings. These findings concur with the growing

evidence demonstrating that people with SMI are less likely to be screened for CVD risk factors, and less likely to receive guideline-directed treatment.[51, 52] Disparities in access and quality of CV care in individuals with SMI are well documented and are significant contributors to the increased morbidity and mortality seen in this population.[51-53] The National Ambulatory Medical Care Survey reported that individuals with SMI receive preventative screening services during only 11% of the visits with their psychiatrists.[53, 54] Ethnic and racial differences have also been associated with disparities in access to holistic CV care.[55] Non-Latino and non-Hispanic Black individuals (62.3%) and Latino or Hispanic individuals (58.6%) are less likely to receive mental health care services than Non-Latino and non-Hispanic White individuals (68.6%).[1] These findings suggest potential systemic discrimination, catalyzing the need for change.

Patient recruitment is a common challenge encountered when conducting research with people with mental health issues due to patient-related factors such as poor motivation and medical mistrust.[81, 82] Various strategies were implemented to boost recruitment, such as in-person recruitment and adding additional referral centers. Efforts towards bundling interventions, such as obtaining blood samples during the initial contact with the participants, or even scheduling participant's CV risk assessment screening on the same day as their other appointments, were implemented to facilitate enrollment. Establishing a large-scale, multicenter referral system for patient recruitment was challenging, as it relied heavily on interdisciplinary communication and collaboration. However, this collaboration was key in increasing patient recruitment. For referred individuals that were unreachable via phone, the consenting process was mediated by the referring HCP. In other words, the referring HCP would dedicate several minutes of their appointment with the patient to call the QI research team, offering an immediate opportunity to obtain consent.

However, this approach relies heavily on busy clinicians and may not be sustainable. Further research is needed to overcome recruitment barriers in people with SMI.

Given the high CV risk factor burden in people with SMI, along with the disparity in access and quality of care, the implementation of a Cardio-Psychiatry clinic is highly relevant. There is a dire need for interdisciplinary collaboration between mental health and CV health professionals to optimize patient outcomes. The innovative nature of the Cardio-Psychiatry clinic could serve as a building block towards a corridor of referral between these two specialties. The Cardio-Psychiatry clinic could also be utilized for clinical trainee rotations, with the idea of promoting holistic care. Given the lack of focused screening services tailored to the SMI population, this initiative could serve as a base for research addressing issues of disparities in care. Most importantly, the Cardio-Psychiatry clinic offers individuals with SMI an opportunity to gain a deeper insight on their CV health, promoting autonomy, self-efficacy, and empowerment.

There are several limitations to this study. This was a single-center study at an academic hospital with a small sample size, which limits generalizability of findings. There was also limited follow-up for study participants. While early identification and management of CV risk factors is beneficial, the lack of follow-up limits insight on the long-term benefits of the intervention. Additional longitudinal research could also address questions of treatment adherence, and patient engagement in the SMI population.

Conclusions:

This QI project aimed to improve access to CV preventative screening in a highly vulnerable population, empowering SMI patients to take charge of their health. Proactive

identification of CV risk factors and overall risk determination for CV related events enabled patients to receive appropriate treatment.

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Table 1. Descriptive Statistics of Cohort

	(N = 23)
Age	52.6 ± 10.8
Female	7 (30%)
Ethnicity	
Non-Latino and non-Hispanic White	14 (61%)
Non-Latino and non-Hispanic Black	6 (26%)
Latino or Hispanic	2 (9%)
Non-Latino and non-Hispanic Asian or Pacific Islander	1 (4%)
Severe Mental Illness	
Schizophrenia	15 (65%)
Bipolar I Disorder	4 (17%)
Schizoaffective Disorder	2 (9%)
Schizoaffective Disorder & Bipolar I Disorder	2 (9%)
Psychiatric Medication	
Second-generation antipsychotic	21 (91%)
First-generation antipsychotic	7 (30%)
Anticholinergic	7 (30%)
Anticonvulsant	7 (30%)
Benzodiazepines	4 (17%)
Cardiovascular Medication	
Oral antihyperglycemic	4 (17%)
Statin	2 (9%)
Calcium channel blocker	2 (9%)
Previous history of risk factor	
Obesity	17 (74%)
Smoking	14 (61%)
Family history	7 (30%)
Hypertension	5 (22%)
Diabetes mellitus	4 (17%)
Obstructive sleep apnea	4 (17%)
Dyslipidemia	3 (13%)
Body Mass Index	35.7 ± 8.10
10-year Framingham risk score	13.8% ± 8.10
PRIMROSE Body Mass Index	3.0% ± 3.00
PRIMROSE lipids	2.4% ± 2.70
30-year Framingham risk score	37.6% ± 13.2
Has primary healthcare provider	17 (74%)
Number of no shows at initial visit	8 (34%)
1 no show	5 (21%)
> 1 no show	3 (13%)

Table 2. Interventions implemented at Cardio-Psychiatry clinic

	(N = 23)
Pharmacological treatment initiated	
Calcium channel blocker	7 (30%)
Statin	7 (30%)
Oral antihyperglycemic	2 (9%)
Number of accepted resources	
Smoking cessation*	5/10 (50%)
Physical activity	18/23 (78%)
Nutrition	18/23 (78%)
Obstructive sleep apnea referral**	1/16 (6%)

*Smoking cessation resources were offered to smokers only.

** Obstructive sleep apnea referrals were offered to patients at intermediate risk using the STOP-bang questionnaire.

Figure 1. Recruitment Overview

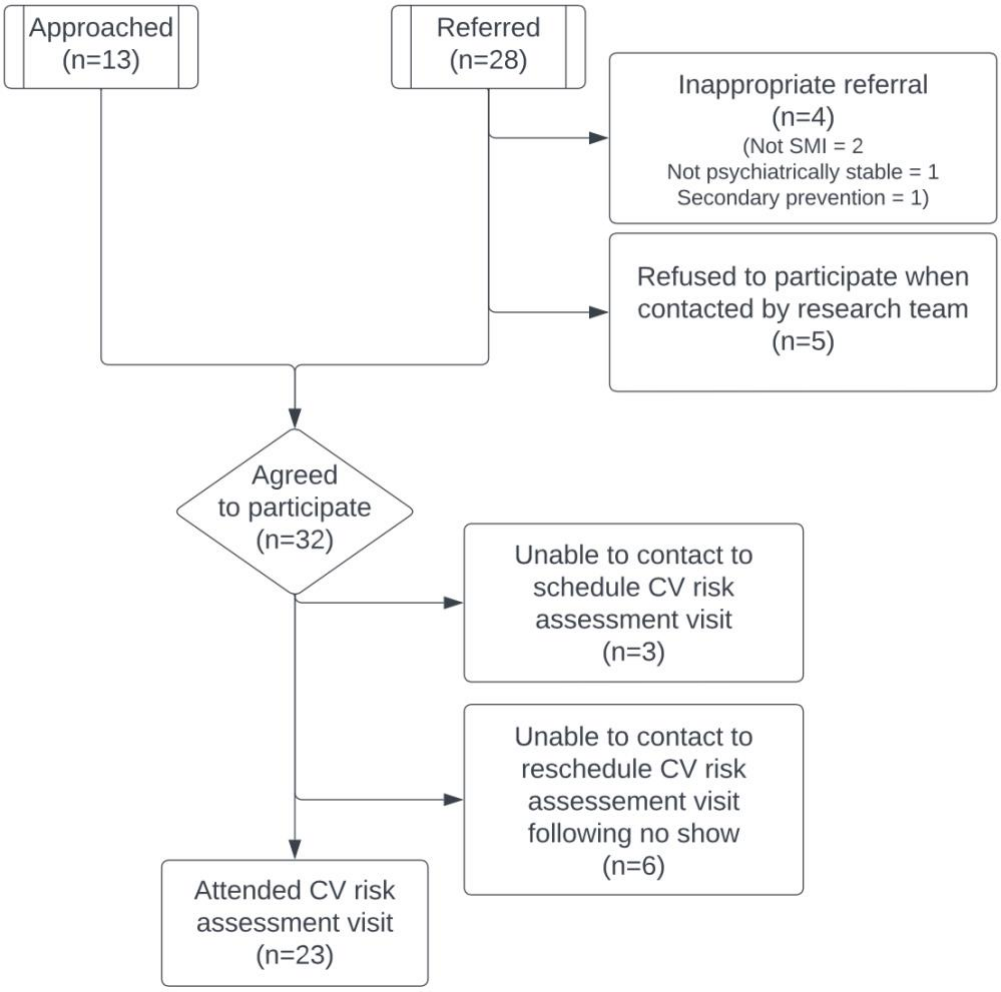


Figure 2. Recruitment Timeline

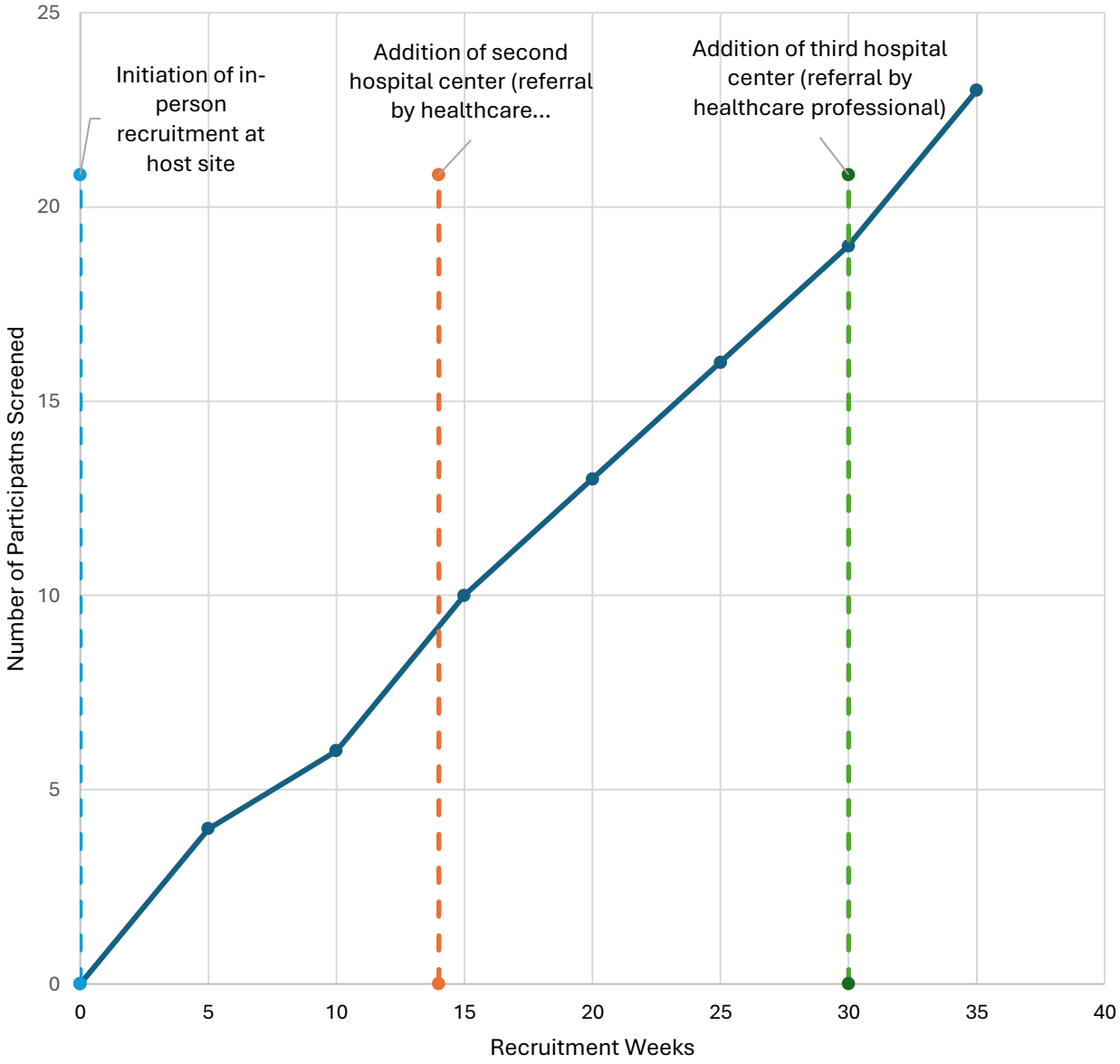
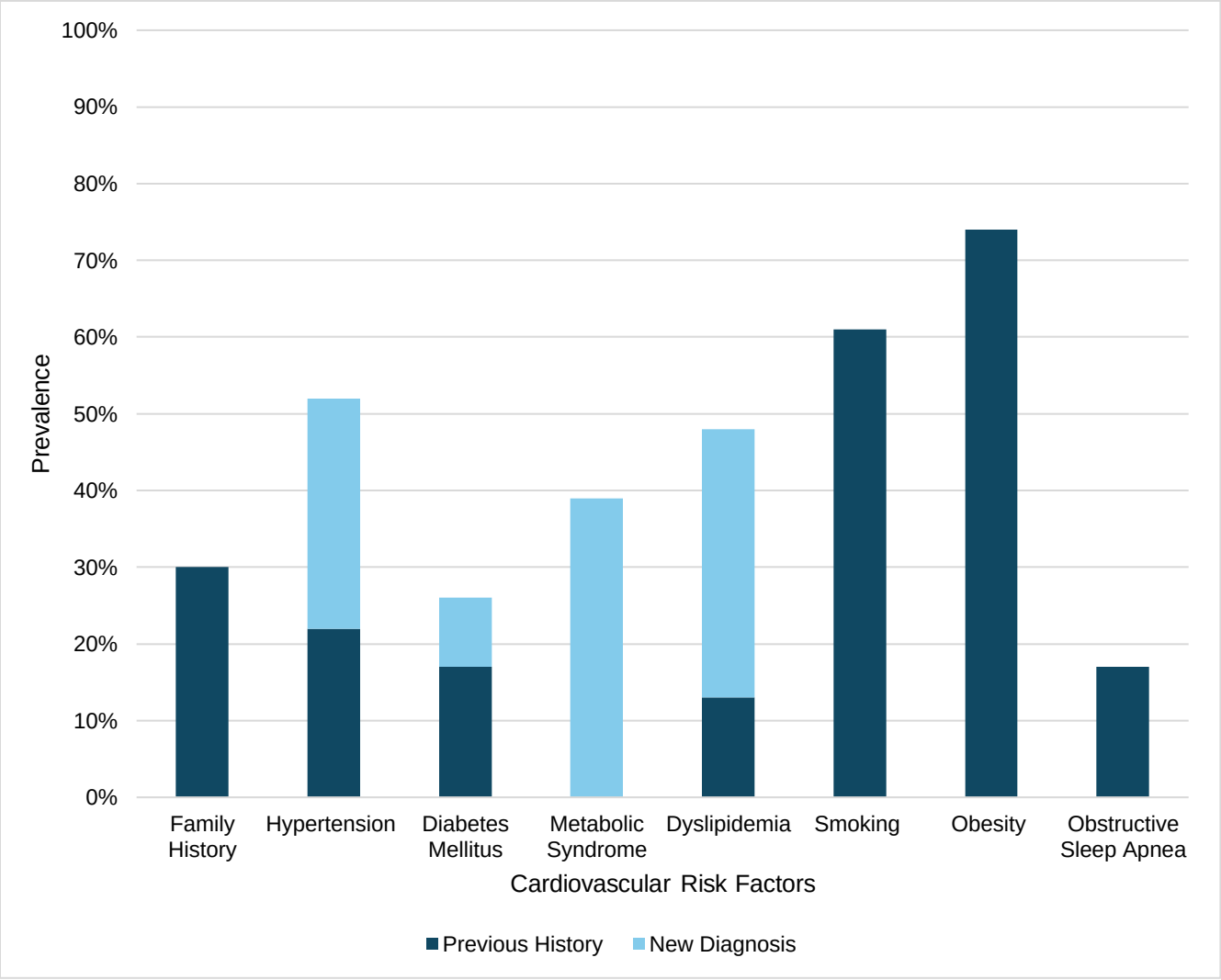


Figure 3. Prevalence of Cardiovascular Risk Factors in Individuals with Severe Mental Illness seen in the Cardio-Psychiatry Clinic



Preamble to Manuscript 2

Individuals with SMI represent a cardio-metabolic vulnerable population, requiring highly coordinated and specialized care. Professional society guidelines are foundational in disseminating knowledge and establishing practice standards. Current practice regarding CV management in people with SMI is highly variable and fails to recognize the compounded risk found in this population. Given the interdependence of CVD and SMI, the is a dire need to explore how professional societies incorporate considerations into their care recommendations.

Cardiovascular Recommendations in Psychiatry Guidelines and Psychiatry Recommendations in Cardiovascular Guidelines: A Systematic Review of Cardiology and Psychiatry Guidelines

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Abstract

Introduction: People with serious mental illness (SMI), such as major depression, schizophrenia, and bipolar disorder, have a much higher rate of cardiovascular (CV) risk factors and disease than the general population. There is a need to explore how CV and psychiatric professional societies describe the interplay of SMI and CV disease to their respective disciplines.

Methods: Major American and European CV and psychiatric professional society guidelines and statements published between 2013-2023 were searched. Primary and secondary prevention CV guidelines were included. Disease-specific psychiatric guidelines for schizophrenia, bipolar, and major depression were included. Relevant text was extracted and classified as recommendations or as supporting text.

Results: There were 26 guidelines (13 CV; 13 psychiatric) included in the analysis. Psychiatric recommendations were included in 5 CV guidelines (38%). The most common recommendations in CV guidelines were for treatment of mental illness to improve CV outcomes (N=5), pharmacological considerations (N=2), and considering mental illness as a risk factor for CV disease (N=2). 13% (1/8) of American CV guidelines had psychiatric recommendations compared with 80% (4/5) of European CV guidelines. CV recommendations were included in 10 psychiatric guidelines (77%). The most common CV recommendations in psychiatric guidelines were for CV disease screening (N=16), CV pharmacological considerations (N=8), and improving CV risk factor control (N=7). 40% (2/5) of American psychiatric guidelines compared with all European psychiatric guidelines (100%; 8/8) had CV recommendations.

Conclusions: CV recommendations were more common in psychiatric guidelines than psychiatric recommendations in CV guidelines. European guidelines had more CV and psychiatric recommendations than comparable American guidelines. Further professional societal efforts are needed to highlight the established relationship between CV disease and psychiatric conditions.

Introduction

Serious mental illness (SMI), such as major depression, schizophrenia, and bipolar disorder, is characterized by severe biopsychosocial impairment and affects about 6% of the population.[1, 2] People with SMI have a mortality rate 2-3 times higher than the general population, leading to a 10- to 25-year shortened life expectancy.[3-5] Similar to the general population, cardiovascular (CV) disease is the leading cause of death in people with SMI. However, people with SMI have a 78% greater risk of developing CV disease and an 85% higher risk of death from CV disease.[6] People with SMI have a higher rate of almost all modifiable CV risk behaviors and conditions, are often exposed to psychopharmacotherapy with CV side effects, and experience disparities in access to care.[7]

Professional society guidelines play an integral role in disseminating knowledge, promoting practice standards, and influencing behavioral change within their respective disciplines. Due to the established interconnectedness of SMI and CV disease, there is a need to understand how CV professional societies incorporate psychiatry-related issues, as well as how psychiatric professional societies include CV-related issues in their guidelines. Thus, the objective of this study is to review CV and psychiatric recommendations in professional society guidelines and statements over the past decade.

Methods

Eligibility Criteria:

We performed a systematic review of major American and European CV and psychiatric professional society guidelines and statements from 2013-2023. For CV guideline topics, we included primary and secondary prevention of CV disease. For psychiatric guideline topics, we

included disease-specific guidelines for schizophrenia, bipolar, and major depression.[6] Types of documents included were professional society guidelines and statements. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Supplemental Data).

Information Sources:

We reviewed CV guidelines from the following American professional societies: American College of Cardiology and American Heart Association. We reviewed CV guidelines from the following European professional societies: European Society of Cardiology and National Institute for Health and Care Excellence (NICE) professional societies. We reviewed psychiatric professional guidelines from the following American societies: Veteran's Administration/Department of Defense, American Psychiatric Association and American College of Physicians. We reviewed psychiatric professional societies from the following European psychiatric societies: NICE and British Association for Pharmacology.

Search Strategy:

We reviewed the full text of each guideline included. In CV guidelines, key terms searched were mental illness, mental health, psychiatric, major depression, bipolar, and schizophrenia. In psychiatric guidelines, key terms searched were: cardiovascular disease, cardiac disease, primary prevention, hypertension, dyslipidemia, metabolic syndrome, and diabetes mellitus. Relevant text was extracted and classified as recommendations or supporting statements. For CV guidelines, we categorized recommendations into the following categories: Pharmacological considerations, considering mental illness as a risk factor for CV disease, screening for mental illness to improve CV outcomes, and treatment of mental illness to improve CV outcomes. For psychiatric guidelines, we categorized recommendations into the following categories: CV pharmacological

considerations, CV risk factor control, CV disease screening, and treatment of mental illness to improve CV outcomes. CV pharmacological consideration refers to choosing which psychotropic medication to prescribe. CV risk factor control includes lifestyle management, comorbidity management, and monitoring.

Results

There were 13 CV guidelines (8 American; 5 European) included in the analysis (Table S1). Five CV guidelines (38%) included psychiatric recommendations (Table 1).[8-12] For primary prevention, none of the American guidelines (0/4; 0%)[13-16] and both of the European guidelines (2/2; 100%)[8, 9] had recommendations regarding psychiatric conditions. Both European primary prevention guidelines included multiple recommendations. Psychiatric-related recommendations involved pharmacological considerations (N=2),[8] considering mental illness as a risk factor for CV disease (N=2),[8, 9] and treatment of mental illness to improve CV outcomes (N=2).[8] At least one phrase about psychiatric conditions was included in the text in half of the American guidelines (2/4; 50%) and in both of the European guidelines (2/2; 100%). For secondary prevention, recommendations regarding psychiatric conditions were included in one-quarter of the American guidelines (1/4; 25%)[10, 17-19] and in two-thirds of the European guidelines (2/3; 67%).[11, 12, 20] Recommendations were about treatment of mental illness to improve CV outcomes (N=3)[10-12] and screening for mental illness in people with CV disease (N=1).[10] At least one phrase about psychiatric conditions was included in the text in half of the American guidelines (2/4; 50%) and in two-thirds of the European guidelines (2/3; 67%).

There were 13 psychiatric guidelines (5 American; 8 European) included in the analysis (Table S2). Psychiatric guidelines were for schizophrenia and psychotic disorders (N=5),[21-25]

major depression (N=5),[26-30] bipolar disorder (N=2),[31, 32] and SMI not otherwise specified (N=1).[33] Ten psychiatric guidelines (77%) included CV recommendations (Table 2). 40% (2/5) of the American guidelines and all of the European guidelines (100%; 8/8) had CV recommendations. Multiple recommendations were included in 70% (7/10) of guidelines that had at least one CV recommendation. Recommendations were about CV disease screening (N=16),[23-25, 29, 31, 32] CV pharmacological considerations (N=8),[21, 23, 24, 30] improving CV risk factor control (N=7),[21, 24, 25, 32, 33] and treatment of mental illness to improve CV outcomes (N=1).[27] At least one phrase about CV conditions was included in the text in 85% (n=11) of psychiatric guidelines.

Discussion

We found that CV disease management recommendations were more commonly made in psychiatric guidelines compared with psychiatric disease recommendations in CV guidelines. European CV guidelines had more psychiatric recommendations than American CV guidelines. Similarly, European psychiatric guidelines had more CV recommendations than corresponding American guidelines. To our knowledge, this is the first study to explore the reporting of CV and psychiatric recommendations in professional society guidelines.

A bidirectional relationship between CVD and SMI has been well-established. CV disease is associated with the development of major depression, particularly following an acute cardiac event, as well as the worsening of pre-existing psychiatric conditions.[34, 35] SMI is associated with high levels of CV risk factors and a high prevalence of CV disease and CV-related mortality.[7] Biological and psychological mechanisms have been proposed to explain this link. Worsened CV outcomes for people with SMI are also partly due to disparities in access to CV care and quality

of care exist. A lack of awareness of CV professionals of the tremendous burden of CV disease in people with SMI might lead to disparities in access to CV care.

The relatively high number of CV recommendations in psychiatric professional guidelines may be reflective of a higher degree of awareness of the CV disease burden in people with SMI amongst psychiatric professionals. As evidenced by the higher rates of CV recommendations and text usage in European psychiatric guidelines compared with American guidelines, this awareness may be greater in Europe. Including CV recommendations in psychiatric guidelines may lead to increased awareness amongst psychiatric professionals about the importance of CV-related care in their patients. Conversely, the low rate of psychiatric-related recommendations in CV guidelines suggests that there may be reduced awareness of the importance of improving CV care for people SMI. The lower rate is even more pronounced in American CV guidelines compared to European CV guidelines.

These findings support the strong need to highlight the importance of considering psychiatric conditions in future CV professional society guidelines. Guidelines should emphasize the strong relationship between these two entities and promote evidence-based recommendations to improve CV outcomes in people with SMI.

There are limitations to our review. We included only major American and European society guidelines. It is possible that the review did not include guidelines from less prominent professional societies. However, the major professional society guidelines included are the ones most widely distributed and most likely to reflect current knowledge and influence clinical practice. Second, we performed a manual search of included guidelines and it is possible that certain textual relevant phrases were not captured in the data extraction process. However, we included key terms and revised the search strategy when new relevant terms were identified. In

addition, the final search strategy was applied uniformly across all the guidelines. Third, the definition for severe mental illness varies and thus we did not include other severe psychiatric diseases, such as anorexia and post-traumatic stress disorder. However, the definition of severe mental illness used was taken from the biggest study of CV disease in severe mental illness to date.[6]

In conclusion, there are a lack of recommendations for psychiatric considerations in CV care, especially in American guidelines. Further efforts are needed to highlight the established relationship between CV disease and psychiatric conditions within professional society guidelines.

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Table 1. Psychiatric recommendations found in cardiovascular guidelines

CV primary prevention recommendations	**Cardiovascular guidelines**
1. Pharmacological considerations	ESC 2021: Cardiovascular disease prevention in clinical practice
2. Mental illness as a risk factor for CV disease	NICE 2023: Cardiovascular disease: risk assessment and reduction ESC 2021: Cardiovascular disease prevention in clinical practice
3. Treatment of mental illness to improve CV outcomes	ESC 2021: Cardiovascular disease prevention in clinical practice
CV secondary prevention recommendations	**Cardiovascular guidelines**
1. Treatment of mental illness to improve CV outcomes	ACC/AHA/SCAI 2021: Coronary artery revascularization ESC 2020: ACS in patients presenting without persistent ST-segment elevation ESC 2019: Diagnosis and management of chronic coronary syndromes
2. Screening for mental illness in people with CV disease	ACC/AHA/SCAI 2021: Coronary artery revascularization

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; ACS, acute coronary syndrome; CV, cardiovascular; ESC, European Society of Cardiology; NICE, National Institute for Health and Care Excellence; SCAI, Society for Cardiovascular Angiography and Interventions.

Table 2. Cardiovascular recommendations found in psychiatric guidelines

CV recommendations	Psychiatric guidelines
1. CV disease screening	NICE 2022: Depression in adults: treatment and management BAP 2020: Evidence-based guidelines for pharmacological treatment of schizophrenia BAP 2016: Evidence-based guidelines for treating bipolar disorder: revised third edition BAP 2016: Management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment NICE 2014: Psychosis and schizophrenia in adults: prevention and management NICE 2014: Bipolar disorder: assessment and management
2. CV pharmacological considerations	VA/DoD 2023: Management of first episode psychosis and schizophrenia BAP 2020: Evidence-based guidelines for pharmacological treatment of schizophrenia BAP 2016: Management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment BAP 2015: Evidence-based guidelines for treating depressive disorders with antidepressants
3. Improving CV risk factor control	VA/DoD 2023: Management of first episode psychosis and schizophrenia EPA 2018: Physical activity as a treatment for severe mental illness BAP 2016: Management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment NICE 2014: Psychosis and schizophrenia in adults: prevention and management NICE 2014: Bipolar disorder: assessment and management
4. Treatment of mental illness to improve CV outcomes	APA 2019: Treatment of depression across three age cohorts

Abbreviations: APA, American Psychiatric Association; BAP, British Association for Psychopharmacology; CV, cardiovascular; CVD; EPA, European Psychiatric Association; NICE, National Institute for Health and Care Excellence; VA/DoD, Department of Veterans Affairs Department of Defense

Table S1. Cardiovascular prevention guidelines and statements

Primary Prevention			
American			
Organization(s)	**Year**	**Title**	**Recommendations and selected discussion**
AHA/ACC/ASE/CHEST/SAEM/ SCCT/SCMR	2021	Chest pain[13]	No recommendations. Psychological syndromes, such as depression, have a close association with chest pain.
ACC/AHA	2019	Primary prevention[14]	No recommendations. Comorbid mental illness is social determinant of health that affects treatment adherence and ASCVD health outcomes.
AHA/ACC/HHS	2014	Strategies to enhance application of CPG[15]	No recommendations.
ACC/AHA	2013	Assessment of cardiovascular risk[16]	No recommendations.
European			
NICE	2023	Cardiovascular disease: Risk assessment and reduction, including lipid modification[9]	Recommendation: *Recognise that CVD risk tools (ex. QRISK3) may underestimate risk in people with SMI. Clinical judgement should inform interpretation, especially for individuals with schizophrenia, bipolar disorder, and other psychoses.*
ESC	2021	Cardiovascular disease prevention[8]	Recommendation: *Mental disorders with either significant functional impairment or decreased use of healthcare systems should be considered as influencing total CVD risk (IC).* Recommendation: *Patients with mental disorders need intensified support and interdisciplinary cooperation to improve adherence to pharmacological and lifestyle interventions (IC, IB).* Recommendation: *ASCVD patients with stress should be considered for referral to psychotherapeutic stress management to improve CV outcomes and reduce stress symptoms (IIa,B).*

			Recommendation*: Patients with CHD and moderate-to-severe major depression should be considered for antidepressive treatment with an SSRI (IIa,B).* Recommendation*: In patients with HF and major depression, SSRIs, SNRIs, and tricyclic antidepressants are not recommended (IIIB.)*
Secondary prevention			
American			
ACC/AHA/SCAI	2021	Coronary artery revascularization[10]	Recommendation: *In patients who have undergone coronary revascularization, screening for depression and referral for treatment when indicated is recommended to improve recovery and quality of life (2b, C-LD).* Recommendation*: In patients who have undergone coronary revascularization who have symptoms of depression, anxiety, or stress, treatment with cognitive behavioural therapy, psychological counselling, and/or pharmacological interventions is beneficial to improve quality or life and cardiac outcomes (1, B-R).*
AHA/ACC	2017	Clinical Performance and Quality Measures for Adults With STEMI and NSTEMI[17]	No recommendations.

ACC/AHA/SCAI	2015	Percutaneous Coronary Intervention for Patients With STEMI[18]	No recommendations.
ACC/AHA	2014	Management of Patients with NSTEMI ACS[19]	No recommendations. Psychiatric disorders are noncardiac causes of chest pain that can mimic ACS.
European			
ESC	2020	ACS in Patients Presenting without Persistent ST-Segment Elevation[11]	Recommendation: *Psychological interventions are recommended to improve symptoms of depression in patients with CAD in order to improve quality-of-life (I, B).*
ESC	2019	Diagnosis and Management of Chronic Coronary Syndromes[12]	Recommendation: *Psychological interventions are recommended to improve symptoms of depression in patients with chronic coronary syndrome (I,B).*
ESC	2017	Management of Acute Myocardial Infarction in Patients Presenting with ST-Segment Elevation[20]	No recommendations.

Legend. Abbreviations. ACC, American College of Cardiology; ACS, acute coronary syndrome; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; ASE, American Society of Echocardiography, CAD, coronary artery disease; CHD, coronary heart disease; CHEST, American College of Chest Physician; CPG, clinical practice guidelines; CV, cardiovascular; CVD, cardiovascular disease; ESC, European Society of Cardiology; HF, heart failure; HHS, Department of Health and Human Services; NICE, National Institute for Health and Care Excellence; NSTEMI, Non–ST-elevation myocardial infarct; SAEM, Society for Academic Emergency Medicine; SCAI, Society for Cardiovascular Angiography and Interventions; SCCT, Society of Cardiovascular Computed Tomography; SCMR, Society for Cardiovascular Magnetic Resonance; SMI, severe mental illness; SNRI, serotonin-noradrenaline reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; STEMI, ST-elevation myocardial infarction

ESC:

Classes of recommendations:

Class I: Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.
Class II: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.
Class IIa: Weight of evidence/opinion is in favour of usefulness/efficacy. Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
Class III: Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.

Level of evidence:

A: Data derived from multiple randomized clinical trials or meta-analyses.
B: Data derived from a single randomized clinical trial or large non-randomized studies.
C: Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

ACC/AHA/SCAI:

Classes of recommendations:

Class 1: Strong (Benefit >>> Risk).
Class 2a: Moderate (Benefit >> Risk)
Class 2b: Weak (Benefit ≥ Risk)
Class 3: No benefit (Moderate, Benefit = Risk)
Class 3: Harm (Strong, Risk > Benefit).

Level of evidence:

LEVEL A: High-quality evidence‡ from more than 1 RCT, Meta-analyses of high-quality RCTs, One or more RCTs corroborated by high-quality registry studies
LEVEL B-R (Randomized): Moderate-quality evidence‡ from 1 or more RCTs, Meta-analyses of moderate-quality RCTs
LEVEL B-NR (Nonrandomized): Moderate-quality evidence‡ from 1 or more well-designed, well- executed nonrandomized studies, observational studies, or registry studies, Meta-analyses of such studies
LEVEL C-LD (Limited Data): Randomized or nonrandomized observational or registry studies with limitations of design or execution, Meta-analyses of such studies, Physiological or mechanistic studies in human subjects
LEVEL C-EO (Expert Opinion): Consensus of expert opinion based on clinical experience

Table S2. Psychiatric guidelines

American			
Organization(s)	**Year**	**Title**	**Recommendations and selected discussion**
VA/DoD	2023	Management of First-Episode Psychosis and Schizophrenia[21]	Recommendations*: Dietary interventions, exercise, psychoeducation, as well as adjuvant pharmacological interventions are suggested in patients treated with antipsychotic medication (Weak for).* Recommendation: M*etformin, Topiramate, or Aripiprazole is suggested for treatment of metabolic side effects of antipsychotic medication and weight loss in individuals with schizophrenia (Weak for).* Coordinated Specialty Care (CSC) places special emphasis on monitoring and managing cardiometabolic risk factors, such as smoking, weight gain, hypertension, dyslipidemia, and pre-diabetes.
VA/DoD	2022	Management of Major Depressive Disorder[26]	No recommendations. MDD co-occurs with many medical illnesses/conditions like diabetes, hypertension, and congestive heart failure, complicating the treatment of medical disorders and MDD, and increasing morbidity and mortality.
APA	2020	Treatment of Patients with Schizophrenia[22]	No recommendations. Increases in morbidity and mortality related to physical health in individuals with schizophrenia are likely associated with such factors as obesity, diabetes, hyperlipidemia, greater use of cigarettes, reduced engagement in health maintenance (e.g. diet, exercise), and disparities in access to preventive health care and treatment for physical conditions. If a patient has a concomitant physical condition (e.g., diabetes, cardiac conduction abnormalities, a seizure disorder), choice of medication will need to consider the likelihood of exacerbating an existing health condition. Factors to consider when making a determination about selecting or changing antipsychotic medications include whether the patient is taking other medications that are known to prolong QTc intervals; whether the patient has factors that would influence drug metabolism, leading to

			higher blood levels of a drug (e.g., poor metabolizer status, pharmacokinetic drug-drug interactions, hepatic or renal disease, drug toxicity); whether the patient is known to have a significant cardiac risk factor (e.g., congenital long QT syndrome, structural or functional cardiac disease, bradycardia, family history of sudden cardiac death.
APA	2019	Treatment of Depression Across Three Age Cohorts[27]	Recommendation: *Patients with depression and Type II diabetes mellitus should be considered for a combination of cognitive-behavioural therapy and usual care (conditional recommendation for use).* Research has shown that among people without CVD but depression at baseline, there is an approximately 200% increase in relative risk (or probability) of developing heart disease compared with nondepressed persons. As noted earlier, depression is frequently found to be comorbid with other mental health problems (e.g., anxiety, posttraumatic stress disorder), as well as in combination with various medical problems (e.g., heart disease, cancer, stroke).
ACP	2016	Nonpharmacologic Versus Pharmacologic Treatment of Adult Patients With Major Depressive Disorder[28]	No recommendations.
European			
NICE	2022	Depression in adults: treatment and management[29]	Recommendation: *Before starting an antipsychotic, check the person's baseline pulse and blood pressure, weight, nutritional status, diet, level of physical activity, fasting blood glucose or HbA1c and fasting lipids.* Recommendation: *Carry out monitoring for people who take an antipsychotic for the treatment of their depression. This may include: weight, fasting blood glucose or HbA1C, fasting lipids, and an electrocardiogram (ECG), as per specified schedule.* Recommendation: *Consider ECG monitoring in people taking lithium who have a high risk of, or existing, CVD.*

BAP	2020	Evidence-based guidelines for the pharmacological treatment of schizophrenia[23]	Recommendation: *Regarding antipsychotic therapy,* • *All patients should have a personal and family CV history taken (D).* • *Attention should be paid to identifying the risk factors for CVD/sudden death in psychiatric patients (D).* • *Treatment with statins should be considered more frequently (D).* • *Avoid high doses/polypharmacy in all patients but especially in those with multiple CV risk factors, unless clinically justified (D).* • *Vigilance for CV events and CV complications of therapy is recommended in all patients (D).*
EPA	2018	Physical activity as a treatment for severe mental illness[33]	Recommendation: *Physical activity should be used to improve physical health in people with SMI (Some evidence, C).*
BAP	2016	Evidence-based guidelines for treating bipolar disorder: revised third edition[31]	Recommendation: *Bipolar patients are at high risk of CV, metabolic and respiratory disease. There should be an annual auditable check for hypertension, central obesity, raised blood glucose, weight, and dyslipidemia annually (S).* Treatment with dopamine antagonist agents should always trigger screening for four cardio-metabolic risk factors (hypertension, central obesity, raised blood glucose, and dyslipidemia**).**
BAP	2016	Management of weight gain, metabolic disturbances and CV risk associated with psychosis and antipsychotic drug treatment[24]	Recommendations: *Regarding physical health risk factors, the following should be assessed (S): body mass index (BMI), HbA1C or random/fasting blood glucose, lipid profile, blood pressure.* • *All measurements below should be assessed before starting an antipsychotic, or as soon as possible and then monitored at specific intervals.* Recommendations: *Regarding obesity,* • *Lifestyle interventions (mostly of the 'behavioural lifestyle intervention' type (S).* • *Antipsychotic switching (B).* • *Adjunctive aripiprazole is recommended as a possible intervention for weight gain associated with clozapine and olanzapine (B).*

			• *Adjunctive Metformin: In the context of recommendations regarding groups at high risk of diabetes in NICE PH38, metformin should be considered as an adjunct to attenuate or reduce weight gain following antipsychotic medication (A).* Recommendations: *Regarding management of increased risks for diabetes and CVD,* • *Annual screening for potential pre-diabetic states is recommended for those with psychosis receiving antipsychotic medications (S).* • *Tobacco smoking is an important additive risk factor for diabetes and CVD, and those who smoke should be referred to smoking cessation services (S).* • *The prescription of metformin for those not responding to intensive lifestyle interventions needs to be considered in the context of the individual (S).* • *Diabetes, dyslipidemia, and hypertension should be managed according to existing standard NICE guidelines for the general population.*
BAP	2015	Evidence-based guidelines for treating depressive disorders with antidepressants[30]	Recommendations: *Regarding comorbid medical illness,* • *Where possible avoid TCAs in patients at high risk of CV disease, arrhythmias and cardiac failure (C).* • *In acute coronary syndromes choose drugs which do not increase the risk of subsequent cardiac events (S): there is best evidence for SSRIs, mirtazapine and bupropion.*
NICE	2014	Psychosis and schizophrenia in adults: prevention and management[25]	Recommendations: *Before starting antipsychotic medication, undertake and record the following baseline investigations: weight (plotted on a chart), waist circumference, pulse and blood pressure, fasting blood glucose or HbA1c, blood lipid profile and prolactin levels, assessment of any movement disorders, assessment of nutritional status, diet and level of physical activity, ECG if findings from physical examination have identified specific CV risk or if there is a personal history of CVD.* Recommendations: *Monitor and record the following regularly and systematically throughout treatment, but especially during titration: weight, waist circumference (plotted on a chart), pulse and blood pressure, fasting blood glucose or HbA1c, and blood lipid levels, adherence, overall physical health.* Recommendation: *The secondary care team should maintain responsibility for at least the first 12 months or until the person's condition has stabilised, whichever is longer. Thereafter, the*

			responsibility for this monitoring may be transferred to primary care. Assessments should be made annually, with a copy of the results sent to the care coordinator, psychiatrists and secondary care team. Recommendation*: Treat people with psychosis or schizophrenia who have diabetes and/or CVD in primary care according to the appropriate NICE guidance.*
NICE	2014	Bipolar disorder: assessment and management[32]	Recommendation: *Ensure that the physical health check for people with bipolar disorder, performed at least annually, includes weight or BMI, diet, nutritional status and level of physical activity; CV status, including pulse and blood pressure; metabolic status, including fasting blood glucose or glycosylated haemoglobin (HbA1c), and blood lipid profile; liver function; renal and thyroid function, and calcium levels, for people taking long-term lithium.* Recommendation: *Before starting antipsychotic medication, measure and record the person's weight or BMI, pulse, blood pressure, fasting blood glucose or HbA1C, blood lipid profile, ECG (if family history suggestive CVD, significant history of cardiac disease/arrhythmia, presence of CV risk factors)* Recommendation*: Monitor the physical health (CVD, diabetes, obesity, and respiratory diseases) of people with bipolar disorder when responsibility for monitoring is transferred from secondary care, and then at least annually. These should be audited in the annual team report, which should be sent to the care coordinator and psychiatrist and put in the secondary care records* Recommendation: *Promptly identify CV risk factors and offer treatment and supportive therapies when indicated, as per NICE's guidelines.* Recommendation*: Trusts should ensure that they take account of relevant guidelines on the monitoring and treatment of CV and metabolic disease in people with bipolar disorder through board-level performance indicators*

Legend. Abbreviations. APA, American Psychiatric Association; APC, American College of Physicians; BAP, British Association for Psychopharmacology; BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease; ECG, electrocardiogram; EPA, European Psychiatric Association; HbA1c, glycated haemoglobin; MDD, Major depressive disorder; NICE, National Institute for Health and Care

Excellence; SMI, severe mental illness; SSRI, selective serotonin reuptake inhibitor; TCA, Tricyclic antidepressant; VA/DoD, Department of Veterans Affairs Department of Defense

BAP:

Categories of evidence for causal relationships and treatment:

Ia: evidence from meta-analysis of randomised controlled trials (RCTs)
Ib: evidence from at least one RCT
IIa: evidence from at least one controlled study without randomisation
IIb: evidence from at least one other type of quasi-experimental study
III: evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
IV: evidence from expert committee reports or opinions and/or clinical experience of respected authorities

Proposed categories of evidence for non-causal relationships:

I: evidence from large representative population samples
IIa: evidence from small, well-designed, but not necessarily representative samples
IIb: evidence from pharmacovigilance studies
III: evidence from non-representative surveys, case reports
IV: evidence from expert committee reports or opinions and/or clinical experience of respected authorities

Strength of recommendation:

A: directly based on category I evidence
B: directly based on category II evidence or extrapolated recommendation from category I evidence
C: directly based on category III evidence or extrapolated recommendation from category I or II evidence
D: directly based on category IV evidence or extrapolated recommendation from category I, II or III evidence

EPA:

Grading of evidence in accordance with SIGN (2011):

1 ++: High-quality meta-analyses, systematic reviews of RCTs or RCTs with a very low risk of blas
1+: Well-conducted meta-analyses, systematic reviews or RCTs with a low risk of bias
1--[a] : Meta-analyses, systematic reviews or RCTs with a high risk of bias
2 ++: High-quality systematic reviews of case control or cohort studies. High-quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+: Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2--[a] : Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3: Nonanalytic studies, eg. case reports, case series
4: Expert opinion

Grading of recommendations, modifed from the SIGN (2011):

A: At least one meta-analysis, systematic review, or other study rated at low risk of bias

B: A body of evidence including studies rated as 2, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as l or II
C: A body of evidence including studies rated as II-III, directly applicable to the target population and demonstrating overall consistency of results.
D: Good practice point recommended good practice based on the clinical experience of the Guidance development group and arrived at through consensus

Table S3. Prisma Checklist

Section and Topic	Item #	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	25
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	4-5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	N/A
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	N/A
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	N/A
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	N/A
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	4-5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A

Section and Topic	Item #	Checklist item	Reported on page #
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	N/A
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	N/A
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	N/A
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	N/A
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	N/A
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	8-9
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	7-8
	23b	Discuss any limitations of the evidence included in the review.	8-9
	23c	Discuss any limitations of the review processes used.	8-9
	23d	Discuss implications of the results for practice, policy, and future research.	8
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	N/A
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	9
Competing interests	26	Declare any competing interests of review authors.	N/A
Availability of data, code and	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from	N/A

Section and Topic	Item #	Checklist item	Reported on page #
other materials		included studies; data used for all analyses; analytic code; any other materials used in the review.	

Discussion

3.0 Key Findings

The bidirectional association between CVD and SMI remains underrecognized. The findings from the quality improvement project and the systematic review of professional guidelines demonstrate the gaps in care experienced by the SMI population. The novel Cardio-Psychiatry clinic revealed smoking and obesity, two of the major predictors of CV related-mortality, to be prevalent in over 60% of participants. While 70% of the cohort had a PCP, uncontrolled CV risk factors were identified and treated in over half of participants. While these findings highlight the increased cardiometabolic vulnerability of people with SMI, they also reinforce existing evidence indicating that individuals with SMI are under-screened for CV risk factors and less likely to receive guideline-recommended treatment upon risk factor identification.[30, 51, 52, 109, 110] Proactive risk stratification is crucial for disease prevention and management in all populations.[9] Considering pre-existing disparities in care, as well as the impact of these findings on such as small cohort, larger scale studies are imperative in capturing the beneficial effect of accessible CV screening in this high-risk population.[30]

The implications of our findings represent individuals with SMI as a cardiometabolic vulnerable population, requiring specialized and coordinated care. While robust data on the cardiometabolic vulnerability of individuals with SMI exists, there is minimal data on CV management of this population. To our knowledge, this systematic review is the first to explore the reporting of CV and psychiatric recommendations in professional society guidelines.

While psychiatric guidelines were most inclusive of CV considerations, less than 40% of CV guidelines included psychiatric considerations. Markedly, all American primary prevention guidelines failed not only at providing management guidance, but there was little describing the

link between CVD and mental illness. These findings magnify the care deficiency experienced by the SMI population, particularly in the United States, supporting the need for future expert guidance. Guidelines should emphasize the interconnectedness between these two disciplines and promote evidence-based recommendations for holistic care.

3.1 Comparing the Literature

SMI and CVD share common biological and behavioural etiologies, explaining the bidirectional association between these two entities.[3, 42] On one hand, sudden cardiac events may trigger the onset of mental illness.[3] Conversely, increasing severity of mental illness has been correlated with worsening comorbid medical conditions such as hypertension, dyslipidemia and diabetes mellitus.[51] While biological and genetic mechanisms are complex and require further research, behavioural mechanisms are consistently reported. Individuals with SMI are more likely to engage in unhealthy lifestyles (high-fat diet, poor physical activity, substance abuse, inadequate medication adherence), all of which exacerbate CV risk.[3, 16, 17, 30] Our data aligns with previous studies reporting elevated prevalences of obesity and smoking.[39, 49, 75-77] Our findings also concur with previous studies showing elevated rates of diabetes, dyslipidemia, metabolic syndrome and hypertension in this population.[16, 18, 47]

These findings stress the importance of utilizing resources for the implementation of primary prevention interventions. While the current evidence has outlined various behavioural interventions aimed at improving lifestyle habits, reported findings are inconsistent. For instance, the CHANGE study enrolled over 400 adults with schizophrenia and obesity into a 12-month lifestyle modification program and care collaboration.[63] Two year follow-up results showed no reduction on 10-year CVD risk between groups.[63] On the other hand, two smaller studies aimed at

reducing obesity rates in schizophrenia spectrum patients reported improvements in weight and BMI.[111, 112] Smoking cessation interventions have been reported as most impactful in reducing CV risk in this population.[11, 62, 113] More specifically, interventions are most effective when they are highly integrated, coordinated and include interventions for both behavioural change and care management.[11, 114] For example, incorporating lifestyle interventions, in concordance with prophylactic use of antidiabetic agents in patients on atypical antipsychotic therapies, even in the absence of baseline dysglycemia.[67] A multimodal approach should be prioritized in the development of future behavioural interventions aimed at reducing CV risk in the SMI population.

3.2 Strategies to Improve CV Health and Disparities in Care

The increased CV morbidity and mortality among individuals with SMI primarily stems from modifiable factors, many of which represent opportunities for improvement of care delivery and patient outcome. The CV risk factor burden must be addressed imperatively, on both the patient and provider-level. While the demand for CV risk screening certainly overweighs its supply, increasing opportunities for primary preventative services is the mainstay of disease prevention. This could be accomplished through encouraging nurse-led interdisciplinary clinics in the primary care setting. In parallel, as SMI patients are often in close contact with their treating psychiatric team, increasing access to preventative services in the psychiatric setting should be considered. Emphasis should be placed on using validated screening tools, like the 30-year FRS, especially in young adults with SMI, with the goal of increasing time spent in optimal midlife health.[30] In other words, as the more traditional 10-year CV risk equation is only validated as of age 40, and SMI patients have a 15-20 year reduced life expectancy, utilizing this tool may result in delayed identification and management of CV risk factors.[30] Furthermore, given the link between

psychopharmacotherapy and heightened CV morbidity, efforts towards prioritizing pragmatic prescribing practices is key. Practitioners should encourage simplified treatment plans, including combined daily doses or tools like the use of a dispill, to facilitate treatment adherence.[11] Comparably, efforts towards encouraging family engagement in the treatment plan have shown favourable outcomes.[11] On the other hand, following sudden cardiac events, all patients should be screened for depressive symptoms and referred for additional psychological support when necessary.

The implementation of a Cardio-Psychiatry clinic is relevant and feasible, as evidenced by the 62% enrolment rate. Our results are consistent with similar studies, reported enrollment rates ranging between 20-60%.[115, 116] Multiple strategies can be implemented at various levels to increase patient recruitment and reduce barriers to care in this high-risk population. Patient recruitment relies heavily on widespread health-care provider awareness. This could be encouraged by distributing informative flyers for providers to share with their patients, presenting the study and its progress during weekly rounds, as well as engaging multiple referring sites.[115] Bundling care, such as scheduling assessments around participants existing appointments was highly effective in motivating patients to participate. Additionally, for individuals with compromised telephone access, the consenting process was mediated by the referring HCP. In other words, the referring HCP allocated several minutes of their appointment with the patient to call the QI research team, presenting an immediate opportunity to obtain consent. Nonetheless, this method depended heavily on busy clinicians and may not be viable in the long term. Additional investigation is necessary to address patient recruitment challenges among individuals with SMI.

While addressing access is key, health-care providers play a pivotal role in health promotion. Patient related factors such as poor self-efficacy, avoidance behaviour, medication

nonadherence, and low SES, often require individuals with SMI to receive continuous therapeutic support. However, the core symptomology of psychiatric disorders often result in individuals with SMI having fewer medical visits, with fewer documented medical problems.[110]

Promoting initiatives like the Cardio-Psychiatry clinic represents increased opportunities to touch base with psychiatric patients and provide adequate medical follow-up. That being said, the development of a trustful patient-provider alliance is essential in the delivery of effective care. The negative attitude of many PCPs towards SMI patients represents a barrier to quality care.[9, 110] PCPs spend less time with individuals with mental illness, as compared to the general population, and often lack knowledge on the management of psychiatric conditions.[110] Conversely, mental-health specialists feel as though they lack fluency with medical management of somatic comorbidities.[110] As a result, individuals with SMI are directly caught in a gap of care. Multidisciplinary collaboration between psychiatry, cardiology and primary care healthcare teams is essential in optimizing patient outcome. The Cardio-Psychiatry initiative fosters a corridor of referrals between these disciplines, promoting collaborative care. It can also be implemented as a clinical trainee rotation, with the aim of raising awareness and bridging the psycho-somatic divide. Additionally, the development of a specialized Cardio-Psychiatry curriculum could increase general practitioners' awareness on these issues, all while reducing the stigma associated with mental illness.[11]

The lack of evidenced-based recommendations on the management of CVD in SMI directly contributes to elevated burden of cardiometabolic diseases in this population. There is a dire need for interdisciplinary consensus and guidance. The systematic review of professional society's guidelines revealed a lack of awareness among both American and European CV specialists, with the former being more pronounced. Conversely, European psychiatric professional societies were

most considerate of CV-related factors. However, recommendations vary. These findings magnify the need for the publication of a best practice guideline, integrating both cardiometabolic and psychiatric perspectives. American and European specialists could collaborate to achieve international consensus on CV management in people with SMI. These recommendations could then be utilized by PCPs, increasing overall awareness, and reducing stigmatization, while providing an improved standard of care.

3.3 Implications and Future Direction

Our findings reveal significant areas for improvement. Cardio-Psychiatry, alternatively referred to as behavioural cardiology, is a developing field of research that investigates the intricate relationship between CV health and mental well-being.[11] This holistic approach is based on the mitigation of psychosocial and biological risk factors through tailored behavioural and pharmacological interventions, patient education, and promotion of self-efficacy.[117] Cardio-Psychiatry also incorporates culturally sensitive care, given the elevated prevalence of SMI among certain ethnicities, and their diminished resource utilization.[60] The Cultural Formulation Interview is a validated tool designed for assessing a patient's cultural background during psychiatric diagnosis and treatment.[60] The Cultural Formulation Interview considers a person's cultural background to shape their perception of mental illness, therapeutic insight, and degree of self-motivation, all of which provide meaningful clinical data.[60] Recovery-oriented care, which focuses on autonomy, empowerment, and shared-decision making is also foundational in Cardio-Psychiatry.[60] Despite increasing efforts in research collaboration and growing recognition of the unaddressed issues in this field, the integration of Cardio-Psychiatry as a distinct area of research and clinical practice has not yet materialized.[11] While the magnitude of interdisciplinary

collaboration required for this paradigm shift is tremendous, it is necessary to palliate the gap in care. Given the saliency of this emerging field, recognition through research grants could support further advancements targeted towards the implementation of interdisciplinary care.

A future direction for this project would include a prospective, randomized control trial exploring the feasibility and efficacy of a multicomponent primary prevention intervention to reduce cardiovascular risk in people with SMI. The publication of a best-practice guideline on how to effectively manage CV risk and disease in people with SMI is also highly relevant. Not only will this address preventative screening, but it will also accompany clinicians on how to optimize holistic care. Further longitudinal studies are needed to study the long-term effects of this intervention, as well as to address questions of treatment adherence in the SMI population.

3.4 Limitations

There are several limitations to our project. First, the QI study was a single-centre study conducted over a limited timeframe, resulting in a relatively small sample size, and affecting the overall generalizability of our findings. Second, our systematic review was limited only to major American and European professional societies and thus other guidelines from less major professional societies were omitted. However, major society guidelines are the most likely to influence clinical practice. Additionally, given the manual search, it is possible that certain textual relevant phrases were not captured.

Conclusion

There is a dire need for collaboration between the divisions of cardiology and psychiatry. Addressing this gap in care is imperative in reducing morbidity and mortality in people with SMI, alleviating one of the largest financial burdens on the healthcare system. The QI project, as well as the literature review of professional guidelines, serve as stepping stones for the emerging field Cardio-Psychiatry.

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