CARDIOVASCULAR RISK AND DISEASE AMONG PEOPLE WITH MENTAL HEALTH DISORDERS IN CANADA

by

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ABSTRACT

Background: Although research has revealed that there is excess cardiovascular morbidity among persons with mental health disorders (MHD), there is limited evidence specific to the Canadian context. It is also unclear if elevated rates of cardiovascular disease (CVD) can be attributed to MHDs themselves or to exposure to psychoactive medications. Moreover, few researchers have extended their investigations to account for psychiatric comorbidity or have applied cardiovascular risk prediction algorithms to conduct comprehensive assessments of this population's heart health.

Methods: Three studies were undertaken utilizing cross-sectional data obtained via the Canadian Community Health Survey Cycle 1.2. MHDs were assessed using the World Mental Health Composite International Diagnostic Interview. Frequency of psychoactive medication use, the presence of heart disease, and stroke and cardiovascular risk factors were also assessed. Framingham risk prediction algorithms were used to calculate cardiovascular risk. Descriptive statistics were employed to estimate the prevalence of CVD in people with a range of MHDs and psychoactive medication use. Associations between MHDs, psychoactive medication use, and cardiovascular risk and CVD were analyzed with logistic regression. Confidence intervals for the proportions and odds ratios were calculated using weighted bootstrapped estimates to take into account the complex survey design and nonresponse.

Results: Our examination of psychiatric comorbidity revealed that a small proportion of Canadians suffer from a heavy burden of MHDs and that disorders often co-occur. Respondents with any lifetime MHD were twice as likely to have a history of heart disease or stroke, and those without heart disease or stroke were more likely to be at high

risk of developing CVD within 30-years compared to people without a diagnosis of a MHD. Similarly, people reporting psychoactive medication use were twice as likely to have heart disease, three times as likely to report having had a stroke, and more likely to be in the highest 30-year risk category for CVD compared to people not reporting psychoactive medication use. Negligible confounding was found between the effects of psychoactive medication use and having a MHD on heart health.

Conclusion: These findings underscore the need for continued monitoring of CVD among Canadians with MHDs and development of effective preventative strategies.

PREFACE

This statement certifies that the work contained in this dissertation was conceived, conducted, and written by myself, Catherine Goldie. All empirical research undertaken for the completion of this dissertation was approved by the University of British Columbia Behavioural Research Ethics Board (project title: "A social ecological examination of cardiovascular risk factors among individuals with severe mental illness," certificate H11-01279). A microdata research contract was granted by Statistics Canada to conduct this research (project title: "A social ecological examination of cardiovascular risk factors among individuals with severe mental illness," project ID: 11-SSH-BCI-2910). Chapters 2, 3 and 4 will be further developed and submitted for publication with the following authors, in order: Catherine Goldie, Joy Johnson, Pamela Ratner, and Victoria Smye. I was responsible for the data analysis and the initial drafts of all chapters. The supervisory committee offered advice with respect to the research question formulation, data analysis plans, interpretation, and writing. The manuscripts have not yet been submitted for peer review or publication.

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LIST OF ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical Classification system
CCHS	Canadian Community Health Survey
CI	Confidence interval
CMHT	Community-based mental health team
CVD	Cardiovascular disease
DIS	Diagnostic Interview Schedule
DSM	Diagnostic and Statistical Manual of Mental Disorders
DSM-III	Diagnostic and Statistical Manual of Mental Disorders (third edition)
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (fourth edition)
ECA	Epidemiologic Catchment Area
ICD	International Classification of Diseases
ICD-10	International Classification of Diseases (tenth revision)
MDE	Major depressive episode
MeSH	Medical Subject Heading
MHD	Mental health disorder
MI	Myocardial infarction
mmHg	Millimeter of mercury
N/A	Not applicable
NCS	National Comorbidity Survey
NCS-R	National Comorbidity Survey Replication
NEMESIS	Netherlands Mental Health Survey and Incidence Study
NPA	Negative percent agreement
OR	Odds ratio
PPA	Positive percent agreement
RCT	Randomized controlled trial
ROC	Receiver operating characteristic
RR	Relative risk
SBP	Systolic blood pressure
SCID	Structured Clinical Interview for DSM-IV Disorders
SD	Standard deviation
SE	Standard error
SMR	Standardized mortality ratio
SNRI	Serotonin-norepinephrine reuptake inhibitors
SSRI	Selective serotonin reuptake inhibitors
TCA	Tricyclic antidepressants
UM-CIDI	University of Michigan-Composite International Diagnostic Interview
WMH-CIDI	World Mental Health Composite International Diagnostic Interview

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CHAPTER 1: INTRODUCTION

1.1 Introduction

In Canada, developments in psychopharmacology, concerns about the civil rights of people with mental health disorders (MHDs), the need for cost-containment, and studies revealing the negative impacts of institutionalization triggered mental healthcare reforms. Beginning in the 1950s, these reforms focused on "de-institutionalization" or rapid closure of psychiatric hospitals and discharge of inpatients into community settings (Krieg, 2001; Morrow, Dagg, & Pederson, 2008; Romanow & Marchildon, 2003; Sealy & Whitehead, 2004). Initially, many communities were unprepared to handle the influx of patients with MHDs; however, infrastructure for community mental health services has since been developed (Romanow & Marchildon, 2003). Multidisciplinary, community-based teams of healthcare professionals are now an integral part of modern mental health services. Community-based mental health teams (CMHT) are responsible for addressing a wide range of health and social needs and are usually composed of providers from several healthcare disciplines, including nursing, occupational therapy, psychiatry, and social work (Tyrer, Coid, Simmonds, Joseph, & Marriott, 2000).

The development of specialized outpatient psychiatric care has resulted in a separation between mental and primary healthcare services for patients with psychiatric disorders and this has had a detrimental impact on their physical health status (Horvitz-Lennon, Kilbourne, & Pincus, 2006; Phelan, Stradins, & Morrison, 2001). This problem has arisen because CMHTs are the primary point of access to the healthcare system for many people with MHDs, yet the provision of health care for other, especially physical, health conditions is not a priority; instead, emphasis is placed on psychological and social issues (Miller, Druss, Dombrowski, &

Rosenheck, 2003; Phelan et al., 2001; Wang et al., 2005). Moreover, for people who are able to access both CMHTs and primary care services, there is poor integration and continuity of care between the two sectors (Horvitz-Lennon et al., 2006; Kates et al., 1997). This fragmentation of services poses significant challenges to effectively meeting the complex care needs of people who have comorbid mental and other chronic illnesses. For example, the coexistence of heart disease complicates the management of psychiatric disorders and can contribute to a diminished quality of life and a worse prognosis (Marano et al., 2011).

There has been some investigation of the intersection between mental and primary healthcare services in Canada, but this has mainly focused on integrating mental healthcare services into primary care. Further examination of how to better implement health care that addresses chronic health conditions, other than MHDs, into CMHTs is needed (Clatney, MacDonald, & Shah, 2008; Palin, Goldner, Koehoorn, & Hertzman, 2011, 2012). Clarity about who should take responsibility for the physical health of people with MHDs needs to be addressed (McIntyre & Romano, 1977). Although primary care providers may be more competent with physical assessment, they can be less confident in working with patients with MHDs. Conversely, CMHTs have expertise in caring for people with psychiatric disorders, but are less familiar with the management of other complex health conditions (Osborn, Nazareth, Wright, & King, 2010). While this fragmentation continues, physical illnesses go undetected or are sub-optimally treated by providers in CMHTs. This occurs because they have competing demands on their time, which limits their ability to focus on issues outside of psychiatry, there is inadequate reimbursement for offering physical health assessment or interventions, and there is limited training and experience in treating non-psychiatric, complex chronic conditions (Horvitz-Lennon

et al., 2006; Jeste, Gladsjo, Lindamer, & Lacro, 1996; Kick, Morrison, & Kathol, 1997; Lawrence & Kisely, 2010; McIntyre et al., 2007; Phelan et al., 2001; Singh, 2000).

Apart from the system-level issues, people with MHDs experience significant provider and personal barriers to accessing high quality health care (Horvitz-Lennon et al., 2006; Miller et al., 2003). For instance, it is known that patients with MHDs are less likely to receive adequate cardiovascular and vascular screening and treatment; this is most frequently manifested through poor control of body weight, blood pressure, cholesterol, and diabetes and through less access to coronary revascularization procedures compared with people without MHDs (Druss, Bradford, Rosenheck, Radford, & Krumholz, 2000; Frayne et al., 2005; Hippisley-Cox, Parker, Coupland, & Vinogradova, 2007; Kisely, Campbell, & Wang, 2009; Nasrallah et al., 2006; Osborn et al., 2010). At the provider level, there is pervasive stigma associated with MHDs that can affect the quality of care people with psychiatric disorders receive (Corrigan & Watson, 2002). For example, some practitioners regard people with MHDs as being difficult or disruptive and attribute abnormal behaviour to individual choice, rather than to being symptoms of an illness, and react by dismissing somatic complaints (Dickerson et al., 2003; Sartorius, 2007). Furthermore, short consultation times and a lack of resources make it difficult for clinicians to both assess a person's mental health status and conduct a physical examination; this limits opportunities for comprehensive health screening (Lester, 2006; Phelan et al., 2001). The situation becomes even more challenging if the person with a MHD has difficulty communicating their health needs because they may be imprecise, apprehensive, or reluctant to discuss their physical health symptoms (Lawrence & Kisely, 2010).

At a patient level, people with MHDs are disadvantaged in their ability to attend to their physical health needs because of cognitive impairment, social isolation, and lack of family

support, self-neglect and lack of motivation are commonly associated with their disorders (Lawrence & Kisely, 2010). Moreover, socio-economic disadvantage is more common among people with MHDs, and is associated with poor health behaviour and reduced access to health care (Muntaner, Eaton, Miech, & O'Campo, 2004). Because of these inequalities, patients with MHDs are less likely to seek consultation for their physical health problems or adhere to treatment than are people without MHDs (Druss & Rosenheck, 1998; Jeste et al., 1996).

It is in this clinical context that pervasive physical health disparities are exacerbated for people with MHDs. It has been well documented that people with MHDs have relatively shorter life expectancy; their mortality rate is two or three times higher than the general population's (Angst, Stassen, Clayton, & Angst, 2002; Brown, 1997; Bushe, Taylor, & Haukka, 2010; Chang et al., 2010; Colton & Manderscheid, 2006; Kawachi, Sparrow, Vokonas, & Weiss, 1994; Saha, Chant, & McGrath, 2007). This mortality gap translates to 13- to 30-year shortened life expectancy, and the gap has widened in recent decades, even in countries with universal health care (De Hert, Correll, et al., 2011). Excess mortality in this population is largely the result of non-psychiatric illnesses, with the most common cause of death being cardiovascular disease (CVD) (Osborn, Levy, et al., 2007). Yet, the nature of the links between CVD and MHDs are not entirely clear, and unpacking these links is challenging.

In what follows, the current state of knowledge related to CVD and MHDs is reviewed. The purpose of this review is two-fold: (a) to examine the current evidence related to elevated CVD and risk among people with MHDs and (b) to discuss measurement issues concerning the key variables used within psychiatric and cardiovascular epidemiology. This review provides a rationale for the series of studies that were undertaken and reported here. After briefly reviewing the search strategy used to identify the relevant literature, the review is prefaced with a general

examination of the association between cardiovascular morbidity and MHDs to provide a frame of reference for the presentation of a conceptual model of the etiology of excess CVD. The discussion of the multifactorial causes of excess cardiovascular mortality, morbidity, and risk among people with MHDs primarily focuses on unhealthful behaviour, side effects of psychoactive medication treatment, and some pathophysiologic characteristics of mental health. The measurement issues are addressed before the justification, objectives, and approach for this work are presented.

1.2 Search strategy

The literature reviewed in Chapters One through Four was drawn from a comprehensive search of English language reports published between 1951 and 2013 encompassing the fields of nursing, medicine (cardiology, psychiatry, and general practice), epidemiology, public health, and rehabilitation sciences. A range of bibliographic databases were searched: PubMed, EMBASE, PsychINFO, CINAHL and the Cochrane Database of Systematic Reviews. To verify that each search was exhaustive, manual searches of references lists from key review papers, as well as internet and grey literature searches using Academic Search Complete, Google Scholar, and previous publications from the Canadian Research Data Centre Network (Statistics Canada) were conducted.

Each search began with broad Medical Subject Heading (MeSH) keywords related to "mental disorders," "cardiovascular diseases," and "epidemiology" before more specific synonyms (appropriate for each chapter) including "schizophrenia," "depression," "bipolar disorder," "anxiety disorders," "comorbidity," "risk," "drug therapy," "antipsychotic agents," "antidepressant agents," "anti-anxiety agents," and "Canada" were used to refine the searches.

Meta-analysis and systematic reviews were favoured over other study designs and priority was given to findings that included adequate sample sizes and validated assessment measures.

1.3 The association between cardiovascular disease and mental health disorders

Numerous studies have demonstrated that individuals with MHDs, such as schizophrenia, depression, bipolar disorder, and anxiety disorders, have greater morbidity associated with CVD compared with people without MHDs (Dossa, Glickman, & Berlowitz, 2011; Enger, Weatherby, Reynolds, Glasser, & Walker, 2004; Goldstein, Fagiolini, Houck, & Kupfer, 2009; Kubzansky, Kawachi, Weiss, & Sparrow, 1998; Rugulies, 2002; Tsai, Lee, Chou, Su, & Chou, 2012). CVD involves a wide class of disorders that affect the heart, the blood vessels of the heart, and the system of blood vessels throughout the body and within the brain (Heart & Stroke Foundation, 2013). CVD manifests itself through coronary death, myocardial infarction (MI), coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, and heart failure (D'Agostino et al., 2008; Pencina, D'Agostino, Larson, Massaro, & Vasan, 2009).

The study of cardiovascular morbidity in Canadians with MHDs has been limited to a few longitudinal studies conducted with provincial-level datasets. Curkendall, Mo, Glasser, Stang, and Jones (2004) conducted a retrospective cohort study of health records from the province of Saskatchewan to compare the prevalence of CVD in patients diagnosed with schizophrenia (N = 3,022) and in age- and sex-matched controls from the general population. They also determined the incidence of cardiovascular morbidity in a follow-up period. The authors found that patients with schizophrenia had increased risk-adjusted odds ratios for heart failure (OR = 1.7, 95% CI [1.4, 2.2]) and stroke (OR = 2.1, 95% CI [1.6, 2.7]). Similarly, the odds of heart failure (OR = 1.6, 95% CI [1.2, 2.0]) and stroke (OR = 1.5, 95% CI [1.2, 2.0]) were also elevated in the follow-

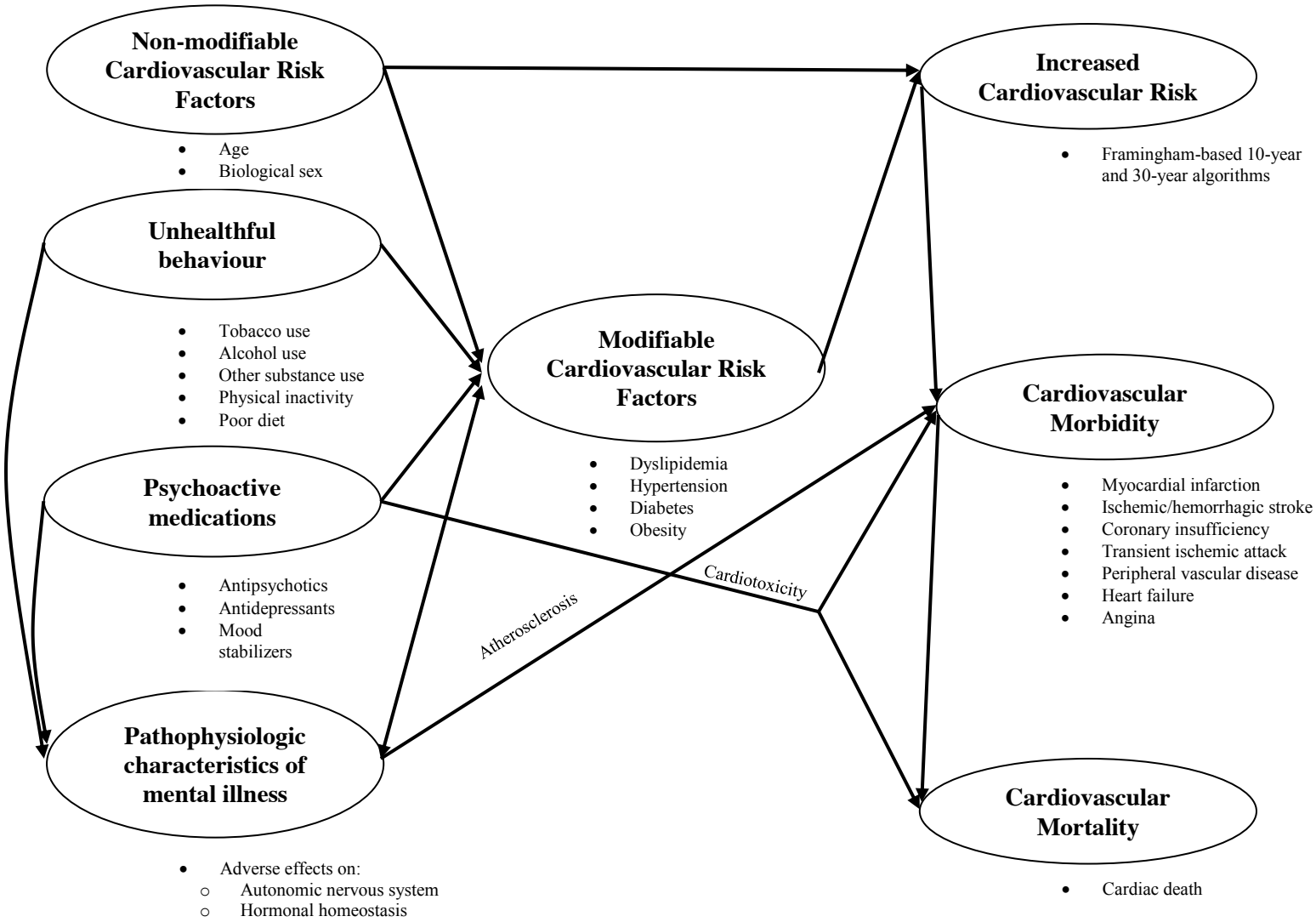
up period. More recently, Callaghan and Khizar (2010) examined the incidence of cardiovascular morbidity among people with bipolar disorder (N = 5,999) by using Province of Ontario emergency department and inpatient hospital records from 2002-2006. The primary outcome was time-to-readmission for any cardiovascular diagnosis. They found that people with bipolar disorder had an adjusted hazard ratio of 1.66 (95% CI [1.37, 2.07]) for subsequent cardiovascular morbidity compared with a population-proxy group (patients with a primary appendicitis-related diagnosis). A more thorough examination of cardiovascular morbidity among Canadians with MHDs is needed, not only to contribute Canadian findings to the international dialogue, but also to better inform approaches to prevention and treatment.

1.4 The etiology of excess cardiovascular morbidity among people with mental health disorders

Figure 1 depicts a conceptual model of excess cardiovascular mortality and morbidity among people with MHDs. The cause of excess cardiovascular mortality, morbidity, and risk among people with MHDs is multifactorial and attributed to a combination of unhealthful behaviours, side effects of psychoactive medication treatment, and pathophysiologic characteristics associated with MHDs. These factors substantially increase the prevalence of modifiable cardiovascular risk factors including dyslipidemia, hypertension, diabetes mellitus, and obesity among people with MHDs compared with the general population. Other non-modifiable risk factors are age, biological sex and genetic background (Barnett et al., 2007; De Hert et al., 2009; Jonas, Franks, & Ingram, 1997; McIntyre, Konarski, Wilkins, Soczynska, & Kennedy, 2006; Osborn et al., 2008; van Reedt Dortland et al., 2010). This model has important implications for the appraisal of cardiovascular risk because the accumulation of cardiovascular risk factors can amplify the risk of cardiovascular injury (Goff et al., 2005; Jackson, Lawes, Bennett, Milne, &

Rodgers, 2005). Moreover, many people with MHDs are less physically active, have comorbid substance use disorders (including tobacco, alcohol, and illicit drug use), and eat a diet that is low in fibre, fruit, and vegetables and high in fat and carbohydrates compared with people without MHDs (Bonnet et al., 2005; Elmslie, Mann, Silverstone, Williams, & Romans, 2001; Lasser et al., 2000; McCreadie, 2003; Osborn, Nazareth, & King, 2007; Rush et al., 2008).

Figure 1: Conceptual model of cardiovascular morbidity and mortality among people with mental health disorders



Previous studies have documented the adverse effects of psychoactive medication use (i.e., antipsychotics, antidepressants, mood stabilizers, anxiolytics) on modifiable cardiovascular risk factors and cardiovascular morbidity (Cohen, Gibson, & Alderman, 2000; Daumit et al., 2008; Pratt et al., 1996). These medications cross the blood-brain barrier and act upon the central nervous system to affect mental processes (e.g., cognition or affect), can induce weight gain, and impair glucose and lipid metabolism that lead to cardiovascular risk factors such as obesity, dyslipidemia, diabetes, and metabolic syndrome (De Hert, Detraux, van Winkel, Yu, & Correll, 2012; Mackin, Bishop, Watkinson, Gallagher, & Ferrier, 2007). The exact psychopharmacological mechanisms underlying these pathways have not been fully elucidated but several explanatory hypotheses exist.

Patient populations that are prescribed antipsychotic, antidepressant, or mood stabilizing medications have varying degrees of weight gain as well as lipid and glucose abnormalities, thereby increasing the risk of obesity, dyslipidemia, diabetes mellitus, and metabolic syndrome (Brauer, Douglas, & Smeeth, 2011; Mackin, 2008; Serretti & Mandelli, 2010). Moreover, antipsychotic medications, tricyclic antidepressant medications, and lithium have known cardiotoxic properties (e.g., they inhibit cardiac sodium, calcium, and potassium channels leading to heart electrophysiology dysfunction and life-threatening arrhythmias) that can manifest in orthostatic hypotension, tachycardia, and ventricular arrhythmias that can prolong the intraventricular conduction time and cause dose-related sudden cardiac death (Chong & Mahendran, 2001; Leung, Barr, Procyshyn, Honer, & Pang, 2012; Ray, Chung, Murray, Hall, & Stein, 2009; Taylor, 2008). Serious conduction alterations such as right and left bundle-branch block or partial or complete atrioventricular block are reflected in electrocardiograms as prolonged PR, QRS, and QT intervals and T-wave flattening or inversion (Marano et al., 2011).

This is a concerning public health issue because psychoactive medication use is common among Canadians, which has substantially increased since the 1980s, yet the impact of psychoactive medication use on CVD and cardiovascular risk has not been quantified on a national level (Beck et al., 2005; Dewa, Remington, Herrmann, Fearnley, & Goering, 2002; Meng, D'Arcy, & Tempier, 2013).

Excess cardiovascular morbidity and mortality among people with MHDs also can be attributed to some pathophysiologic characteristics of MHDs. For example, it is known that psychological stress associated with MHDs can have negative effects on physical health and can be both a cause and consequence of CVD (Figueredo, 2009). A considerable amount of research in this area has been provided by the INTERHEART and INTERSTROKE studies (O'Donnell et al., 2010; Yusuf et al., 2004). Both studies used standardized case-control designs to examine acute myocardial infarction (MI) (N = 15,152 cases and 14,820 controls, in 52 countries) and stroke (N = 2,337 with ischemic stroke, N = 663 with hemorrhagic stroke, and 3,000 controls, in 22 countries). The authors documented that psychosocial stress (i.e., depression, locus of control, perceived stress, and life events) contributed to an increased risk of myocardial infarction (MI) (OR = 2.67 [99% CI: 2.21, 3.22]) and stroke (OR = 1.30 [99% CI: 1.06, 1.60]) (O'Donnell et al., 2010; Yusuf et al., 2004). Other types of psychological stress have been implicated in increasing the risk of CVD, including anxiety, hostility, and hopelessness (Das & O'Keefe, 2008).

The pathophysiological mechanisms underlying psychological stress appear to adversely affect the autonomic nervous system (e.g., reducing heart variability and impairing vagal control) and hormonal homeostasis (e.g., causing chronic elevation in cortisol from repeated stress), resulting in metabolic abnormalities, inflammation, insulin resistance, and endothelial

dysfunction, which promote or accelerate atherosclerosis (Carney et al., 1995; Das & O'Keefe, 2008; Kubzansky et al., 1998; Marano et al., 2011; McEwen, 2003). It is not clear which of the above explanatory hypotheses are most responsible for excess CVD among people with MHDs and their validity needs to be examined further.

1.5 Measurement of key variables

When critically examining cardiovascular morbidity among people with MHDs, the approaches used to measure MHDs and CVD must be carefully considered. Determining whether an individual has a MHD is important for the clinical treatment of patients, as well as for the surveillance of a population's mental health status. However, categorizing MHDs into discrete disorders is a problematic undertaking because the disorders cannot be empirically or objectively verified or validated, in part because of the subjectivity of the diagnostic process and because many people experience multiple psychiatric disorders either concurrently or over the course of their lifetime. Without established neurobiological evidence of abnormality to support diagnostic categories, it can be challenging to differentiate between symptoms of psychiatric illnesses; many are not mutually exclusive. Whereas detailed description of the incidence and prevalence of myocardial infarction and ischemic or hemorrhagic stroke are important metrics for surveying population health, analysis of risks to cardiovascular health is key for developing an understanding of how to prevent disease and injury. Capturing these data is also challenging. Several multivariate risk prediction algorithms, derived from cohort studies and randomized trials, have been developed to quantitatively estimate an individual's chance of developing CVD (Anderson, Odell, Wilson, & Kannel, 1991; Brindle et al., 2006; Conroy et al., 2003; D'Agostino et al., 2000; D'Agostino, Wolf, Belanger, & Kannel, 1994; D'Agostino et al., 2008; Hippisley-Cox, Coupland, et al., 2007; Pencina et al., 2009; Ridker, Buring, Rifai, & Cook, 2007; Ridker,

Paynter, Rifai, Gaziano, & Cook, 2008; Wilson et al., 1998; Woodward, Brindle, & Tunstall-Pedoe, 2007). Determining which measure of cardiovascular risk is best suited to community-based samples is a key to ensuring that valid data are collected. Some of challenges associated with measuring MHDs and cardiovascular risk in community-based samples are considered.

1.5.1 Mental health disorders

The establishment of the Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association (2013), has improved the reliability of psychiatric diagnosis by providing a common language and authoritative taxonomy for the classification of MHDs. The DSM is a rule-based classification system that contains extensive descriptive criteria to aid clinicians in the diagnosis of MHDs by utilizing information related to patients' current presentation. It uses specifiers that describe the severity and course of illness, and provides the principal diagnosis or reason for a healthcare visit when multiple diagnoses are present.

Clinicians and psychiatric epidemiologists have operationalized the DSM in different ways to suit their needs and the settings in which they work. Trained clinicians regularly use semi-structured interviews in their clinical practice, including the Structured Clinical Interview for DSM-IV Disorders (SCID), to assist them with confirming or documenting the presence of Axis 1 (e.g., clinical disorders such as depression or schizophrenia) and Axis 2 (e.g., developmental and personality disorders) disorders (First, Gibbon, & Spitzer, 1997). The most significant challenge to operationalizing the DSM in psychiatric epidemiology is the lack of experienced clinicians to interview and diagnose a large number of respondents in a short period of time. Trained lay interviewers are regularly used to survey community-based populations, but they lack the skills necessary to make independent diagnostic decisions; therefore, they must rely on

established measurement tools that restrict the interviewer's judgment. Consequently, researchers must trust that the respondents' self-reported symptoms and past diagnoses are accurate, which can be problematic because it is known that self-reported data are subject to bias (Podsakoff, MacKenzie, Lee, & Podsakoff, 2003). For example, for a variety of reasons, respondents may not be able to answer the survey questions accurately. Although it is assumed that respondents are fully informed of their most recent diagnosis, many people do not know or cannot recall their diagnosis. Others, whose symptoms are treated, may consider themselves "cured" and may not report having a disorder (Atkinson, Zibin, & Chuang, 1997). In addition, respondents might not be motivated to answer questions accurately because doing so may engender embarrassing or stigmatizing experiences. They may also struggle to comprehend the questions or tasks asked of them, especially if they are complicated, have vaguely defined terms, or require careful recall (Kessler et al., 2004). These issues can further complicate classification and necessitate novel methods to verify self-reported MHDs. By considering multiple indicators of mental health status commonly used within epidemiological surveys, concordance between indicators of mental health status and psychoactive medication use can be assessed.

Psychiatric comorbidity, the presence of symptoms that meet criteria for more than one psychiatric disorder within an individual respondent, is commonly reported with both the SCID and WMH-CIDI (Cassano, Pini, Saettoni, Rucci, & Dell'Osso, 1998; Kessler, Chiu, Demler, & Walters, 2005). This practice has developed because MHDs do not always occur independently of one another (Andrews, Slade, & Issakidis, 2002; Bijl, Ravelli, & van Zessen, 1998). Consequently, the reporting of prevalence rates of single, mutually exclusive disorders is not adequate because it fails to capture the complexity of respondents' mental health status. Furthermore, patterns of psychiatric comorbidity may be important to understanding whether

particular disorder combinations or pairings place affected people at increased risk for CVD. There has been a limited amount of research in this area; however, there is some evidence to suggest that outpatients with coronary heart disease have a range of psychiatric disorders and that psychiatric comorbidity is common (Bankier, Januzzi, & Littman, 2004). Incorporating measures of psychiatric comorbidity with psychiatric epidemiological research is necessary because it provides richer diagnostic and risk prediction information.

1.5.2 Cardiovascular risk prediction

CVD risk prediction scores have been widely adopted, especially those derived from the Framingham Heart Study (Dawber, Kannel, & Lyell, 1963; Dawber, Meadors, & Moore, 1951), have been adapted for use in primary care as simplified charts, tables, computer programs, and web-based tools, and are routinely recommended in policy documents and guidelines (ATP-III, 2002; Kannel, Feinleib, McNamara, Garrison, & Castelli, 1979; McPherson, Frohlich, Fodor, Genest, & Canadian Cardiovascular Society, 2006). Framingham-based algorithms use sex-specific functions to calculate the multivariable risk of CVD within a defined time period (e.g., 10 years) for people without established CVD. This is done by assigning weights or points for risk factors (i.e., age, diabetes, tobacco smoking, systolic blood pressure, total cholesterol, and HDL cholesterol) and then applying a scoring algorithm to estimate an absolute probability of developing CVD. Low-moderate risk is considered < 10%, moderately high risk is 10% to 20%, and high risk is > 20%. In most cohorts, Framingham-based scores have demonstrated very good discrimination, as evidenced by C statistics that range from 0.75 to 0.80 (D'Agostino et al., 2008; Lloyd-Jones, 2010; Pencina et al., 2009).

In clinical practice, cardiovascular risk prediction algorithms are used to assist healthcare providers to match the intensity of their treatment with the probability of disease, as well as to

facilitate risk communication with patients (ATP-III, 2002; McPherson et al., 2006). Depending on their absolute risk, patients may be offered blood pressure and cholesterol lowering pharmacotherapy, in addition to advice about relevant health behaviour (e.g., smoking cessation and physical activity) (Brindle et al., 2006). Framingham risk estimation also can be used on a population level to study particular sub-groups that are known to be vulnerable to CVD for the purpose of informing prevention interventions. Framingham-based algorithms are suitable for use in large survey research because they utilize non-laboratory based predictors that can be assessed via self-report. A number of recent studies have quantified the short-term risk of coronary heart disease, using Framingham-based estimates in people with schizophrenia or other psychosis in hospital and community-based samples (Cohn, Prud'homme, Streiner, Kameh, & Remington, 2004; Goff et al., 2005; McCreadie, 2003; Osborn, Nazareth, & King, 2006). There is a need for studies assessing both short- (i.e., 10-year) and long-term (i.e., 30-year) cardiovascular risk in community samples of people with MHDs. This is because 10-year Framingham risk prediction algorithms may underestimate the true risk burden in community samples, particularly in younger individuals and women (Pencina et al., 2009; Sniderman & Furberg, 2008). The clustering of risk factors among people with MHDs at younger ages and increasing life expectancy suggest the need for longer-term risk prediction tools to facilitate better monitoring of this public health problem (Cohn et al., 2004).

1.5.3 Study justification

Although we know that cardiovascular morbidity is elevated among community-dwelling persons with MHDs in international samples, we do not have a reliable estimate of the burden of disease in Canada. Moreover, although a substantial body of evidence exists to explain the etiology of excess cardiovascular morbidity among people with MHDs, the relative contribution

of MHDs and psychoactive medication use has yet to be delineated in a Canadian sample. It is of particular interest whether MHDs incur additional cardiovascular risk and disease beyond that of psychoactive medication use alone. Further research is needed to explore and contrast both short- and long-term projections of cardiovascular risk among people with MHDs living in community settings as comprehensive assessments of a population's heart health is essential for enhanced surveillance. To date, few researchers have extended their investigations to account for patterns of psychiatric comorbidity and psychoactive medication polypharmacy (i.e., concurrent use of two or more psychoactive medications). These factors should also be investigated to determine if they place affected people at increased risk for CVD; such study will further our understanding of the prevalence and patterns of psychiatric disorders and psychoactive medication use, and provide richer diagnostic and risk prediction information.

Lastly, relatively little attention has been paid to how MHDs and psychoactive medication use are measured within community-based surveys. Although psychoactive medication use can be employed as an indicator of treatment for MHDs, previous work has demonstrated that there is a substantial mismatch between medication use and self-reported MHDs (Beck et al., 2005). A critical assessment of agreement between different indicators of mental health status and of psychoactive medication use commonly used within community-based surveys is needed to evaluate their consistency and to enrich our discussion of CVD and MHDs.

1.6 Study objectives

The overall aim of this research was to examine short- and long-term cardiovascular risk and disease among people with MHDs or using psychoactive medications. To achieve this, methodological issues surrounding identifying groups of people with MHDs within a population

health survey had to be addressed before the association between MHDs and a history of heart disease and stroke, and 10-year and 30-year cardiovascular risk could be examined. This investigation then examined whether having a MHD manifests additional cardiovascular risk and disease beyond that of psychoactive medication use. Taken together, these objectives were intended to fill the gaps in the existing literature and were sequentially addressed through three epidemiological studies. The specific objectives were as follows:

1. **To describe the extent of psychiatric comorbidity found among major mental health disorders, identify the most common disorder pairings, and measure the strength of association between disorders**. In Chapter 2, we examine psychiatric comorbidity in a community-based population and a discussion of the implications for improved surveillance of MHDs. An analytic technique is described that accounts for psychiatric comorbidity as well as an investigation of psychoactive medication polypharmacy and classification agreement between multiple indicators of mental health status commonly used within community-based surveys.

2. **To ascertain the associations between mental health disorders and a history of heart disease and stroke, and 10-year and 30-year cardiovascular risk**. Chapter 3 describes an investigation of the associations between cardiovascular risk and cardiovascular disease, and MHDs in the Canadian population. This investigation applied the analytic technique used to account for psychiatric comorbidity presented in Chapter 2 and highlights a novel application of cardiovascular risk prediction algorithms. Findings from this chapter inform a discussion of the opportunities for Canadian health professionals to play a greater role in improving the cardiovascular health of people living with MHDs.

3. **To determine the associations between psychoactive medication use and a history of heart disease and stroke, and 10-year and 30-year cardiovascular risk**. Chapter 4 provides an examination of the associations between psychoactive medication use and cardiovascular risk and cardiovascular disease in the Canadian population. This analysis was undertaken to extend the findings described in Chapter 3 and to determine whether MHDs incurred additional cardiovascular risk and disease beyond that of psychoactive medication use. The same analytic techniques described in Chapter 3 are used and are extended to examine psychoactive medication polypharmacy. The chapter concludes with a discussion of the implications for Canadian healthcare professionals.

1.7 Approach

The three studies included in this dissertation utilized data from the Canadian Community Health Survey (CCHS) Cycle 1.2 ("Mental Health and Well-being") that was conducted by Statistics Canada in May through December 2002. The survey was a nationally representative, face-to-face, household survey of 36,984 English, French, Mandarin, and Punjabi speaking Canadians aged 15 years or older, living in privately occupied dwellings in ten provinces. People living on Indian reserves, on Canadian Forces' bases, in institutions, in some remote areas, or who were homeless were excluded from the sampling frame. The CCHS Cycle 1.2 measured the mental health of Canadians by providing cross-sectional estimates of mental health status, mental health system utilization, and mental health determinants across community settings in Canada (Statistics Canada, 2002).

The CCHS Cycle 1.2 respondents were selected from a multistage stratified cluster design in which the household was the final sampling unit. Each province was divided into three types of

regions (major urban centres, cities, and rural regions) before clusters within each stratum were selected based on socio-economic characteristics. Dwelling lists were then prepared for each cluster and households were selected from these lists (Statistics Canada, 2002). This technique ensured that the probability of selecting a sampling unit was proportional to the size of the population (Statistics, 1998). In all of the selected dwellings, a knowledgeable household member was asked to supply basic demographic information about all of the residents. Depending on the composition of the household, one member was then selected for a more in-depth interview. In cases where this initial household visit resulted in non-response, telephone follow-ups were conducted. Data collection by telephone was authorized only when travel to the respondent's home was prohibitive or the respondent refused to conduct the interview in person; this resulted in 14% of the interviews being completed by telephone. In total, 48,047 households were selected to participate and a national response rate of 77% was achieved (Statistics, 2002).

The content of the CCHS Cycle 1.2 was based on a selection of MHDs from the World Mental Health–Composite International Diagnostic Interview (WMH-CIDI) and other Statistics Canada surveys such as the National Population Health Survey, the CCHS Cycle 1.1, and the Health Promotion Survey (Kessler & Ustun, 2004; Statistics Canada, 2002). Priority content areas for the CCHS Cycle 1.2 were selected through consultations with mental health experts from the World Health Organization, academia, federal and provincial governments, professional associations, and consumers of mental health services.

1.8 Summary

In summary, this dissertation consists of five chapters. Chapter 1 provides a general examination of the associations between cardiovascular morbidity and MHDs, presents a conceptual model of the etiology of excess CVD among people with MHDs, and focuses on

three broad factors known to increase CVD and risk. Gaps in the existing literature and measurement approaches were identified. Chapter 2 describes novel methods to examine psychiatric comorbidity in community-based population health surveys. The chapter provides a discussion of the implications for improved surveillance of MHDs. Chapter 3 presents an investigation of the associations between cardiovascular risk and CVD, and MHDs in the Canadian population. Chapter 4 describes an examination of the associations between psychoactive medication use and cardiovascular risk and cardiovascular disease in the Canadian population. Finally, Chapter 5 provides a review the key findings of the studies undertaken, a discussion of the unique contributions arising from this work, some avenues for future research, the limitations of the work, and some recommendations for healthcare providers and epidemiologists.

CHAPTER 2: EXAMINING PSYCHIATRIC COMORBIDITY IN COMMUNITY-BASED POPULATION HEALTH SURVEYS: IMPLICATIONS FOR IMPROVED SURVEILLANCE OF MENTAL HEALTH DISORDERS

2.1 Introduction

Recent emphasis placed on the reporting of the co-occurrence of MHDs in community-based population health surveys has drawn attention to the fact that psychiatric comorbidity is frequently observed but not well understood (Andrews et al., 2002; Bijl et al., 1998; Bourdon, Rae, Locke, Narrow, & Regier, 1992; Kessler et al., 2005; Kessler et al., 1994; Regier et al., 1990). Psychiatric comorbidity is a term applied to individuals who report symptoms that meet the criteria for more than one MHD (Andrews et al., 2002). Historically, psychiatric epidemiologists have explored single disorders and overlooked methods to meaningfully account for the complexity of multiple diagnoses. This practice is problematic because patterns of psychiatric comorbidity may be important to understanding whether particular disorder combinations or pairings place affected people at increased risk for other health conditions. This type of information could assist healthcare professionals to tailor treatment to ensure optimal quality of life and health outcomes for affected people.

Although psychiatric comorbidity has been discussed as a by-product of structured diagnostic interviews, which commonly are used in population health surveys and based on established psychiatric classification tools, several studies have demonstrated that certain disorders are strongly associated with one another and have a tendency to co-occur (Andrews et al., 2002; Boyd et al., 1984; Maj, 2005). Irrespective of the underlying etiology, patterns of psychiatric comorbidity should be investigated because they are associated with greater severity

of illness, physical morbidity, and healthcare service utilization (Andrews et al., 2002; Bourdon et al., 1992; Kessler et al., 2005; Kessler et al., 1994; Regier et al., 1990).

Improved reporting of psychiatric comorbidity in community-based population health surveys can further our understanding of the prevalence and pattern of psychiatric disorders, and provide richer diagnostic and risk prediction information about affected people. The primary objectives of this study were to report the prevalence rates of MHDs and to explore the extent of psychiatric comorbidity, the most common disorder pairings or combinations, and the strength of the associations between specific psychiatric disorders within a community-based sample of Canadians. A secondary objective was to critically assess the agreement between indicators of mental health status and of psychoactive medication use commonly included in community-based surveys to investigate their consistency

2.2 Background

2.2.1 Psychiatric comorbidity

The term 'psychiatric comorbidity' was derived from the notion of 'medical comorbidity,' which was originally described by Alvan Feinstein (1970) as "any distinct clinical entity that has existed or that may occur during the clinical course of a patient who has the index disease under study" (pp. 456-457). Psychiatric comorbidity is increasingly used in the research literature to refer to reports of symptoms that meet the criteria for more than one MHD (e.g., major depressive disorder and panic disorder) (Andrews et al., 2002; Maj, 2005; Pincus, Tew, & First, 2004). Multiple interpretations of the phenomenon exist; it can be understood as the existence of two or more distinct psychiatric disorders within an individual (either occurring separately or one contributing to the development of another) or the identification of multiple manifestations of a single, complex disorder (Lilienfeld, Waldman, & Israel, 1994; Maj, 2005;

Pincus et al., 2004). Both propositions are speculative because the psychopathology underlying the presence of multiple disorders remains poorly understood (Maj, 2005; Pincus et al., 2004).

2.2.2 Categorizing mental health disorders using diagnostic tools

Determining whether an individual has a MHD is important for the clinical treatment of patients, as well as for the surveillance of a population's mental health status. However, categorizing MHDs into discrete disorders is a problematic undertaking because the disorders cannot be empirically or objectively verified or validated, in part because of the subjectivity of the diagnostic process, many people experience multiple psychiatric disorders concurrently or over the course of their lifetime. Without established neurobiological evidence of abnormality to support diagnostic categories, it can be challenging to differentiate between symptoms of these illnesses; many are not mutually exclusive. The establishment of the Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association (2013) and the International Classification of Diseases (ICD), published by the World Health Organization (2010), has improved the reliability of psychiatric diagnosis by providing a common language and authoritative taxonomy for the classification of MHDs. The DSM and the ICD are compatible publications with different uses. The DSM is a rule-based classification system that contains extensive descriptive criteria to aid clinicians to diagnose MHDs by utilizing information related to patients' current presentation, uses specifiers that describe the severity and course of illness, and provides the principal diagnosis or reason for a healthcare visit when multiple diagnoses are present. Each disorder included in the manual is accompanied by a set of diagnostic criteria containing information about the disorder, such as associated features, prevalence, familial patterns, age, culture and gender-specific features, and differential diagnosis. Information about treatment for each disorder is not included in the manual

(American Psychiatric Association, 2000). The ICD is a medical classification list that contains code numbers used for reimbursement and monitoring of morbidity and mortality statistics by national and international health agencies.

Although the DSM has been instrumental in creating a nosological framework for MHDs and has greatly enhanced diagnostic agreement in the field of psychiatry, there are several shortcomings to its use that weaken its utility as a taxonomic classification system. Warelow and Holmes (2011) offered their critique of the DSM and described it as a guideline, rather than a precise tool, because the language used to describe diagnostic criteria for disorder categories is "open-ended," "ambiguous," "evasive," and requires a substantial degree of clinical judgment to aid interpretation (pp. 384-386). This results in an overlap among the disorder categories because the natural boundaries between discrete entities are not well defined. The categories can perhaps best be thought of as flexible concepts, justified only by whether they provide a useful framework for organizing and explaining the complexity of a patient's experience or the ability to guide decisions about treatment (Kendell & Jablensky, 2003). Moreover, concepts of psychiatric disease are not static and continue to evolve over time; the DSM continuously attempts to draw a line between normal and abnormal aspects that are inherent to the human condition (Warelow & Holmes, 2011).

Recent revisions of the DSM (III thru V) have intrinsically encouraged the practice of making multiple diagnoses by splitting diagnostic categories into a large number of relatively narrowly defined psychiatric disorders and listing few exclusionary hierarchies; meaning that one disorder does not take precedence over one or more subordinate diagnoses (Pincus et al., 2004). Exclusionary or hierarchy-free diagnostic classification systems assume that symptoms of a subordinate diagnosis are associated with features of the primary disorder and do not

warrant an additional diagnosis (Tew & Pincus, 2007). Therefore MHDs are not prioritized in favour of capturing a comprehensive picture of psychiatric symptoms and characterizing the complexity of clinical presentations (Andrews, Slade, & Issakidis, 2002; Pincus, Tew, & First, 2004). This dramatic change in thinking from previous versions of the DSM (I and II), which followed a one disease-one diagnosis model, resulted in a substantial increase in the prevalence rates of observed psychiatric comorbidity and made it more complicated for researchers to define homogeneous samples of respondents (Boyd et al., 1984; Maj, 2005; Mayes & Horwitz, 2005).

2.2.3 Operationalization of the Diagnostic and Statistical Manual of Mental Disorders

Clinicians and psychiatric epidemiologists have operationalized the DSM in different ways to suit their goals and the settings in which they work. Trained clinicians regularly use semi-structured interviews in their clinical practice, including the Structured Clinical Interview for DSM-IV Disorders (SCID), to assist them with confirming or documenting the presence of Axis 1 (e.g., clinical disorders such as depression or schizophrenia) and Axis 2 (e.g., developmental and personality disorders) disorders (First, Spitzer, Gibbon, & Williams, 1997). The SCID was modelled on the clinical interview and contains questions that efficiently elicit information necessary to judge whether a patient satisfies the diagnostic criteria of particular disorders. As diagnostic decisions can differ between clinicians, assurance that a psychiatric disorder has been correctly identified can only be verified by testing agreement between clinicians (i.e., establishing inter-rater reliability). The inter-rater reliability of the SCID has been established through several studies; the results have revealed moderate to excellent agreement of the Axis I disorders, and most categorically and dimensionally measured personality disorders have shown excellent agreement (Lobbestael, Leurgans, & Arntz, 2011; Maffei et al., 1997; Segal, Hersen, Hasselt, Kabacoff, & Roth, 1993).

The most significant challenge to operationalizing the DSM in psychiatric epidemiology is the lack of experienced clinicians to interview and diagnose a large number of respondents in a short period of time. Trained lay interviewers are regularly used to survey community-based populations, but they lack the skills necessary to make independent diagnostic decisions; therefore, they must rely on established measurement tools that restrict their reliance on judgment. Consequently, researchers must trust that the respondents' self-reported symptoms and past diagnoses are accurate, which can be problematic because it is known that self-reported data are subject to bias (Podsakoff et al., 2003). For example, respondents may not be able to answer the survey questions accurately; although it is assumed that respondents are fully informed of their most recent diagnosis, many people do not know or forget the characteristics of their MHDs or are treated with medications that relieve their symptoms so that they do not report having them (Atkinson et al., 1997). In addition, respondents might not be motivated to answer questions accurately because doing so may engender embarrassing or stigmatizing experiences. They may also struggle to comprehend the questions or tasks asked of them, especially if they are complicated, have vaguely defined terms, or require precise recall (Kessler et al., 2004). These issues can complicate classification and necessitate novel methods to verify self-reported MHDs.

2.3.4 The World Mental Health Composite International Diagnostic Interview

There is methodological complexity involved in developing a fully-structured psychiatric diagnostic interview to be used by lay interviewers. Fortunately, a significant amount of research has been devoted towards the development of instruments designed to measure community-based population mental health status. The first instrument created was the Diagnostic Interview Schedule (DIS), which was exclusively based on the criteria of the DSM III

(American Psychiatric Association, 1980; Robins, Helzer, Croughan, & Ratcliff, 1981). The DIS was subsequently expanded to become the World Health Organization's Composite International Diagnostic Interview (CIDI), which operationalized both the DSM-IV and ICD-10 criteria to assign diagnostic categories to respondents and to facilitate cross-national comparative research (Robins, Wing, Wittchen, & Helzer, 1988; World Health, 1990). The CIDI has demonstrated good inter-rater reliability and test-retest reliability (Wittchen, 1994). Most recently, the CIDI was modified in response to the findings of clinical reappraisal studies to become the World Mental Health Composite International Diagnostic Interview (WMH-CIDI). The WMH-CIDI includes broader areas of assessment than does the CIDI, such as measures of risk factors, consequences, patterns, and correlates of treatment and treatment adequacy, and is now used in almost all major psychiatric epidemiological surveys (Kessler et al., 2004).

In the absence of an objective biological or gold standard test to verify the presence of MHDs in a patient, semi-structured clinical interviews are seen as the reference standard against which to judge fully structured psychiatric diagnostic interview tools. Kessler et al. (2004) explained that current investigations in the field have adopted the goal of clinical calibration rather than validation to assess concordance between the WMH-CIDI and semi-structured clinical interviews such as the SCID. This means that the focus is directed toward achieving consistency in diagnoses rather than "correctness." Diagnostic concordance between the WMH-CIDI version 3.0 and the SCID have demonstrated moderate to good levels of agreement for lifetime and 12-month prevalence estimates when evaluated among 21,425 respondents in France, Italy, Spain, and the USA (Haro et al., 2006). Haro et al. (2006) plotted a receiver operating characteristic (ROC) curve (i.e., a visual depiction of classification accuracy) for DSM-IV anxiety, mood, and substance disorders assessed with the WMH-CIDI for individual

disorders and the SCID. They found that the area under the curve was .76 for having any lifetime disorder (range .62–.93). The area under the curve is equal to the probability that a classifier will rank a randomly chosen positive instance higher than a randomly chosen negative one (i.e., true positive rate versus false positive rate). These values suggest that the accuracy of the measure is fair (Fawcett, 2006).

2.3.5 Evidence of psychiatric comorbidity in community-based mental health surveys

Several psychiatric epidemiological studies of the prevalence of specific MHDs have found relatively high rates of psychiatric comorbidity. The Epidemiologic Catchment Area (ECA) survey, conducted by the US National Institute of Mental Health, was the first to document this observation (Regier et al., 1984). In the first wave of that survey, Boyd et al. (1984) examined a sample of 11,519 household respondents living in three cities in northeastern USA and found that the presence of any psychiatric disorder (as measured by the DIS) significantly increased the odds of having another co-occurring disorder. In the second and third waves, Bourdon et al. (1992) assessed 18,344 household respondents in five cities and 1,947 institutionalized respondents and found that some respondents with a single MHD had co-occurring disorders: 23% of respondents with disorders in the past month, 25% of respondents with disorders in the past six months, and 35% of respondents with disorders sometime in their lifetime. The authors concluded that psychiatric comorbidity was more extensive in the general population than they had expected.

The findings of the ECA survey provided the impetus for Kessler et al. (1994) to conduct the National Comorbidity Survey (NCS), which advanced the study of psychiatric epidemiology because it was designed to not only ascertain the prevalence but also the causes and consequences of psychiatric disorders. It included a stratified multistage area probability sample

of 8,098 community-dwelling people aged 15-54 years, living in 48 states. Using a modified version of the CIDI (University of Michigan (UM)-CIDI), it was found that 48% of the sample had been diagnosed with at least one DSM-III-R disorder, and 21% reported one, 13% reported two, and 14% reported three or more disorders (American Psychiatric Association, 1987; Wittchen, Kessler, Zhao, & Abelson, 1995). Even more compelling, 79% of the respondents who reported lifetime disorders and 82% who reported 12-month disorders had psychiatric comorbidity. It was found that 6 of 10 disorders reported to have occurred in the past year occurred in 14% of the sample with a lifetime history of three or more disorders. The authors highlighted this finding to emphasize that the majority of MHDs in the US is concentrated in one sixth of the population. These people are burdened with a high level of psychiatric comorbidity and more detailed examinations should be conducted of their particular types of comorbidity (Kessler et al., 1994).

The NCS was followed by the US National Comorbidity Survey Replication (NCS-R), which was conducted with a nationally representative sample of 9,282 English-speaking respondents, 18 years of age and older. It generated a multi-stage clustered area probability sample and surveyed respondents with the WMH-CIDI to estimate the prevalence of 12-month diagnoses according to the DSM-IV and ICD-10 (Kessler et al., 2005). Kessler et al. (2005) reported that 55% of the sample had a single psychiatric disorder, 22% had two disorders, and 23% had three or more disorders. The tetrachoric correlations among the 12-month disorders were almost all positive (98%) and statistically significant (72%). The strongest correlations ($r >$ .60) represented well-known conditions: bipolar disorder (major depressive episode with mania or hypomania), double depression (major depressive episode with dysthymia), anxious depression (major depressive episode with generalized anxiety disorder), comorbid mania or

hypomania, and attention-deficit or hyperactivity disorder, panic disorder with agoraphobia, comorbid social phobia with agoraphobia, and comorbid substance disorders (both alcohol abuse and dependence with drug abuse and dependence). These psychiatric comorbidities were consistent with the ECA study and the NCS in demonstrating that the majority of DSM disorders are positively correlated and that a high level of psychiatric comorbidity is present among people with histories of MHDs in the past 12 months.

Kessler et al. (2005) emphasized the importance of considering disease severity alongside psychiatric comorbidity. Respondents with serious MHDs were identified as having the following: a 12-month suicide attempt with serious lethality intent; work disability or substantial limitation due to a mental or substance disorder; positive screening results for non-affective psychosis; bipolar I or II disorder; substance dependence with serious role impairment; an impulse control disorder with repeated serious violence; or any disorder that resulted in 30 or more days of role impairment in the year. It was found that disease severity was strongly related to psychiatric comorbidity; 9.6% of respondents with one disorder, 25.5% with two disorders, and 49.9% with three or more disorders were identified as suffering from a severe MHD.

Studies conducted outside of the USA have contributed to our understanding of psychiatric comorbidity. Andrews et al. (2002) used data from the Australian National Survey of Mental Health and Well-Being (10,641 adults, 18 years of age and older) to evaluate the relationships between comorbidity, disability, and health service utilization associated with MHDs occurring within a 12-month period. Using the CIDI, they found that 40% of people with one psychiatric disorder (N = 1,372) met the criteria for an additional disorder, and the greater the number of disorders that a person had, the greater his or her disability, distress, neuroticism, and healthcare utilization. Odds ratios were calculated for 66 comorbid disorder pairs and it was

found that almost all (83%) of the combinations or pairings had odds ratios greater than 1.0, which indicated strong associations between disorders (i.e., the likelihood of co-occurrence).

The Netherlands Mental Health Survey and Incidence Study (NEMESIS) was a prospective study of 7,076 people from the Dutch population (Bijl et al., 1998). The investigators ascertained the lifetime, 12-month, and 1-month prevalence rates of psychiatric diagnoses in people aged 18-64 years according to CIDI classifications and the DSM-III-R. Bijl et al. (1998) reported that 41.2% of respondents with lifetime disorders, 23.2% of respondents with 12-month disorders, and 16.5% of respondents with disorders occurring in the past month were classified as having one or more diagnoses. Upon further evaluation, it was found that among the people who had suffered from a psychiatric disorder, almost one half (45%) had experienced more than one. Moreover, 9.2% of the respondents who disclosed three or more disorders within the previous 12 months accounted for one third of all MHDs reported. The authors also found that comorbidity was more common among women than among men (lifetime disorders: $55\%_{women}$ vs. $36\%_{men}$ and 12-month disorders: $44\%_{women}$ vs. $26\%_{men}$). This demonstrates that psychiatric comorbidity is a relatively common occurrence and those affected bear a disproportionate burden of illness.

In Canada, the largest psychiatric epidemiological study that has been carried out in a community-based sample was the Canadian Community Health Survey (CCHS) Cycle 1.2. The CCHS is a cross-sectional survey that is administered by Statistics Canada and operates on a yearly collection cycle (prior to 2007, data collection occurred every two years) with changing areas of focus. The objectives of Cycle 1.2 were to measure the mental health status of Canadians by providing cross-sectional estimates of mental health status, mental health system utilization, and mental health determinants (Statistics, 2002). Analyses of the data from this

survey have been reported in numerous publications and have answered a variety of research questions about the state of mental health in Canada. No study has explicitly examined the extent of psychiatric comorbidity in the Canadian population.

Smaller community-based prevalence studies have been conducted in Edmonton, Alberta and in Ontario. Bland, Newman, and Orn (1988) surveyed 3,258 Edmonton residents aged 18 years and older, and used the DIS to estimate the 6-month prevalence rates of 13 DSM-III disorders; however, the extent of psychiatric comorbidity in the sample was not reported. Offord et al. (1996) used cross-sectional data from the Mental Health Supplement of the Ontario Health Survey to report the past-year prevalence rates of 14 DSM-III-R psychiatric disorders, using the UM-CIDI. The community-based sample consisted of 9,953 respondents selected from across the province, and aged 15 to 64 years. Psychiatric comorbidity was a common finding; almost one in four respondents (24.2%) who were identified as having one disorder reported additional disorders. Further investigation of the Canadian national prevalence rates and patterns of psychiatric comorbidity is warranted because it represents an important indicator of mental health status. Without monitoring trends in psychiatric comorbidity, population mental health and illness cannot be accurately estimated or fully understood.

The current study was informed by and extended beyond previous epidemiological studies, which documented the presence and extent of psychiatric comorbidity, to identify the most common disorder pairings, and measure the strength of the associations between disorders. Additional objectives were to consider multiple indicators of mental health status commonly used within community-based surveys and ascertain classification agreement between them.

2.3 Methods

2.3.1 Data source and sample

The data for this secondary analysis were obtained via the CCHS Cycle 1.2, which was a nationally representative household survey of 36,984 English, French, Mandarin, and Punjabi speaking Canadians aged 15 years or older, living in privately-occupied dwellings in the ten provinces. Its target population was residents in all provinces with the exclusion of populations on Indian reserves and Canadian Forces' bases, and in healthcare institutions and some remote areas. The CCHS respondents were selected from a multistage stratified cluster design in which the household was the final sampling unit. Each province was divided into three types of regions (major urban centres, cities, and rural regions) before clusters within each stratum were selected based on socio-economic characteristics. Dwelling lists were then prepared for each cluster and households were selected from these lists (Statistics Canada, 2002). This technique ensured that the probability of selecting a sampling unit was proportional to the size of the population (Statistics Canada, 1998).

Face-to-face interviews were carried out between May and December 2002 by trained lay interviewers using a computer-assisted personal interviewing method (Statistics Canada, 2002). The interviewers explained the study and obtained verbal informed consent before commencing an interview. In all of the selected dwellings, a knowledgeable household member was asked to supply basic demographic information about all of the residents. Depending on the composition of the household, one member was then selected for a more in-depth interview. In cases where this initial household visit resulted in non-response, telephone follow-ups were conducted. Data collection by telephone was authorized only when travel was prohibitive or the respondent refused to conduct the interview in person; this resulted in 14% of the interviews being completed by telephone. In total, 48,047 households were selected to participate in Cycle 1.2

and a national response rate of 77% was achieved (Statistics, 2002).

2.3.2 Measures

Diagnostic information related to mental health was gathered using a modified version of the WMH-CIDI, which was operationalized to meet the needs of the CCHS Cycle 1.2. Because of this modification, which did not measure all of the DSM-IV and ICD-10 disorders, the instrument is referred to as the "CCHS 1.2/WMH-CIDI." The CCHS 1.2/WMH-CIDI determined the lifetime and 12-month prevalence rates of seven major MHDs: major depressive episode, manic episode, social phobia, panic disorder, agoraphobia, alcohol dependence, and substance use disorder. Schizophrenia was not assessed with the structured diagnostic interview; rather, it was assessed as a self-reported chronic health condition. The respondents were asked if they had ever been diagnosed with schizophrenia by a health professional. This is a common survey practice because schizophrenia is rarely reported in psychiatric epidemiological surveys; the number of respondents meeting the diagnostic criteria is very small. Lifetime prevalence of a disorder is the proportion of the sample who ever experienced the disorder, while 12-month prevalence is the proportion that experienced a disorder sometime during the 12 months preceding the interview. To reduce respondent burden, a screening section of questions preceded all of the survey modules related to the disorders. Negative responses to the screening questions prompted a conditional "skip logic" feature to avoid respondents being asked the full roster of questions associated with each disorder, when not relevant. Asking the respondents if they took any of the following medications within the previous 12 months assessed psychoactive medication use: anxiolytics, antipsychotics, antidepressants, or mood stabilizers (e.g., "In the past 12 months, did you take medications to reduce anxiety or nervousness (such as Ativan, Valium or Serax)?").

2.3.3 Analysis

To estimate the prevalence rates and most common disorder pairings for each lifetime and 12-month psychiatric disorder, homogenous subsets of respondents were created. Respondents who were identified as having the disorder alone (e.g., depression), the disorder and its most common pairing (e.g., depression and social phobia only), and the disorder plus any other disorder except its most common pairing (e.g., depression and any other disorder not including social phobia) were classified into discrete categories. The same procedure was used to classify people taking psychoactive medications. Respondents were identified as taking a particular medication alone (e.g., antidepressant medication only), the medication and its most common pairing (e.g., antidepressants and anxiolytics only), and the medication plus any other psychoactive medication except its most common pairing (e.g., antidepressants with other medications, not anxiolytics).

Second, to determine the number of comorbid disorders reported by the total sample, respondents were classified according to the total number of lifetime and 12-month MHDs for which they met the diagnostic criteria for eight possible disorders (i.e., none, one, two, or three or more disorders). The total number of disorders was contrasted with psychoactive medication use. Third, the bivariate associations among the eight lifetime and 12-month disorders and psychoactive medication use were explored by examining a series of unadjusted logistic regression models containing only pairs of disorders. Finally, as a means of validating the CCHS 1.2/WMH-CIDI disorder classifications, self-reported psychoactive medication use was treated as a proxy indicator of mental health status and responses were contrasted using positive percent agreement (PPA) with mental health status and negative percent agreement (NPA).

Clinical diagnostic tools are usually described in terms of their ability to correctly identify people who have a disorder (i.e., sensitivity) as well as correctly identify people who do

not have a disorder (i.e., specificity). However, when a new classification tool (e.g., psychoactive medication use) is compared to a non-reference or "gold" standard (i.e., disorders identified with the CCHS 1.2/WMH-CIDI), sensitivity and specificity are not appropriate terms to describe the results; "correctness" of the new tool cannot be estimated directly because a respondent's true condition is unknown. The solution to this problem is the use of PPA and NPA to describe how often the new tool being assessed agrees with a non-reference standard (US Department of Health and Human Services, 2007).

The PPA was calculated via a contingency table and the following formulas were employed: PPA = 100% * (a/(a+c)), where "a" was the number of respondents with a MHD and reported to be taking psychoactive medications and "c" was the number of respondents with a MHD not reported to be taking a psychoactive medication. NPA = 100% * (d/(b+d)), where "b" was the number of respondents without a MHD and reported to be taking psychoactive medications and "d" was the number of respondents without a MHD not reported to be taking a psychoactive medication. Agreement between the CCHS 1.2/WMH-CIDI classification and psychoactive medication use was considered slight if it was found to be between 0.0% and 20.0%, fair if it was between 21.0% and 40.0%, moderate if it was between 41.0% and 60.0%, substantial if it was between 61.0% and 80.0% and almost perfect if it was between 81.0% and 100.0% (Zegers et al., 2010). Psychoactive medication use was considered an appropriate indicator of mental illness because it is reasonable to assume that respondents who are prescribed and currently taking psychoactive medications suffer from some type of psychiatric disorder (e.g., respondents who reported taking antipsychotic medications likely had schizophrenia).

There were two methods used in the CCHS Cycle 1.2 to describe respondents' psychoactive medication use. The first method asked respondents if they took anxiolytics to

reduce anxiety or nervousness, antipsychotics for the treatment of psychotic behaviour, or antidepressants or mood stabilizers within the past 12 months. The second method required the interviewer to visually inspect any bottles, tubes, or boxes of medication that the respondent reported taking within the last two days. The interviewer then recorded these medications using codes from the Anatomical Therapeutic Chemical (ATC) Classification System (World Health Organization, 2009). Individual responses from these two questions were contrasted and the PPA and NPA were calculated.

Confidence intervals (95%) for the reported percentages and odds ratios were calculated using weighted bootstrapped estimates to account for the complex survey design and to extrapolate findings to the Canadian population. Hierarchy-free diagnoses (one disorder does not take precedence over another diagnosis) were used throughout the analyses and in the reporting of psychiatric comorbidity. A conservative α level of $p \leq .001$ was used to assess the statistical significance of the comorbid disorder pairings to account for multiple estimations. All of the analyses were conducted using the Stata version 12 software package (StataCorp., 2011).

Statistics Canada provided probability weights in the survey data files. The following characteristics were used to form the adjustment strategy for weighting in the CCHS Cycle 1.2 (applied in this order): initial weight (overall probability of selection), sample increase or decrease (necessary modifications made to obtain the desired sample within a health region), stabilization (to compensate for oversampling), removal of out-of-scope dwellings, household non-response, creation of person level weight (converted from household weights), person non-response (based on sex, age group, urban/rural indicator, education, marital status, and the size of the household), and post stratification (to ensure that the sum of the final weights corresponded to population estimates). The population estimates for the CCHS Cycle 1.2 were based on the

1996 Census in addition to estimates of birth, death, immigration, and emigration counts (Statistics, 2002).

2.4 Results

2.4.1 The prevalence of psychiatric disorders

The results presented in Table 2-1 show hierarchy-free prevalence rates of seven CCHS 1.2/WMH-CIDI lifetime and 12-month disorders, and the prevalence rates for lifetime schizophrenia and 12-month psychoactive medication use (which were not measured via the CCHS 1.2/WMH-CIDI). The most common individual CCHS 1.2/WMH-CIDI lifetime and 12-month psychiatric disorder was having a major depressive episode. About 12.2% (95% CI [11.7, 12.7]) of the respondents were identified as having a lifetime episode and 4.8% (95% CI [4.5, 5.1]) reported experiencing an episode in the past 12 months. The most common psychoactive medication used by the respondents was antidepressants, with 6.7% (95% CI [6.3, 7.0]) of the sample having reported using them within the past 12 months. Mood disorders (i.e., major depressive episode or manic episode) represented the most common diagnostic category with 13.3% (95% CI [12.7, 13.8]) of the respondents reporting lifetime and 5.2% (95% CI [4.9, 5.6]) reporting 12-month mood disorders.

Psychiatric comorbidity was most frequently observed with two co-occurring disorders. Six of the seven disorders were most commonly paired with depression, which was itself most commonly paired with social phobia. Drug dependence most commonly co-occurred with alcohol dependence. There were pairings among the various psychoactive medications used; all of the psychoactive medications were most commonly paired with antidepressants, which were most commonly paired with anxiolytics.

Table 2-1: Lifetime and 12-Month Prevalence Rates of CCHS 1.2/WMH-CIDI Disorders, Most Common Disorder Pairings, and Psychoactive Medication Use

Disorder	Lifetime Prevalence % [95% CI]	12-month Prevalence % [95% CI)
Schizophrenia[a] alone	0.1 [0.1, 0.1]	-
with major depressive episode	0.1 [0.1, 0.1]	-
with other disorders, not major depressive episode	0.1 [0.0, 0.1]	-
All schizophrenia	0.3 [0.2, 0.3]	
Major Depressive Episode alone	7.8 [7.4, 8.2]	3.0 [2.7, 3.2]
with social phobia	2.9 [2.7, 3.1]	0.9 [0.8, 1.1]
with other disorders, not social phobia	1.5 [1.3, 1.7]	0.9 [0.8, 1.0]
All major depressive episode	12.2 [11.7, 12.7]	4.8 [4.5, 5.1]
Manic Episode alone	0.6 [0.5, 0.8]	0.3 [0.2, 0.3]
with major depressive episode	1.3 [1.1, 1.4]	0.5 [0.4, 0.6]
with other disorders, not major depressive episode	0.5 [0.4, 0.6]	0.2 [0.1, 0.3]
All manic episode	2.4 [2.1, 2.6]	1.0 [0.8, 1.1]
Any mood disorder	13.3 [12.7, 13.8]	5.2 [4.9, 5.6]
Social Phobia alone	4.2 [3.9, 4.5]	1.7 [1.5, 1.9]
with major depressive episode	2.9 [2.7, 3.1]	0.9 [0.8, 1.1]
with other disorders, not major depressive episode	1.0 [0.8, 1.2]	0.4 [0.3, 0.5]
All social phobia	8.1 [7.7, 8.5]	3.0 [2.8, 3.3]
Panic Disorder alone	1.5 [1.3, 1.6]	0.7 [0.6, 0.9]
with major depressive episode	1.4 [1.3, 1.6]	0.5 [0.5, 0.6]
with other disorders, not major depressive episode	0.8 [0.6, 1.0]	0.3 [0.2, 0.3]
All panic disorder	3.7 [3.4, 4.0]	1.5 [1.4, 1.7]
Agoraphobia alone	0.5 [0.4, 0.6]	0.3 [0.2, 0.5]
with major depressive episode	0.6 [0.5, 0.7]	0.2 [0.2, 0.3]
with other disorders, not major depressive episode	0.4 [0.3, 0.6]	0.2 [0.1, 0.2]
All agoraphobia	1.5 [1.4, 1.7]	0.7 [0.6, 0.9]
Any anxiety disorder	11.3 [10.8, 11.7]	4.6 [4.3, 5.0]
Alcohol dependence alone	-	1.8 [1.6, 2.0]
with major depressive episode	-	0.4 [0.3, 0.5]
with other disorders, not major depressive episode	-	0.4 [0.3, 0.5]
All alcohol dependence	-	2.6 [2.4, 2.8]
Drug Dependence alone	-	0.3 [0.2, 0.4]
with alcohol dependence	-	0.3 [0.2, 0.4]
	-	0.2 [0.1, 0.2]

Disorder	Lifetime Prevalence % [95% CI]	12-month Prevalence % [95% CI)
with other disorders, not alcohol dependence		
All drug dependence	-	0.8 [0.6, 0.9]
Any substance use disorder	-	3.0 [2.8, 3.3]
Psychoactive medication use[a,b]		
Anxiolytics alone	-	3.0 [2.7, 3.2]
with antidepressants	-	3.0 [2.8, 3.2]
with other medications, not antidepressants	-	0.2 [0.1, 0.3]
All anxiolytics	-	6.2 [5.8, 6.5]
Antipsychotics alone	-	0.1 [0.0, 0.1]
with antidepressants	-	0.4 [0.3, 0.5]
with other medications, not antidepressants	-	0.1 [0.1, 0.2]
All antipsychotics	-	0.6 [0.5, 0.7]
Antidepressants alone	-	3.3 [3.1, 3.5]
with anxiolytics	-	3.0 [2.8, 3.2]
with other medications, not anxiolytics	-	0.4 [0.3, 0.5]
All antidepressants	-	6.7 [6.3, 7.0]
Mood stabilizers alone	-	0.2 [0.2, 0.3]
with antidepressants	-	0.9 [0.7, 1.0]
with other medications, not antidepressants	-	0.2 [0.1, 0.2]
All mood stabilizers	-	1.3 [1.1, 1.4]
Any psychoactive medication use	-	10.2 [9.7, 10.6]

Note. N = 36,984 respondents representing 24,996,593 Canadians. All psychiatric disorders were identified with a hierarchy-free method. The sum of each disorder category (i.e., any mood disorder, anxiety disorder, substance use disorder or psychoactive medication use) is less than the stated rates of distinct disorders because of comorbidity. The dash represents data that were not available or suppressed because of imprecise estimates. % = percent. CI = confidence interval.

[a] Not measured by structured diagnostic interview (CCHS 1.2/WMH-CIDI).

[b] Measured by self-reported medication use (within the last 12 months) or verified by interviewer's visual inspection of prescription bottle, tube or box (used within the last two days).

2.4.2 Comorbidity

The lifetime and 12-month comorbidity prevalence rates are presented in Tables 2-2 and 2-3. As shown in the second column of Table 2-2, 79.8% (95% CI [79.2, 80.4]) of the respondents reported no lifetime MHDs, 14.5% (95% CI [14.0, 15.0]) had one, 4.1% (95% CI [3.8, 4.5]) had two, and 1.6 % (95% CI [1.4, 1.8]) reported three or more disorders. Although

most of the disorders occurred in isolation, 28.3% of the respondents who met the criteria for a lifetime disorder and 24.3% of the respondents who met the criteria for one 12-month disorder also endorsed symptoms of additional disorders. In Table 2-2, column 4, it is shown that an even greater percentage (39.8%) of the 12-month disorders occurred in respondents with a lifetime history of comorbidity indicating that comorbidity is more frequently apparent in respondents with active disorders.

The bivariate associations between the hierarchy-free lifetime and 12-month MHDs are reported in Tables 2-4, 2-5 and 2-6. The odds ratios (ORs) can be interpreted as follows: a history of schizophrenia in one's lifetime increases the odds of having a major depressive episode in one's lifetime by a factor of 5.1. Table 2-4 demonstrates that all of the bivariate associations among the lifetime disorders are statistically significant ($p \leq .001$) and range from OR = 3.3 (95% CI [1.7, 6.5]) for schizophrenia and panic disorder to 14.8 (95% CI [7.7, 28.3]) for schizophrenia and manic episode. This indicates that there are strong associations in all of the disorder pairings and signifies that the risk of having a second disorder is significantly greater in the presence of a first disorder.

Tables 2-5 and 2-6 provide the bivariate associations between the 12-month disorders, between the psychoactive medications used within the last 12-months, and between the 12-month disorders and psychoactive medications used. All of the ORs between the 12-month psychiatric disorders are statistically significant (ORs range from 2.8 (95% CI [1.6, 4.8]) for agoraphobia and alcohol dependence to 25.7 (95% CI [17.6, 37.4]) for alcohol and drug dependence). The strongest bivariate associations represented well-established syndromes: bipolar disorder (major depressive episode with manic episode) (OR = 25.4, 95% CI [19.4, 33.3]), panic disorder and agoraphobia (OR = 15.9, 95% CI [10.5, 24.2]), and comorbid

substance use disorders (alcohol dependence and drug dependence) (OR = 25.7, 95% CI [17.6, 37.4]).

Table 2-2: Concentration of Lifetime Disorders, 12-Month Disorders, and Psychoactive Medication Use Among Respondents with any Lifetime Psychiatric Comorbidity

Number of lifetime disorders	Rate within entire sample[a]	Rate within sample with any lifetime disorder[b]	Rate within sample with any 12-month disorder[c]	Rate within sample taking any psychoactive medication[d]
	% [95% CI]	% [95% CI]	% [95% CI]	% [95% CI]
0	79.8 [79.2, 80.4]	N/A	N/A	45.9 [43.9, 47.9]
1	14.5 [14.0, 15.0]	71.7 [70.3, 73.2]	60.3 [58.1, 62.4]	29.6 [27.8, 31.5]
2	4.1 [3.8, 4.5]	20.4 [19.0, 21.8]	25.6 [23.5, 27.6]	15.2 [13.4, 17.0]
≥ 3	1.6 [1.4, 1.8]	7.9 [7.1, 8.7]	14.2 [12.6, 15.8]	9.3 [8.1, 10.5]
Total	100.0	100.0	100.0	100.0

Note. All psychiatric disorders were identified with a hierarchy-free method. % = percent. CI = confidence interval. N/A = not applicable.

[a] Based on reports of 36,984 respondents representing 24,996,593 people in the Canadian population.

[b] Based on reports of 7,626 respondents representing 5,060,001 people in the Canadian population.

[c] Based on reports of 3,459 respondents representing 2,210,327 people in the Canadian population.

[d] Based on reports of 4,528 respondents representing 2,545,284 people in the Canadian population. Measured by self-reported medication use (within the last 12 months) or verified by interviewer's visual inspection of prescription bottle, tube or box (used within the last two days).

Table 2-3: Concentration of 12-Month Disorders and Psychoactive Medication Use Among Respondents with 12-Month Psychiatric Comorbidity

Number of 12-month disorders	Rate within entire sample[a]	Rate within sample with any 12-month disorder[b]	Rate within sample taking any psychoactive medication[c]
	% [95% CI]	% [95% CI]	% [95% CI]
0	89.4 [88.9, 89.8]	N/A	65.2 [63.1, 67.2]
1	8.1 [7.7, 8.4]	75.7 [73.9, 77.6]	22.4 [20.6, 24.2]
2	1.8 [1.6, 2.0]	16.6 [14.9, 18.2]	7.5 [6.4, 8.6]
≥3	0.8 [0.7-0.9]	7.7 [6.7- 8.7]	4.9 [4.0, 5.8]
Total	100.0	100.0	100.0

Note. All psychiatric disorders were identified with a hierarchy-free method. % = percent. CI = confidence interval. N/A = not applicable.

[a] Based on reports of 36,984 respondents representing 24,996,593 people in the Canadian population.

[b] Based on reports of 4,134 respondents representing 2,658,580 people in the Canadian population (this number does not match

column 4 of Table 2 because alcohol and drug dependence were measured in the past year, but not included within the lifetime disorder sample (this difference equates to 675 respondents).

[c] Based on reports of 4,528 respondents representing 2,545,284 people in the Canadian population. Measured by self-reported medication use (within the last 12 months) or verified by interviewer's visual inspection of prescription bottle, tube or box (used within the last two days).

Table 2-4: The Strength of Association Between Lifetime CCHS 1.2/WMH-CIDI Disorders

Disorder	**Mood disorders**			**Anxiety disorders**		
	Schizophrenia	Major Depressive Episode	Manic Episode	Social Phobia	Panic Disorder	Agoraphobia
			OR[95% CI]			
Schizophrenia	-					
Major Depressive Episode	5.1* [2.9, 8.8]	-				
Manic Episode	14.8* [7.7, 28.3]	9.3* [7.6, 11.2]	-			
Social Phobia	6.7* [3.3, 13.7]	5.1* [4.5, 5.7]	8.3* [6.8, 10.0]	-		
Panic disorder	3.3* [1.7, 6.5]	5.2* [4.4, 6.2]	7.3* [5.7, 9.3]	6.6* [5.3, 8.1]	-	
Agoraphobia	10.6* [5.0, 22.7]	4.8* [3.8, 6.1]	7.1* [4.9, 10.3]	6.0* [4.5, 8.0]	13.3* [9.8, 18.1]	-

Note. All psychiatric disorders were identified with a hierarchy-free method. % = percent. CI = confidence interval. OR = Odds ratio.
*p < .001.

Table 2-5: The Strength of Association Between 12-Month CCHS 1.2/WMH-CIDI Disorders

Disorder	Mood disorders		Anxiety disorders			Substance use	
	Major depressive episode	Manic episode	Social Phobia	Panic Disorder	Agoraphobia	Alcohol dependence	Drug dependence
	OR [95% CI]						
Major depressive episode	-						
Manic Episode	25.4* [19.4, 33.3]	-					
Social Phobia	11.1* [9.2, 13.5]	16.5* [12.2, 22.2]	-				
Panic Disorder	12.6* [10.0, 16.0]	15.6* [11.1, 21.9]	10.3* [7.8, 13.6]	-			
Agoraphobia	9.1* [6.2, 13.4]	16.8* [9.2, 30.7]	10.5* [7.2, 15.3]	15.9* [10.5, 24.2]	-		
Alcohol dependence	3.7* [3.0, 4.7]	7.3* [5.2, 10.4]	3.3* [2.5, 4.4]	3.2* [2.3, 4.5]	2.8* [1.6, 4.8]	-	
Drug dependence	7.3* [5.1, 10.5]	17.0* [11.1, 25.8]	4.1* [2.7, 6.3]	7.3* [4.3, 12.3]	7.0* [3.8, 12.9]	25.7* [17.6, 37.4]	-
Anxiolytic use	6.7* [5.8, 7.8]	7.7* [5.8, 10.4]	5.2* [4.3, 6.3]	9.6* [7.6, 12.3]	7.1* [5.0, 10.2]	1.3 [0.9, 1.7]	2.4* [1.5, 3.7]
Antipsychotic use	11.5* [8.2, 16.1]	15.5* [8.9, 26.8]	9.2* [6.0, 13.9]	8.0* [4.7, 13.4]	10.7* [5.3, 21.6]	2.0 [0.9, 4.2]	6.6* [3.3, 13.2]
Antidepressant use	13.6* [11.8, 15.6]	8.3* [6.3, 11.1]	6.4* [5.3, 7.7]	10.5* [8.3, 13.4]	6.1* [4.1, 8.8]	2.1* [1.7, 2.7]	3.5* [2.4, 5.2]
Mood stabilizer use	15.0* [11.2, 20.0]	14.7* [9.7, 22.2]	7.8* [5.6, 10.7]	8.4* [5.8, 12.2]	6.7* [3.8, 11.7]	2.7* [1.7, 4.4]	3.7* [1.9, 7.0]

Note. All psychiatric disorders were identified with a hierarchy-free method. Psychoactive medication use was measured by self-reported medication use (within the last 12 months) or verified by interviewer's visual inspection of prescription bottle, tube or box (used within the last two days). % = percent. CI = confidence interval. OR = Odds ratio.
*p < .001.

Table 2-6: The Strength of Association Between Psychoactive Medication Use

Disorder	Psychoactive medication use			
	Anxiolytic use	Anti-psychotic use	Antidepressant use	Mood stabilizer use
	OR [95% CI]			
Major depressive episode				
Manic Episode				
Social Phobia				
Panic Disorder				
Agoraphobia				
Alcohol dependence				
Drug dependence				
Anxiolytic use	-			
Antipsychotic use	21.7* [16.1, 29.4]	-		
Antidepressant use	23.2* [20.4, 26.4]	31.3* [22.5, 43.4]	-	
Mood stabilizer use	21.7* [16.8, 28.1]	70.5* [49.1, 101.3]	33.1* [25.4, 43.0]	-

Note. All psychiatric disorders were identified with a hierarchy-free method. Psychoactive medication use was measured by self-reported medication use (within the last 12 months) or verified by interviewer's visual inspection of prescription bottle, tube or box (used within the last two days). % = percent. CI = confidence interval. OR = Odds ratio.
*p < .001.

2.4.3 Psychoactive medication use

Table 2-1 illustrates that three of the four psychoactive medications were most commonly used in combination with antidepressant medications, which was itself most commonly used with anxiolytic medications. The rate of psychotropic medication use was greater than would be expected given the prevalence of each disorder category; the prevalence of any mood disorders occurring within the past 12 months was 5.2% (95% CI [4.9, 5.6]), whereas the prevalence of all antidepressant and mood stabilizer medication use within the past 12 months was 6.7% (95% CI [6.3, 7.0]) and 1.3% (95% CI [1.1, 1.4]), respectively. When psychoactive medication use within the past 12 months was stratified by the number of co-occurring lifetime and 12-month disorders (see Tables 2-2 and 2-3), it was found that 45.9% (95% CI [43.9, 47.9]) and 65.2% (95% CI [63.1, 67.2]) reported taking psychoactive medications even though they were not identified as having a lifetime or 12-month disorder, respectively.

In Table 2-5, the ORs for 12-month disorders and psychoactive medication use ranged from 2.1 (95% CI [1.7, 2.7]) for alcohol dependence and antidepressant medication use to 15.5 (95% CI [8.9, 26.8]) for manic episode and antipsychotic medication use. Two disorder-psychoactive medication use combinations were found to have no statistically significant association: alcohol dependence and anxiolytic medication use (OR = 1.3, 95% CI [0.9, 1.7]) as well as alcohol dependence and antipsychotic medication use (OR = 2.0, 95% CI [0.9, 4.2]). In Table 2-6, statistically significant associations were found between all the psychoactive medications pairings (ORs ranged from 21.7, 95% CI [16.1, 29.4] for anxiolytic and antipsychotic medication use to 70.5, 95% CI [49.1, 101.3]) for antipsychotic and mood stabilizer medication use).

2.4.4 Agreement between indicators of mental health status

To examine the concordance between the two methods of assessing psychoactive medication use and between the MHDs and psychoactive medication use, the PPA and NPA were calculated. Table 2-7 illustrates that between the two indicators used to identify respondents' use of psychoactive medications, the PPA was found to be moderate for antipsychotic medication use (50.5%, 95% CI [41.9, 59.1]); substantial for anxiolytic (66.7%, 95% CI [62.5, 70.8]) and mood stabilizer (72.9%, 95% CI [65.2, 80.6]) medication use and almost perfect (82.3 %, 95% CI [79.9, 84.6]) for antidepressant medication use. Table 2-8 shows that the PPA between identified MHDs and psychoactive medication use was slight-to-moderate: 10.7% (95% CI [8.6, 12.9]) for mood stabilizer medication use and any mood disorder to 59.3% (95% CI [44.8, 73.9]) for antipsychotic medication use and self-reported schizophrenia. The NPA was almost perfect for all the comparisons.

Table 2-7: Positive and Negative Percent Agreement for Psychoactive Medication Use

Psychoactive medication use	Positive percent agreement[a]	Negative percent agreement[b]
	% (95% CI)	
Anxiolytic medication use		
Self-report vs. interviewer inspection	66.7 [62.5, 70.8]	95.8 [95.5, 96.1]
Antipsychotic medication use		
Self-report vs. interviewer inspection	50.5 [41.9, 59.1]	99.9 [99.8, 99.9]
Antidepressant medication use		
Self-report vs. interviewer inspection	82.3 [79.9, 84.6]	98.0 [97.8, 98.2]
Mood stabilizer medication use		
Self-report vs. interviewer inspection	72.9 [65.2, 80.6]	99.3 [99.2, 99.4]

Note. Two methods were used in the CCHS Cycle 1.2 to identify respondents' psychoactive medication use. The first method asked respondents to report if they took anxiolytics, antipsychotics, antidepressants or mood stabilizers within the past 12 months. The second method required the interviewer to visually inspect any medication bottles, tubes or boxes that the respondent reported taking within the last two days. The interviewer inspection was considered the non-reference standard. Bootstrapped weighted estimates are presented. CI = confidence interval.

Table 2-8: Positive and Negative Percent Agreement for Mental Health Disorders and Psychoactive Medication Use

Mental health disorders and psychoactive medication use	Positive percent agreement[b]	Negative percent agreement[c]
	% (95% CI)	
Antipsychotic medication use vs. schizophrenia[a] (lifetime)	59.3 [44.8, 73.9]	99.6 [99.5, 99.6]
Antidepressant medication use vs. major depressive episode	41.1 [38.0, 44.2]	95.1 [94.8, 95.4]
Mood stabilizer medication use vs. manic episode	14.4 [9.8, 18.9]	98.9 [98.7, 99.0]
Antidepressant medication use vs. any mood disorder	39.8 [36.9, 42.8]	95.2 [94.9, 95.5]
Mood stabilizer medication use vs. any mood disorder	10.7 [8.6, 12.9]	99.3 [99.1, 99.4]
Anxiolytic medication use vs. social phobia	23.2 [19.9, 26.6]	94.5 [94.1, 94.8]
Anxiolytic medication use vs. panic disorder	36.2 [30.9, 41.6]	94.4 [94.1, 94.8]
Anxiolytic medication use vs. agoraphobia	31.1 [23.7, 38.6]	94.0 [93.7, 94.4]
Anxiolytic medication use vs. any anxiety disorder	25.9 [23.0, 28.7]	94.8 [94.5, 95.1]

Note. Respondents with mental health disorders occurring within the past 12-months were identified using the CCHS 1.2/WMH-CIDI. Respondents' psychoactive medication use was identified by either self-reported medication use or through interviewers' visual inspection of medication bottles, tubes or boxes. The disorders identified through the WMH-CIDI were considered the reference standard. Bootstrapped weighted estimates are presented. CI = confidence interval.

[a]Not identified using the CCHS 1.2/WMH-CIDI.

2.5 Discussion

The findings confirm that MHDs are widespread in the Canadian population. Approximately one of every five respondents reported at least one lifetime MHD and one of every ten respondents reported at least one 12-month MHD. The prevalence estimates for single disorders match previously reported estimates derived from the CCHS Cycle 1.2; however, other researchers have not explicitly explored patterns of comorbidity among psychiatric disorders, most common disorder pairings or agreement between multiple indicators of mental illness (Lesage et al., 2006; Patten et al., 2006; Sareen et al., 2007; Tellez-Zenteno, Patten, Jetté, Williams, & Wiebe, 2007). Neglecting to investigate details of psychiatric comorbidity incorrectly assumes that MHDs occur independently of one another and that clear boundaries can be identified; we have shown that this is not the case. Characteristics of psychiatric comorbidity should be examined in all community-based mental health surveys to enrich our understanding of this phenomenon. This information will not only improve surveillance but can have a tangible impact on how healthcare professionals view, assess, and treat people with MHDs. For example, when a clinician encounters a patient who is suffering from a major depressive episode and alcohol dependence, he or she may feel less inclined to decide which is the primary condition, and instead create a treatment plan that addresses both concurrently.

Previous analyses of the CCHS Cycle 1.2 have examined particular MHDs (e.g., major depressive episode or post-traumatic stress disorder) and treated them as correlates of various outcomes (e.g., suicide or obesity) without a critical investigation of psychiatric comorbidity (Cheung & Dewa, 2006; McIntyre et al., 2006; Schaffer, Cairney, Cheung, Veldhuizen, & Levitt, 2006). This is a limitation of the current evidence; we have demonstrated that respondents can have more than one disorder and by overlooking psychiatric comorbidity, inadvertent omitted variable bias can be introduced (Clarke, 2005). For example, examining a single diagnosis only

may mask the effects of other important variables (e.g., medication use and other MHDs). Because of these analytic omissions in previous CCHS Cycle 1.2 analyses, our findings can only be compared with previous international psychiatric epidemiological studies that examined lifetime and 12-month psychiatric comorbidity and utilized established measurement instruments (e.g., the DIS, CIDI, UM-CIDI and WMH-CIDI).

It is apparent that prevalence estimates from earlier psychiatric epidemiological studies, which utilized diagnostic classification instruments with exclusionary hierarchies (e.g., the DIS), reported lower prevalence estimates of each MHD, compared with later studies that utilized a version of the CIDI (Bijl et al., 1998; Bland et al., 1988; Bourdon et al., 1992; Kessler et al., 2005; Kessler et al., 1994; Offord et al., 1996; Regier et al., 1990). This could be expected because co-occurring disorders were prioritized in earlier instruments and secondary disorders that were considered 'due to' another priority disorder were excluded (Bourdon et al., 1992). Notwithstanding the effect of differences among the diagnostic classification instruments, our appraisal of the Canadian prevalence of MHDs, estimated via the CCHS Cycle 1.2, was lower than USA rates derived from the NCS and NCS-R (Kessler et al., 2005; Kessler et al., 1994). The rate of psychiatric comorbidity was also lower in the CCHS Cycle 1.2 than previously found in the NCS and NCS-R (Kessler et al., 2005; Kessler et al., 1994). This discrepancy is most likely the result of the CCHS 1.2/WMH-CIDI instrument. It assessed a limited number of MHDs (i.e., eight in total) compared with the NCS and NCS-R, which measured a broader range of anxiety, mood, and impulse-control disorders (i.e., 18 in total) using the full version of the WMH-CIDI. The implication of this finding is that the prevalence of having any MHD and the proportion of people that suffer from psychiatric comorbidity are probably underestimated in the CCHS Cycle 1.2. Moreover, the NCS and NCS-R offered initial non-responders a financial

incentive to participate, whereas the CCHS Cycle 1.2 did not. Because it is known that respondents with psychiatric illnesses are more reluctant to respond to mental health surveys compared with people without MHDs, this incentive could have increased participation and increased the observed rates of MHDs in the NCS and NCS-R (Kessler, Little, & Groves, 1995).

The relative magnitude of the association between the disorders paired for the lifetime and 12-month disorders was similar to the findings of the ECA study and the Australian National Survey of Mental Health and Well-being. All of the disorder pairings demonstrated strong associations, which signifies that the risk of having a second disorder is significantly greater in the presence of a first disorder. The ORs for comorbidity with two disorders, occurring within the past 12-months, were noticeably greater than were those for lifetime comorbidity. This finding has been reported previously by Kessler (1995) and Andrews (2002), but its interpretation is uncertain without further study. Patterns of comorbidity have implications for the classification of MHDs because these strong associations may actually indicate shared underlying or clustered symptomology or psychopathology.

This is the first study to examine agreement between the two methods used in the CCHS Cycle 1.2 to identify respondents' psychoactive medication use. We found that concordance between two different indicators was moderate to almost perfect (contingent on the type of psychoactive medication used). This finding indicates that varying timeframes (e.g., past 12-months versus past 2 days) and data collection methods (e.g., self report vs. interviewer verification) do influence the proportion of respondents who are identified as using psychoactive medications. This has implications for how psychoactive medication use is measured and reported in future mental health surveys.

Psychoactive medication use was also found to be relatively common and unexpectedly

reported by many respondents without identified lifetime or 12-month MHDs. This finding suggests that traditional measurement tools used to identify people with evidence of MHDs in community-based surveys (e.g., the WMH-CIDI) may fail to identify respondents who have other indications of mental illness. This is a significant finding that has not been previously reported. Results from other psychiatric epidemiological surveys have documented low psychotropic drug utilization rates among people with MHDs, but they have not explicitly examined psychotropic medication use among people without identified MHDs (Alonso et al., 2004; Beck et al., 2005; Sewitch, Cole, McCusker, Ciampi, & Dyachenko, 2008).

A definitive explanation for the mismatch between psychoactive medication use and MHDs is elusive given the available information within the survey. However, there are four potential explanations for our findings. The first is that the CCHS 1.2/WMH-CIDI did not measure a broad enough range of MHDs and this resulted in underreporting of psychiatric illness. Alternatively, respondents may have been unable (e.g., memory deficits) or preferred not to disclose their current or past symptoms of mental illness to Statistics Canada interviewers. This could result from widespread social stigma associated with their disorders; it is known that many individuals respond to questions about their mental health status based on what they believe will be viewed favourably by interviewers (Corrigan et al., 2000; van de Mortel, 2008). Moreover, it is known that compromised autobiographic memory is a prominent symptom of many MHDs; some individuals who have suffered from MHDs have difficulty associating dates with episodic symptoms due to inaccurate long-term recall. These cognitive deficits could influence their ability to accurately report their psychiatric history. Simon and VonKorff (1995) explained that recall errors are not random in psychiatric populations; underestimation of lifetime morbidity occurs more frequently in cross-sectional surveys than does overestimation. They also

suggest that recall of episodes of illness may be influenced by a person's current emotional state; for example, people currently experiencing depression are more likely to recall previous episodes than are those with similar histories who are not currently experiencing symptoms. Stability of long-term recall has been consistently related to the severity of the episode and the receipt of treatment; therefore, mild episodes that do not require treatment are forgotten over a 1-5 year period and more severe episodes are remembered past 5 years (Beekman, Copeland, & Prince, 1999; Simon & VonKorff, 1995) .

The third reason for the observed discrepancy between psychoactive medication use and MHDs may result from off-label psychoactive prescription drug use (e.g., medications used for purposes other than for what they were approved for). Examples of this include antidepressant medications prescribed for smoking cessation (e.g., bupropion) (Campion, Checinski, & Nurse, 2008), or chronic pain (e.g., tricyclic antidepressants) (Maizels & McCarberg, 2005), antipsychotic medications used for delirium (e.g., haloperidol) (Lonergan, Britton, Luxenberg, & Wyller, 2007) or anxiolytics used to assist sleep (e.g., lorazepam) (Roth, Hartse, Saab, Piccione, & Kramer, 1980). The fourth reason respondents may not report symptoms of mental illness, even though they are taking psychoactive medications, is because of a treatment effect whereby symptoms are controlled through medication use and therefore not reported (Roe, Goldblatt, Baloush-Klienman, Swarbrick, & Davidson, 2009). This is commonly seen when people discontinue taking their antidepressant medications because they "feel better" (p. 1405) (Bull et al., 2002).

2.5.1 Limitations

There are several limitations associated with the CCHS Cycle 1.2 survey and our analysis that warrant discussion. The sample from which these findings are derived under-represents

several important segments of the Canadian population in which MHDs are known to be prevalent. For example, people who are homeless or who live in institutions were not included in the CCHS 1.2 sampling frame, yet these are the people most likely to have MHDs (Argintaru et al., 2013; Krausz et al., 2013; Lafortune, 2010). Further, these analyses utilized retrospective self-reported data; the validity of this data collection approach is often questioned because the information cannot be verified. The CCHS 1.2/WMH-CIDI is a structured diagnostic interview administered by lay interviewers. Although this is a practical necessity in epidemiological surveys, it results in limited diagnostic precision because the interviewers were not trained clinicians and were required to keep their interactions within a predetermined script.

It should be noted that there are several estimates included in the sample that have relatively wide confidence intervals (e.g., the prevalence rate of schizophrenia); because bootstrapping techniques were applied to obtain relatively accurate standard errors, the lack of precision is most likely a consequence of small numbers. For this reason, the corresponding percentages or ORs that had wide confidence intervals must be interpreted with caution. Furthermore, the CCHS 1.2 was a cross-sectional survey so the reported bivariate associations cannot be said to reflect causal effects and are unadjusted for demographics correlates. This means that confounders were not accounted for in these analyses. Finally, the PPA and NPA were estimated to evaluate the agreement between methods used to identify respondents' psychoactive medication use as well as to evaluate the agreement between psychoactive medication use and respondents identified as having MHDs through the CCHS 1.2/WMH-CIDI. It should be reiterated that agreement should not be interpreted as meaning "correct" or that the disorder status is known with certainty; it is simply a measure of concordance.

2.5.2 Implications

Going forward, publications arising from the CCHS or other community-based health surveys should include measures of psychiatric comorbidity when reporting prevalence estimates of MHDs. Surveillance of psychiatric comorbidity could be improved by using some or all of the analytic techniques reported here. Reporting the extent of psychiatric comorbidity by examining the number of psychiatric disorders identified in individual respondents, identifying common disorder and psychoactive medication use pairings, and measuring the strength of association between disorders as well as between disorders and psychoactive medication use will greatly improve our understanding of how MHDs co-occur and provide information about the strengths and limitations of the instruments used to identify people with MHDs. Moreover, critical appraisal of the methods used to identify people with MHDs in community-based mental health surveys is necessary. Aside from expanding the CCHS 1.2/WMH-CIDI to include more disorders, alternative indicators of mental health status should be identified (e.g., psychoactive medication use or disease severity) and contrasted with more traditional measures (e.g., WMH-CIDI). Ideally, any discrepancies encountered could be clarified during data collection. For example, the precision of data collection could be improved by asking detailed psychoactive medication use questions alongside the CCHS 1.2/WMH-CIDI diagnostic questions and following up when inconsistencies are encountered. Psychiatric epidemiologists should also be aware that reported psychoactive medication use varies depending on the timeframe and method used for measurement.

The above recommendations are written with the intention of increasing recognition of psychiatric comorbidity in community-based health surveys. If implemented, they will further our understanding of how to accurately identify, categorize, and investigate the breadth of MHDs suffered in the community.

2.6 Conclusion

Psychiatric comorbidity is commonly identified in community-based surveys and should be examined in meaningful ways. The reporting of prevalence rates of single, mutually exclusive disorders is not adequate because it fails to capture the complexity of respondents' mental health status. This paper adds to the discussion of psychiatric comorbidity by contributing detailed findings of the prevalence and extent of psychiatric comorbidity within the Canadian population as well as contributing novel recommendations for future surveillance efforts. It also addresses several critical gaps in the research literature. Specifically, it offers an example of how to examine individual disorders alone and in combination with others, offers meaningful ways to investigate and discuss the concentration and association between psychiatric disorders, and considers the utility of examining alternative and multiple indicators of mental health status. Increasing recognition and dialogue related to psychiatric comorbidity will further our understanding of the complexities inherent in mental health diagnoses and measurement.

CHAPTER 3: THE ASSOCIATION BETWEEN CARDIOVASCULAR RISK AND CARDIOVASCULAR DISEASE, AND MENTAL HEALTH DISORDERS IN THE CANADIAN POPULATION

3.1 Introduction

People with MHDs are known to have poorer physical health and to suffer from higher rates of morbidity and mortality due to cardiovascular disease (CVD) compared with the general population (De Hert et al., 2009; Dickey, Normand, Weiss, Drake, & Azeni, 2002; Fleischhacker et al., 2008; Hennekens, 2007). The elevated rate of CVD can be partially attributed to an excess of established cardiovascular risk factors, including obesity, tobacco use, diabetes mellitus, hypertension, and dyslipidemia (D'Agostino et al., 2008; Hamer, Batty, Stamatakis, & Kivimaki, 2010; Lasser et al., 2000; McElroy, 2009). The presence of multiple cardiovascular risk factors can result in greater risk for cardiovascular injury. Several cardiovascular risk prediction algorithms have been developed to assess an individual's probability of developing CVD, but these techniques are rarely used in psychiatric epidemiology, particularly within the Canadian context. Research investigating CVD and cardiovascular risk among Canadians with MHDs is needed to better inform approaches to prevention and treatment.

The purpose of this study was to describe the association between MHDs and heart disease, stroke, and 10-year and 30-year cardiovascular risk using data from the Canadian Community Health Survey (CCHS) Cycle 1.2.

3.2 Background

3.2.1 Mental health disorders and cardiovascular mortality

CVD is defined as injuries to the cardiovascular system: the heart, the blood vessels of the heart, and the system of blood vessels throughout the body and within the brain (Heart &

Stroke Foundation, 2013). CVD manifests itself through coronary death, myocardial infarction (MI), coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, and heart failure (D'Agostino et al., 2008; Pencina et al., 2009).

It has been well documented that people with MHDs have relatively shorter life expectancy because their rate of mortality is two or three times higher than the general population's (Angst et al., 2002; Brown, 1997; Bushe et al., 2010; Chang et al., 2010; Colton & Manderscheid, 2006; Dembling, Chen, & Vachon, 1999; Harris & Barraclough, 1998; Kawachi et al., 1994; Osborn, Levy, et al., 2007; Saha et al., 2007). This mortality gap translates to a 13- to 30-year shortened life expectancy and has widened in recent decades, even in countries with universal health care (De Hert, Correll, et al., 2011). Excess mortality in this population is largely the result of physical illnesses, such as CVD, and not suicide (De Hert, Correll, et al., 2011; Lawrence, Holman, Jablensky, & Hobbs, 2003).

A meta-analysis of 37 studies (N = 22,296) conducted in 25 different countries demonstrated that people with schizophrenia have a mean all-cause standardized mortality ratio (SMR) of 2.98 (standard deviation (SD) = 1.75); the SMRs for MI and cerebrovascular disease are 2.01 (SD = 0.83) and 0.87 (SD = 0.38), respectively (Saha et al., 2007). Angst et al. (2002) examined data from 12 community and psychiatric inpatient samples (N = 71,444), between 1976 and 2000, and found that the all-cause SMRs for patients diagnosed with major depressive and bipolar disorders ranged from 1.23 to 2.50. In the second part of their Zurich-based study, Saha et al. followed 306 psychiatric hospital in-patients that were diagnosed with major depressive disorder (N = 186) or bipolar disorder (N = 220) for 34 to 38 years and found an overall SMR of 1.61 (95% CI [1.43, 1.80]). Apart from suicide, cardiovascular and cerebrovascular diseases accounted for a higher than expected mortality rate; the SMR for CVD

was 1.61 (95% CI [1.31, 1.96]) and cerebrovascular disease was 1.33 (95% CI [0.96, 1.81]). Similarly, Kawachi, Sparrow, Vokonas, and Weiss (1994) conducted a 32-year follow-up study of the association between anxiety and fatal coronary heart disease in a cohort of community-dwelling men in the greater-Boston area (N = 2,271). The authors documented an age-adjusted odds ratio (OR) of 3.20 (95% CI [1.27, 8.09]) for fatal coronary heart disease among men who scored two or more on an anxiety symptoms scale compared with men reporting no anxiety.

3.2.2 Mental health disorders and cardiovascular morbidity

Because CVD is a chronic condition with varying survival rates, estimates of cardiovascular morbidity (e.g., non-fatal heart disease or stroke) are also regularly reported. Numerous studies have demonstrated that individuals with MHDs have greater morbidity associated with heart disease and stroke compared with people without MHDs (Chauvet-Gelinier, Trojak, Verges-Patois, Cottin, & Bonin, 2013; Dickey et al., 2002; Dossa et al., 2011; Enger et al., 2004; Hemingway & Marmot, 1999; Kubzansky et al., 1998; Lin, Hsiao, Pfeiffer, Hwang, & Lee, 2008; Nielsen, Vestergaard, Christensen, Christensen, & Larsen, 2013; Rugulies, 2002; Tsai et al., 2012). These findings were confirmed by the World Mental Health Survey Initiative, which conducted 18 epidemiologic surveys in 17 countries with 85,052 people (Ormel et al., 2007). The initiative investigated the cross-cultural associations between MHDs and heart disease and found that age- and gender-adjusted pooled ORs were 2.1 (95% CI [1.9, 2.5]) for mood disorders, 2.2 (95% CI [1.9, 2.5]) for anxiety disorders, and 1.4 (95% CI [1.0, 1.9]) for alcohol abuse or dependence for persons with heart disease compared with those without. The cardiovascular morbidity of people with schizophrenia and the association between MHDs and stroke, specifically, are rarely examined in epidemiological surveys because of small numbers.

The study of cardiovascular morbidity in Canadians with MHDs has been limited to a few longitudinal studies conducted with provincial-level datasets. Curkendall, Mo, Glasser,

Stang, and Jones (2004) conducted a retrospective cohort study of health records from the province of Saskatchewan to compare the prevalence of CVD in patients diagnosed with schizophrenia (N = 3,022) and in age- and sex-matched controls from the general population. They also determined the incidence of cardiovascular morbidity in a follow-up period. They found that patients with schizophrenia had increased risk-adjusted odds ratios for heart failure (OR = 1.7, 95% CI [1.4, 2.2]), stroke (OR = 2.1, 95% CI [1.6, 2.7]), and transient cerebral ischemia (OR = 2.6, 95% CI [1.7, 3.7]). The odds of having MI, ischemic heart disease, or ventricular arrhythmia were not significantly different from those in the comparison group. However, the odds of incident ventricular arrhythmia (OR = 2.3, 95% CI [1.2, 4.3]), heart failure (OR = 1.6, 95% CI [1.2 to 2.0]), and stroke (OR = 1.5, 95% CI [1.2, 2.0]) were elevated. More recently, Callaghan and Khizar (2010) examined the incidence of cardiovascular morbidity among people with bipolar disorder (N = 5,999) by using Province of Ontario emergency department and inpatient hospital records from 2002-2006. The primary outcome was time-to-readmission for any cardiovascular diagnosis. They found that people with bipolar disorder had an adjusted hazard ratio of 1.66 (95% CI [1.37, 2.07]) for subsequent cardiovascular morbidity compared with a population-proxy group (patients with a primary appendicitis-related diagnosis). The findings of these studies are limited to particular disorders and in two provinces, a more thorough examination of cardiovascular morbidity among Canadians with MHDs is warranted. Moreover, an investigation of the influence of psychiatric comorbidity on CVD is needed.

Psychiatric comorbidity is a term applied to individuals who report symptoms that meet the criteria for more than one MHD (Andrews et al., 2002). In the previous chapter, we revealed that MHDs do not occur independently of one another. Indeed, 28.3% of the respondents who

met the criteria for one lifetime disorder also endorsed symptoms for additional disorders. However, psychiatric comorbidity was most frequently observed with two co-occurring disorders. Bankier, Januzzi, and Littman (2004) demonstrated that psychiatric comorbidity among outpatients with coronary heart disease is common; the mean number of comorbid psychiatric disorders per person (N = 100) was 1.7. However, they recommended that larger epidemiological studies be undertaken to confirm this finding. Because patterns of comorbidity may contribute to our understanding of the disorder combinations or pairings that place affected people at risk for yet other health conditions, it is important to incorporate appropriate measures into population health research.

3.2.3 Mental health disorders and modifiable cardiovascular risk factors

The etiology of excess cardiovascular morbidity among people with MHDs is multifactorial and attributed to a combination of genetic, behavioural, and socioeconomic influences that are compounded by the side effects of psycho-pharmacological treatments that are known to increase the prevalence of cardiovascular risk factors (De Hert et al., 2009; Newcomer & Hennekens, 2007). A considerable amount of research has been dedicated towards identifying modifiable cardiovascular risk factors in the general population. The INTERHEART and INTERSTROKE studies have been the most influential works in this area; they documented nine risk factors that account for 90% of the risk associated with acute MI in men and 94% of the risk in women and ten risk factors that account for 90% of the risk associated with stroke for people of all ages and in all regions of the world (O'Donnell et al., 2010; Yusuf et al., 2004).

The INTERHEART study used a standardized case-control design to examine acute MI in 15,152 cases and 14,820 controls, in 52 countries. They determined that tobacco smoking (OR = 2.87 [99% CI: 2.58, 3.19]), raised ApoB/ApoA1 ratio (LDL-C/HDL-C) (OR = 3.25 [99% CI: 2.81, 3.76]), hypertension (OR = 1.91 [99% CI: 1.74, 2.10]), diabetes mellitus (OR = 2.37

[99% CI: 2.07, 2.71]), abdominal obesity (OR = 1.12 [99% CI: 1.0, 1.25]), and psychosocial factors (e.g., depression, locus of control, perceived stress, and life events) (OR = 2.67 [99% CI: 2.21, 3.22]) contributed to an increased risk of MI, whereas moderate alcohol consumption (OR = 0.99, 95% CI [0.82, 1.02]), daily consumption of fruits and vegetables (OR = 0.70, 99% CI [0.62, 0.79]), and regular physical activity (OR = 0.86, 99% CI [0.76, 0.97]) were protective against MI (Yusuf et al., 2004). The INTERSTROKE study used the same method to examine modifiable risk factors for stroke using case-control pairs (N = 2,337 with ischemic stroke, N = 663 with hemorrhagic stroke, and 3,000 controls) in 22 countries and identified the following risk factors: hypertension (OR = 2.64, 99% CI [2.26, 3.08]), tobacco smoking (OR = 2.09, 99% CI [1.75, 2. 51]), waist-to-hip ratio (OR = 1.65, 99% CI [1.36, 1.99]), diet risk score (higher scores indicate an increasingly unhealthful cardiovascular diet) (OR = 1.35, 99% CI [1.11, 1.64]), diabetes mellitus (OR = 1.36, 99% CI [1.10, 1.68]), alcohol intake (i.e., > 30 drinks per month) (OR = 1.51, 99% CI [1.18, 1.92]), psychosocial stress (OR = 1.30, 99% CI [1.06, 1.60]), depression (OR = 1.35, 99% CI [1.10, 1.66]), cardiac causes (i.e., atrial fibrillation or flutter, previous MI, rheumatic valvular disease, or prosthetic heart valve) (OR = 2.38, 99% CI [1.77, 3.20]), and ratio of apolipoproteins (B to A1) (OR = 1.89, 99% CI [1.49, 2.40]) increased the risk of stroke, whereas regular physical activity (OR = 0.69, 99% CI [0.53, 0.90]) was protective against stroke (O'Donnell et al., 2010).

It is known that the prevalence rates of modifiable cardiovascular risk factors, including tobacco smoking, dyslipidemia, hypertension, diabetes mellitus, and obesity are substantially elevated in people with MHDs compared with the general population (Barnett et al., 2007; De Hert et al., 2009; Goff et al., 2005; Jonas et al., 1997; Lasser et al., 2000; McIntyre et al., 2006; Osborn et al., 2008; van Reedt Dortland et al., 2010). Moreover, many people with MHDs are

less physically active, have comorbid substance use disorders, and eat a diet that is low in fibre, fruit, and vegetables and high in fat and carbohydrates compared with people without MHDs (Bonnet et al., 2005; Elmslie et al., 2001; McCreadie, 2003; Osborn, Nazareth, et al., 2007; Rush et al., 2008; Westreich, 2005). This has important implications for the appraisal of cardiovascular risk in this group because cardiovascular risk factors can cluster to amplify the risk of injury (Jackson et al., 2005).

3.2.4 Cardiovascular risk prediction

Several multivariate risk prediction algorithms, derived from cohort studies and randomized trials, have been developed to quantitatively estimate an individual's chance of developing CVD (Anderson et al., 1991; Brindle et al., 2006; Conroy et al., 2003; D'Agostino et al., 2000; D'Agostino et al., 1994; D'Agostino et al., 2008; Hippisley-Cox, Coupland, et al., 2007; Pencina et al., 2009; Ridker et al., 2007; Ridker et al., 2008; Wilson et al., 1998; Woodward et al., 2007). CVD risk prediction scores are widely adopted, especially those derived from the Framingham Heart Study (Dawber et al., 1963; Dawber et al., 1951), and have been adapted for use in primary care as simplified charts, tables, computer programs, and web-based tools, and are routinely recommended in policy documents and guidelines (ATP-III, 2002; Kannel et al., 1979; McPherson et al., 2006). Framingham-based algorithms use sex-specific functions to calculate the multivariable risk of CVD within a defined time period (e.g., 10 years) for people without established CVD. This is done by assigning weights or points for risk factors (i.e., age, diabetes, tobacco smoking, systolic blood pressure, total cholesterol, and HDL cholesterol) and then applying a scoring algorithm to estimate an absolute probability of developing CVD. Low-moderate risk is considered < 10%, moderately high risk is 10%-20%, and high risk is > 20%. In most cohorts, Framingham-based scores have demonstrated very

good discrimination, as evidenced by C statistics that range from 0.75 to 0.80 (D'Agostino et al., 2008; Lloyd-Jones, 2010; Pencina et al., 2009).

In clinical practice, cardiovascular risk prediction algorithms are used to assist healthcare providers match the intensity of their treatment to the probability of disease, as well as to facilitate risk communication with patients (ATP-III, 2002; McPherson et al., 2006). Depending on their absolute risk, patients may be offered blood pressure and cholesterol lowering pharmacotherapy, in addition to advice about relevant health behaviour (e.g., smoking cessation and physical activity) (Brindle et al., 2006). Risk estimation also can be used on a population-level to study particular sub-groups that are known to be vulnerable to CVD for the purpose of informing prevention interventions. A number of recent studies have quantified the risk of coronary heart disease, using Framingham-based estimates in people with schizophrenia or other psychosis in hospital and community-based samples (Cohn et al., 2004; Goff et al., 2005; McCreadie, 2003; Osborn et al., 2006). A few have extended their investigation to include participants with other MHDs taking antipsychotic medications (Correll, Frederickson, Kane, & Manu, 2006; Mackin et al., 2007). However, cardiovascular risk prediction techniques have not been applied in community-based mental health surveys with respondents who suffer from a variety of MHDs. The Canadian Community Health Survey (CCHS) Cycle 1.2 offered a unique opportunity to apply these techniques for the Canadian population.

3.3 Methods

3.3.1 Data source and sample

Cross-sectional data about mental health status, CVD, and cardiovascular risk factors were derived from the CCHS Cycle 1.2 conducted by Statistics Canada (Statistics Canada, 2002). This nationally representative household survey targeted residents in all provinces, with

the exclusion of populations on Indian reserves and Canadian Forces' bases, and in healthcare institutions and some remote areas. The CCHS respondents were selected from a multistage stratified cluster design in which the household was the final sampling unit. Each province was divided into three types of regions (i.e., major urban centres, cities, and rural regions) before clusters within each stratum were selected based on socio-economic characteristics. Dwelling lists were then prepared for each cluster and households were selected from the lists. This technique ensured that the probability of selecting a sampling unit was proportional to the size of the population (Statistics Canada, 1998).

Face-to-face interviews were carried out between May and December 2002 by trained lay interviewers using a Computer-Assisted Personal Interviewing (CAPI) method (Statistics Canada, 2002). The interviewers explained the study and obtained verbal informed consent before commencing an interview. In all of the selected dwellings, a knowledgeable household member was asked to supply basic demographic information about all of the residents. Depending on the composition of the household, one member was then selected for a more in-depth interview. In cases where this initial household visit resulted in non-response, telephone follow-ups were conducted. Data collection by telephone was authorized only when travel was prohibitive or the respondent refused to conduct the interview in person; this resulted in 14% of the interviews being completed by telephone. In total, 48,047 households were selected to participate in Cycle 1.2 and a national response rate of 77% was achieved (Statistics Canada, 2002).

3.3.2 Demographic measures

Sex (male or female), age in years, marital status (single vs. married or common-law), total household income based on number of members (low income vs. middle or high income),

education level (< than secondary graduate [< 12 years of basic education] vs. ≥ secondary graduate), immigrant status (immigrant [immigrated from overseas] vs. non-immigrant [Canadian born]), and ethnicity/race ("white" vs. not "white") were treated as demographic correlates. Low income was defined as < $15,000 if 1 or 2 people; < $20,000 if 3 or 4 people; < $30,000 if 5 or more people living in a household (Statistics Canada, 2002).

3.3.3 Measures of mental health status

Mental health status was measured with a modified version of the World Mental Health Composite International Diagnostic Interview (WMH-CIDI), which was modified to meet the needs of the CCHS Cycle 1.2 (i.e., fewer disorders were assessed) and based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 1994; Kessler et al., 2004; Statistics Canada, 2002). The CCHS 1.2/WMH-CIDI is a fully-structured psychiatric diagnostic interview administered by trained lay interviewers to determine the lifetime prevalence rates of five major MHDs. These include major depressive episode, manic episode, social phobia, panic disorder, and agoraphobia. Hierarchy-free diagnoses (one disorder did not take precedence over another diagnosis) were considered throughout the analyses. The lifetime prevalence of a disorder is the proportion of the sample who ever experienced the disorder. Schizophrenia was not measured with the structured diagnostic interview; rather, it was assessed as a self-reported chronic health condition diagnosed by a health professional. To reduce the respondents' burden, screening questions preceded the CCHS 1.2/WMH-CIDI survey modules. Negative responses to the screening questions prompted a conditional "skip logic" feature to avoid the full roster of questions associated with each disorder being posed when they were not relevant.

The respondents were classified as having a MHD if they had at least one lifetime MHD or if they had been treated with at least one psychoactive medication (e.g., anxiolytics, antidepressants, antipsychotics, or mood stabilizer medications) within the past 12 months. There were two methods used in the CCHS Cycle 1.2 to identify respondents who took psychoactive medications. The first asked the respondents to report if they took anxiolytics to reduce anxiety or nervousness, antipsychotics for the treatment of psychotic behaviour, or antidepressants or mood stabilizers within the past 12 months. The second method required the interviewer to visually inspect any medications that the respondent reported taking within the last two days. The interviewer then recorded these medications using codes from the Anatomical Therapeutic Chemical (ATC) Classification System (World Health Organization, 2009).

3.3.4 Measures of cardiovascular disease

The CCHS Cycle 1.2 included indicators of heart disease and stroke in the self-reported chronic conditions module; the question stem stated, "We are interested in long-term conditions which are expected to last or have already lasted 6 months or more and that have been diagnosed by a health professional." The respondents answered "yes" or "no" to the questions: "Do you have heart disease?" and "Do you suffer from the effects of a stroke?" Self-reported CVD diagnoses have been shown to have acceptable validity, with under-reporting occurring more frequently than over-reporting of the diagnosis (Kehoe, Wu, Leske, & Chylack, 1994; Kriegsman, Penninx, van Eijk, Boeke, & Deeg, 1996).

3.3.5 Measures of cardiovascular risk

Cardiovascular risk was calculated with algorithms from the Framingham Heart Study to estimate short- and long-term risk of CVD (D'Agostino et al., 2008; Pencina et al., 2009). The 10-year risk of cardiovascular disease was calculated in men and women without established CVD, aged 30-74 years, to predict "general" cardiovascular outcomes, such as coronary death,

myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, and heart failure using a simple point-based or "score sheet" system. The point-based system assigned each risk factor level an integer number. These risk factor values were summed to derive a score, and then the risk for that score was determined from a look-up table (D'Agostino et al., 2008).

The 30-year risk of cardiovascular disease derived risk estimates using Cox regression (i.e., equation-based) models for men and women without established CVD or cancer, aged 20-59 years, to predict the likelihood of "hard" outcomes such as coronary death, myocardial infarction, and stroke. Individuals with cancer were excluded from the analysis. Simple non-laboratory-based predictors were used in the calculations of 30-year risk, including: sex (male or female), age (years), body mass index (self-reported weight and height [kg/(m)]), self-reported systolic blood pressure (SBP) (mmHg), diabetes status (yes/no), treatment for hypertension (yes/no), and smoking (yes/no) (Pencina et al., 2009).

Diabetes status ("Do you have diabetes") and SBP ("Do you have high blood pressure?") were collected through the self-reported chronic conditions module of the CCHS. Both risk algorithms required a quantitative measurement of SBP (in mmHg), which was not available in the CCHS Cycle 1.2. Accordingly, the respondents who reported having high blood pressure were assumed to have SBP = 140-159 mmHg, respondents with or without reported high blood pressure who indicated that they were taking an antihypertensive drug were assumed to have SBP = 130-139 mmHg, and respondents without high blood pressure and who did not report taking an antihypertensive drug were considered to have SBP = 120-129 mmHg (Hackam et al., 2013). The rationale for these decisions was based on a therapeutic paradigm that prescribers "treat to target" or keep blood pressure below a level that is known to induce cardiovascular

events (i.e., 140/90 mmHg) (Atar, Birkeland, & Uhlig, 2010). Hypertension drug therapy was determined via the ATC codes. A self-reported proxy measure for smoking status was used because the CCHS Cycle 1.2 did not directly ask the respondents about their tobacco use patterns. This variable was included in the stress module and asked the respondents, "When dealing with stress, how often do you try to feel better by smoking more cigarettes than usual?" The respondents were classified as smokers if they responded with "often," "sometimes," "rarely," or "never" and as non-smokers if they indicated that they "do not smoke."

3.3.6 Analysis

To investigate the relationships between MHDs and CVD risk and CVD, three groups of respondents were created for each specific MHD. This approach was taken to incorporate measures of psychiatric comorbidity into our analysis. We sought to determine whether particular MHDs or disorder combinations place affected people at greater risk of CVD. One group was respondents who were identified as having one MHD alone (e.g., a major depressive episode only), a second group had a disorder and its most common disorder pairing (e.g., a major depressive episode and social phobia alone), and a third group was respondents who reported having a specific MHD with any other disorder (a major depressive episode alone or with any other MHD, including social phobia).

The demographic characteristics of the respondents with specific MHDs were characterized with proportions and bivariate ORs. Age was stratified into three categories to correspond with the Framingham scoring algorithms (i.e., 15-34 years, 35-64 years, and $\geq$ 65 years). Descriptive statistics were used to describe the prevalence of heart disease and stroke among the respondents with lifetime MHDs before cross-tabulations were produced, and the associations between the specific MHDs and heart disease and stroke were described with unadjusted and demographically adjusted ORs. Short- (10-year) and long-term (30-year)

cardiovascular risk estimates were dichotomized at the median to estimate the strength of their relationship with lifetime MHDs (Allan et al., 2013). The estimates for cardiovascular risk were adjusted for marital status, household income, education level, immigrant status, and ethnicity/race. Sex and age were not treated as covariates because they were included in the risk prediction algorithms. Confidence intervals (95%) for the proportions and odd ratios (ORs) were estimated using the balanced repeated replication method with Stata version 12 software to adjust for clustered sampling and the sample weights (Rust & Rao, 1996; StataCorp., 2011).

3.4 Results

3.4.1 Sample characteristics

The sample consisted of 36,984 respondents and was weighted to represent 24,996,593 people in the Canadian population. Table 3-1 presents the rates of having any lifetime MHD and of having schizophrenia, alone or in combination with other MHDs. Respondents with any MHD, in their lifetime, were more likely to be women (29.7%), middle-aged (i.e., 35-64 years; 27.7%), single (28.2%), have low household income (34.8%), born in Canada (i.e., not immigrants; 26.9%), and "white" (26.5%). The respondents with schizophrenia, specifically, were more likely to be male, single, and have low income. The rates of lifetime mood disorders (see Table 3-2) and anxiety disorders (see Table 3-3, 3-4) indicate that these respondents were more likely to be female, middle-aged, single, have low income, secondary school graduates, "white," and born in Canada. Five of the six MHDs were most commonly paired with having had a major depressive episode, which was itself most commonly paired with social phobia.

Table 3-1: Lifetime Mental Health Disorders and Schizophrenia by Demographic Factors

Demographic factor	**Mental health disorder** (any)[a] vs. no disorder	**Schizophrenia alone**[b] vs. else[c]	**Schizophrenia with MDE** vs. else[d]	**Schizophrenia alone or with any other mental health disorder including MDE** vs. else[e]
	% [95% CI] OR [95% CI]			
Sex				
Male vs. female	20.0 [19.1, 20.9]/ 29.7 [28.7, 30.7] 0.6 [0.5, 0.6]	0.1 [0.0, 0.2]/ 0.1 [0.0, 0.1] 2.2 [0.9, 5.6]	0.1 [0.1, 0.1]/ 0.1 [0.0, 0.2] 1.0 [0.5, 2.1]	0.3 [0.2, 0.4]/ 0.2 [0.1, 0.3] 1.6 [0.9, 2.7]
Age				
35-64 years vs. 15-34 years	27.7 [26.8, 28.7]/ 21.8 [21.0, 22.6] 1.4 [1.3, 1.5]	0.1 [0.0, 0.1]/ 0.1 [0.0, 0.2] 0.5 [0.2, 1.1]	0.1 [0.1, 0.2]/ 0.1 [0.0, 0.1] 1.5 [0.7, 3.4]	0.2 [0.2, 0.3]/ 0.3 [0.1, 0.4] 1.0 [0.5, 1.8]
≥ 65 years vs. 15-34 years	20.5 [19.2, 21.8]/ 25.7 [25.0, 26.4] 0.7 [0.7, 0.8]	0.1 [0.0, 0.2]/ 0.1 [0.0, 0.1] 1.3 [0.4, 3.7]	- -	0.2 [0.0, 0.3]/ 0.3 [0.2, 0.3] 0.6 [0.3, 1.4]
Marital Status				
Single vs. not single	28.2 [27.2, 29.2]/ 22.9 [22.0, 23.7] 1.3 [1.2, 1.4]	0.1 [0.1, 0.2]/ 0.0 [0.0, 0.1] 3.1 [1.2, 7.8]	0.2 [0.1, 0.3]/ 0.0 [0.0, 0.1] 5.1 [1.9, 13.4]	0.5 [0.3, 0.6]/ 0.1 [0.1, 0.2] 4.1 [2.2, 7.4]
Total household income				
Low income vs. middle or high income	34.8 [32.4, 37.1]/ 24.1 [23.4, 24.8] 1.7 [1.5, 1.9]	0.2 [0.1, 0.3]/ 0.1 [0.0, 0.1] 3.0 [1.2, 7.1]	0.5 [0.3, 0.7]/ 0.1 [0.0, 0.1] 7.7 [3.7, 16.0]	0.8 [0.6, 1.1]/ 0.2 [0.1, 0.3] 4.4 [2.6, 7.6]
Education level				
< than secondary graduate vs. ≥ secondary graduate	25.1 [23.9, 26.2]/ 24.8 [24.1, 25.5] 1.0 [0.9, 1.1]	0.1 [0.0, 0.1]/ 0.1 [0.0, 0.1] 0.8 [0.3, 2.1]	0.2 [0.1, 0.3]/ 0.1 [0.0, 0.1] 2.2 [1.1, 4.5]	0.3 [0.2, 0.5]/ 0.2 [0.1, 0.3] 1.5 [0.9, 2.6]
Immigrant status				
Immigrant vs. non-immigrant	17.9 [16.4, 19.4]/ 26.9 [26.2, 27.7] 0.6 [0.5, 0.7]	0.1 [0.0, 0.1]/ 0.1 [0.0, 0.1] 0.7 [0.2, 2.2]	- -	0.1 [0.0, 0.2]/ 0.3 [0.2, 0.4] 0.4 [0.1, 0.9]
Ethnicity/race				
"White" vs. not "white"	26.5 [25.9, 27.2]/ 16.6 [14.8, 18.4]	0.1 [0.0, 0.1]/ 0.1 [0.0, 0.2]	0.1 [0.1, 0.1]/ 0.1 [0.0, 0.2]	0.3 [0.2, 0.3]/ 0.2 [0.1, 0.4]

Demographic factor	**Mental health disorder** (any)[a] vs. no disorder	**Schizophrenia alone**[b] vs. else[c]	**Schizophrenia with MDE** vs. else[d]	**Schizophrenia alone or with any other mental health disorder including MDE** vs. else[e]
	% [95% CI] OR [95% CI]			
	1.8 [1.6, 2.1]	0.8 [0.2, 3.2]	1.0 [0.3, 3.3]	1.0 [0.5, 2.3]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. Cells with a dash are suppressed data because the numbers were too small for disclosure. Major depressive episode (MDE). % = percent; OR = odds ratio; CI = confidence interval.
[a]Respondents identified as having evidence of at least one lifetime mental health disorder or taking at least one psychoactive medications within the past 12-months.
[b]Not measured by structured diagnostic interview (CCHS 1.2/WMH-CIDI).
[c]Indicates that the comparison is all respondents in the sample not including people with the listed disorder alone.
[d]Indicates that the comparison is all respondents in the sample not including people with the listed disorder in combination with its most common disorder pairing.
[e]Indicates that the comparison is all respondents in the sample who have the listed disorder in any combination.

Table 3-2: Lifetime Mood Disorders by Demographic Factors

Demographic factor	Major depressive episode alone vs. else[a]	MDE with social phobia vs. else[b]	MDE alone or with any other mental health disorder including social phobia vs. else[c]	Manic episode alone vs. else[a]	Manic episode with MDE vs. else[b]	Manic episode alone or with any other mental health disorder including MDE vs. else[c]	Any mood disorder[d] vs. else
	% [95% CI] OR [95% CI]						
Sex							
Male vs. female	5.7 [5.2, 6.2]/ 9.7 [9.0, 10.3] 0.6 [0.5, 0.6]	2.3 [2.0, 2.7]/ 3.4 [3.1, 3.8] 0.7 [0.6, 0.8]	9.2 [8.5, 9.9]/ 15.1 [14.4, 15.9] 0.6 [0.5, 0.6]	0.7 [0.6, 0.9]/ 0.5 [0.4, 0.7] 1.4 [1.0, 2.0]	1.1 [0.9, 1.4]/ 1.4 [1.2, 1.6] 0.8 [0.7, 1.1]	2.4 [2.1, 2.7]/ 2.3 [2.0, 2.6] 1.0 [0.9, 1.2]	10.4 [9.7, 11.1]/ 16.0 [15.2, 16.8] 0.6 [0.6, 0.7]
Age							
35-64 years vs. 15-34 years	9.1 [8.5, 9.8]/ 6.2 [5.7, 6.7] 1.5 [1.4, 1.7]	3.3 [3.0, 3.7]/ 2.4 [2.1, 2.7] 1.4 [1.2, 1.6]	14.3 [13.5, 15.1]/ 10.0 [9.4, 10.5] 1.5 [1.4, 1.7]	0.7 [0.5, 0.8]/ 0.6 [0.5, 0.8] 1.0 [0.8, 1.5]	1.3 [1.1, 1.5]/ 1.2 [1.0, 1.4] 1.1 [0.9, 1.4]	2.5 [2.2, 2.9]/ 2.2 [1.9, 2.5] 1.2 [1.0, 1.4]	15.4 [14.6, 16.2]/ 10.9 [10.3, 11.5] 1.5 [1.4, 1.6]
≥ 65 years vs. 15-34 years	5.3 [4.6, 6.0]/ 8.2 [7.7, 8.6] 0.6 [0.5, 0.7]	0.7 [0.4, 1.0]/ 3.3 [3.0, 3.5] 0.2 [0.1, 0.3]	6.6 [5.8, 7.4]/ 13.2 [12.6,13.7] 0.5 [0.4, 0.5]	0.1 [0.0, 0.2]/ 0.7 [0.6, 0.9] 0.2 [0.1, 0.4]	0.1 [0.0, 0.2]/ 1.5 [1.3, 1.6] 0.1 [0.0, 0.3]	0.3 [0.1, 0.5]/ 2.7 [2.5, 2.9] 0.1 [0.1, 0.2]	6.7 [5.9, 7.5]/ 14.4 [13.8, 15.0] 0.4 [0.4, 0.5]
Marital Status							
Single vs. not single	8.6 [8.0, 9.2]/ 7.2 [6.6, 7.8] 1.2 [1.1, 1.4]	3.8 [3.4, 4.2]/ 2.4 [2.1, 2.6] 1.6 [1.4, 1.9]	14.6 [13.8, 15.4]/ 10.7 [10.1, 11.4] 1.4 [1.3, 1.6]	0.9 [0.7, 1.1]/ 0.5 [0.3, 0.6] 1.9 [1.4, 2.8]	2.0 [1.7, 2.3]/ 0.8 [0.7, 0.9] 2.5 [2.0, 3.2]	3.5 [3.1, 4.0]/ 1.6 [1.4, 1.9] 2.2 [1.8, 2.7]	16.0 [15.2, 16.8]/ 11.5 [10.8, 12.2] 1.5 [1.3, 1.6]
Total household income							
Low income vs. middle or high income	9.4 [7.6, 11.3]/ 7.6 [7.2, 8.0] 1.3 [1.0, 1.6]	4.5 [3.7, 5.3]/ 2.8 [2.6, 3.1] 1.6 [1.3, 2.0]	16.6 [14.6, 18.6]/ 11.9 [11.3, 12.4] 1.5 [1.3, 1.7]	0.6 [0.3, 0.8]/ 0.6 [0.5, 0.8] 0.9 [0.6, 1.5]	2.7 [2.2, 3.3]/ 1.1 [0.9, 1.3] 2.5 [1.9, 3.3]	4.0 [3.3, 4.7]/ 2.2 [1.9, 2.4] 1.9 [1.5, 2.3]	17.8 [15.8, 19.8]/ 12.9 [12.3, 13.4] 1.5 [1.3, 1.7]
Education level							
< than secondary graduate vs. ≥ secondary graduate	6.3 [5.5, 7.0]/ 8.2 [7.7, 8.7] 0.8 [0.7, 0.9]	2.2 [1.8, 2.5]/ 3.2 [2.9, 3.5] 0.7 [0.6, 0.8]	10.1 [9.3, 11.0]/ 12.9 [12.3, 13.4] 0.8 [0.7, 0.8]	0.7 [0.5, 1.0]/ 0.6 [0.5, 0.7] 1.3 [0.9, 1.9]	1.4 [1.0, 1.7]/ 1.2 [1.1, 1.4] 1.1 [0.8, 1.5]	2.7 [2.2, 3.2]/ 2.2 [2.0, 2.5] 1.2 [1.0, 1.5]	11.4 [10.5, 12.3]/ 13.8 [13.2, 14.4] 0.8 [0.7, 0.9]

Demographic factor	Major depressive episode alone vs. else[a]	MDE with social phobia vs. else[b]	MDE alone or with any other mental health disorder including social phobia vs. else[c]	Manic episode alone vs. else[a]	Manic episode with MDE vs. else[b]	Manic episode alone or with any other mental health disorder including MDE vs. else[c]	Any mood disorder[d] vs. else
	% [95% CI] OR [95% CI]						
Immigrant status							
Immigrant vs. non-immigrant	5.9 [4.9, 6.8]/ 8.2[7.8, 8.7] 0.7 [0.6, 0.8]	1.9 [1.3, 2.4]/ 3.2 [3.0, 3.4] 0.6 [0.4, 0.8]	8.7 [7.5, 9.9]/ 13.2 [12.6, 13.7] 0.6 [0.5, 0.7]	0.7 [0.4, 1.0]/ 0.6 [0.5, 0.8] 1.1 [0.7, 1.7]	0.5 [0.3, 0.7]/ 1.4 [1.3, 1.6] 0.3 [0.2, 0.6]	1.6 [1.1, 2.0]/ 2.6 [2.3, 2.8] 0.6 [0.4, 0.8]	9.7 [8.4, 11.0]/ 14.2 [13.6, 14.8] 0.6 [0.6, 0.8]
Ethnicity/race							
"White" vs. not "white"	8.2 [7.8, 8.7]/ 5.1 [4.0, 6.2] 1.7 [1.3, 2.1]	3.1 [2.9, 3.3]/ 1.9[1.3, 2.6] 1.6 [1.1, 2.3]	13.0 [12.4, 13.5]/ 8.1[6.8, 9.5] 1.7 [1.4, 2.0]	0.7 [0.5, 0.8]/ 0.6 0.3, 0.8] 1.2 [0.7, 2.0]	1.3 [1.1, 1.4]/ 1.2[0.7, 1.7] 1.0 [0.7, 1.7]	2.4 [2.1, 2.6]/ 2.3 [1.6, 3.0] 1.0 [0.7, 1.4]	14.0 [13.4, 14.5]/ 9.2 [7.8, 10.7] 1.6 [1.3, 1.9]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. Cells with a dash are suppressed data because the numbers were too small for disclosure. Major depressive episode (MDE). % = percent; OR = odds ratio; CI = confidence interval.

[a]Indicates that the comparison is all respondents in the sample not including people with the listed disorder alone.

[b]Indicates that the comparison is all respondents in the sample not including people with the listed disorder in combination with its most common disorder pairing.

[c]Indicates that the comparison is all respondents in the sample who have the listed disorder in any combination.

[d]Any mood disorder includes respondents with major depressive episode and manic episode (comparison is people without mood disorders).

Table 3-3: Lifetime Social Phobia and Panic Disorder by Demographic Factors

Demographic factor	Social phobia alone vs. else[a]	Social phobia with MDE vs. else[b]	Social phobia alone or with any other mental health disorder including MDE vs. else[c]	Panic disorder alone vs. else[a]	Panic disorder with MDE vs. else[b]	Panic disorder alone or with any other mental health disorder including MDE vs. else[c]
	% [95% CI] OR [95%CI]					
Sex						
Male vs. female	4.2 [3.7, 4.6]/ 4.1 [3.7, 4.5] 1.0 [0.9, 1.2]	2.3 [2.0, 2.7]/ 3.4 [3.1, 3.8] 0.7 [0.6, 0.8]	7.5 [6.9, 8.2]/ 8.7 [8.1,9.2] 0.9 [0.8, 1.0]	1.2 [1.0, 1.4]/ 1.7 [1.4, 1.9] 0.7 [0.6, 0.9]	0.9 [0.7, 1.1]/ 1.9 [1.6, 2.1] 0.5 [0.4, 0.6]	2.8 [2.4, 3.2]/ 4.6 [4.2, 5.0] 0.6 [0.5, 0.7]
Age						
35-64 years vs.15-34 years	4.1 [3.8, 4.5]/ 4.1 [3.7, 4.6] 1.0 [0.9, 1.2]	3.3 [3.0, 3.7]/ 2.4 [2.1, 2.7] 1.4 [1.2, 1.6]	8.8 [8.2, 9.4]/ 7.4 [6.8, 7.9] 1.2 [1.1, 1.4]	1.6 [1.4, 1.9]/ 1.2 [1.0, 1.4] 1.4 [1.1, 1.8]	1.7 [1.5, 2.0]/ 1.1 [0.9, 1.2] 1.7 [1.3, 2.1]	4.5 [4.1, 5.0]/ 2.8 [2.5, 3.1] 1.7 [1.4, 1.9]
≥ 65 years vs. 15-34 years	1.7 [1.3, 2.0]/ 4.6 [4.2, 4.9] 0.4 [0.3, 0.5]	0.7 [0.4, 1.0]/ 3.3 [3.0, 3.5] 0.2 [0.1, 0.3]	2.6 [2.1, 3.1]/ 9.1 [8.6, 9.5] 0.3 [0.2, 0.3]	1.0 [0.7, 1.3] /1.5 [1.3, 1.7] 0.6 [0.4, 0.9]	0.3 [0.1, 0.4]/ 1.6 [1.4, 1.8] 0.2 [0.1, 0.3]	1.4 [1.1, 1.8]/ 4.1 [3.8, 4.4] 0.3 [0.3, 0.5]
Marital Status						
Single vs. not single	4.6 [4.1, 5.1]/ 3.8 [3.5, 4.2] 1.2 [1.0, 1.4]	3.8 [3.4, 4.2]/ 2.4 [2.1, 2.6] 1.6 [1.4, 1.9]	9.5 [8.8, 10.1]/ 7.3 [6.8, 7.8] 1.3 [1.2, 1.5]	1.3 [1.0, 1.5]/ 1.5 [1.3, 1.8] 0.8 [0.7, 1.1]	1.8 [1.5, 2.1]/ 1.2 [1.0, 1.4] 1.6 [1.2, 2.0]	3.9 [3.5, 4.3]/ 3.6 [3.2, 4.0] 1.1 [0.9, 1.3]
Total household income						
Low income vs. middle or high income	3.8 [3.1, 4.5]/ 4.2 [3.8, 4.5] 0.9 [0.7, 1.1]	4.5 [3.7, 5.3]/ 2.8 [2.6, 3.1] 1.6 [1.3, 2.0]	9.8 [8.7, 10.9]/ 8.0 [7.6, 8.4] 1.2 [1.1, 1.4]	2.2 [1.4, 3.1]/ 1.4 [1.2, 1.5] 1.7 [1.1, 2.4]	2.4 [1.8, 2.9]/ 1.4 [1.2, 1.5] 1.7 [1.3, 2.3]	5.6 [4.5, 6.7]/ 3.6 [3.3, 3.9] 1.6 [1.3, 2.0]
Education level						
< than secondary vs. ≥secondary graduate	4.2 [3.6, 4.7]/ 4.1 [3.8, 4.5] 1.0 [0.8, 1.2]	2.2 [1.8, 2.5]/ 3.2 [2.9, 3.5] 0.7 [0.6, 0.8]	7.3 [6.6, 8.0]/ 8.4 [7.9, 8.9] 0.9 [0.8, 1.0]	1.4 [1.1, 1.7]/ 1.5 [1.2, 1.7] 1.0 [0.7, 1.3]	1.1 [0.9, 1.4]/ 1.5 [1.3, 1.7] 0.7 [0.6, 1.0]	3.3 [2.8, 3.8]/ 3.8 [3.5, 4.2] 0.9 [0.7, 1.0]
Immigrant status						
Immigrant vs. non-immigrant	3.0 [2.4, 3.6]/ 4.5 [4.1, 4.8] 0.7 [0.5, 0.8]	1.9 [1.3, 2.4]/ 3.2 [3.0, 3.4] 0.6 [0.4, 0.8]	5.5 [4.7, 6.4]/ 8.9 [8.4, 9.3] 0.6 [0.5, 0.7]	0.7 [0.5, 1.0]/ 1.6 [1.4, 1.8] 0.5 [0.3, 0.7]	0.7 [0.5, 1.0] /1.6 [1.4, 1.8] 0.5 [0.3, 0.7]	1.8 [1.4, 2.2]/ 4.2 [3.9, 4.6] 0.4 [0.3, 0.5]

Demographic factor	Social phobia alone vs. else[a]	Social phobia with MDE vs. else[b]	Social phobia alone or with any other mental health disorder including MDE vs. else[c]	Panic disorder alone vs. else[a]	Panic disorder with MDE vs. else[b]	Panic disorder alone or with any other mental health disorder including MDE vs. else[c]
	% [95% CI] OR [95%CI]					
Ethnicity/race						
"White" vs. not "white"	4.4 [4.1, 4.7]/ 3.1 [2.3, 3.9] 1.4 [1.1, 1.9]	3.1 [2.9, 3.3]/ 1.9 [1.3, 2.6] 1.6 [1.1, 2.3]	8.6 [8.1, 9.0]/ 5.9 [4.7, 7.0] 1.5 [1.2, 1.9]	1.6 [1.4, 1.8]/ 0.7 [0.4, 1.0] 2.3 [1.5, 3.7]	1.6 [1.4, 1.7]/ 0.6 [0.4, 0.8] 2.6 [1.8, 3.9]	4.1 [3.7, 4.4]/ 1.7 [1.2, 2.1] 2.5 [1.9, 3.4]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. Cells with a dash are suppressed data because the numbers were too small for disclosure. Major depressive episode (MDE). % = percent; OR = odds ratio; CI = confidence interval.

[a]Indicates that the comparison is all respondents in the sample not including people with the listed disorder alone.

[b]Indicates that the comparison is all respondents in the sample not including people with the listed disorder in combination with its most common disorder pairing.

[c]Indicates that the comparison is all respondents in the sample who have the listed disorder in any combination.

[d]Any anxiety disorder includes respondents with social phobia, panic disorder and agoraphobia (comparison is people without anxiety disorders).

Table 3-4: Lifetime Agoraphobia and Any Anxiety Disorder by Demographic Factors

Demographic factor	Agoraphobia alone vs. else[a]	Agoraphobia with MDE vs. else[b]	Agoraphobia alone or with any other mental health disorder including MDE vs. else[c]	Any anxiety disorder[d] vs. else
	% [95% CI] OR [95%CI]			
Sex				
Male vs. female	0.2 [0.1, 0.3]/ 0.8 [0.6, 1.0] 0.3 [0.1, 0.4]	0.4 [0.3, 0.5]/ 0.8 [0.6, 1.0] 0.5 [0.3, 0.7]	0.8 [0.6, 1.0]/ 2.2 [1.9, 2.5] 0.4 [0.3, 0.5]	9.6 [8.9, 10.3]/ 12.9 [12.2, 13.6] 0.7 [0.7, 0.8]
Age				
35-64 years vs.15-34 years	0.7 [0.5, 0.8]/ 0.3 [0.2, 0.4] 2.1 [1.4, 3.2]	0.7 [0.5, 0.8]/ 0.5 [0.4, 0.6] 1.3 [0.9, 1.8]	1.9 [1.6, 2.2]/ 1.1 [0.9, 1.3] 1.7 [1.3, 2.2]	12.7 [11.9, 13.4]/ 9.7 [9.1, 10.4] 1.3 [1.2, 1.5]
≥ 65 years vs. 15-34 years	0.3 [0.2, 0.4]/ 0.5 [0.4, 0.7] 0.6 [0.3, 1.0]	0.3 [0.1, 0.5]/ 0.6 [0.5, 0.8] 0.5 [0.2, 0.9]	0.7 [0.5, 1.0]/ 1.7 [1.5, 1.9] 0.4 [0.3, 0.6]	4.3 [3.7, 4.9]/ 12.5 [12.0, 13.0] 0.3 [0.3, 0.4]
Marital Status				
Single vs. not single	0.6 [0.4, 0.9]/ 0.4 [0.3, 0.5] 1.5 [0.9, 2.4]	0.8 [0.6, 1.0]/ 0.5 [0.3, 0.6] 1.7 [1.2, 2.5]	1.8 [1.5, 2.2]/ 1.3 [1.1, 1.6] 1.4 [1.1, 1.8]	12.9 [12.2, 13.7]/ 10.2 [9.6, 10.8] 1.3 [1.2, 1.4]
Total household income				
Low income vs. middle or high income	1.2 [0.3, 2.0]/ 0.4 [0.3, 0.5] 2.7 [1.2, 6.3]	1.0 [0.6, 1.5]/ 0.6 [0.4, 0.7] 1.9 [1.2, 3.0]	2.6 [1.6, 3.5]/ 1.4 [1.2, 1.6] 1.8 [1.2, 2.8]	14.8 [13.2, 16.4]/ 11.0 [10.5, 11.5] 1.4 [1.2, 1.6]
Education level				
< than secondary vs. ≥secondary graduate	0.6 [0.3, 1.0]/ 0.4 [0.3, 0.6] 1.4 [0.8, 2.6]	0.7 [0.5, 1.0]/ 0.6 [0.4, 0.7] 1.3 [0.9, 2.0]	1.8 [1.4, 2.3]/ 1.4 [1.2, 1.6] 1.3 [0.9, 1.7]	10.7 [9.8, 11.6]/ 11.5 [10.9, 12.1] 0.9 [0.8, 1.0]
Immigrant status				
Immigrant vs. non-immigrant	0.6 [0.2, 1.0]/ 0.5 [0.4, 0.6] 1.3 [0.6, 2.6]	0.3 [0.1, 0.4]/ 0.7 [0.6, 0.8] 0.4 [0.2, 0.7]	1.1 [0.6, 1.5]/ 1.7 [1.5, 1.9] 0.6 [0.4, 1.0]	7.6 [6.6, 8.6]/ 12.3 [11.8, 12.9] 0.6 [0.5, 0.7]

Demographic factor	Agoraphobia alone vs. else[a]	Agoraphobia with MDE vs. else[b]	Agoraphobia alone or with any other mental health disorder including MDE vs. else[c]	Any anxiety disorder[d] vs. else
	% [95% CI] OR [95%CI]			
Ethnicity/race				
"White" vs. not "white"	0.4 [0.3, 0.5]/ 0.9 [0.3, 1.4] 0.5 [0.2, 1.0]	0.7 [0.6, 0.8]/ 0.2 [0.1, 0.3] 4.1 [2.1, 7.7]	1.6 [1.4, 1.8]/ 1.3 [0.8, 1.9] 1.2 [0.8, 1.9]	11.9 [11.4, 12.4]/ 8.0 [6.7, 9.3] 1.6 [1.3, 1.9]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. Cells with a dash are suppressed data because the numbers were too small for disclosure. Major depressive episode (MDE). % = percent; OR = odds ratio; CI = confidence interval.

[a]Indicates that the comparison is all respondents in the sample not including people with the listed disorder alone.

[b]Indicates that the comparison is all respondents in the sample not including people with the listed disorder in combination with its most common disorder pairing.

[c]Indicates that the comparison is all respondents in the sample who have the listed disorder in any combination.

[d]Any anxiety disorder includes respondents with social phobia, panic disorder and agoraphobia (comparison is people without anxiety disorders).

3.4.1 The relationships between mental health disorders and cardiovascular risk.

Table 3-5 illustrates that respondents who were identified as having had any lifetime MHD were less likely (OR = 0.8, 95% CI [0.8, 0.9]) to be in the highest 10-year risk category for CVD, relative to those who reported no MHD. This same group was 20% more likely (OR = 1.2, 95% CI [1.1, 1.4]) to be in the highest 30-year risk category for CVD. These findings were consistent across all of the lifetime mood and anxiety disorders. However, many of the ORs for the specific MHDs and the 10- and 30-year cardiovascular risk estimates were not elevated.

Table 3-5: Lifetime Mental Health Disorders and Cardiovascular Risk

Mental health status	10-year CVD risk[h]		30-year CVD risk[h]	
	unadjusted OR [95% CI]	adjusted[i] OR [95% CI]	unadjusted OR [95% CI]	adjusted[i] OR [95% CI]
Mental health disorder (any)[a] vs. no disorder	0.9 [0.8, 1.0]	0.8 [0.8, 0.9]	1.2 [1.0, 1.3]	1.2 [1.1, 1.4]
Schizophrenia alone[b] vs. else[c]	0.9 [0.3, 2.8]	0.7 [0.2, 2.4]	0.8 [0.2, 2.7]	1.1 [0.3, 3.9]
Schizophrenia with MDE vs. else[d]	1.5 [0.6, 3.5]	1.4 [0.5, 4.0]	1.3 [0.6, 3.1]	2.3 [0.8, 6.5]
Schizophrenia alone or with any other mental health disorder including MDE vs. else[e]	1.2 [0.7, 2.2]	1.0 [0.5, 2.1]	0.8 [0.4, 1.7]	1.2 [0.5, 2.7]
MDE alone vs. else[c]	0.8 [0.7, 0.9]	0.8 [0.7, 0.9]	1.1 [1.0, 1.3]	1.2 [1.0, 1.4]
MDE with social phobia vs. else[d]	0.8 [0.6, 0.9]	0.8 [0.6, 1.0]	1.1 [0.9, 1.4]	1.2 [1.0, 1.6]
MDE alone or with any other mental health disorder including social phobia vs. else[e]	0.8 [0.7, 0.9]	0.8 [0.7, 0.9]	1.1 [1.0, 1.3]	1.2 [1.1, 1.4]
Manic episode alone vs. else[c]	0.8 [0.5, 1.3]	0.8 [0.4, 1.4]	1.3 [0.9, 2.1]	1.7 [1.0, 2.6]
Manic episode with MDE vs. else[d]	0.9 [0.6, 1.3]	0.8 [0.5, 1.3]	1.0 [0.7, 1.3]	1.2 [0.8, 1.7]
Manic episode alone or with any other mental health disorder including MDE vs. else[e]	0.8 [0.6, 1.1]	0.8 [0.6, 1.1]	1.1 [0.9, 1.5]	1.4 [1.1, 1.8]
Any mood disorder[f]	0.8 [0.7, 0.9]	0.8 [0.7, 0.9]	1.1 [1.0, 1.3]	1.3 [1.1, 1.4]
Social phobia alone vs. else[c]	0.8 [0.7, 1.0]	0.8 [0.7, 1.0]	1.0 [0.8, 1.3]	1.0 [0.8, 1.2]
Social phobia with MDE vs. else[d]	0.8 [0.6, 0.9]	0.8 [0.6, 1.0]	1.1 [0.9, 1.4]	1.2 [1.0, 1.6]

Mental health status	10-year CVD risk[h]		30-year CVD risk[h]	
	unadjusted OR [95% CI]	adjusted[i] OR [95% CI]	unadjusted OR [95% CI]	adjusted[i] OR [95% CI]
Social phobia alone or with any other mental health disorder including MDE vs. else[e]	0.8 [0.7, 0.9]	0.8 [0.7, 0.9]	1.1 [0.9, 1.3]	1.1 [1.0, 1.3]
Panic disorder alone vs. else[c]	0.8 [0.6, 1.1]	0.7 [0.5, 1.0]	1.2 [0.9, 1.6]	1.1 [0.8, 1.6]
Panic disorder with MDE vs. else[d]	0.8 [0.6, 1.1]	0.8 [0.5, 1.1]	1.2 [0.9, 1.6]	1.2 [0.9, 1.7]
Panic disorder alone or with any other mental health disorder including MDE vs. else[e]	0.8 [0.6, 0.9]	0.7 [0.5, 0.9]	1.2 [1.0, 1.5]	1.2 [0.9, 1.5]
Agoraphobia alone vs. else[c]	0.7 [0.4, 1.1]	0.6 [0.4, 1.1]	1.0 [0.6, 1.7]	1.1 [0.6, 2.1]
Agoraphobia with MDE vs. else[d]	0.8 [0.5, 1.3]	0.6 [0.4, 1.0]	0.7 [0.5, 1.2]	0.7 [0.4, 1.3]
Agoraphobia alone or with any other mental health disorder including MDE vs. else[e]	0.8 [0.6, 1.1]	0.7 [0.5, 1.0]	0.9 [0.6, 1.3]	0.9 [0.6, 1.4]
Any anxiety disorder[g]	0.8 [0.7, 0.9]	0.7 [0.6, 0.8]	1.1 [1.0, 1.2]	1.1 [1.0, 1.3]

Note. Findings are based on reports of 17 307 respondents representing n= 12,909,158 people in the Canadian population. Respondents with a previous history of heart disease or stroke were excluded from the 10-year risk analysis. Respondents with a previous history of heart disease, stroke and cancer were excluded from the 30-year risk analysis. Cells with a dash represent sample sizes too small for disclosure. Major depressive disorder (MDE). %=percent; OR=odds ratio; CI= confidence interval.

[a]Respondents identified as having evidence of at least one lifetime mental health disorder or taking at least one psychoactive medications within the past 12-months

[b]Not measured by structured diagnostic interview (CCHS 1.2/WMH-CIDI)

[c]Indicates that the comparison is all respondents in the sample not including people with the listed disorder alone

[d]Indicates that the comparison is all respondents in the sample not including people with the listed disorder in combination with its most common disorder pairing

[e]Indicates that the comparison is all respondents in the sample who have the listed disorder in any combination

[f]Any mood disorder includes respondents with major depressive episode and manic episode (comparison is people without mood disorders)

[g]Any anxiety disorder includes respondents with social phobia, panic disorder and agoraphobia (comparison is people without anxiety disorders)

[h]Dichotomized at the median (high vs. low risk)

[i]Estimates are adjusted for marital status, household income, education level, immigrant status and ethnicity/race. All variables made a significant contribution to the outcome except household income

3.4.2 The relationships between mental health disorders and CVD

The respondents who reported having had any MHD, in the lifetime, were twice as likely to report having heart disease (OR = 2.0, 95% CI [1.8, 2.2]) or stroke (OR = 2.3, 95% CI [1.7, 3.0]) compared with people without any MHDs, after adjusting for differences in socio-demographics (see Table 3-6). People who had agoraphobia with a major depressive episode had the highest prevalence rates of heart disease (10.2%, 95% CI [4.5, 16.0]) and people with schizophrenia had the highest prevalence of stroke (1.9%, 95% CI [0.1, 3.9]). People with agoraphobia alone had the lowest rates of heart disease (2.8%, 95% CI [0.9, 4.6]) while people who had a manic episode with a major depressive episode had the lowest rates of stroke (0.4%, 95% CI [0.0, 0.8]). Respondents with any mood or any anxiety disorder were one and one half times more likely to have heart disease (OR = 1.5, 95% CI [1.3, 1.8], OR = 1.5, 95% CI [1.2, 1.8], respectively) and almost two times more likely to have had a stroke (OR = 1.8, 95% CI [1.1, 2.7], OR = 1.8, 95% CI [1.1, 2.8], respectively) compared with people without mood or anxiety disorders, after adjusting for sociodemographic differences.

The association between CVD and each MHD alone, adjusted for socio-demographic differences (e.g., a major depressive episode alone; OR = 1.2, 95% CI [1.0, 1.6]) was stronger when considered in combination with the disorder's most common pairing (e.g., major depressive disorder and social phobia OR = 1.5, 95% CI [1.0, 2.1]) (after adjustment). The same pattern was evident for people who reported having a previous stroke. This was the case for all of the MHDs except panic disorder.

Table 3-6: Lifetime Mental Health Disorders and Cardiovascular Disease

	Heart Disease vs. no heart disease	**Heart Disease** vs. no heart disease	**Heart Disease** vs. no heart disease	**Stroke** vs. no stroke	**Stroke** vs. no stroke	**Stroke** vs. no stroke
	% [95% CI]	unadjusted OR [95% CI]	adjusted[h] OR [95% CI]	% [95% CI]	unadjusted OR [95% CI]	adjusted[i] OR [95% CI]
Mental health disorder (any)[a] vs. no disorder	7.7 [7.1, 8.4]/ 4.7 [4.4, 5.0]	1.7 [1.5, 1.9]	2.0 [1.8, 2.2]	1.6 [1.3, 2.0]/ 0.8 [0.7, 0.9]	2.1 [1.6, 2.7]	2.3 [1.7, 3.0]
Schizophrenia alone[b] vs. else[c]	8.4 [0.1, 16.8]/ 5.4 [5.2, 5.7]	1.6 [0.5, 5.5]	1.6 [0.4, 7.1]	-	-	-
Schizophrenia with MDE vs. else[d]	-	-	-	-	-	-
Schizophrenia alone or with any other mental health disorder including MDE vs. else[e]	7.6 [2.0, 13.2]/ 5.4 [5.2, 5.7]	1.4 [0.6, 3.4]	1.7 [0.7, 4.3]	1.9 [0.1, 3.9]/ 1.0 [0.9, 1.1]	2.0 [0.6, 6.5]	2.3 [0.7, 7.6]
MDE alone vs. else[c]	6.0 [4.8, 7.2]/ 5.4 [5.1, 5.7]	1.1 [0.9, 1.4]	1.2 [1.0, 1.6]	1.4 [0.8, 1.9]/ 1.0 [0.8, 1.1]	1.4 [0.9, 2.0]	1.6 [1.0, 2.7]
MDE with social phobia vs. else[d]	4.7 [3.2, 6.2]/ 5.5 [5.2, 5.7]	0.9 [0.6, 1.2]	1.5 [1.0, 2.1]	1.5 [0.5, 2.6]/ 1.0 [0.9, 1.1]	1.4 [0.9, 2.2]	2.6 [1.2, 5.8]
MDE alone or with any other mental health disorder including social phobia vs. else[e]	6.1 [5.1, 7.0]/ 5.3 [5.0, 5.6]	1.1 [1.0, 1.4]	1.5 [1.3, 1.8]	1.3 [0.9, 1.8]/ 1.0 [0.8, 1.1]	1.4 [0.9, 2.0]	1.8 [1.2, 2.8]
Manic episode alone vs. else[c]	4.8 [1.0, 8.7]/ 5.4 [5.2, 5.7]	0.9 [0.3, 2.3]	1.6 [0.6, 4.5]	-	-	-
Manic episode with MDE vs. else[d]	4.7 [2.5, 6.8]/ 5.5 [5.2, 5.7]	0.8 [0.5, 1.4]	1.8 [1.0, 3.1]	0.4 [0.0, 0.8]/ 1.0 [0.9, 1.1]	0.4 [0.1, 1.2]	0.8 [0.2, 2.3]
Manic episode alone or with any other mental health disorder including MDE vs. else[e]	4.4 [2.8, 6.1]/ 5.4 [5.2, 5.7]	0.8 [0.5, 1.2]	1.6 [1.0, 2.5]	0.4 [0.1, 0.7]/ 1.0 [0.9, 1.1]	0.4 [0.2, 0.8]	0.8 [0.4, 1.7]
Any mood disorder[f]	5.9 [5.0, 6.8]/ 5.4 [5.1, 5.7]	1.1 [0.9, 1.3]	1.5 [1.3, 1.8]	1.2 [0.8, 1.7]/ 1.0 [0.8, 1.1]	1.3 [0.9, 1.9]	1.8 [1.1, 2.7]
Social phobia alone vs. else[c]	3.8 [2.5, 5.1]/ 5.5 [5.2, 5.8]	0.7 [0.5, 1.0]	1.0 [0.7, 1.5]	0.9 [0.1, 1.7]/ 1.0 [0.9, 1.1]	0.9 [0.3, 2.7]	1.5 [0.5, 4.4]
Social phobia with MDE vs. else[d]	4.7 [3.2, 6.2]/ 5.5 [5.2, 5.7]	0.9 [0.6, 1.2]	1.5 [1.0, 2.1]	1.5 [0.5, 2.6]/ 1.0 [0.9, 1.1]	1.6 [0.7, 3.3]	2.6 [1.2, 5.8]

	Heart Disease vs. no heart disease	**Heart Disease** vs. no heart disease	**Heart Disease** vs. no heart disease	**Stroke** vs. no stroke	**Stroke** vs. no stroke	**Stroke** vs. no stroke
	% [95% CI]	unadjusted OR [95% CI]	adjusted[h] OR [95% CI]	% [95% CI]	unadjusted OR [95% CI]	adjusted[i] OR [95% CI]
Social phobia alone or with any other mental health disorder including MDE vs. else[e]	4.1 [3.2, 4.9]/ 5.6 [5.3, 5.9]	0.7 [0.6, 0.9]	1.2 [0.9, 1.5]	1.1 [0.5, 1.7]/ 1.0 [0.9, 1.1]	1.1 [0.6, 2.0]	1.9 [1.1, 3.4]
Panic disorder alone vs. else[c]	8.9 [6.0, 11.9]/ 5.4 [5.1, 5.7]	1.7 [1.2, 2.5]	2.0 [1.3, 3.0]	1.6 [0.3, 3.0]/ 1.0 [0.9, 1.1]	1.7 [0.6, 4.6]	1.3 [0.4, 4.3]
Agoraphobia alone vs. else[c]	2.8 [0.9, 4.6]/ 5.5 [5.2, 5.7]	0.5 [0.2, 1.0]	0.6 [0.2, 1.3]	-	-	-
Agoraphobia with MDE vs. else[d]	10.2 [4.5, 16.0] / 5.4 [5.1, 5.7]	2.0 [1.0, 3.9]	2.8 [1.4, 5.6]	-	-	-
Agoraphobia alone or with any other mental health disorder including MDE vs. else[e]	6.5 [3.8, 9.3]/ 5.4 [5.1, 5.7]	1.2 [0.8, 1.9]	1.7 [1.0, 2.7]	1.2 [0.3, 2.1]/ 1.0 [0.9, 1.1]	1.3 [0.5, 2.9]	1.7 [0.7, 4.2]
Any anxiety disorder[g]	5.2 [4.4, 6.0]/ 5.5 [5.2, 5.8]	0.9 [0.8, 1.1]	1.5 [1.2, 1.8]	1.2 [0.7, 1.6]/ 1.0 [0.9, 1.1]	1.2 [0.8, 1.8]	1.8 [1.1, 2.8]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. Cells with a dash are suppressed data due to numbers too small to disclosure. Major depressive episode (MDE). % = percent; OR = odds ratio; CI = confidence interval.

[a]Respondents identified as having evidence of at least one lifetime mental health disorder or taking at least one psychoactive medications within the past 12-months

[b]Not measured by structured diagnostic interview (CCHS 1.2/WMH-CIDI)

[c]Indicates that the comparison is all respondents in the sample not including people with the listed disorder alone

[d]Indicates that the comparison is all respondents in the sample not including people with the listed disorder in combination with its most common disorder pairing

[e]Indicates that the comparison is all respondents in the sample who have the listed disorder in any combination

[f]Any mood disorder includes respondents with major depressive episode and manic episode (comparison is people without mood disorders)

[g]Any anxiety disorder includes respondents with social phobia, panic disorder and agoraphobia (comparison is people without anxiety disorders)

[h]Estimates for heart disease are adjusted for sex, age, marital status, household income, education level, immigrant status and ethnicity/race. All variables made a significant contribution to the outcome except for marital status

[i]Estimates for stroke are adjusted for sex, age, marital status, household income, education level, immigrant status and ethnicity/race. The following variables were not significant predictors of the outcome: marital and immigrant status and race/ethnicity.

3.5 Discussion

This study documented the association between MHDs, CVD, and 10- and 30-year cardiovascular risk among Canadians. Using data from the CCHS Cycle 1.2, respondents who were identified as having any lifetime MHD were twice as likely to have had heart disease or suffered from the effects of a stroke compared with Canadians without a MHD. The association was more pronounced once the differences in socio-demographic characteristics were taken into account. Our results are consistent with previous population-level cohort and cross-sectional survey studies that have quantified the association between MHDs and heart disease (Callaghan & Khizar, 2010; Curkendall et al., 2004; Goodwin, Davidson, & Keyes, 2009; Nielsen et al., 2013; Ormel et al., 2007; Rugulies, 2002). However, our investigation of the association between MHDs and stroke revealed a stronger relationship than what has been reported previously in prospective studies (Dossa et al., 2011; Tsai et al., 2012).

There are several possible mechanisms that explain the association between MHDs and CVD. First, psychoactive medications, such as antipsychotics, antidepressants, and mood stabilizers are commonly prescribed to people with MHDs; they are known to induce cardiovascular and metabolic abnormalities, such as weight gain and impaired glucose and lipid metabolism that lead to obesity, dyslipidemia, diabetes, and metabolic syndrome, which increase the risk of CVD (De Hert et al., 2012; Mackin et al., 2007; Newcomer, 2007). Psychotropic medications also have arrhythmogenic effects on myocardial repolarization, which can prolong the QT interval and cause sudden cardiac death (Mackin, 2008; Ray et al., 2009). Second, having a MHD is associated with unhealthful behaviour, such as smoking, poor diet, physical inactivity and substance misuse (Dickey et al., 2002; McCreadie, 2003). Third, people

with MHDs frequently receive insufficient health care. They are less likely than people without MHDs to spontaneously report health symptoms, some characteristics of their disorders (e.g., cognitive impairment and social isolation) may contribute to limited help seeking and adherence to treatment (e.g., cognitive deficits may make it more difficult for individuals to remember appointments), and the stigma they experience may adversely affect the quality of care that they do receive (Corrigan, 2004; Hemingway & Marmot, 1999; Kaufman, McDonell, Cristofalo, & Ries, 2012; McCabe & Leas, 2008; Phelan et al., 2001; Robson & Gray, 2007; Üstün & Sartorius, 1995). It is known that people with MHDs are less likely to undergo coronary revascularization procedures compared with people without MHDs (Druss et al., 2000). Fourth, there may be some physiological consequences associated with MHDs that can explain why CVD rates are elevated in this group. One hypothesis states that allostatic load (i.e., the chronic elevation in cortisol from repeated stress) is increased in people with MHDs, which can promote or advance atherosclerosis (McEwen, 2003). Other studies have demonstrated that people with anxiety disorders have abnormal cardiac autonomic control, which may increase their risk of fatal ventricular arrhythmias (Kubzansky et al., 1998).

Our analysis found that respondents who were identified as having any lifetime MHDs were more likely to be at lower risk (vs. high) of developing CVD within 10 years compared with people without MHDs, and higher 30-year risk of developing CVD. This was an unexpected finding; previous research has documented elevated 10-year CVD risk among people with severe MHDs (e.g., schizophrenia, major depressive episode and bipolar disorders) (Cohn et al., 2004; Goff et al., 2005; Osborn et al., 2006). The most likely explanation for these findings arises from the characteristics of our sample. There

was a greater proportion of people in the middle-aged group with MHDs, which could have conferred a protective, short-term benefit (compared with older-aged people) of minimizing the risk of cardiovascular injury (Lakatta, 2002). This is because age is the most heavily weighted variable in the 10-year risk prediction model and was not controlled for in our statistical analysis (this is because it was incorporated into the risk prediction calculation itself). Another alternative for these divergent findings could be attributed to differences between the methods used to calculate short- (i.e., point-based system) and long-term (i.e., equation-based) cardiovascular risk estimates. It is known that simplified points-based systems used to predict 10-year cardiovascular risk often misclassify respondents compared with equation-based 10-year cardiovascular risk algorithms (Gordon, Polansky, Boscardin, Fung, & Steinman, 2010). Therefore, it is possible that the simplified points-based system used to calculate 10-year cardiovascular risk might provide a less accurate risk estimate compared with equation-based algorithms used to calculate 30-year risk. Further investigation into this area is needed; there has been limited comparison of the risk group classification derived from 10-year points-based and 30-year equation-based algorithms. It should be noted that the ORs for several of the specific MHDs and the 10-year cardiovascular risk estimate were not statistically significant or were small in magnitude.

It was our intent to determine whether certain MHD pairings placed people at greater risk for CVD. Our findings suggest that the strength of the associations between heart disease and stroke and each MHD alone was greater when combined with its most common disorder pairing. This finding contributes to the accumulating evidence that

psychiatric comorbidity may be associated with greater likelihood of CVD, but this association needs further examination (Bankier et al., 2004).

Continued investigation of the mechanisms underlying the association between comorbid MHDs and CVD, in Canadian populations, is needed. A better understanding of the antecedents to this health disparity could inform clinical and public health interventions to improve the cardiovascular health of Canadians living with MHDs. Prospective studies are needed to tease out the relative contributions of illness, health behaviour, and pharmacotherapy in the development of CVD and cardiovascular risk.

3.5.1 Limitations

The CCHS 1.2 was a cross-sectional survey so the reported bivariate associations between MHDs and CVD and cardiovascular risk cannot be said to reflect causal effects. Future prospective studies are needed to document the risk of developing CVD among a sample of Canadians with single and comorbid MHDs. This study did not exert control over or account for the effects of concurrent psychoactive medication use on CVD and CVD risk in respondents with MHDs; this is a significant limitation of this study. The relative contribution of medications to CVD and cardiovascular risk should be assessed in future work.

It also should be noted that certain liberties were taken to estimate CVD risk with the available data. For example, the CCHS Cycle 1.2 did not provide a cholesterol measure, so it was not possible to utilize other established cardiovascular risk algorithms that require this information or that incorporate newer biomarkers of cardiovascular risk (e.g., homocysteine, folic acid, C reactive protein, and interleukin 6) (de Ruijter et al., 2009). Decision rules also were applied for the categorical measurement of SBP and a weak self-reported proxy measure of smoking status was used. The reliability of these

methods has not been tested so the findings should be interpreted with caution. It also is known that 10-year cardiovascular risk algorithms have a tendency to under-predict cardiovascular risk in certain populations (Lloyd-Jones, 2010; Silver, Huang, Nash, & Prasad, 2011).

The sample from which these findings are derived under-represents several important segments of the Canadian population in which MHDs are known to be prevalent. For example, people who are homeless or who live in institutions were not included in the CCHS 1.2 sampling frame, yet these are the people more likely to have MHDs and are the most marginalized by social and structural inequity (Argintaru et al., 2013; Krausz et al., 2013; Lafortune, 2010). Further, these analyses utilized retrospective self-reported data; the validity of this data collection approach is often questioned because the information cannot be verified. It is known that compromised autobiographic memory is a prominent symptom of many MHDs (Simon & VonKorff, 1995).

The CCHS 1.2/WMH-CIDI is a structured diagnostic interview administered by lay interviewers. Although this is a practical necessity in epidemiological surveys, it results in limited diagnostic precision because the interviewers are not trained clinicians and must keep their interactions within a predetermined script. Finally, several of the reported estimates had relatively wide confidence intervals (e.g., the prevalence rate of schizophrenia); because bootstrapping techniques were applied to obtain relatively accurate standard errors, the lack of precision is most likely a consequence of small numbers. For this reason, the corresponding proportions or ORs, with wide confidence intervals, must be interpreted with caution.

3.5.2 Implications for healthcare providers

In Canada, mental healthcare reform has focused on "de-institutionalization" or closure of psychiatric hospitals and the subsequent development of community mental health teams (Romanow & Marchildon, 2003). Such multidisciplinary teams are usually composed of providers from several healthcare disciplines, including nursing, occupational therapy, psychiatry and social work and are responsible for treating a range of health and social needs (Tyrer et al., 2000). However, physical health care is not necessarily given priority, in this setting, because many mental health practitioners emphasize psychological and social treatment at the expense of physical assessment. This bias can be problematic because community mental heath teams are often the only contact that people with MHDs have with the healthcare system, which creates a separation of physical and mental health care services (Kates et al., 1997; Phelan et al., 2001). Moreover, it is known that there is inequity in mental health services use by education level; mental health service use has also been found to be higher among the more educated people (Steele, Dewa, Lin, & Lee, 2007). This makes access even more difficult for a subset of this population. Phelan et al. (2001) explained that if a person with a MHD was to seek consultation with a primary care provider, it is unlikely that her or his physical health conditions would be adequately addressed. The orientation of primary care is reactive, with short consultation times making it difficult for practitioners to assess a person's mental health status and to conduct a physical examination, especially if the person is imprecise, apprehensive, and reluctant to discuss physical health symptoms.

A confluence of patient, provider, and system factors has created a situation in which quality physical health care is unavailable for Canadians with MHDs. There is an

opportunity for all healthcare providers to play a greater role in improving the physical health of people living with MHDs. This descriptive study demonstrates that people with MHDs are more likely to suffer from cardiovascular injury than are people without MHDs.

Healthcare providers, especially nurses who work in a variety of settings, have the capacity to combat this health inequity by placing special emphasis on routinely monitoring physical health signs and symptoms (e.g., weight, blood pressure, and fasting glucose and lipids) in this population, offering effective interventions, and promoting healthful lifestyles (e.g., diet, exercise, and smoking cessation counselling) through education and advocating for continued funding of existing programs. Furthermore, when lifestyle interventions fail, collaboration with other healthcare providers should be sought to ensure that physical health is made a priority.

To tackle systemic barriers to physical healthcare provision, improved integration of primary and mental healthcare services is needed to better address the complex care needs of people who have comorbid mental and physical illnesses and to strengthen continuity of care (Horvitz-Lennon et al., 2006; Kates et al., 1997). This can be accomplished by clarifying who should take responsibility for the physical health of people with MHDs, offering physical health assessment and interventions within community-based mental health teams or through the creation of liaison roles to coordinate services and improve communication and advocacy (Druss et al., 2010; Lawrence & Kisely, 2010).

3.6 Conclusion

This descriptive study documented the association between specific groupings of MHDs, CVD, and cardiovascular risk among community-dwelling Canadians. It utilized a novel approach by investigating 10- and 30-year cardiovascular risk using Framingham-based algorithms with available survey data. Our findings suggest that Canadians with lifetime MHDs are two times more likely to suffer from heart disease or stroke compared with people without MHDs. Our investigation of cardiovascular risk was less conclusive because the respondents with MHDs were less likely to be at greater short-term risk for CVD, but were more likely to at greater long-term risk. These findings represent an important public health inequity that needs to be addressed so that it does not progress further. Healthcare providers are uniquely situated to play a key role in improving the cardiovascular health of people living with MHDs in Canada.

CHAPTER 4: THE ASSOCIATION BETWEEN CARDIOVASCULAR RISK AND CARDIOVASCULAR DISEASE, AND PSYCHOACTIVE MEDICATION USE IN THE CANADIAN POPULATION

4.1 Introduction

It has been well documented that cardiovascular disease (CVD) is a major contributor to excess morbidity and mortality among people with MHDs (Angst et al., 2002; Chauvet-Gelinier et al., 2013; Kawachi et al., 1994; Osborn, Levy, et al., 2007; Saha et al., 2007). Previous studies have demonstrated that increased CVD in this group can be partially attributed to psychoactive medication use (i.e., antipsychotics, antidepressants, mood stabilizers, and anxiolytics) because the drugs induce cardiovascular and metabolic abnormalities, including weight gain, impaired glucose and lipid metabolism, which lead to obesity, dyslipidemia, diabetes, and metabolic syndrome (De Hert et al., 2012; Mackin et al., 2007). The exact psychopharmacological mechanisms underlying these outcomes have not been fully elucidated but several explanatory hypotheses exist. This phenomenon is a major public health concern because psychoactive medication use is common among Canadians, including those with and without MHDs, and their use has substantially increased since the 1980s. Yet the impact of psychoactive medication use on CVD and cardiovascular risk has not been quantified on a national level (Beck et al., 2005; Dewa et al., 2002; Meng et al., 2013). Moreover, it is not known how anxiolytic medication use and psychotropic medication polypharmacy (i.e., concurrent use of two or more psychoactive medications) affect CVD and risk. This chapter provides evidence of the prevalence of psychoactive medication use in the Canadian population, and of the association between psychoactive medication use, CVD, and cardiovascular risk.

4.2 Background

Psychoactive medications, including antipsychotics, antidepressants, mood stabilizers and anxiolytics, are chemical substances that, when taken or administered into one's system, cross the blood-brain barrier to act upon the central nervous system to affect mental processes (e.g., cognition or affect) (World Health Organization, 2013). These drugs are the cornerstone of pharmacological treatment for MHDs because they confer many benefits to users, but they also differentially and adversely affect the cardiovascular system. CVD is defined as injuries to the cardiovascular system: the heart, the blood vessels of the heart, and the system of blood vessels throughout the body and within the brain (Heart & Stroke Foundation, 2013). CVD manifests itself through coronary death, myocardial infarction (MI), coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, and heart failure (D'Agostino et al., 2008; Pencina et al., 2009). Patterns of psychoactive medication use have been examined in Canada with data from the Canadian Community Health Survey (CCHS) Cycle 1.2, but their influence on CVD and cardiovascular risk has yet to be quantified on a population level.

4.2.1 Antipsychotic medications

The primary indication for antipsychotic or neuroleptic medication use is the treatment of schizophrenia and related psychotic conditions. Most antipsychotic drugs are also approved to treat a broad range of symptoms associated with bipolar mania and depression when affected people do not respond to standard antidepressant treatment (De Hert et al., 2012). The first generation of antipsychotics, known as typical antipsychotics, were developed in the 1950s and approved for use in Canada in the 1970s. A second generation of antipsychotic medications, referred to as atypical antipsychotics, were

developed and introduced in the 1990s (clozapine in 1992, risperidone in 1993, and olanzapine and quetiapine in 1998) and have largely replaced typical antipsychotics as a first-line therapy (Dewa et al., 2002). Widespread use of atypical antipsychotic therapy has led to improved treatment adherence (because they target both positive and negative signs and symptoms of schizophrenia), relapse prevention, and a reduced risk of acute and chronic extrapyramidal adverse effects (including motor symptoms such as tardive dyskinesia, dystonia. and akathisia) (Leucht et al., 2009; Rummel-Kluge et al., 2012). However, patient populations that are prescribed antipsychotic medications have varying degrees of weight gain as well as lipid and glucose abnormalities, thereby increasing the risk of obesity, dyslipidemia, diabetes mellitus, metabolic syndrome (abdominal obesity, hypertension, dyslipidemia, and glucose intolerance or insulin resistance), and associated cardiovascular morbidity and mortality (Allison et al., 1999; ATP-III, 2002; Brauer et al., 2011; De Hert et al., 2012; Parsons et al., 2009). Moreover, it is know that antipsychotic medications have cardiotoxic properties (e.g., they inhibit cardiac sodium, calcium, and potassium channels leading to heart electrophysiology dysfunction and life-threatening arrhythmias), which can manifest in orthostatic hypotension, tachycardia, and ventricular arrhythmias that can prolong the QT interval and cause dose-related sudden cardiac death (Leung et al., 2012; Mackin, 2008; Ray et al., 2009).

People with severe MHDs are at risk for CVD notwithstanding the use of antipsychotic drugs. Drug naïve and first-episode patients with schizophrenia and bipolar disorder are known to be at increased risk of being overweight (BMI = 25-30 kg/m^2), being obese (BMI $\geq$ 30 kg/m^2), and having central obesity (waist circumference > 102 cm in men and > 88 cm in women) compared with the general population (De Hert, Correll,

et al., 2011; Maina, Salvi, Vitalucci, D'Ambrosio, & Bogetto, 2008; Thakore, Mann, Vlahos, Martin, & Reznek, 2002). People with schizophrenia have a 2.8 to 3.5 greater risk of obesity and people with bipolar disorder are 1.2 to 1.5 times more likely to be obese (Coodin, 2001; De Hert, Correll, et al., 2011; McIntyre et al., 2006).

To further compound the association between MHDs and obesity, weight gain is a well-established adverse effect of antipsychotic treatment and affects between 15% and 72% of patients depending on personal (e.g., genetics, demographic, and illness characteristics, pre-treatment diet, activity levels, and body composition) and treatment-related (e.g., dose, and adherence) factors (Coodin, 2001; De Hert, Correll, et al., 2011). Studies of genetic predictors of weight gain associated with antipsychotic medication use have suggested that there are specific gene polymorphisms (e.g., on HTR2C and LEPR) that may be responsible for this adverse side effect (De Hert, Correll, et al., 2011). Adiposity-dependent and adiposity-independent insulin resistance can lead to impaired glucose regulation and lipid metabolism (Newcomer, 2007). The mechanisms underlying antipsychotic-induced weight gain and metabolic dysfunction are not fully understood but are postulated to be related to the receptor affinity of antipsychotic drugs for histamine H_1, serotonin 5-HT_{2C} and 5-HT_{1A}, muscarinic M_3, dopamine D_2, and adrenergic receptors (Chang & Lu, 2012; De Hert et al., 2012).

The amount of observed weight gained differs by antipsychotic medication. Among typical antipsychotics, the low-potency agents (e.g., chlorpromazine and thioridazine) are associated with a higher risk of weight gain compared with mid- or high-potency (e.g., haloperidol) agents. However, weight gain and dyslipidemia are even greater for individuals taking second-generation agents, especially clozapine and

olanzapine (De Hert et al., 2008). The harmful effects of these medications on lipid metabolism can be independent of weight gain or in addition to weight-related effects. Other second-generation antipsychotics confer intermediate (e.g., iloperidone, quetiapine, risperidone, paliperidone, sertindole, and zotepine) and low (e.g., amisulpride, aripiprazole, asenapine, lurasidone, and ziprasidone) risks of weight gain but it should be emphasized that there are no atypical antipsychotic medications that are considered weight neutral (De Hert et al., 2012).

The evidence documenting an association between antipsychotic agents and CVD is limited. Brauer et al. (2011) conducted a systematic review of the literature to determine whether the use of antipsychotic agents was associated with the incidence of myocardial infarction (MI) in adults and found no association with current use of atypical (relative risk (RR) = 0.98, 95% CI [0.88, 1.09]) or typical antipsychotic agents (RR = 0.99, 95% CI [0.96, 1.03)]. Daumit et al. (2008) prospectively examined the effects of several antipsychotic medications on estimates of 10-year coronary heart disease risk, calculated with a Framingham risk equation, for 1,125 patients enrolled in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial. They found that the adjusted mean change in 10-year coronary heart disease risk differed significantly for the antipsychotic agents examined: olanzapine was associated with a 0.5% (standard error (SE) 0.3) increase and quetiapine a 0.3% (SE 0.3) increase in risk, whereas the risk decreased for patients treated with perphenazine (-0.5%, SE 0.3), risperidone (-0.6%, SE 0.3), and ziprasidone (-0.6%, SE 0.4).

4.2.2 Antidepressant medications

Antidepressant medications are primarily used in the treatment of mood disorders, such as major depressive episode and bipolar disorders. They also are used for a variety of other conditions including anxiety, eating, and post-traumatic stress disorders. The major classes of drugs used to treat depression are referred to as first-generation (e.g., monoamine oxidase inhibitors and tricyclic antidepressants (TCAs)), second-generation (e.g., selective serotonin reuptake inhibitors (SSRIs)), and third-generation (e.g., serotonin-norepinephrine reuptake inhibitors (SNRIs)) antidepressants. Patterns of antidepressant medication use have changed over time, with both an overall increase in their use and a shift in use among the antidepressant classes (Beck et al., 2005; Benazon, Mamdani, & Coyne, 2005; Paulose-Ram, Jonas, Orwig, & Safran, 2004). SSRIs and SNRIs have gained considerable popularity because they have fewer and more benign side effects than did their predecessors (Pacher & Kecskemeti, 2004).

Antidepressant medication use often affects body weight, but the amount of change varies because the symptoms associated with mood disorders, alone, can cause both positive and negative changes in appetite and energy output. For example, weight gain during initial antidepressant treatment can result from improvement in patients who experienced weight loss as a symptom of depression with melancholic features or it can be a residual symptom in patients who overeat when depressed. Nevertheless, significant weight gain that continues despite achieving full remission of depressive symptoms is generally attributed to the adverse effects of antidepressant treatment (Fava, 2000). Serretti and Mandelli (2010) conducted a comprehensive meta-analysis to compare the effect of different antidepressants on body weight and found that antidepressant

medications differ in their ability to induce weight gain. TCAs are the most potent weight gain–inducing medication because they have a high affinity for α-adrenergic, histaminergic, and cholinergic receptors, which are responsible for appetite. Conversely, SSRIs act selectively to enhance serotonin function and have a weight-reducing or anorexigenic effect.

Many antidepressant medications also have cardiotoxic properties; TCAs are associated with an increased risk of arrhythmias and worsening of established CVD, whereas SSRIs have neutral or beneficial effects that reduce the risk of arrhythmias (Hamer, Batty, Seldenrijk, & Kivimaki, 2011; Taylor, 2008). The most common manifestation of TCAs is the slowing of intraventricular conduction, manifested by prolonged PR, QRS, and QT intervals, on standard electrocardiograms, and orthostatic hypotension. SSRIs have significant advantages over TCAs in producing fewer cardiotoxic side effects; these newer compounds exhibit a lower risk of inducing hypotension and a higher margin of safety in acute overdose than TCAs (Glassman, 1998; Pacher & Kecskemeti, 2004).

Cohen et al. (2000) prospectively investigated the association between the use of antidepressant medications and incident MI in a cohort of 2,247 people who received at least one prescription for an antidepressant medication and 52,750 controls. They found that antidepressant users had a RR of MI of 2.2, 95% CI [1.3, 3.7] compared with nonusers. Furthermore, the RR of MI was 2.2, 95% CI [1.2, 3.8] in users of TCAs and 0.8, 95% CI [0.2, 3.5] in users of SSRIs, as compared with subjects who did not use antidepressants.

4.2.3 Mood stabilizer medications

Mood stabilizers are used in the treatment of bipolar disorder and most commonly include lithium and anticonvulsants, including sodium valproate or carbamazepine (Kilbourne et al., 2007). This class of psychotropic medication is also associated with weight gain, impaired glucose tolerance, and metabolic dysfunction (Mackin, 2008). Mood stabilizing medications carry with them varying magnitudes of risk; substantial weight gain is frequently observed with lithium and valproate treatment, whereas other medications in this class have intermediate (e.g., carbamazepine and gabapentin), weight neutral (e.g., lamotrigine and oxcarbazepine), and weight loss (e.g., topiramate and zonisamide) effects (De Hert, Correll, et al., 2011). Stimulation of appetite and enhanced energy storage is thought to be the mechanisms responsible for weight gain associated with these medications (Breum et al., 1992; Luef, Lechleitner, Bauer, Trinka, & Hengster, 2003). Moreover, there is evidence to suggest that mood stabilizers including lithium and carbamazepine are associated with sinus node arrhythmias, while valproate does not cause drug-related cardiotoxicity (Chong & Mahendran, 2001). There is some evidence to suggest that lithium is associated with an increased risk of MI (odds ratio (OR) = 10.1, 95% CI [1.0, 99.3]); but further investigation is needed because of this study's small sample size (Pratt et al., 1996).

4.2.4 Anxiolytic medications

Anxiolytic medications are used for the treatment of anxiety disorders, such as social phobia, panic disorder, and agoraphobia. Beck et al. (2005) examined psychoactive medication use in Canada using the CCHS Cycle 1.2 and found that 7.2% of those with anxiety disorders had taken a sedative-hypnotic (e.g., benzodiazepines and non-benzodiazepine compounds, mostly zopiclone) in the previous two days. Further

analysis of this subgroup revealed that the most commonly used anxiolytic medication was benzodiazepines (6.6%, 95% CI [5.5, 7.6]). Literature exploring the association between benzodiazepines, CVD, and cardiovascular risk is limited and inconclusive. Volgelzangs et al. (2010) documented an association between benzodiazepine use and heart disease (OR = 1.6, 95% CI [1.0, 2.7]) among people with current depressive or anxiety disorders (N = 1,170) using data from the Netherlands Study of Depression and Anxiety. However, Pratt et al. (1996) examined psychoactive medication use and the risk of MI in the Baltimore cohort of the Epidemiologic Catchment Area Study (N = 1, 551) and found that there was no increased risk associated with benzodiazepine use (OR = 1.3, 95% CI [0.7, 2.4]).

4.2.5 Psychoactive medication use in Canada

The CCHS Cycle 1.2 offered a unique opportunity to investigate psychotropic medication use in Canada. In an earlier phase of this research, we found that 10.2%, 95% CI [9.7, 10.6] of CCHS Cycle 1.2 respondents were identified (either through self-reported use within the past 12 months or visual verification of medications used within the past two days) as having taken psychoactive medications (i.e., antipsychotics 0.6%, 95% CI [0.5, 0.7]; antidepressants 6.7%, 95% CI [6.3, 7.0]; mood stabilizers 1.3%, 95% CI [1.1, 1.4]; and anxiolytics 6.2%, 95% CI [5.8, 6.5]). Significant psychotropic medication polypharmacy (i.e., concurrent use of two or more psychoactive medications) existed, the median number of psychoactive medications used was two, and antidepressants were most commonly paired with other psychoactive medications. Similar findings have been documented in other population-based mental health surveys

(Faries, Ascher-Svanum, Zhu, Correll, & Kane, 2005; Mojtabai & Olfson, 2010; Paulose-Ram et al., 2004; Procyshyn, Kennedy, Tse, & Thompson, 2001).

Although psychoactive medication use can be employed as an indicator of treatment for MHDs, it is known that there is a substantial mismatch between medication use and people identified as having MHDs. Among the CCHS Cycle 1.2 respondents who were identified as using psychoactive medications, 65.2%, 95% CI, [63.1, 67.2] had not reported any symptoms of mental illness within the past 12 months (as determined with the CCHS Cycle 1.2 World Mental Health Composite International Diagnostic Interview [CCHS 1.2/WMH-CIDI]). When we investigated this issue further, we found that the positive percent agreement between various MHDs and psychoactive medication use was slight-to-moderate: 10.7%, 95% CI [8.6, 12.9] positive agreement for reported mood stabilizer medication use and any mood disorder, 25.9%, 95% CI [23.0, 28.7] for anxiolytic medication use and any anxiety disorder, and 59.3%, 95% CI [44.8, 73.9] agreement for antipsychotic medication use and self-reported schizophrenia. The negative percent agreement was high for all the comparisons. Similar findings have been reported in other publications arising from analyses of the CCHS Cycle 1.2 and in other international investigations of psychoactive medication use (Alonso et al., 2004; Beck et al., 2005; Sewitch et al., 2008).

Although Beck et al. (2005) used a more conservative method to identify CCHS Cycle 1.2 respondents taking psychotropic medications; they reported that 7.2%, 95% CI [6.9, 7.6] of Canadians had taken at least one psychoactive medication within the past two days (identified using visual verification of medication label and including sleep-aid medications). Moreover, among Canadians with any lifetime MHDs, only 19.3%, 95%

CI [18.0, 20.6] reported taking psychoactive medications. This frequency was much greater among people with schizophrenia (64.0%, 95% CI [49.9, 78.0]): 47.9% (95% CI [34.3, 61.5] of people with schizophrenia used antipsychotic agents, 25.2% (95% CI [15.3, 35.1] used antidepressants, and 19.2% (95% CI [11.2, 27.1]) used sedative-hypnotics (i.e., medications commonly used for sleep or anxiety). However, only 8.2%, 95% CI [5.8, 10.5] of those with bipolar disorder were taking a mood stabilizer, whereas 20.1%, 95% CI [16.7, 23.5] took an antidepressant. These findings not only signify a discrepancy between psychoactive medication use and MHDs in the CCHS Cycle 1.2, but also highlight that people with specific illnesses take a variety of medications for which their principal MHD is not the primary indication.

4.2.6 Psychoactive medication use in Canada: Opportunities for further investigation

Investigation of the association between psychoactive medication use and CVD in Canada has been limited to a few provincial, retrospective cohort studies conducted in Ontario and British Columbia; these studies contrasted the association between typical and atypical antipsychotic medication use and the occurrence of stroke or mortality among older adults (≥ 65 years) (Gill et al., 2005; Herrmann, Mamdani, & Lanctot, 2004; Schneeweiss, Setoguchi, Brookhart, Dormuth, & Wang, 2007). Although very useful, these studies had a narrow approach to investigating psychoactive medication use and CVD. A more global investigation of psychoactive medication use and CVD and cardiovascular risk is needed to better understand the breadth of this problem in Canada.

There also is some evidence to suggest that psychoactive medication polypharmacy (i.e., two psychoactive medications taken together), between and within medication classes, is associated with an elevation in cardiovascular risk factors and

cardiac arrhythmias. Correll et al. (2007) investigated whether the co-prescribing of two or more atypical antipsychotics was associated with an increased prevalence of metabolic syndrome. They found that patients (N = 364) receiving antipsychotic monotherapy had higher rates of metabolic syndrome and lipid markers of insulin resistance than did patients receiving antipsychotic polytherapy. In contrast, Sala et al. (2005) conducted a small observational study of hospitalized patients (N =38) to compare the effects of antipsychotic monotherapy and psychoactive medication polytherapy (between antipsychotic, antidepressant, and mood stabilizing medications) on cardiac electrophysiology. They demonstrated that there was no significant prolongation of the QT interval following monotherapy with an antipsychotic agent, while the combination of antipsychotic and antidepressant medications caused significant QT prolongation. Further investigation into psychiatric polypharmacy (between and within medication classes) and cardiovascular risk and morbidity is needed and the CCHS Cycle 1.2 is an ideal platform to examine some of these associations.

4.3 Methods

4.3.1 Data source and sample

Cross-sectional data about psychoactive medication use, mental health status, CVD, and cardiovascular risk were derived from the CCHS Cycle 1.2, conducted by Statistics Canada (Statistics Canada, 2002). The CCHS Cycle 1.2 survey methodology is described in detail elsewhere (Gravel & Béland, 2005). Briefly, this nationally representative household survey targeted residents in all provinces and territories, with the exclusion of populations on Indian reserves and Canadian Forces' bases, and in healthcare institutions and some remote areas. The CCHS respondents were selected

from a multistage stratified cluster design in which the household was the final sampling unit. Each province was divided into three types of regions (i.e., major urban centres, cities, and rural regions) before clusters within each stratum were selected based on socio-economic characteristics. Dwelling lists were then prepared for each cluster and households were selected from the lists. This technique ensured that the probability of selecting a sampling unit was proportional to the size of the population (Statistics Canada, 1998).

Face-to-face interviews were carried out between May and December 2002 by trained lay interviewers using a computer-assisted personal interviewing method (Statistics Canada, 2002). The interviewers explained the study and obtained verbal informed consent before commencing an interview. In all of the selected dwellings, a knowledgeable household member was asked to supply basic demographic information about all of the residents. Depending on the composition of the household, one member was then selected for a more in-depth interview. In cases where this initial household visit resulted in non-response, telephone follow-ups were conducted. Data collection by telephone was authorized only when travel was prohibitive or the respondent refused to conduct the interview in person; this resulted in 14% of the interviews being completed by telephone. In total, 48,047 households were selected to participate in Cycle 1.2 and a national response rate of 77% was achieved (Statistics Canada, 2002).

4.3.2 Demographic measures

Sex (male or female), age (in years), marital status (single vs. married or common-law), total household income based on number of members (low income vs. middle or high income), education level (< than secondary school graduate [< 12 years of

basic education] vs. ≥ secondary school graduate), immigrant status (immigrant [immigrated from overseas] vs. non-immigrant [Canadian born]), and ethnicity/race ("white" vs. not "white") were treated as demographic correlates. Low income was defined as < $15,000 if 1 or 2 people; < $20,000 if 3 or 4 people; < $30,000 if 5 or more people living in a household (Statistics Canada, 2002).

4.3.3 Measures of psychoactive medication use

There were two methods used in the CCHS Cycle 1.2 to identify people that were taking psychoactive medications. The first asked respondents to self-report if, within the past 12 months, they took anxiolytics ("Did you take medication to reduce anxiety or nervousness such as, Ativan, Valium or Serax?"), antipsychotics ("Did you take medication for the treatment of psychotic behaviours such as, Haldol, Risperdol, or Seroquel?"), antidepressants ("Did you take antidepressants such as Prozac, Paxil or Effexor?") or mood stabilizers ("Did you take mood stabilizers such as Lithium, Tegretol or Epival?").The second method required the interviewer to visually inspect any medications that the respondent reported taking within the last two days. The interviewer then recorded these medications using codes from the Anatomical Therapeutic Chemical (ATC) Classification System (World Health Organization, 2009). A comprehensive list of anxiolytics (i.e., ATC code N05B*), antipsychotics (i.e., ATC codes N05AA, N05AB, N05AC, N05AD, N05AE, N05AF, N05AG, N05AH, N05AX), antidepressants (i.e., ATC code N06A*), and mood stabilizer (i.e., ATC codes N03AF, N03AG, NO3AX, N05AN) medications was collected. An individual was classified as having used a specific psychoactive medication if a positive response was received through either method.

4.3.4 Measures of mental health disorders

Respondents with mental heath disorders were identified using a modified version of the World Mental Health Composite International Diagnostic Interview (WMH-CIDI), which was adapted to meet the needs of the CCHS Cycle 1.2 (i.e., fewer disorders were assessed) and based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 1994; Kessler et al., 2004; Statistics Canada, 2002). The CCHS 1.2/WMH-CIDI is a fully-structured psychiatric diagnostic interview administered by trained lay interviewers to determine the lifetime prevalence rates of five major MHDs. These include major depressive episode, manic episode, social phobia, panic disorder, and agoraphobia. Hierarchy-free diagnoses (one disorder did not take precedence over another diagnosis) were considered throughout the analyses. The lifetime prevalence of a disorder is the proportion of the sample who ever experienced the disorder. Schizophrenia was not measured with the structured diagnostic interview; rather, it was assessed as a self-reported chronic health condition diagnosed by a health professional. An individual was classified as having any MHD if she or he had at least one lifetime MHD.

4.3.5 Measures of cardiovascular risk

Cardiovascular risk was calculated with algorithms from the Framingham Heart Study to estimate short- and long-term risk of CVD (D'Agostino et al., 2008; Pencina et al., 2009). The 10-year risk of cardiovascular disease was calculated in men and women without established CVD, aged 30-74 years, to predict "general" cardiovascular outcomes, such as coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, and heart failure using a simple point-based or "score sheet" system. The point-based

system assigns each risk factor level an integer number. These risk factor values are summed to derive a score, and then the risk for that score is determined from a look-up table (D'Agostino et al., 2008).

The 30-year risk of cardiovascular disease derives risk estimates using cox regression (i.e., equation-based) models for men and women without established CVD or cancer, aged 20-59 years, to predict the likelihood of "hard" outcomes such as coronary death, myocardial infarction, and stroke. Individuals with cancer were excluded from the analysis because their disease can influence mortality within the projected time frame and is therefore viewed as a confounding variable to the associations of interest. Simple, non-laboratory-based predictors were used in the calculations of 30-year risk, including: sex (male or female), age (years), body mass index (self-reported weight and height [kg/(m)]), self-reported systolic blood pressure (SBP) (mmHg), diabetes status (yes/no), treatment for hypertension (yes/no), and smoking (yes/no) (Pencina et al., 2009).

Diabetes status ("Do you have diabetes?") and SBP ("Do you have high blood pressure?") were collected through the self-reported chronic conditions module. Both risk algorithms required a quantitative measurement of SBP (in mmHg), which was not available in the CCHS Cycle 1.2. Accordingly, the respondents who reported having high blood pressure were assumed to have SBP = 140-159 mmHg, respondents with or without reported high blood pressure who indicated that they were taking an antihypertensive drug were assumed to have SBP = 130-139 mmHg, and respondents without high blood pressure and who did not report taking an antihypertensive drug were considered to have SBP = 120-129 mmHg (Hackam et al., 2013). The rationale behind these decisions is based on a therapeutic paradigm that prescribers "treat to target" or

keep blood pressure below a measurement that is known to induce cardiovascular events (i.e., 140/90 mmHg) (Atar et al., 2010). Hypertension drug therapy was determined via the ATC codes. A self-reported proxy measure for smoking status was used because the CCHS Cycle 1.2 did not directly ask the respondents about their tobacco use patterns. An item was included in the stress module and asked the respondents, "When dealing with stress, how often do you try to feel better by smoking more cigarettes than usual?" The respondents were classified as smokers if they responded with "often," "sometimes," "rarely," or "never" and as non-smokers if they indicated that they "do not smoke."

4.3.6 Measures of cardiovascular disease

The CCHS Cycle 1.2 included indicators of heart disease and stroke in the self-reported chronic conditions module; the question stem stated, "We are interested in long-term conditions which are expected to last or have already lasted 6 months or more and that have been diagnosed by a health professional." The respondents answered "yes" or "no" to the questions: "Do you have heart disease?" and "Do you suffer from the effects of a stroke?" Self-reported CVD diagnoses have been shown to have acceptable validity, with under-reporting occurring more frequently than over-reporting of the diagnosis (Kehoe et al., 1994; Kriegsman et al., 1996).

4.3.7 Analysis

To investigate the relationships between psychoactive medication use and cardiovascular risk and CVD, three subgroups of respondents were created for each specific medication class. This approach was taken to incorporate measures of psychoactive medication polypharmacy into the analysis. We sought to determine whether particular medication combinations place affected people at an increased risk of CVD. One group was respondents who took a single medication (e.g., an antidepressant

only compared to respondents who took antidepressant medications in combination with other medications or respondents who did not take any psychoactive medications), a second group took two medications (e.g., the most common pairings, such as an antidepressant and anxiolytic compared to respondents who took antidepressant medications alone or in other combinations or respondents who did not take any psychoactive medications), and a third group was respondents who took a medication in any combination (e.g., antidepressants alone or with any other psychoactive medication, including anxiolytics compared to people who took other psychoactive medications or no psychoactive medications).

The demographic characteristics of the respondents taking specific psychoactive medications were described with proportions and bivariate ORs. Age was stratified into three categories to correspond with the Framingham scoring algorithms (i.e., 15-34 years, 35-64 years, and ≥ 65 years). Descriptive statistics were used to describe the prevalence of heart disease and stroke among the respondents taking psychoactive medications within the past 12 months, and the associations between the specific psychoactive medications and heart disease and stroke were described with unadjusted ORs, demographically adjusted ORs, and ORs adjusted by lifetime MHDs. Short- (10-year) and long-term (30-year) cardiovascular risk estimates were dichotomized at the median and the strength of their relationship with psychoactive medications was estimated (Allan et al., 2013). The estimates for cardiovascular risk were adjusted for marital status, household income, education level, immigrant status, ethnicity/race, and lifetime mental health status; sex and age were not treated as confounders because they were included in the risk prediction algorithms. Confidence intervals (95%) for the proportions and ORs

were estimated using the balanced repeated replication method with Stata version 12 software to adjust for clustered sampling and the sample weights (Rust & Rao, 1996; StataCorp., 2011).

4.4 Results

4.4.1 Sample characteristics

The sample consisted of 36,984 respondents and was weighted to represent 24,996,593 people in the Canadian population. Tables 4-1 and 4-2 present the rates of psychoactive medication use within the past 12 months. Respondents taking any psychoactive medications were more likely to be women, older (> 34 years), single, low-income earners, with less than a secondary school education, born in Canada (i.e., not immigrants), and "white." Similarly, people taking any combination of anxiolytic, antidepressant, and mood stabilizer medications were more likely to be female, have low incomes, limited education, be born in Canada, and be single and "white." However, respondents using antipsychotic medications alone or with any other psychoactive medications were likely to be older (i.e., > 34 years), single, have low income, less than a secondary school education and born in Canada.

Table 4-1: Twelve-month Psychoactive Medication Use and Anxiolytic Medication Use by Demographic Factors

	Psychoactive medication use (any) vs. no psychoactive med. use[a]	**Anxiolytic** use alone vs. else[b]	**Anxiolytic use with antidepressant** vs. else[c]	**Anxiolytic use alone or with any other psychoactive med. including antidepressant** vs. else[d]	**Antipsychotic** use alone vs. else[b]	**Antipsychotic medication use with antidepressant** vs. else[c]	**Antipsychotic use alone or with any other psychoactive med. including antidepressant** vs. else[d]
				% [95% CI] OR [95% CI]			
Sex							
Male vs. Female	7.0 [6.4, 7.6]/ 13.3 [12.6,13.9] 0.5 [0.4, 0.5]	2.1 [1.8,2.5]/ 3.8 [3.4, 4.2] 0.6 [0.5,0.7]	2.1 [1.8, 2.4]/ 3.9 [3.5, 4.2] 0.5 [0.5, 0.6]	4.3 [3.9, 4.8]/ 7.9 [7.4, 8.5] 0.5 [0.5, 0.6]	0.1 [0.0, 0.1]/ 0.1 [0.0, 0.1] 0.7 [0.3, 1.7]	0.4 [0.3, 0.5]/ 0.4 [0.3, 0.5] 1.0 [0.7, 1.4]	0.5 [0.4, 0.7]/ 0.6 [0.5, 0.8] 0.8 [0.6, 1.1]
Age							
35-64 yrs. vs. 15-34 yrs.	11.8 [11.1,12.5]/ 8.4 [7.9, 8.9] 1.5 [1.3, 1.6]	3.0 [2.6,3.4]/ 3.0 [2.7,3.3] 1.0 [0.9, 1.2]	3.7 [3.4, 4.1]/ 2.2 [1.9, 2.4] 1.8 [1.5, 2.0]	6.9 [6.4, 7.5]/ 5.3 [4.9, 5.7] 1.3 [1.2, 1.5]	0.1 [0.0, 0.1]/ 0.1 [0.0, 0.1] 1.1 [0.4, 2.7]	0.5 [0.4, 0.7]/ 0.3 [0.2, 0.3] 2.0 [1.3, 3.0]	0.7 [0.6, 0.9]/ 0.5 [0.4, 0.6] 1.5 [1.1, 2.1]
≥ 65 yrs. vs. 15-34 yrs.	14.0 [13.0,15.1]/ 9.5 [9.0, 10.0] 1.6 [1.4, 1.7]	7.3 [6.5,8.0]/ 2.2 [2.0, 2.5] 3.4 [2.9, 4.0]	2.7 [2.3, 3.2]/ 3.0 [2.8, 3.3] 0.9 [0.7, 1.1]	10.3 [9.4, 11.2]/ 5.4 [5.1, 5.8] 2.0 [1.8, 2.3]	0.1 [0.0, 0.2]/ 0.1 [0.0, 0.1] 1.8 [0.6, 5.1]	0.2 [0.1, 0.4]/ 0.4 [0.3, 0.5] 0.6 [0.3, 1.0]	0.6 [0.4, 0.8]/ 0.6 [0.5, 0.7] 1.1 [0.7, 1.6]
Marital status							
Single vs. Not single	11.4 [10.7,12.1]/ 9.4 [8.8, 10.0] 1.2 [1.1, 1.4]	3.0 [2.7,3.4]/ 2.9 [2.6, 3.3] 1.0 [0.9, 1.2]	3.6 [3.3, 4.0]/ 2.6 [2.3, 2.9] 1.4 [1.2, 1.6]	7.0 [6.5, 7.5]/ 5.7 [5.2, 6.1] 1.3 [1.1, 1.4]	0.1 [0.1, 0.2]/ 0.0 [0.0, 0.1] 3.6 [1.3, 10.6]	0.6 [0.5, 0.7]/ 0.3 [0.2, 0.4] 2.1 [1.4, 3.2]	1.0 [0.8, 1.1]/ 0.4 [0.2, 0.5] 2.7 [1.9, 3.9]
Total household income							
Low income vs. middle or high income	18.4 [16.8,20.0]/ 9.5 [9.0, 10.0] 2.1 [1.9, 2.4]	6.2 [5.3,7.2]/ 2.7 [2.4, 3.0] 2.4 [2.0, 2.9]	5.4 [4.7, 6.2]/ 2.8 [2.5, 3.1] 2.0 [1.7, 2.4]	12.2 [11.0,13.3]/ 5.6 [5.2, 6.0] 2.3 [2.0, 2.6]	0.3 [0.1, 0.4]/ 0.0 [0.0, 0.1] 6.4 [2.4, 17.2]	1.3 [1.0, 1.6]/ 0.3 [0.2, 0.4] 4.2 [2.9, 6.0]	2.0 [1.6, 2.4]/ 0.4 [0.3, 0.5] 4.8 [3.6, 6.5]
Education level							
< than secondary graduate vs. secondary graduate	12.3 [11.4,13.1]/ 9.4 [8.9, 9.9] 1.3 [1.2, 1.5]	4.6 [4.1,5.1]/ 2.4 [2.1, 2.7] 1.9 [1.6, 2.3]	3.2 [2.8, 3.7]/ 2.9 [2.6, 3.2] 1.1 [0.9, 1.3]	8.1 [7.4, 8.7]/ 5.5 [5.1, 5.9] 1.5 [1.3, 1.7]	0.1 [0.0, 0.2]/ 0.1 [0.0, 0.1] 1.9 [0.8, 4.7]	0.6 [0.4, 0.8]/ 0.3 [0.2, 0.4] 1.8 [1.2, 2.7]	0.9 [0.7, 1.1]/ 0.5 [0.4, 0.6] 1.9 [1.4, 2.6]

	Psychoactive medication use (any) vs. no psychoactive med. use[a]	**Anxiolytic** use alone vs. else[b]	**Anxiolytic use with antidepressant** vs. else[c]	**Anxiolytic use alone or with any other psychoactive med. including antidepressant** vs. else[d]	**Antipsychotic** use alone vs. else[b]	**Antipsychotic medication use with antidepressant** vs. else[c]	**Antipsychotic use alone or with any other psychoactive med. including antidepressant** vs. else[d]
Immigrant status							
Immigrant vs. non-immigrant	6.2 [5.4, 7.0]/ 11.4 [10.9,11.9] 0.5 [0.4, 0.6]	1.8 [1.4, 2.3]/ 3.3 [3.0,3.6] 0.5 [0.4, 0.7]	1.6 [1.2, 2.1]/ 3.4 [3.1, 3.7] 0.5 [0.4, 0.6]	3.6 [3.0, 4.2]/ 6.9 [6.5, 7.4] 0.5 [0.4, 0.6]	0.1 [0.0, 0.2]/ 0.1 [0.0, 0.1] 1.6 [0.5, 4.9]	0.1 [0.0, 0.2]/ 0.5 [0.4, 0.6] 0.3 [0.1, 0.6]	0.3 [0.2, 0.4]/ 0.7 [0.6, 0.8] 0.4 [0.3, 0.7]
Ethnicity/race							
"White" vs. not "white"	11.3 [10.8,11.8]/ 4.6 [3.9, 5.4] 2.6 [2.2, 3.1]	3.3 [3.1,3.6]/ 1.1 [0.8, 1.5] 3.0 [2.1, 4.3]	3.3 [3.1, 3.6]/ 1.4 [0.9, 1.8] 2.5 [1.7, 3.5]	6.9 [6.5, 7.3]/ 2.6 [2.0, 3.2] 2.8 [2.2, 3.5]	0.1 [0.0, 0.1]/ 0.2 [0.0, 0.3] 0.3 [0.1, 1.2]	0.5 [0.4, 0.5]/ 0.1 [0.1, 0.2] 3.2 [1.6, 6.4]	0.6 [0.5, 0.7]/ 0.4 [0.2, 0.6] 1.6 [0.9, 2.7]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. % = percent; OR = odds ratio; CI = confidence interval.

[a]Psychoactive medication use represents people identified as taking at least one anxiolytic, antipsychotic, antidepressant, or mood stabilizer medication within the last year.

[b]Indicates that the comparison is all respondents in the sample not including people taking the listed medication alone (e.g., comparison group includes respondents who took anxiolytic medications in combination with other medications, respondents who took antipsychotic, antidepressant or mood stabilizing medications or respondents who did not take any psychoactive medications).

[c]Indicates that the comparison is all respondents in the sample not including people taking the listed medication in combination with its most common pairing (e.g., comparison group includes respondents who took anxiolytic medications alone or in other combinations, respondents who took antipsychotic, antidepressant or mood stabilizing medications or respondents who did not take any psychoactive medications)

[d]Indicates that the comparison is all respondents in the sample who did not take the listed medication (e.g., the comparison group is people who took other psychoactive medications or no psychoactive medications).

Table 4-2: Twelve-month Antidepressant and Mood Stabilizer Medication Use by Demographic Factors

	Antidepressant use alone vs. else[b]	**Antidepressant use with anxiolytic** vs. else[c]	**Antidepressant use alone or with any other psychoactive meds. including anxiolytic** vs else[d]	**Mood stabilizer** use alone vs. else[b]	**Mood stabilizer use with antidepressant** vs. else[c]	**Mood stabilizer use alone or with any other psychoactive meds. including antidepressants** vs else[d]
	% [95% CI] OR [95% CI]					
Sex						
Male vs. Female	2.1 [1.8, 2.4]/ 4.5 [4.1, 4.8] 0.5 [0.4, 0.5]	2.1 [1.8, 2.4]/ 3.9 [3.5, 4.2] 0.5 [0.5, 0.6]	4.5 [4.1, 4.9]/ 8.8 [8.2, 9.3] 0.5 [0.4, 0.6]	0.2 [0.1, 0.2]/ 0.3 [0.2, 0.4] 0.5 [0.3, 1.0]	0.7 [0.5, 0.8]/ 1.1 [0.8, 1.3] 0.6 [0.5, 0.8]	0.9 [0.7, 1.1]/ 1.6 [1.4, 1.9] 0.6 [0.4, 0.7]
Age						
35-64 yrs. vs. 15-34 yrs.	4.0 [3.6, 4.4]/ 2.5 [2.3, 2.8] 1.6 [1.4, 1.9]	3.7 [3.4, 4.1]/ 2.2 [1.9, 2.4] 1.8 [1.5, 2.0]	8.2 [7.6, 8.8]/ 5.0 [4.6, 5.3] 1.7 [1.5, 1.9]	0.3 [0.2, 0.4]/ 0.2 [0.1, 0.2] 1.7 [0.9, 3.2]	1.1 [0.8, 1.3]/ 0.6 [0.5, 0.7] 1.8 [1.3, 2.4]	1.6 [1.3, 1.9]/ 0.9 [0.8, 1.1] 1.7 [1.3, 2.2]
≥ 65 yrs. vs. 15-34 yrs.	3.0 [2.4, 3.5]/ 3.3 [3.1, 3.6] 0.9 [0.7, 1.1]	2.7 [2.3, 3.2]/ 3.0 [2.8, 3.3] 0.9 [0.7, 1.1]	6.0 [5.3, 6.8]/ 6.8 [6.4, 7.2] 0.9 [0.8, 1.0]	0.2 [0.1, 0.3]/ 0.2 [0.2, 0.3] 0.8 [0.4, 1.7]	0.4 [0.2, 0.5]/ 0.9 [0.8, 1.1] 0.4 [0.2, 0.6]	0.9 [0.6, 1.1]/ 1.3 [1.2, 1.5] 0.6 [0.5, 0.9]
Marital status						
Single vs. Not single	3.5 [3.2, 3.8]/ 3.1 [2.8, 3.5] 1.1 [1.0, 1.3]	3.6 [3.3, 4.0]/ 2.6 [2.3, 2.9] 1.4 [1.2, 1.6]	7.7 [7.1, 8.3]/ 6.0 [5.6, 6.5] 1.3 [1.2, 1.4]	0.2 [0.1, 0.2]/ 0.3 [0.2, 0.4] 0.5 [0.3, 0.9]	1.1 [0.9, 1.4]/ 0.7 [0.5, 0.8] 1.7 [1.2, 2.2]	1.6 [1.3, 1.8]/ 1.1 [0.9, 1.3] 1.4 [1.1, 1.8]
Total household income						
Low income vs. middle or high income	4.7 [3.8, 5.6]/ 3.3 [3.0, 3.5] 1.5 [1.2, 1.8]	5.4 [4.7, 6.2]/ 2.8 [2.5, 3.1] 2.0 [1.7, 2.4]	11.0 [9.7, 12.3]/ 6.4 [6.0, 6.8] 1.8 [1.6, 2.1]	0.3 [0.1, 0.5]/ 0.2 [0.1, 0.3] 1.2 [0.5, 3.0]	1.7 [1.3, 2.2]/ 0.8 [0.6, 0.9] 2.2 [1.6, 3.1]	2.5 [2.0, 3.1]/ 1.1 [1.0, 1.3] 2.2 [1.7, 2.9]
Education level						
< than secondary graduate vs. secondary graduate	3.4 [3.0, 3.9]/ 3.2 [3.0, 3.5] 1.1 [0.9, 1.3]	3.2 [2.8, 3.7]/ 2.9 [2.6, 3.2] 1.1 [0.9, 1.3]	7.0 [6.4, 7.7]/ 6.5 [6.1, 7.0] 1.1 [1.0, 1.2]	0.2 [0.1, 0.4]/ 0.2 [0.1, 0.3] 1.2 [0.6, 2.2]	0.7 [0.5, 1.0]/ 0.9 [0.7, 1.1] 0.8 [0.6, 1.2]	1.2 [1.0, 1.5]/ 1.3 [1.1, 1.5] 1.0 [0.7, 1.3]
Immigrant status						
Immigrant vs. non-immigrant	2.1 [1.6, 2.6]/ 3.6 [3.4, 3.9] 0.6 [0.4, 0.7]	1.6 [1.2, 2.1]/ 3.4 [3.1, 3.7] 0.5 [0.4, 0.6]	4.0 [3.3, 4.6]/ 7.5 [7.1, 7.9] 0.5 [0.4, 0.6]	0.2 [0.1, 0.3]/ 0.3 [0.2, 0.3] 0.6 [0.3, 1.4]	0.3 [0.1, 0.5]/ 1.0 [0.9, 1.2] 0.3 [0.2, 0.5]	0.6 [0.4, 0.8]/ 1.5 [1.3, 1.7] 0.4 [0.3, 0.6]

	Antidepressant use alone vs. else[b]	**Antidepressant use with anxiolytic** vs. else[c]	**Antidepressant use alone or with any other psychoactive meds. including anxiolytic** vs else[d]	**Mood stabilizer** use alone vs. else[b]	**Mood stabilizer use with antidepressant** vs. else[c]	**Mood stabilizer use alone or with any other psychoactive meds. including antidepressants** vs else[d]
	% [95% CI]					
Ethnicity/race						
"White" vs. not "white"	3.6 [3.4, 3.9]/ 1.6 [1.2, 2.1] 2.3 [1.6, 3.1]	3.3 [3.1, 3.6]/ 1.4 [0.9, 1.8] 2.5 [1.7, 3.5]	7.4 [7.0, 7.8]/ 3.1 [2.4, 3.8] 2.5 [2.0, 3.1]	0.3 [0.2, 0.3]/ 0.1 [0.0, 0.2] 3.6 [0.6, 6.2]	1.0 [0.8, 1.2]/ 0.2 [0.1, 0.3] 5.3 [3.0, 9.2]	1.4 [1.2, 1.6]/ 0.4 [0.2, 0.6] 3.4 [2.1, 5.5]

Note. Findings are based on reports of 36,984 respondents representing N = 24,996,593 people in the Canadian population. % = percent; OR = odds ratio; CI = confidence interval.

[b]Indicates that the comparison is all respondents in the sample not including people taking the listed medication alone (e.g., comparison group includes respondents who took antidepressant medications in combination with other medications, respondents who took antipsychotic, anxiolytic or mood stabilizing medications or respondents who did not take any psychoactive medications).

[c]Indicates that the comparison is all respondents in the sample not including people taking the listed medication in combination with its most common pairing (e.g., comparison group includes respondents who took antidepressant medications alone or in other combinations, respondents who took antipsychotic, anxiolytic or mood stabilizing medications or respondents who did not take any psychoactive medications).

[d]Indicates that the comparison is all respondents in the sample who did not take the listed medication (e.g., the comparison group is people who took other psychoactive medications or no psychoactive medications).

4.4.2 Relationships between psychoactive medications and cardiovascular risk

Table 4-3 illustrates that there was no association found between psychoactive medication use and 10-year cardiovascular risk (OR = 1.1, 95% CI [0.9, 1.2]) after controlling for differences in sociodemographic characteristics. This same group was 50% more likely (OR = 1.5, 95% CI [1.2, 1.7]) to be in the highest 30-year risk category for CVD after adjustment for sociodemographic variables. This trend was consistent across respondents who were identified as taking any antipsychotic, antidepressant, or mood stabilizer medications. However, individuals who reported taking anxiolytic medications had positive associations for both outcomes (i.e., they were in the higher risk group for 10-year and 30-year cardiovascular risk). Adjustment for lifetime history of MHDs did not affect the observed positive association between psychoactive medication use and 30-year cardiovascular risk. However, it did influence the association between psychoactive medication use and 10-year cardiovascular risk, causing it to reach statistical significance (OR = 1.2, 95% CI [1.1, 1.4]). There was no evidence to suggest that psychoactive medication polypharmacy increased the likelihood of being at high (vs. low) risk of developing CVD within 10- or 30-years compared with singular psychoactive medication use.

Table 4-3: Twelve-month Psychoactive Medication Use and 10-Year and 30-Year Cardiovascular Risk

	Framingham 10-year cardiovascular risk[e]			Framingham 30-year cardiovascular risk[e]		
	unadjusted	adjusted for demographics[f]	adjusted for demographics[f] and lifetime mental health disorders[g]	unadjusted	adjusted for demographics[f]	adjusted for demographics[f] and lifetime mental health disorders[g]
	OR [95% CI]					
Psychoactive medication use (any) vs. no psychoactive medication use[a]	1.2 [1.1, 1.4]	1.1 [0.9, 1.2]	1.2 [1.1, 1.4]	1.4 [1.2, 1.6]	1.5 [1.2, 1.7]	1.4 [1.2, 1.7]
Anxiolytics use alone vs. else[b]	1.7 [1.3, 2.1]	1.3 [1.1, 1.7]	1.4 [1.1, 1.8]	1.6 [1.2, 2.2]	1.6 [1.2, 2.3]	1.6 [1.1, 2.2]
Anxiolytic use with antidepressants vs. else[c]	1.2 [1.0, 1.4]	1.1 [0.9, 1.3]	1.3 [1.1, 1.6]	1.4 [1.1, 1.7]	1.4 [1.1, 1.8]	1.3 [1.0, 1.7]
Anxiolytic use alone or with any other psychoactive medications including antidepressants vs. else[d]	1.4 [1.3, 1.6]	1.2 [1.0, 1.4]	1.4 [1.2, 1.6]	1.4 [1.2, 1.7]	1.5 [1.3, 1.8]	1.4 [1.2, 1.7]
Antipsychotic use alone vs. else[b]	1.8 [0.5, 6.2]	2.0 [0.5, 8.7]	2.5 [0.6, 11.1]	1.4 [0.3, 6.6]	2.8 [0.6, 12.6]	2.5 [0.6, 11.2]
Antipsychotic use with antidepressants vs. else[c]	1.4 [0.9, 2.2]	1.1 [0.7, 1.9]	1.3 [0.8, 2.2]	1.7 [1.0, 3.1]	2.0 [1.0, 3.7]	1.8 [0.9, 3.4]
Antipsychotic use alone or with any other psychoactive medications including antidepressants vs. else[d]	1.5 [1.0, 2.2]	1.2 [0.8, 1.9]	1.5 [0.9, 2.3]	1.4 [0.9, 2.2]	1.8 [1.1, 3.1]	1.7 [1.0, 2.8]
Antidepressant use alone vs. else[b]	0.9 [0.8, 1.1]	0.9 [0.7, 1.0]	1.0 [0.8, 1.2]	1.2 [1.0, 1.5]	1.2 [0.9, 1.5]	1.1 [0.9, 1.5]
Antidepressant use with anxiolytics vs. else[c]	1.2 [1.0, 1.4]	1.1 [0.9, 1.3]	1.3 [1.1, 1.6]	1.4 [1.1, 1.7]	1.4 [1.1, 1.8]	1.3 [1.0, 1.7]
Antidepressant use alone or with any other psychoactive medications including anxiolytics vs. else[d]	1.0 [0.9, 1.2]	0.9 [0.8, 1.1]	1.1 [0.9, 1.3]	1.3 [1.1, 1.6]	1.4 [1.2, 1.7]	1.3 [1.1, 1.6]
Mood stabilizer use alone vs. else[b]	0.9 [0.5, 1.8]	0.7 [0.4, 1.4]	0.8 [0.4, 1.6]	0.9 [0.4, 2.1]	0.9 [0.3, 2.5]	0.8 [0.3, 2.3]
Mood stabilizer use with antidepressants vs. else[c]	0.9 [0.6, 1.3]	0.9 [0.5, 1.4]	1.0 [0.6, 1.6]	1.8 [1.2, 2.8]	2.1 [1.3, 3.5]	1.9 [1.2, 3.2]
Mood stabilizer use alone or with any other psychoactive medications including antidepressants vs. else[d]	0.9 [0.7, 1.3]	0.9 [0.6, 1.3]	1.0 [0.7, 1.5]	1.6 [1.1, 2.3]	1.9 [1.2, 2.9]	1.8 [1.1, 2.7]

Note. Findings are based on reports of 18,931 respondents representing N = 13,881,375 people in the Canadian population. Respondents who were 30-74 years old were included whereas people with a previous history of heart disease or stroke were excluded from the 10-year risk analysis. Respondents who were 20-59 years old were included whereas people with a previous history of heart disease, stroke and cancer were excluded from the 30-year risk analysis. % = percent; OR = odds ratio; CI = confidence interval.

[a]Psychoactive medication use represents people identified as taking at least one anxiolytic, antipsychotic, antidepressant or mood stabilizer medication within the last year.

[b]Indicates that the comparison is all respondents in the sample not including people taking the listed psychoactive medication alone.

[c]Indicates that the comparison is all respondents in the sample not including people who were taking the listed psychoactive medication combination.

[d]Indicates that the comparison is all respondents in the sample who did not take the listed medication in any combination.

[e]Variable is dichotomized at the median (high vs. low).

[f]Estimates are adjusted for the following demographic variables: marital status, household income, education level, immigrant status and ethnicity/race. All variables made a significant contribution to the outcome except household income.

[g]Estimates are adjusted for the following lifetime mental health disorders: schizophrenia, major depressive episode, manic episode, social phobia, panic disorder and agoraphobia.

4.4.3 Relationships between psychoactive medication use and cardiovascular disease

Overall, the prevalence of heart disease was 12.3% (95% CI [11.0, 13.6]) among people taking any psychoactive medications compared with 4.7% (95% CI [4.4, 4.9]) in those who had not taken a psychoactive medication in the past 12 months (see Table 4-4). This equates to more than a two-fold increase in the odds of having heart disease (OR = 2.4, 95% CI [2.1, 2.8]) after adjusting for sociodemographic differences. Similarly, the prevalence of stroke was 2.8% (95% CI, [2.3, 3.4]) among respondents taking any psychoactive medications compared with 0.8%, 95% CI [0.7, 0.9]) in those who had not taken a psychoactive medication in the past 12 months; this is almost a three-fold increase in the odds of stroke (OR = 2.7, 95% CI [2.0, 3.6]) after adjusting for sociodemographic differences (see Table 4-5).

Almost all of the psychoactive medications had a positive association with heart disease; the only exceptions to this were antipsychotic medications used alone and mood stabilizers used in any combination with other psychoactive medications. Similarly, most of the psychoactive medications had a positive association with stroke (except for anxiolytic medications used alone). There was no association between psychoactive medication use and 10-year cardiovascular risk (OR = 1.1, 95% CI [0.9, 1.2]). Psychoactive medication polypharmacy did not confer greater odds of having heart disease or stroke compared with singular psychoactive medication use.

To account for the effect of any lifetime history of MHDs on CVD, odds ratios were adjusted accordingly and the positive associations between psychoactive medication use and heart disease and stroke persisted but the magnitude of association was reduced slightly. This indicates that there was a negligible confounding effect found between psychoactive medications and lifetime MHDs.

Table 4-4: Twelve-month Psychoactive Medication Use and Heart Disease

	Prevalence of heart disease	Heart disease vs. no heart disease		
		unadjusted	adjusted for demographics[e]	adjusted for demographics[e] and lifetime mental health disorders[f]
	% [95% CI]	OR [95% CI]		
Psychoactive medication use (any) vs. no psychoactive medication use[a]	12.3 [11.0, 13.6]/ 4.7 [4.4, 4.9]	2.9 [2.5, 3.3]	2.4 [2.1, 2.8]	2.3 [1.9, 2.7]
Anxiolytics use alone vs. else[b]	19.7 [16.9, 22.5]/ 5.0 [4.7, 5.3]	4.7 [3.9, 5.6]	2.7 [2.2, 3.4]	2.6 [2.1, 3.3]
Anxiolytic use with antidepressants vs. else[c]	10.9 [8.5, 13.3]/ 5.3 [5.0, 5.6]	2.2 [1.7, 2.9]	2.2 [1.7, 2.9]	1.9 [1.5, 2.5]
Anxiolytic use alone or with any other psychoactive medications including antidepressants vs. else[d]	15.2 [13.5, 17.0]/ 4.8 [4.5, 5.1]	3.6 [3.1, 4.1]	2.7 [2.2, 3.2]	2.5 [2.1, 3.0]
Antipsychotic use alone vs. else[b]	16.0 [1.2, 30.8]/ 5.4 [5.2, 5.7]	3.3 [1.0, 11.0]	2.8 [0.7, 10.5]	2.4 [0.6, 9.4]
Antipsychotic use with antidepressants vs. else[c]	14.4 [7.2, 21.6]/ 5.4 [5.1, 5.7]	2.9 [1.6, 5.4]	3.3 [1.7, 6.7]	2.7 [1.4, 5.4]
Antipsychotic use alone or with any other psychoactive medications including antidepressants vs. else[d]	14.2 [8.2, 20.2]/ 5.4 [5.1, 5.7]	2.9 [1.8, 4.8]	2.8 [1.6, 5.0]	2.4 [1.4, 4.2]
Antidepressant use alone vs. else[b]	7.9 [5.7, 10.0]/ 5.4 [5.1, 5.6]	1.5 [1.1, 2.1]	1.5 [1.1, 2.1]	1.3 [1.0, 1.9]
Antidepressant use with anxiolytics vs. else[c]	10.9 [8.5, 13.3]/ 5.3 [5.0, 5.6]	2.2 [1.7, 2.9]	2.2 [1.7, 2.9]	1.9 [1.5, 2.5]
Antidepressant use alone or with any other psychoactive medications including anxiolytics vs. else[d]	9.2 [7.7, 10.7]/ 5.2 [4.9, 5.5]	1.9 [1.5, 2.2]	1.9 [1.5, 2.3]	1.7 [1.4, 2.0]
Mood stabilizer use alone vs. else[b]	6.1 [0.1, 12.2]/ 5.4 [5.2, 5.7]	1.1 [0.3, 4.7]	1.3 [0.3, 5.2]	1.2 [0.3, 4.7]
Mood stabilizer use with antidepressants vs. else[c]	5.8 [3.2, 8.4]/ 5.4 [5.2, 5.7]	1.1 [0.6, 1.8]	1.3 [0.8, 2.3]	1.1 [0.6, 1.9]
Mood stabilizer use alone or with any other psychoactive medications including antidepressants vs. else[d]	6.7 [4.2, 9.3]/ 5.4 [5.1, 5.7]	1.3 [0.8, 1.9]	1.4 [0.9, 2.2]	1.2 [0.8, 1.9]

Note. Findings are based on reports of 36,960 respondents representing N= 24,984,278 people in the Canadian population. Cells with a dash represent sample sizes too small for disclosure. %=percent; OR=odds ratio; CI= confidence interval.

[a]Psychoactive medication use represents people identified as taking at least one anxiolytic, antipsychotic, antidepressant or mood stabilizer medication within the last year

[b]Indicates that the comparison is all respondents in the sample not including people taking the listed psychoactive medication alone

[c]Indicates that the comparison is all respondents in the sample not including people who were taking the listed psychoactive medication combination

[d]Indicates that the comparison is all respondents in the sample who did not take the listed medication in any combination

[e]Estimates are adjusted for the following demographic variables: sex, age, marital status, household income, education level, immigrant status and ethnicity/race. All variables made a significant contribution to the outcome except marital status

[f]Estimates are adjusted for the following lifetime mental health disorders: schizophrenia, major depressive episode, manic episode, social phobia, panic disorder and agoraphobia

Table 4-5: Twelve-month Psychoactive Medication Use and Stroke

	Prevalence of stroke	Stroke vs. no stroke		
		unadjusted	adjusted for demographics[e]	adjusted for demographics[e] and lifetime mental health disorders[f]
	% [95% CI]	OR [95% CI]		
Psychoactive medication use (any) vs. no psychoactive medication use[a]	2.8 [2.3, 3.4]/ 0.8 [0.7, 0.9]	3.7 [2.8, 4.7]	2.7 [2.0, 3.6]	2.5 [1.8, 3.4]
Anxiolytics use alone vs. else[b]	2.8 [1.8, 3.8]/ 0.9 [0.8, 1.1]	3.0 [2.1, 4.5]	1.4 [0.9, 2.2]	1.4 [0.9, 2.1]
Anxiolytic use with antidepressants vs. else[c]	2.5 [1.6, 3.4]/ 1.0 [0.8, 1.1]	2.7 [1.8, 4.0]	2.6 [1.7, 3.9]	2.2 [1.4, 3.4]
Anxiolytic use alone or with any other psychoactive medications including antidepressants vs. else[d]	2.8 [2.1, 3.5]/ 0.9 [0.8, 1.0]	3.3 [2.4, 4.4]	2.1 [1.5, 2.9]	1.9 [1.3, 2.7]
Antipsychotic use alone vs. else[b]	-	-	-	-
Antipsychotic use with antidepressants vs. else[c]	3.5 [0.2, 6.8]/ 1.0 [0.9, 1.1]	3.6 [1.1, 12.0]	3.6 [1.1, 12.3]	2.8 [0.8, 10.1]
Antipsychotic use alone or with any other psychoactive medications including antidepressants vs. else[d]	4.0 [0.9, 7.1]/ 1.0 [0.9, 1.1]	4.2 [1.6, 11.0]	3.5 [1.3, 9.5]	2.8 [1.0, 8.2]
Antidepressant use alone vs. else[b]	2.7 [1.4, 4.1]/ 0.9 [0.8, 1.1]	3.0 [1.7, 5.2]	2.7 [1.4, 5.3]	2.3 [1.2, 4.6]
Antidepressant use with anxiolytics vs. else[c]	2.5 [1.6, 3.4]/ 1.0 [0.8, 1.1]	2.7 [1.8, 4.0]	2.6 [1.7, 3.9]	2.2 [1.4, 3.4]
Antidepressant use alone or with any other psychoactive medications including anxiolytics vs. else[d]	2.8 [2.0, 3.5]/ 0.9 [0.8, 1.0]	3.2 [2.3, 4.5]	3.1 [2.1, 4.4]	2.7 [1.8, 4.1]
Mood stabilizer use alone vs. else[b]	-	-	-	-
Mood stabilizer use with antidepressants vs. else[c]	3.7 [1.7, 5.8]/ 1.0 [0.9, 1.1]	3.9 [2.1, 7.4]	5.4 [2.8, 10.3]	4.3 [2.2, 8.5]
Mood stabilizer use alone or with any other psychoactive medications including antidepressants vs. else[d]	3.5 [1.8, 5.1]/ 1.0 [0.8, 1.1]	3.7 [2.1, 6.5]	4.5 [2.5, 7.8]	3.6 [2.0, 6.6]

Note. Findings are based on reports of 36,974 respondents representing N= 24,992,487 people in the Canadian population. Cells with a dash are suppressed data due to numbers too small to disclose. %=percent; OR=odds ratio; CI= confidence interval.

[a]Psychoactive medication use represents people identified as taking at least one anxiolytic, antipsychotic, antidepressant or mood stabilizer medication within the

last year
[b]Indicates that the comparison is all respondents in the sample not including people taking the listed psychoactive medication alone
[c]Indicates that the comparison is all respondents in the sample not including people who were taking the listed psychoactive medication combination
[d]Indicates that the comparison is all respondents in the sample who did not take the listed medication in any combination
[e]Estimates are adjusted for the following demographic variables: sex, age, marital status, household income, education level, immigrant status and ethnicity/race. All variables made a significant contribution to the outcome except marital status
[f]Estimates are adjusted for the following lifetime mental health disorders: schizophrenia, major depressive episode, manic episode, social phobia, panic disorder and agoraphobia

4.5 Discussion

This study documented the association between psychoactive medication use, CVD, and short- and long-term cardiovascular risk in Canada. Using data from the CCHS Cycle 1.2, we found that respondents using any psychoactive medications within the past 12 months were twice as likely to have heart disease and three times as likely to suffer from the effects of a stroke compared with Canadians who did not use any psychoactive medications. Furthermore, although there was no association found between psychoactive medication use and 10-year cardiovascular risk, people using psychoactive medications were one and a half times more likely to be at high risk of developing CVD within the next 30 years. Moreover, the presence of mental health diagnoses did not engender additional cardiovascular morbidity or risk beyond psychoactive medication use alone. The findings that women are more likely to use psychoactive medications and that use increases with age have been well described through analyses of the CCHS Cycle 1.2 data and other international psychiatric epidemiological surveys (Alonso et al., 2004; Beck et al., 2005; Paulose-Ram et al., 2004).

This cross-sectional investigation took a broad approach to examining individual psychoactive medication classes and CVD using national survey data, consequently, epidemiological comparisons are limited. Previous studies investigating the associations between antipsychotic, mood stabilizer, or anxiolytic medications and CVD have resulted in either inconclusive findings, or were too narrow in scope (e.g., they focused on a specific medication and a specific cardiovascular outcome) medications to fully contrast this analysis. However, our findings related to the association between antidepressant medication use and heart disease are consistent with previous prospective studies that have quantified this association (Cohen et al., 2000). Our results contribute to an accumulating body of evidence that illustrate the association between psychoactive medication use and cardiovascular morbidity. In

particular, our results are among the first to quantify the association between anxiolytic and mood stabilizer medication use and CVD in a large sample of population-based respondents.

This study used Framingham-based algorithms to investigate short (10-year) and long-term (30-year) risk of CVD among people using psychoactive medications. Our investigation of 10-year cardiovascular risk and psychoactive medications yielded unanticipated findings given the severe cardiometabolic side effects linked to psychoactive medication use previously described in this paper. However, we also documented a significant positive association between 30-year cardiovascular risk group and psychoactive medication use. These divergent findings could either signify that people taking psychoactive medications are more likely to be at higher long-term (compared with short-term) risk of developing CVD or result from differences in the sample or methods used to calculate short- (i.e., a point-based system) and long-term (i.e., an equation-based) cardiovascular risk estimates.

The most likely explanation for these findings arises from the characteristics of our sample. There was a large proportion of middle-aged people who were taking psychoactive medications, this characteristic of the sample could have conferred a protective, short-term benefit (compared with older-aged people) of minimizing the risk of cardiovascular injury (Lakatta, 2002). Age was not controlled in the statistical analysis for the 10- and 30-year risk prediction models because it was incorporated into the risk prediction calculations themselves. Alternatively, although clinical guidelines support the use of points-based and equation-based risk algorithms, points-based systems have been shown to misclassify 15% of respondents compared with equation-based 10-year cardiovascular risk algorithms (Gordon et al., 2010). Therefore, it is possible that the simplified points-based system used to calculate the 10-year cardiovascular risk estimates might have provided less accurate estimates compared with

equation-based algorithms used to calculate the 30-year risk. Further investigation in this area is needed because there has been limited study of the comparison of risk group classification by 10-year points-based and 30-year equation-based algorithms.

We adjusted our estimates by lifetime MHDs because our previous work using the CCHS Cycle 1.2 dataset demonstrated that respondents who were identified as having any MHD were twice as likely to have heart disease or suffer from the effects of a stroke than were Canadians without MHDs. However, a significant limitation of this previous analysis was that it did not control for the confounding influence of concurrent psychoactive medication use among respondents with MHDs. Moreover, it has been shown that excess cardiovascular morbidity and mortality among persons with MHDs can also be attributed to pathophysiologic characteristics of their disorders. The pathophysiological mechanisms underlying these relationships appear to adversely affect the autonomic nervous system (e.g., reducing heart variability and impairing vagal control) and hormonal homeostasis (e.g., causing chronic elevation in cortisol from repeated stress), resulting in metabolic abnormalities, inflammation, insulin resistance, and endothelial dysfunction which promote or accelerate atherosclerosis (Carney et al., 1995; Das & O'Keefe, 2008; Kubzansky et al., 1998; Marano et al., 2011; McEwen, 2003).

Adjusting for MHDs in the present analysis caused slight reductions in the magnitude of the observed associations between psychoactive medication use and CVD and 30-year cardiovascular risk. This indicates that the associations presented represent unconfounded relationships between psychoactive medications and long-term cardiovascular risk, heart disease and stroke. Further investigation of this relationship is needed and should control for both MHDs and psychoactive medication use by examining the association between homogenous groups of respondents and CVD (i.e., four groups of respondents with/without MHDs taking/not taking

psychoactive medications).

It was our intent to determine if psychoactive medication polypharmacy placed respondents at greater risk of CVD and excess cardiovascular risk. Although many of the respondents used two types of psychoactive medications (most commonly paired with antidepressants), we did not document an association between psychoactive medication polypharmacy and increased CVD or cardiovascular risk. This could be the result of our analytic approach as well as limitations of the CCHS Cycle 1.2. For example, we examined psychoactive medication polypharmacy between medication classes (i.e., concurrent use of antipsychotic and antidepressant medications) but did not examine specific medications within drug categories (e.g., concurrent use of two antipsychotic medications). Additionally, the CCHS Cycle 1.2 did not provide the means to assess treatment quality such as medication dose, duration, and adherence. These details could provide valuable insights into the relationship between psychoactive medication polypharmacy and CVD. There is an urgent need for large, controlled, prospective studies examining the effect of psychoactive medication polypharmacy on cardiovascular morbidity.

Overall, these findings serve as a foundation for future investigations of psychoactive medication use and CVD and risk in Canada. Continued examination of the mechanisms responsible for the described associations and explanations of the statistically non-significant associations are needed and can be achieved through a variety of research designs. Nevertheless, this investigation has shed light on a concerning public health problem that needs to be addressed in clinical practice.

4.5.1 Implications for healthcare professionals

Healthcare professionals have a responsibility to mitigate excessive cardiovascular morbidity and mortality suffered by patients using psychoactive medications. Rigorous

screening and proactive interventions are needed to manage the cardiometabolic and cardiotoxic consequences associated with the use of psychoactive medications. Routine monitoring of patients' fasting glucose, body mass index, fasting triglycerides, fasting cholesterol, waist circumference, high-density lipoprotein/low-density lipoprotein, blood pressure, signs of diabetes, and cardiac rhythm is necessary for all patients receiving psychoactive medication treatment, something that is frequently overlooked in clinical practice (De Hert, Vancampfort, et al., 2011; Kilbourne et al., 2007; Sala et al., 2005). Patients with established risk factors should receive extra attention. Clinicians should also consider pharmacologic as well as non-pharmacologic interventions to reduce or alleviate cardiovascular morbidity in this population.

Healthcare providers can actively manage cardiometabolic risk in patients who are using psychoactive medications through non-pharmacological interventions that emphasize maintaining a healthful lifestyle. Daily consumption of fruits and vegetables, regular exercise, and smoking cessation can drastically reduce a patients' cardiovascular and metabolic risk (Lang, Barr, & Procyshyn, 2013; O'Donnell et al., 2010; Yusuf et al., 2004). In the event that these lifestyle interventions are inadequate, clinicians should consider socio-economic barriers to well-being as well as with pharmacological approaches. For example, weight gain and metabolic abnormalities associated with certain classes of psychoactive medications should be assessed on an individualized basis and lower-risk agents should be considered. The risks to physical health and psychiatric benefits of particular psychoactive medications should be carefully weighed because it is known that different medications are associated with varying degrees of cardiometabolic and cardiotoxic risks. Initiating weight-lowering medications and treating significant cardiovascular and metabolic abnormalities can also benefit patients. For example, it is known that metformin addition attenuates olanzapine-induced weight gain in drug naïve first-

episode schizophrenia patients (Wu et al., 2008).

4.5.2 Limitations

There are several limitations associated with the CCHS Cycle 1.2 and with our analyses. The CCHS 1.2 was a cross-sectional survey so the reported bivariate associations between MHDs and CVD and cardiovascular risk cannot be said to reflect causal mechanisms. The sample from which these findings are derived under-represents several important segments of the Canadian population in which psychoactive medication use is most prevalent. For example, people who resided in institutions including hospitals, nursing homes, and prisons or people who were homeless were not included in the CCHS 1.2 sampling frame (Lasser & Sunderland, 1998; Shelton, Ehret, Wakai, Kapetanovic, & Moran, 2010). Further, these analyses utilized some retrospective self-reported data; the validity of this data collection approach is often questioned because the information cannot be verified.

Lifetime mental health status was assessed using the CCHS 1.2/WMH-CIDI, which is a structured diagnostic interview, administered by lay interviewers. Although this is a practical necessity in epidemiological surveys, it results in limited diagnostic precision because the interviewers are not trained clinicians and must keep their interactions within a predetermined script. Moreover, the CCHS 1.2/WMH-CIDI only assessed a limited number of MHDs. Thus respondents identified as having any lifetime MHD may be underestimated, while those with no lifetime disorder may have been overestimated.

The lack of control exerted over medication treatment quality such as dose, duration, and adherence is a significant limitation of this study. The relative contribution of specific medications to CVD and cardiovascular risk should be assessed in future work. It should also be noted that atypical antipsychotic medications were approved for use in Canada in the 1990s, and

this survey was conducted in 2002; it is not clear how the timing of their introduction influenced the findings presented in this analysis. Moreover, the associations reported between individual psychoactive medications and the primary outcomes of this study were made in comparison to people taking other medications as well as no medications. We see this as both a strength and a limitation as this method allowed us to use the whole sample in our analysis and our findings reflect an inclusive comparison group. However, if comparisons had been limited to respondents not taking any psychoactive medications, the reported associations may have been stronger.

It also should be noted that certain liberties were taken to estimate CVD risk with the available data. For example, the CCHS Cycle 1.2 did not provide a cholesterol measure, thus, it was not possible to employ other established cardiovascular risk algorithms that require this information or that incorporate newer biomarkers of cardiovascular risk (e.g., homocysteine, folic acid, C reactive protein, and interleukin 6) (de Ruijter et al., 2009). Decision rules also were applied for the categorical measurement of systolic blood pressure and a rather weak self-reported measure of smoking status was used. The reliability of these methods has not been tested; consequently, the findings should be interpreted with caution. It also is known that 10-year cardiovascular risk algorithms have a tendency to under-predict cardiovascular risk in certain populations (e.g., among people who are younger or among specific subgroups, including kidney transplant recipients) (Lloyd-Jones, 2010; Silver et al., 2011).

Finally, several of the reported estimates had relatively wide confidence intervals (e.g., the prevalence rate of schizophrenia); because bootstrapping techniques were applied to obtain relatively accurate standard errors, the lack of precision is most likely a consequence of small numbers. For this reason, the corresponding proportions or ORs, with wide confidence intervals,

must be interpreted with caution, and where associations would not found, the possibility of insufficient statistical power must be kept in mind.

4.6 Conclusion

This study contributes several noteworthy findings that enrich our knowledge of psychoactive medication use and CVD and risk among Canadians. We have demonstrated that people who take psychoactive drugs are more likely to have heart disease, stroke, and be at high risk of suffering from long-term cardiovascular injury. These findings were not influenced by demographic variables or lifetime MHDs. We also showed that short-term cardiovascular risk predictions were not associated with the taking of psychoactive medications, and the concurrent use of two medications (from different classes) did not appear to increase the odds of CVD or of being in the higher grouping of cardiovascular risk. This analysis used some novel approaches to estimating cardiovascular risk and examining psychoactive medication polypharmacy that could be refined in future work given the limitations of the CCHS Cycle 1.2 and analytical approach. These findings emphasize a need for healthcare professionals to play a more active role in monitoring the physical health of people using psychoactive medications in Canada and offering effective interventions to combat cardiovascular morbidity.

CHAPTER 5: CONCLUSION

5.1 Summary of findings

In this dissertation associations were examined between MHDs, psychoactive medication use, and cardiovascular risk and disease in a representative sample of Canadians. In Chapter 1, it was demonstrated that while a substantial amount of evidence exists of there being a relationship between cardiovascular morbidity and MHDs, there is a lack of evidence specific to the Canadian context. A broad conceptual model of explanatory pathways of the excess cardiovascular morbidity in persons with MHDs was presented and an argument was put forward for the need to examine the relative contribution of MHDs and psychoactive medications to short- and long-term projections of cardiovascular risk and cardiovascular disease (CVD). In this chapter, measurement issues related to the key variables were considered.

Chapter 2 highlighted the importance of measuring psychiatric comorbidity within community-based population health surveys. The findings illustrated that a small proportion of Canadians suffer from a heavy burden of MHDs and that disorders often co-occur. Strong associations were found between all of the disorders paired, signifying that the risk of having a second disorder is significantly greater in the presence of a disorder. It was hypothesized that these patterns of comorbidity may have implications for the classification of MHDs because strong associations could indicate shared underlying or clustered symptomology or psychopathology. Psychiatric comorbidity was more apparent among respondents with disorders occurring within the last 12-months compared to disorders occurring anytime during one's lifetime. Moreover, psychoactive medication use was found to be relatively common and unexpectedly reported by many respondents without identified lifetime or 12-month MHDs. This pointed to the limitation of traditional measurement tools (e.g., the World Mental Health

Composite International Diagnostic Interview (WMH-CIDI)) used to identify people with evidence of MHDs in community-based surveys, which often overlook respondents who have other indications of mental illness. To investigate this further, concordance between the two methods of assessing psychoactive medication use in the CCHS Cycle 1.2 were examined and reasonable consistency was found. However, much weaker agreement was documented between a history of MHDs and psychoactive medication use. Several possible explanations for this mismatch were discussed.

In Chapter 3 an innovative method to assess cardiovascular risk at a population level was used and the resulting findings underscored the association between MHDs and CVD. In particular, our analysis revealed that respondents who were identified as having any lifetime MHD were more likely to be at lower risk (vs. high) of developing CVD within 10 years compared with people without MHDs, and relatively higher 30-year risk of developing CVD. Respondents who reported having had any lifetime MHD were twice as likely to report having heart disease or stroke compared with people without any MHD, after adjusting for differences in socio-demographics. Drawing on insights from Chapter 2, the associations between cardiovascular risk and disease were examined for each MHD alone (e.g., major depressive episode only), with its most common disorder pairing (e.g., major depressive episode and social phobia alone), and in any combination with other disorders (major depressive episode alone or with any other MHD, including social phobia). The association between CVD and each MHD alone was stronger when considered in combination with the disorder's most common pairing. This finding contributes to an accumulating body of evidence that psychiatric comorbidity may be associated with a greater likelihood of CVD.

Finally, in Chapter 4 we investigated whether MHDs confounded the relationship between exposure to antipsychotic medications and cardiovascular risk and disease. This was achieved by examining the association between psychoactive medication use and 10-year and 30-year cardiovascular risk and CVD; then adjusting the observed associations by MHD status. After adjustment for sociodemographic differences, there was no association found between psychoactive medication use and 10-year cardiovascular risk. However, people using psychoactive medications were one and a half times more likely to be at higher risk of developing CVD within 30 years. Moreover, people taking any psychoactive medications had a two-fold increased risk of heart disease and almost a three-fold increased risk of stroke compared with people not taking psychoactive medications. Although almost of the psychoactive medications had positive associations with heart disease and stroke, there was no indication that psychoactive medication polypharmacy conferred a greater risk for cardiovascular risk or CVD over single psychoactive medication use. Lastly, mental health diagnoses did not incur additional cardiovascular morbidity or risk beyond that associated with psychoactive medication use.

5.2 Unique contributions

The studies that compose this dissertation make several unique contributions to a growing body of literature about CVD among individuals with MHDs. They also highlight novel measurement approaches to investigating cardiovascular risk, psychiatric comorbidity, psychoactive medication polypharmacy, and agreement between indicators of MHDs and psychoactive medication use commonly used in community-based mental health surveys. Although these findings are outlined in the individual chapters, there are four key contributions worth revisiting—they are the most significant.

To begin, this study documents the prevalence and association between: (a) specific groupings of MHDs and cardiovascular risk and disease and (b) specific groupings of psychoactive medication use and cardiovascular risk and disease among Canadians. It also provides evidence to suggest that the presence of mental health diagnoses add a negligible contribution to long-term cardiovascular risk, heart disease, and stroke once psychoactive medication use is considered.

Second, this study used 10- and 30-year cardiovascular risk prediction algorithms from the Framingham Heart Study to measure short- and long- term cardiovascular risk among CCHS respondents with MHDs or taking psychoactive medications (D'Agostino et al., 2008; Pencina et al., 2009). Although Framingham-based 10-year cardiovascular risk prediction algorithms have been used in psychiatric epidemiology, this study also employed long-term risk prediction techniques (Cohn et al., 2004; Goff et al., 2005; McCreadie, 2003). This was done because respondents of community mental health surveys include younger respondents; therefore longer-term risk prediction tools are better suited to assess their risk of developing disease.

Third, this dissertation explicitly measured patterns of comorbidity among psychiatric disorders using a Canadian community-based mental health survey. Findings from Chapter 2 highlight that MHDs do not occur independently of one another and that future surveillance could be improved through regular reporting of the number of psychiatric disorders identified in individual respondents, most common disorder pairings within a sample and by measuring the strength of association between disorders. These creative methods have advanced our understanding of the prevalence and patterns of major psychiatric disorders in Canada and can be used to provide richer diagnostic and risk prediction information about affected people.

Finally, our approach to identifying people with MHDs was unique in that it questioned the validity of CCHS 1.2/WMH-CIDI disorder classifications by treating self-reported psychoactive medication use as a proxy indicator of mental health status and contrasted responses using positive and negative percent agreement. Our findings from this analysis showed slight-to-moderate agreement between MHDs and psychoactive medication use; indicating that psychoactive medication use was relatively common and reported by many respondents without identified lifetime or 12-month MHDs. This finding points to traditional measurement tools (e.g., WMH-CIDI) used to identify people with evidence of MHDs in community-based surveys often omitting respondents who have other indications of mental illness. Data collection should be improved in future surveys by asking detailed psychoactive medication use questions alongside diagnostic questions and following up when inconsistencies are encountered.

5.3 Limitations

Although specific limitations of each chapter were described in detail, several broad limitations that involve the CCHS Cycle 1.2 sampling frame, data collection techniques, and interpretation of findings span the entire dissertation and warrant further discussion. The CCHS Cycle 1.2 sample under-represents several important segments of the Canadian population in which MHDs are known to be prevalent. For example, people who were homeless or who lived in institutions were not included in the CCHS 1.2 sampling frame, yet these are the people most likely to have MHDs (Argintaru et al., 2013; Krausz et al., 2013; Lafortune, 2010). Future mental health surveys should consider expanding their data collection techniques to include respondents from these groups to achieve a more representative sample.

The CCHS Cycle 1.2 utilized the WMH-CIDI, which is a structured diagnostic interview,

administered by lay interviewers to identify respondents with MHDs (Kessler et al., 2004). Although this is a practical necessity in epidemiological surveys of large populations, this data collection tool has limited diagnostic precision because the interviewers are not trained clinicians and must keep their interactions within a predetermined script. Further, this technique utilized retrospective self-reported data; the validity of this data collection approach is often questioned because reported information cannot be verified through other means. Researchers must trust that the respondents' self-reported symptoms and past diagnoses are accurate. This can be problematic because respondents may not be able to answer questions accurately; many people do not know or forget the characteristics of their MHDs or are treated with medications that relieve their symptoms so that they do not report having them (Atkinson et al., 1997). In addition, respondents might not be motivated to answer questions truthfully because of a fear that doing so may engender embarrassing or stigmatizing experiences. They may also struggle to comprehend the questions or tasks asked of them, especially if they are complicated, have vaguely defined terms, or require careful recall (Kessler et al., 2004).

There are also a few limitations that affect the interpretation of the reported findings. The CCHS 1.2 was a cross-sectional survey so the reported bivariate associations cannot be said to reflect causal effects. Future prospective studies are needed to document the risk of developing CVD among a sample of Canadians with MHDs or people using psychoactive medications. Further, it should be noted that there are several estimates included in the sample that have relatively wide confidence intervals; because bootstrapping techniques were applied to obtain relatively accurate standard errors, the lack of precision is a consequence of small numbers. For this reason, the corresponding proportions or ORs with wide confidence intervals, must be interpreted with caution.

5.4 Recommendations for research and practice

While specific implications have been outlined in the context of each chapter, the collective work of this dissertation informs recommendations for research and practice. The findings from this dissertation also serve as a foundation for further investigation into the etiology of excess CVD among Canadians with MHDs and impetus for examination of effective clinical interventions to mitigate cardiovascular risk.

5.4.1 Recommendations for research

Continued population-level surveillance of cardiovascular risk and CVD among people with MHDs or taking psychoactive medications is necessary to advance our understanding of the mechanisms responsible for the association between excess cardiovascular morbidity and MHDs. To do this effectively, thoughtful consideration must be given to how MHDs and cardiovascular outcomes are identified, classified and reported. This dissertation has demonstrated that future mental health surveys could be improved by using the full version of the WMH-CIDI to capture a broad array of MHDs and avoid underestimating the prevalence of MHDs within a population. Moreover, incorporating measures of disease severity to enrich diagnostic information, collecting detailed information about psychiatric comorbidity and psychoactive medication polypharmacy to examine their relationship to other health conditions and testing agreement between indicators of mental health status are beneficial practices that should be continued. Further, the feasibility of including homeless individuals within the sampling frame should be considered as they represent an important subgroup of community members known to have high rates of MHDs and suffer from structural inequities.

The degree of psychiatric comorbidity within a sample should be examined by noting the number of disorders identified in individual respondents, distinguishing common disorder

pairings, and measuring the strength of association between disorders. Researchers should also be aware that the prevalence of psychoactive medication use varies depending on the timeframe (e.g., past-12months vs. 2 days) and method (e.g., self-report vs. visual verification) used to measure it. Critical appraisal of the methods used to identify people with MHDs is also essential as it provides feedback on the reliability of diagnostic tools in place. To accomplish this, alternative or proxy indicators of mental health status should be identified (e.g., psychoactive medication use or disease severity) and contrasted with more traditional measures (e.g., WMH-CIDI) to ensure consistency.

Careful selection of measures used to identify people who have or are at increased risk CVD is important. Simple non-laboratory-based multivariate risk prediction algorithms that utilize sex, age, body mass index, systolic blood pressure, diabetes and smoking status, treatment for hypertension can be used in epidemiological studies to gain information about a population's cardiovascular health (D'Agostino et al., 2008). It is preferable to have direct measures of these predictors so that assumptions about proxy measures can be avoided. It is also possible to utilize more complex cardiovascular risk prediction calculations suited to specific groups (e.g., women or certain ethnicities), such as the Reynolds Rick Score, QRISK, ETHRISK or SCORE, by obtaining lipid measurements (e.g., total cholesterol, high density lipoprotein) and combining them with non-laboratory based predictors (Brindle et al., 2006; Conroy et al., 2003; Hippisley-Cox, Coupland, et al., 2007; Ridker et al., 2007). This dissertation has also demonstrated that calculating both short- and long-term cardiovascular risk is advisable in community-based samples as long-term estimates may reveal findings not captured in short-term estimates. Moreover, the collection of detailed CVD outcomes (e.g., beyond dichotomous responses to questions about whether a respondent has a previous history of heart disease and stroke) could

allow for more complex analysis to be conducted and more precise conclusions to be drawn. Agreement or classification accuracy should also be investigated between of points-based and equation-based 10-year cardiovascular risk algorithms to determine if they are equivalent when applied in the context described in chapters 3 and 4. If some or all of these recommendations were implemented in population health research, our understanding of how to accurately identify, categorize, and investigate the breadth of mental and cardiovascular illnesses suffered in community samples would be greatly improved.

Finally, because cross-sectional data cannot infer causation, prospective studies are needed to confirm the observed associations and investigate their underlying etiologies. For example, this study did not explicitly examine the contribution of unhealthful behaviours or access to physical healthcare to increased cardiovascular risk and disease. It would be particularly informative to identify a large sample of participants experiencing a variety of single and comorbid MHDs and follow them for an extended period of to time to learn about how symptoms of their disorders or medication side effects influence their health decisions or behaviours and how they use healthcare services. Moreover, using larger multivariate models that incorporate key interaction terms could also provide additional information about the relative influence of predictive variables. For example, the relationship between CVD and MHDs could be simultaneously adjusted by psychoactive medication use, healthcare services provision, health behaviours and number of MHDs.

5.4.2 Recommendations for practice

The findings of this research demonstrated that Canadians with MHDs are more likely to suffer from CVD than Canadians without MHDs. Healthcare providers have an opportunity to play a key role in mitigating this relationship by improving the healthcare that people with

MHDs receive. Systemic and provider-level barriers have contributed to a situation in which quality primary health care is inaccessible for many Canadians with MHDs.

To tackle systemic barriers to primary healthcare provision, improved integration of primary and mental healthcare services is needed to better address the complex care needs of people who have comorbid mental and physical illnesses and to strengthen continuity of care (Horvitz-Lennon et al., 2006; Kates et al., 1997). This can be accomplished by clarifying who should take responsibility for the full range of health issues experienced by people with MHDs. Offering health assessment, interventions, and health education within community-based mental health teams and creating liaison roles to coordinate services and improve communication and advocacy are two ways that services could be improved (Druss et al., 2010; Lawrence & Kisely, 2010).

Mental healthcare providers are uniquely positioned to improve their patients' general physical health by offering preventative screening and treatment for patients at high risk for or established CVD. Currently, mental healthcare providers do not routinely conduct physical health assessments of their patients; nor do they monitor for adverse physical effects of psychoactive medications (Horvitz-Lennon et al., 2006). Given the prevalence of cardiovascular risk and disease among people with MHDs or taking psychoactive medications, these practices are problematic.

Mental healthcare providers can play a key role in improving the health of their patients by being vigilant in conducting structured physical assessments, especially routine cardiovascular risk screening, before and after initiating psychopharmacological treatment, nurses in particular can offer health promotion interventions to target known cardiovascular risk factors and be conscientious of the impact of psychoactive medications on cardiovascular risk

factors (Jeste et al., 1996; Lawrence & Kisely, 2010; Osborn et al., 2010). Future research into effective implementation of health promotion programs will be particularly valuable. For example, evaluation of the feasibility and efficacy of routine structured cardiovascular screening and/or cardiac rehabilitation programs offered in other settings could be implemented in community-based mental health teams (CMHTs) (Mesidor, Gidugu, Rogers, Kash-Macdonald, & Boardman, 2011). Moreover, the effectiveness of targeted cardiovascular risk reduction interventions offered in CMHTs such as tobacco reduction/cessation, diet and exercise, stress reduction education should be investigated. Psychoactive medications should also be used cautiously with patients at risk for or who have existing cardiovascular morbidity because of the myriad of side effects that these medications have on the cardiovascular system, including orthostatic hypotension, tachycardia, reduction in heart rate variability and slowing of intraventricular conduction (Marano et al., 2011).

Future efforts should be devoted towards developing better policies that facilitate access to primary healthcare services, guidelines for safe cardiometabolic medication treatment and health promotion interventions to be offered in clinical settings.

5.6 Conclusion

The findings of this dissertation research have underscored the association between MHDs, psychoactive medication use and long-term cardiovascular risk and disease in Canada. They have also illustrated the importance of measuring psychiatric comorbidity and alternate indicators of mental health status (e.g. psychoactive medication use) within community-based population health surveys. The findings underscore the need for Canadian healthcare professionals to play a more active role in monitoring the physical health of people with MHDs or using psychoactive medications and offering effective interventions to combat cardiovascular

morbidity. There is a continued need to better understand the etiology of this health disparity and develop proactive practices to bring about further improvements in the physical health and lives of people with MHDs.

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