

**Prospective Associations between Diet Quality and Mental Health in Adults**

by

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A thesis submitted in partial fulfillment of the requirements for the degree of

Master of Science

in

Epidemiology

School of Public Health  
University of Alberta

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## **Abstract**

Mental illnesses are highly prevalent in Canada and pose a significant personal, societal, and economic burden. In recent years, a relationship between diet and mental illness has emerged, highlighting diet as a potential public health target for the prevention of mental illness. This thesis assesses the relationship between diet quality and the number of physician visits for mental illness in Albertan adults.

A prospective study was conducted with survey data from adults enrolled in Alberta's Tomorrow Project and linked administrative health data from Alberta Health. The sociodemographic and lifestyle characteristics of individuals were compared according to categories of the number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses. An updated Healthy Eating Index was developed for the Canadian context (HEI-C 2015) to evaluate diet quality. The relationship between HEI-C 2015 scores and the number of physician visits for mental illness was assessed. Four washout periods were used to exclude participants with physician visits for mental illness prior to baseline to assess the temporal nature of the relationship.

Physician visits for mental illnesses were more common among those with: low household incomes, no university degree, unattached marital status, non-full-time employment, low physical activity, current smoking status, disease comorbidities, dietary supplement use, low alcohol consumption, adherence to red meat and processed meat recommendations, non-adherence to sugar recommendations, and poor diet quality.

Diet quality, measured with the HEI-C 2015, was inversely associated with the number of physician visits for depression, affective disorders, and other mental illnesses. Results remained

significant with washout periods of six months, one year, and variable washout from 2000 to cohort enrollment, but not two years.

As the number of individuals living with mental illness is predicted to rise in Canada with a growing and aging population, preventive strategies are urgently needed. Diet has been highlighted as a potential risk factor, impacting the development and progression of mental illness. Our findings suggest that adults seeking physician care for mental illnesses differ from those not seeking care, in terms of both sociodemographic and lifestyle risk factors. Further, diet quality may be an important risk factor to consider when examining physician visits for depression, affective disorders, and other mental illnesses in this age group. The modifiable nature of diet makes it an important target in population-level primary prevention interventions of mental illness. Future research should build on these results to address gaps in the research and inform public health interventions on dietary improvement.

## **Preface**

The research projects, of which this thesis is a part, received research ethics approval from the Human Research Ethics Board (REB) at the University of Alberta. All the work presented in this thesis was conducted by Shelby Marozoff under the supervision and guidance of the supervisory committee.

Alberta's Tomorrow Project is only possible due to the commitment of its research participants, its staff and its funders: Alberta Health and the Alberta Cancer Prevention Legacy Fund, Alberta Cancer Foundation, Canadian Partnership Against Cancer and substantial in kind funding from Alberta Health Services. The views expressed herein represent the views of the author and not of Alberta's Tomorrow Project or any of its funders.

This study is based in part on data provided by Alberta Health. The interpretation and conclusions contained herein are those of the researchers and do not necessarily represent the views of the Government of Alberta. Neither the Government nor Alberta Health express any opinion in relation to this study.

No part of this thesis has been previously published.

## **Acknowledgements**

I would like to thank all the people who made this thesis possible.

First, thank you to my supervisor Dr. Katerina Maximova, who showed me encouragement, patience, and support throughout this project. I can't thank you enough for taking me on as a student. Thank you to my co-supervisor Dr. Paul Veugelers, who contributed enthusiasm and knowledge – it has been a joy to learn from you. I would like to acknowledge my committee member, Dr. Dean Eurich for sharing his expertise and feedback throughout this project. I am also grateful to Dr. Ming Ye, for all the time he devoted to answering my numerous questions about study design, data availability, and statistical analyses. Finally, I would like to extend my thanks to my external examiner, Dr. Arto Ohinmaa and my chair, Dr. Stephanie Yanow for their time.

Thank you to the ATP team and all participants; without you this project would not have been possible.

I would also like to thank my friends and family, who offered continual encouragement and good humour throughout these two years. To my parents – thank you for your love and endless support.

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## List of Abbreviations

ABC: Alberta Blue Cross  
AH: Alberta Health  
AHEI: Alternative Healthy Eating Index  
AI: Adequate Intake  
ATC: Anatomical Therapeutic Chemical Classification  
ATP: Alberta's Tomorrow Project  
AUC: Area Under the (receiver operating characteristic) Curve  
BDI: Beck Depression Inventory  
BMI: Body Mass Index  
CCHS: Canadian Community Health Survey  
CES-D: Centre for Epidemiologic Studies Depression Scale  
CDHQ-I: Canadian Diet History Questionnaire I  
CFG: Canada's Food Guide  
CIDI: Composite International Diagnostic Interview  
DGA: Dietary Guidelines for Americans  
DGI: Dietary Guidelines Index  
DQI: Diet Quality Index  
DQI-I: Diet Quality Index International  
DQI-R: Diet Quality Index Revised  
DR: Diet Record  
DSM: Diagnostic and Statistical Manual of Mental Disorders  
FFQ: Food Frequency Questionnaire  
GBD: Global Burden of Disease  
GHQ: General Health Questionnaire  
HADS: Hospital Anxiety and Depression Scale  
HDI: Healthy Diet Indicator  
HEI: Healthy Eating Index  
HEI-C: Healthy Eating Index Canada  
HLQ: Health and Lifestyle Questionnaire  
HR: Hazard Ratio  
ICD: International Classification of Diseases  
LAMAD: Literature-Based Adherence Score to the Mediterranean Diet  
MD: Mediterranean Diet  
MDQI: Mediterranean Diet Quality Index  
MDS: Mediterranean Dietary Scale  
MET: Metabolic Equivalent of Task  
MMDS: Modified Mediterranean Diet Score  
MUFA: Monounsaturated Fatty Acids  
MVPA: Moderate-to-Vigorous Physical Activity

NBM: Negative Binomial regression Models  
OR: Odds Ratio  
PDP: Pro-vegetarian Dietary Pattern  
PIN: Pharmaceutical Information Network  
PUFA: Polyunsaturated Fatty Acid  
PYTPAQ: Past-Year Total Physical Activity Questionnaire  
RCT: Randomized Controlled Trials  
RDA: Recommended Dietary Allowance  
rMED: Relative Mediterranean Diet Score  
RNI: Recommended Nutrient Intake  
RR: Relative Risk  
SCID: Structured Clinical Interview for DSM  
SD: Standard Deviation  
SES: Socioeconomic Status  
SFA: Saturated Fatty Acids  
UL: Tolerable Upper Intake Level  
USDA: United States Department of Agriculture  
WHO: World Health Organization  
YLD: Years Lived with Disability

## Chapter 1: Introduction

Mental illnesses account for almost one quarter (22.9%) of the world's non-fatal burden of disease, measured in years lived with disability (YLDs) (1). This makes them the leading global cause of YLDs, ahead of musculoskeletal disorders, HIV/AIDS and tuberculosis, and diabetes (1). The global non-fatal burden of mental illness increased by an estimated 13.5% between 2007 and 2017, likely due to shifting age distributions and improvements in longevity (2). The 2017 Global Burden of Disease (GBD) study estimated the annual prevalence of mental illness to be close to one billion cases globally, with over three million incident cases occurring that year (2). Globally, depressive disorders account for the greatest non-fatal burden of mental and substance use disorders, an estimated 42.5% of that burden (1). Following depression, in decreasing order, the global burden of mental illness is mainly comprised of anxiety disorders (15.3%), drug use disorders (9.4%), alcohol use disorders (7.9%), schizophrenia (7.4%), and bipolar disorder (7.4%) (1).

In Canada, the national 12-month prevalence of mental illness is estimated to be 19.8% of the population, or affecting almost 1 in 5 Canadians (3). In 2011, over 6.8 million Canadians were living with a prevalent mental illness that met diagnostic criteria, which is more than double the number of citizens with heart disease (estimated 1.4 million) or type 2 diabetes (estimated 2.2 million) (3). As the Canadian population grows and ages, the number of individuals suffering from mental illness is predicted to increase 31% by 2041, growing to over 8.9 million prevalent cases (20.9% of the population) (3). One Canadian study used health-adjusted life years, which integrate premature death and reduced functioning, to measure the impact of mental illnesses and found that their burden on the Ontario population was over 1.5 times greater than that of all cancers and seven times that of all infectious diseases (4). Given

that the Canadian population is living longer and aging, decreasing the burden of mental illness should be a public health priority.

The 2012 cycle of the Canadian Community Health Survey (CCHS) examined the prevalence of specific mental illnesses in a representative sample of the general population. It was found that 5.4% of Canadians aged 15 years and older met the criteria for a 12-month prevalence of a mood disorder, with 4.7% of the population experiencing symptoms consistent with depression and 1.5% consistent with bipolar disorder (5). That same study found that an estimated 2.6% of the population had a symptom profile consistent with generalized anxiety disorder, and 10.1% met the criteria for either a drug or alcohol use disorder over the past year (5). Other mental illnesses including psychotic disorders and personality disorders were not assessed in the CCHS 2012, suggesting an underestimation of the true prevalence of mental illness in Canada. Overall, mental illnesses pose a substantial burden both in Canada and globally.

The development of mental illness is influenced by a number of factors, including sociodemographic, genetic, and lifestyle factors. A meta-analysis found the following individual-level sociodemographic factors to be independently associated with worse mental health: low income, marital status/not living with a partner, lack of emotional/social support, female gender, low educational attainment, low socioeconomic status (SES), unemployment, financial strain, perceived discrimination, negative subjective health, and loneliness, among others (6). At a contextual level, a variety of sociodemographic risk factors are associated with the development of mental illnesses, such as neighbourhood deprivation, perceived community violence, and poor air and water quality (6). Exposure to a range of social stressors plays an important role in initiation of mental illness.

The risk of mental illness has a hereditary component – they run in families. However, the idea of a single causative gene being responsible for a particular mental illness is incorrect. A recent genome-wide association study found that of the 18 genes that have been researched most frequently in terms of risk of depression, none were linked to depression measured numerous ways, including lifetime diagnosis, current severity, lifetime symptom count, lifetime episode count and others (7). Similar results have arisen with respect to schizophrenia (8). It is more likely that risk of mental illness is influenced by numerous genes, each of which on its own does not have a significant effect.

A number of lifestyle behaviours have shown strong associations with mental illnesses. For instance, physical activity improves mood and reduces depression and anxiety symptoms (9). A significant body of research supports its relationship with mental illnesses through both primary and secondary prevention (9). The present recommendations for Canadian adults are 150 minutes per week of moderate-to-vigorous physical activity, with only 17% of men and 14% of women meeting these recommendations (10). Alcohol use is also associated with mental illness. An increased number of alcoholic drinks per occasion is linked to a greater risk of depression and evidence suggests that alcohol dependence or abuse may lead to depression (11). In Canada, an estimated 22 million individuals consume alcohol each year, and it is the most widely used psychoactive drug after caffeine, making it a particularly important risk factor (11). Other lifestyle behaviours that show a relationship with mental illness include smoking, unhealthy body mass index (BMI) (i.e., underweight or obese), and irregular sleep cycles (12). Healthy and unhealthy lifestyle behaviours tend to occur in clusters and individuals who display more healthy lifestyle choices show higher life satisfaction and lower psychological distress (12). These



lifestyle behaviours, along with socioeconomic and genetic factors all influence the development and course of mental illness.

Diet has also been proposed as a potential risk factor for mental illness. Analyses from nationally representative dietary studies suggest that Canadians are falling short of the recommendations of Canada's Food Guide (CFG) (13). For instance, in 2004, only 26% of the population over two years of age met the minimum recommended number of daily vegetables and fruit servings for their age and sex group in CFG 2007 (13). From 2004 to 2015, this number of daily vegetables and fruit servings decreased by 0.6 servings per day (13). Similarly, the number of recommended milk and alternatives servings according to CFG 2007 decreased between 2004 and 2015 in the population (13). In 2004, Canadians consumed an estimated 1.7 servings per day, which decreased by 0.1 servings per day by 2015 (13). Poor quality diets are a leading contributor to the global burden of chronic disease (14) and more recently are being investigated as a contributor to mental illness. Both cross-sectional and longitudinal studies have shown a relationship between poor quality diets and increased mental illness symptoms, and vice versa (15-19). Similar results have been shown with adherence to Mediterranean diets being protective against the development of symptoms of mental illness (20-23). Diet as a modifiable risk factor could have a substantial impact on the burden of mental illness in Canada.

Due to their considerable prevalence, mental illnesses place a substantial burden on the health care system through direct and indirect economic costs. Their total direct cost to the national health care system reached \$22.6 billion, or 8.9% of the estimated \$200.5 billion spent on health care in Canada in 2011 (3, 24). Over the following 30 years, these direct costs are expected to reach \$105.6 billion (3). Direct costs to the health care system only include public and private expenses associated with the services and supports of mental health treatment, care,

and recovery, and are a small fraction of the total costs to Canada's economy incurred by mental illnesses (25).

A report from the Public Health Agency of Canada using provincial and territorial administrative health data found that approximately five million (13.6%) Canadians over one-year old accessed health care services for a mental illness in 2009/10 (26). The age-standardized annual prevalence of health care usage related to mental health varied throughout the provinces and territories, from 11% to 16.8%. Alberta displayed an annual age-standardized prevalence of 13.9%, placing it centrally in terms of health services burden. In the same year, individuals with mental illnesses accounted for 25.5% of all acute care hospital days, which amounts to almost 3.6 million days (27). Diagnoses of mental illness, whether most responsible or comorbid, were associated with hospital stays over 2.5 times as long as those not involving a mental health diagnosis (27). These numbers include only acute care hospitalizations and do not include psychiatric hospitals or emergency departments. As hospitalizations in general hospitals only account for an estimated 86.8% of mental health hospitalizations (28), these statistics are likely understated. As the Canadian population grows and ages, the burden of increasing numbers of individuals suffering from mental illnesses will significantly impact the ability of the health care system to provide essential mental health care.

The indirect costs of mental illnesses, which include disability claims, lost productivity at school and work through absenteeism or poor performance, and social and judicial services, add an additional economic burden (25). Approximately 2 in 9 workers (21.4% of the working population) have had their work productivity impacted by a mental illness (3). The annual productivity impact of mental illnesses on the workforce is estimated to be over \$6.3 billion, and predicted to increase to \$16.0 billion by 2041 (3). These workplace costs, together with social,

educational, and judicial costs place the indirect economic burden of mental illness between \$10.5 and \$51.0 billion in Canada presently, depending on the cost components and methods used to estimate economic impact (29-31).

Maintaining the status quo in terms of mental illness prevention, treatment, and awareness will allow this enormous health and economic burden to persist. Research is currently needed into novel preventive strategies for these disorders. The high prevalence of unhealthy diets and other lifestyle behaviours in Canada, along with their putative association with mental illnesses make them an ideal target for addressing this public health burden. The objective of this thesis is to improve understanding of diet quality as a potential risk factor for mental health service utilization in adults.

This thesis employs a “paper-based” format and includes an introduction, a literature review, two chapters that align with the objectives of this thesis, and a discussion of the findings. The first chapter provides a general introduction to mental illness and its burden in Canada and globally. Chapter two is a literature review of diet and mental illness. Chapters three and four comprise the two epidemiological studies of this thesis, both prospective cohort studies using the Alberta’s Tomorrow Project (ATP) dataset and linked administrative health care records. The first study describes the factors associated with the utilization of health services for mental illness in Alberta. The second study examines the association between diet quality and mental illness in a large prospective cohort, accounting for multiple potential confounders, and using administrative health data to define the outcome. The fifth chapter provides a discussion of the main findings, methodological considerations, strengths and limitations, and ultimate conclusions and recommendations.

## **Chapter 2: Literature Review**

This literature review discusses the research on diet and mental illness in adults. It is organized as follows: I first discuss measurement techniques, treatments, and preventive strategies for mental illnesses. This is followed by a discussion of diet in Canada and assessment techniques commonly used in research. Next, I discuss the literature examining diet as a preventive strategy for mental illness and possible confounders in this relationship. The end of this chapter details the gaps in the literature and research objectives.

### **2.1 What is Mental Health and Mental Illness?**

The World Health Organization (WHO) defines mental health as “a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community” (32). Since its inception, the WHO has included mental health in its definition of health “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (32). Mental health is an integral part of overall health and is more than the absence of mental illness. While mental health is the range of emotions, thoughts, and feelings experienced by everyone, mental illnesses are diagnosed disorders that alter thinking, mood, and/or behaviour (33).

Mental illnesses extend to all aspects of an individual’s life, including relationships, career, education, community engagement, and health. The symptoms of these illnesses can range from mild to severe, and depend on the type of mental illness, the individual, and complex interactions of psychosocial, environmental, and biological factors (33). Mental illnesses may present anywhere from a single, brief episode to a chronic disorder. A number of different

mental illnesses have been identified, and the International Classification of Diseases (ICD), 10<sup>th</sup> revision has specified over 400 sub-types (34). Some of the more prevalent mental illnesses include:

- Depression, a disorder which may manifest as sadness, low self-esteem, or feelings of guilt; other symptoms include withdrawal from friends and family and difficulties with sleep (34)
- Bipolar I disorder, a disorder of moods that alternate between periods of exaggerated euphoria, irritability, or both (manic phase) and episodes of depression (depressive phase) (35)
- Generalized anxiety disorder, a disorder which manifests as persistent, excessive, and unrealistic worry about everyday things (35)
- Schizophrenia, a group of disorders characterized by disturbances in thought (e.g., delusions, hallucinations), mood (e.g., blunted, flattened, inappropriate affect), sense of self, and abnormal purposeless behaviour, repetitious activity, or inactivity (34)

Mental illnesses exist in all age, gender, and racial groups, cultures, and social strata, and are a significant issue in populations both in Canada (3-5) and globally (1,2).

## **2.2 Assessing Mental Illness and its Challenges**

How mental illnesses are defined and measured has far-reaching implications for the individuals diagnosed, medical professionals, and society as a whole. Despite increased awareness and knowledge of mental illnesses in recent decades, understanding of their etiology and progression is still incomplete. As a result, the definitions of specific mental illnesses put forward by the major diagnostic manuals – the ICD and the Diagnostic and Statistical Manual of

Mental Disorders (DSM) – often diverge from one another and have been subject to much revision (36).

It is challenging to assign a dichotomy of presence or absence of disease because mental illnesses present in gradients of severity (36). Individuals diagnosed with different mental illnesses often have a number of symptoms in common (36), which speaks to the multidimensional nature of mental illness. Despite this knowledge, classification systems such as the ICD and DSM organize mental illnesses into discrete categories (36), and clinicians diagnose and conceptualize mental illnesses as distinct from normal functioning and one another (37). Diagnoses are made on the basis of thresholds for each component of a mental illness. For example, in the ICD 10<sup>th</sup> revision a depressive episode includes emotional, behavioural, cognitive, and physical components which must be present in the individual for a diagnosis to be made (35, 36). However, these thresholds appear somewhat subjective and “subthreshold” mental problems are common, particularly in childhood. Overall, a number of challenges in measuring mental illnesses arise from the ambiguity and arbitrariness inherent in their definitions.

### **2.2.1 Clinical Interviews for Evaluating Mental Illness**

No biological measurement tool exists at present to aid in quantitatively defining the presence or absence of mental illness (36). Clinicians rely on the presentation and description of symptoms provided by patients and observers to inform diagnoses. Clinical interviews are one technique for assessing mental illness in research and in medical practice. A number of different clinical interviews exist and they may be fully- or semi-structured, or unstructured. Whereas an unstructured clinical interview is more conversation-based and used primarily in clinical

practice, structured clinical interviews are standardized sets of questions, rigorously tested, and used predominantly in research (37).

Two of the most common structured clinical interviews are the Structured Clinical Interview for DSM (SCID) from the American Psychiatric Association and the Composite International Diagnostic Interview (CIDI) from the WHO. No reliability or validity data is available for the SCID-5, the most recent iteration published in 2013. A prior version, SCID-III-R, shows wide variation in reliability (interrater kappa: 0.64-0.93 depression; 0.40-0.91 dysthymia; 0.56-0.95 anxiety disorder) (38). Validity studies of the SCID-III-R have found it to be good (bipolar I disorder sensitivity: 76%, specificity: 93%; depression sensitivity: 84%, specificity: 91%; schizophrenia sensitivity: 74%, specificity: 96%, as compared to SCID-based clinician diagnosis, medical records, and follow-up interview) (39). The SCID is often considered the “gold standard” of clinical interviews, and used extensively in psychiatry, however it is a significant limitation that little is published on the validity and reliability of more recent versions (38).

The CIDI, first developed in 1990, assesses mental illnesses according to criteria in the ICD 10<sup>th</sup> revision and the DSM 3<sup>rd</sup> revision (40). It has been updated with subsequent versions of the DSM and the most recent version, the WHO World Mental Health CIDI 3.0, was published in 2004 (40). The CIDI has been found to have moderate concordance to the SCID (AUC: 0.76 for dichotomous presence of lifetime anxiety, mood, and substance use disorders) (40). These clinical interviews, despite being two of the most commonly used assessment tools in mental illness case ascertainment, only perform moderately well in assessing mental health status.

### **2.2.2 Rating Scales for Evaluating Mental Illness**

Many rating scales exist for mental illnesses and are widely used in epidemiologic research due to their structured and standardized format (41). Rating scales consist of a list of items relevant for the mental illness being evaluated and are either self-completed or filled out by an observer (clinician, trained evaluator, or personal informant) (41). Psychiatric rating scales can be used to assess the severity of mental illness and changes in severity over time, along with assisting in making diagnoses and measuring the side effects of medications (42). The general premise is to assign numerical scores to observations, statements, symptoms, or behaviours, from which diagnoses can be made (42).

Some of the more valuable and frequently used rating scales include the General Health Questionnaire (GHQ) (60, 30, 28, or 12 items) and the Beck Depression Inventory (BDI). The GHQ, which assesses anxiety, mood, and somatoform disorders, has moderate validity (sensitivity: 78%, specificity: 72%) compared to standardized clinical interview (GHQ-30) (43) and reliability (Cronbach's  $\alpha$ : 0.53-0.9) (GHQ-12) (44). The BDI, which assesses the severity of depression in adults and adolescents, has been revised to create the BDI-1A and the BDI-II. The BDI-II as well has good reliability ( $\alpha$ : 0.94) and validity (sensitivity: 94%, specificity: 92%) compared to physician diagnosis (45). While rating scales have the advantages of brevity and standardization, along with the most frequently used ones being valid and reliable, they are not a "gold standard". Individual rating scales are only applicable for certain mental illnesses and their brevity suggests that potentially important information may be missed.

### **2.2.3 Self-Report of Physician Diagnoses for Evaluating Mental Illness**

In order to assess the presence of mental illness in individuals, certain studies have used self-report of physician diagnoses. In such studies, a positive response to the question "Have you ever been diagnosed as having depression by a medical doctor?" would define a case of mental



illness (21). One study which utilized self-report for evaluating mental illness, also conducted a validation study in a subsample of the cohort, taking the SCID-I as gold standard. They found the percentage of confirmed depression to be 74% and the percentage of confirmed non-depression to be 81% (46). The estimated sensitivity and specificity were 0.37 and 0.96, respectively, making self-report of medical diagnosis an adequate method (46). It is possible that stigma may play a role in disclosure of diagnosis in epidemiologic studies, and the sensitivity and specificity of this method would likely differ depending on the level of acceptance of mental illnesses in a population.

#### **2.2.4 Use of Administrative Health Databases for Evaluating Mental Illness**

In Canada, medically necessary hospital and physician services are covered through the universal health care system and delivered by the provinces and territories. Administrative health data provides information on who accesses these services. The administrative health databases in Alberta include practitioner (i.e., physician or allied health professional) claims, inpatient care, ambulatory care, health benefits claims, pharmaceutical dispenses, vital statistics, and population registries (47). There are a number of benefits to administrative datasets including large sample sizes, low costs, increased generalizability, a wide variety of data fields, and often decades of follow-up (48), making them ideal for epidemiologic studies.

For mental illnesses, practitioner claims data is particularly valuable as it provides information on who sought health care for a mental illness through the traditional medical system. Practitioner claims provide fee-for-service and shadow billing claims information for insured health services (47). However, not all individuals with symptoms of mental illness seek physician care, as barriers such as stigma and accessibility concerns exist. Prevalence estimates from administrative databases may underestimate the true prevalence of mental illness in a

population. Furthermore, physicians still rely on assessment methods such as clinical interviews, ratings scales, and their personal expertise to make a diagnosis of mental illness. The validity and reliability of physician diagnosis is only as accurate as these methods. For assessing mental illnesses, administrative health databases have been used less than the other methods, although they provide important information on health service utilization.

## **2.3 Prevention and Treatment of Mental Illness**

### **2.3.1 Current Approaches to Treatments of Mental Illness**

While the number of treatments for mental illnesses and their efficacy has increased in recent decades, there is still significant room for improvement. Substantial numbers of individuals with mental illnesses are unable to become fully symptom-free with treatment or maintain symptomatic improvement. For example, it is estimated that contemporary treatments are effective for only one third of mood disorder cases (49). Further, these particular mental illnesses are especially recurrent; over 50% of individuals who recover from a first episode suffer additional episodes in their lifetime and an estimated 80% relapse following two lifetime episodes (50). Relapse is common with all mental illnesses and frequently occurs following treatment discontinuation, but also occurs even when following treatment as prescribed.

Contemporary treatments for mental illnesses primarily involve brain-stimulation treatments, psychosocial treatments, and pharmacology. Brain-stimulation treatments involve methods such as electroconvulsive therapy, which has been used for decades, as well as more invasive techniques such as deep-brain stimulation. One systematic review found electroconvulsive therapy to be significantly more effective than simulated electroconvulsive therapy or pharmacotherapy for the treatment of depression (51), although others have noted that

there is limited evidence for its long-term efficacy in a variety of mental illnesses (52). Deep-brain stimulation has been found to reduce symptoms in approximately half (53%) of individuals with treatment-resistant depression (53) and a recent meta-analysis found it to be effective in reducing symptoms in 60.0% of individuals with treatment-resistant obsessive-compulsive disorder (54). Despite these numbers, brain-stimulation treatments still involve adverse side effects including mood changes, infections, suicidality, and intracranial hemorrhage (55) and are only used in more severe and resistant cases.

Psychosocial treatments in mental health settings involve techniques such as psychotherapy, cognitive behavioural therapy, and motivational interviewing (56). These methods aim to help individuals' mental health through the identification and alteration of thoughts and beliefs that contribute to psychiatric problems. As with other treatments, the goals of psychosocial approaches are symptom reduction, functional improvements, and ideally, remission of the disorder (57). Of the psychosocial treatments, cognitive behavioural therapy is the most widely studied (57). A review of meta-analyses found it to be effective for a wide range of mental problems particularly for anxiety disorders, somatoform disorders, bulimia, anger control problems, and general stress (57). Although strong evidence exists on the effectiveness of psychosocial treatments, certain mental illnesses do not respond well including substance use disorders, psychotic disorders, and personality disorders (57). Psychosocial treatments are an important treatment strategy for mental illnesses, but do not solve the problem of increasing incident cases being diagnosed each year.

Pharmacological treatments have played a central, though only moderately effective role in reducing the global burden of mental illnesses. As with the treatments highlighted above, they are subject to a number of limitations. Commonly prescribed psychopharmaceuticals include

antipsychotics, antidepressants, mood stabilizers, and anxiolytics, although other medications not indicated for mental illness are often prescribed as well. Side effects are common with psychopharmaceuticals; an estimated half of individuals taking antipsychotic medications fail to comply fully with the prescription (58). A series of three National Institute of Mental Health sponsored trials examined the long-term effects and usefulness of accepted contemporary psychopharmacological treatments in real-world patients with comorbidities (59-61). Collectively, these trials demonstrated that psychopharmacological approaches are less capable of managing the symptoms of mental illnesses than previously demonstrated in trials sponsored by the pharmaceutical industry. For instance, 74% of individuals taking antipsychotics discontinued treatment before 18 months (59) in the trial investigating chronic schizophrenia. Only 37% of individuals prescribed an initial antidepressant went into remission after 14 weeks, in the trial examining depression (60). Finally, in the trial examining bipolar affective disorder, only 24% of individuals receiving psychopharmacological treatment went in to remission for 8 consecutive weeks, a proportion smaller than the 27% who went into remission whilst prescribed a placebo (61). While present treatments exist for all mental illnesses, there is a need for more effective strategies and treatments that prevent the development and progression of mental illnesses.

### **2.3.2 Established and Novel Preventive Strategies for Mental Illness**

Psychiatry has traditionally been based on tertiary prevention – the reduction of severity, discomfort, or disability in established illness (62). Primary and secondary preventive strategies have made major contributions to risk aversion of common chronic diseases, such as cardiovascular disease and certain cancers (62). However, there is robust scientific evidence suggesting that mental illnesses can be prevented as well. As a result of research into the

modifiable risk factors for mental illness, prevention strategies are now being developed to address these factors appropriately. Some of the more common established preventive strategies for mental illnesses include stress reduction and physical activity promotion, for example. Of the lifestyle behaviours affecting the development of mental illness, these are two of the most modifiable in the general population. Based on the success of these lifestyle interventions, diet has more recently been investigated as a primary prevention target for mental illness.

Stress has been highlighted as an important risk factor in the development of mental illness. A large body of evidence exists linking stressful or traumatic life events with the development of mental illness (63). However, it has been shown that chronic daily stress is also a significant predictor of mental health and well-being (63). The cumulative effects of day-to-day stresses such as family responsibilities, financial constraints, and dissatisfaction with studies or job are correlated with both depression and anxiety (63). Interventions targeting daily stress have been shown to be effective at reducing stress, depression, and anxiety, particularly those that target both stressful environments and individual skills and behaviours (62). Workplace stress-reduction interventions have been highlighted as particularly effective, as most adults spend large amounts of time in work environments, and for many employment is a significant source of stress (62). Workplace interventions are common for physical health purposes, but more recently are being suggested as important and cost-effective strategies for the prevention of mental illness.

Physical activity has been linked to a reduction in many mental illness symptoms (9). In clinical populations, physical activity interventions have been found to have moderate-to-strong anti-depressive effects, and less consistently, anti-anxiety effects (64). More recently, physical activity has been investigated as a prevention tool for mental illnesses in non-clinical populations

(64). Physical activity interventions defined as bodily movements produced by skeletal muscles and requiring energy expenditure, were found to be associated with a reduction in depressive symptoms in a recent meta-meta-analysis of randomized trials (64). Smaller, but still significant effects have been found for the reduction of anxiety symptoms in the general population. Given that so few Canadians meet current physical activity guidelines (10), physical activity interventions could have a large impact on the mental health status of individuals with and without mental illness.

Diet has been highlighted as an emerging strategy for the prevention of mental illness. Early research focused on specific nutrients, such as vitamin D (65, 66), B vitamins (67, 68), and folate (69, 70), and their association with illness. However, more recent research has highlighted the need to examine diet as a whole. This shift has largely been motivated by an understanding that individuals do not consume single nutrients or foods in isolation, and their investigation ignores the complex interactions of nutrients in daily diets (71). Further, what is eaten in excess is as important as what is eaten in insufficient quantities (72). Based on this premise of investigating diet as a whole, emerging research has found associations between overall diet and several mental illnesses both cross-sectionally and longitudinally (15-19). Diet displays particular significance as a risk factor for mental illness due to its modifiable nature and the possibility of mental illness prevention via diet warrants further investigation.

## **2.4 Diet and Dietary Assessment**

In Canada, poor dietary habits are the leading contributor to the burden of chronic disease, ahead of smoking, physical activity, and alcohol (14, 73). Despite the established knowledge on the importance of healthy and balanced food choices, Canadian diets fall short of the recommendations put forward by CFG or disease-specific recommendation guides. CFG is

an educational tool developed by Health Canada with the aim of helping Canadians meet nutrient standards and prevent nutrition-related chronic diseases (74). CFG was first developed in 1942 with a focus on malnutrition and ensuring Canadians were receiving key nutrients (74). It has since been revised multiple times to reflect the present state of nutrition knowledge and the nutrition-related diseases affecting the population. The most recent update, in 2019, takes a more holistic approach to diet, highlighting cultural traditions, shared meals, food literacy, and food waste, and not simply required servings of food groups (75).

The previous CFG, which was in place from 2007 to 2019 included age- and sex-specific recommendations on the amounts and types of food to consume within four food groups: vegetables and fruit, grain products, milk and alternatives, and meat and alternatives (74). However, nationally-representative dietary surveys have found that Canadians consistently fail to meet these recommendations (13). The 2015 CCHS found that Canadian adults aged 18-54 years were consuming on average, 4.6 daily vegetables and fruit servings (13), falling short of the recommended 7-8 servings for women and 8-10 servings for men (74). Similarly, adults consumed an average of 5.9 daily servings of grain products (13), which is less than CFG 2007's recommended 6-7 servings for women and 8 servings for men (74). Milk and alternatives servings were also below recommended intakes, with adults consuming an estimated 1.6 daily servings (13) out of the recommended 2 for both men and women (74). However, Canadian adults reported consuming 2.7 daily servings of meat and alternatives (13), out of the recommended 2 and 3 servings for men and women, respectively (74). Of the four food groups, meat and alternatives daily intake increased from 2004 to 2015, whereas vegetables and fruit, grain products, and milk and alternatives daily intake all decreased (13).

Canadians consume a large amount of “other foods and beverages”, which are not part of CFG 2007’s four food groups. In 2015, Canadian adults reported consuming on average, 62 kcal daily from high-calorie beverages (>40 kcal/100g) and 25 kcal daily from low-calorie beverages ( $\leq$ 40 kcal/100g) (13). High-calorie beverages include non-diet sodas, fruit drinks, and sweetened iced tea, for example, and low-calorie beverages include diet sodas, unsweetened or lightly sweetened tea and coffee (13). This consumption of beverages, while large, is lower than the reported daily intake in 2004 and the daily consumption of high-calorie beverages decreased by 30 kcal ( $p < 0.05$ ) for adults in this time period (13). In 2015, Canadian adults also reported consuming an estimated 138 kcal daily from high fat and/or high sugar foods, such as candies, chocolates, syrups, sauces, and fruit jams (13). This is similar to the 132 daily kcal reported in 2004 (13). While the reduction in high-calorie beverages was substantial between surveys, daily intakes of most food groups and “other foods and beverages” either stagnated or worsened over time (13).

One study which used recommendations from CFG 2007, along with the 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult, Canadian Cancer Society recommendations, and recommendations from the 2015 GBD study, evaluated Canadians’ adherence and their resulting economic burden (73). Not meeting the recommendations for intake for both protective foods (vegetables, fruit, whole grains, milk, nuts and seeds) and harmful foods (processed meat, red meat, sugar-sweetened beverages) resulted in an estimated \$13.8 billion economic burden in Canada, of which \$5.1 billion was direct health care costs and \$8.7 billion was indirect costs (73). These direct health care costs represented an estimated 3.9% of all hospital, physician, and drug costs in Canada in 2014 (73). The high cost of poor-quality diets in Canada suggest that



investments promoting healthy eating may result in substantial savings to both direct health care and indirect costs as well as lower risks of developing chronic diseases.

#### **2.4.1 Dietary Assessment Approaches**

Diet is challenging to assess due to its multiple intercorrelated components (76). Dietary assessment methods must also account for the daily variation but underlying consistency that is characteristic of individuals' diets (76). A number of individual-level methods for dietary assessment have been developed that allow investigation of the dietary causes of disease, namely biochemical and food intake methods.

Biochemical indicators or nutritional “biomarkers” are useful techniques for evaluating dietary exposures in epidemiologic studies. They have three uses in such a context; biomarkers can: 1) be used as surrogates for dietary intake when investigating disease occurrence, 2) serve as a measure of nutritional status, and 3) validate other forms of dietary assessment (76). While they have the benefit of being objective measures, it cannot be assumed that there will be a close relationship between the amount of a particular nutrient in the diet and the values obtained via biochemical measurements (77). Dietary intake is one of many determinants of nutritional status – others include homeostatic mechanisms, bioavailability, and genetics – all of which influence the concentration of a particular nutrient in blood or tissues (76). For financial reasons as well as ease, reported food intake measures are preferentially used over “biomarkers” in epidemiological studies investigating diet.

Several methods for assessing dietary intake through participant self-report exist. Two methods, the 24-hour dietary recall and the diet record (DR) method, are based on foods and their amount consumed by an individual on one or more particular days (76). The 24-hour recalls

are generally conducted by trained dietary interviewers who ask questions regarding all foods or drinks consumed within the previous 24-hour period (76). Information on food preparation methods, recipe ingredients, brand names, and portion sizes is solicited (76). A large source of error in the 24-hour recall method stems from the need to accurately recall entire dietary intake of a particular day (76). The DR method is a detailed record of the amounts of foods and beverages consumed on one or more particular days, recorded at time of consumption by the participant in order to minimize the role of memory (78). Both the 24-hour recall and the DR method permit the incorporation of foods from all cultures, and provide quantitative estimates of the energy, foods, and nutrients consumed (78). Further, these methods have the benefit of capturing situational factors surrounding diet including time of day and location of meal consumption.

Food frequency questionnaire (FFQ) is another self-report technique for assessing dietary intake in epidemiologic studies. FFQ differs from 24-hour recall and DR in that they capture the average long-term diet (76). Instead of assessing a day's consumption, FFQ provide information on average intake over weeks, months, or years. While FFQ sacrifice precise measurements on foods consumed, methods of cooking, and combinations of foods in meals, FFQ accurately describe the frequency of consumption of a wide range of foods over a long time period (78) making them a more meaningful method for investigating the dietary causes of chronic diseases. FFQ are the most widely used method of dietary assessment in epidemiology due to lower associated costs, a reduced burden on subjects, and ease in processing (76).

#### **2.4.2 Whole Diet Analyses**

Diet quality indices use information from dietary assessment approaches to evaluate overall diet quality, often through comparison to age- and sex-specific guidelines and Dietary

Reference Intakes (79). They assess the intake of essential nutrients, foods, and food groups to evaluate up to four components of diet: diversity, moderation, adequacy, and balance (79-81). In epidemiologic studies of adults, indices of diet quality have primarily been used in, and some are validated for, the evaluation of chronic disease morbidity and mortality (79). In the first decades of research on diet quality, most indices were developed based on the American dietary guidelines and the Mediterranean diet (81). The Mediterranean diet has received particular attention due to extensive research highlighting the association between adherence and reduced risk of cardiovascular disease and certain cancers (80). A number of diet quality indices have since been created based on the Mediterranean Diet as a result (80). Table 2.1 provides an overview of the popular diet quality indices used in North America for adult populations. Diet quality indices have been developed to examine adherence to the dietary recommendations of Australia, France, Denmark, and other countries, but are not included in the table below. Separate indices evaluating adherence to the Mediterranean Diet are displayed in Table 2.2. All indices vary in their components and as such, provide a different view of an individual's diet.

Table 2.1. Dietary indices evaluating adherence to North American dietary recommendations in adults

<b>Index Author (Year)</b>	<b>Index Components</b>	<b>Scoring System and Range</b>	<b>Purpose</b>
<b>Diet Quality Index (DQI)</b> Patterson et al. (1994) (82)	Total fat, SFA, cholesterol, vegetables and fruits, starches and complex carbohydrates, protein, sodium, calcium	0-2 points for each component Total score: 0 (excellent diet) to 16 (poor diet)	Reflects adherence to 1989 National Research Council Diet and Health
<b>Diet Quality Index Revised (DQI-R)</b> Haines et al. (1999) (83)	Total fat, SFA, cholesterol, fruit, vegetables, grains, calcium, iron, dietary diversity, dietary moderation	0-10 points for each component Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to American 1992 Food Guide Pyramid and 1995 DGA
<b>Diet Quality Index International (DQI-I)</b> Kim et al. (2003) (84)	Overall food group variety, within-group variety for protein source, vegetable group, fruit group, grain group, fiber, protein, iron, calcium, vitamin C, total fat, SFA, cholesterol, sodium, empty calorie foods, macronutrient ratio, fatty acid ratio	0-20 points for variety; 0-40 points for adequacy; 0-30 points for moderation; 0-10 points for overall balance Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to worldwide (WHO) and individual national (American) dietary guidelines, 1992 Food Guide Pyramid, and prior diet quality indices
<b>Healthy Eating Index (HEI)</b> Kennedy et al. (1995) (85)	Grains, vegetables, fruits, milk, meat, total fat, SFA, cholesterol, sodium, variety	0-10 points for each component Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 1990 DGA and 1992 Food Guide Pyramid
<b>Healthy Eating Index 2005 (HEI-2005)</b> Guenther et al. (2007) (86)	Total fruit, whole fruit, total vegetables, dark green and orange vegetables and legumes, total grains, whole grains, milk, meat and beans, oils, SFA, sodium, calories from solid fats, alcoholic beverages, and added sugars	0-5 points for fruits, vegetables, and grains; 0-10 points for milk, meat and beans, oils, SFA, and sodium; 0-20 points for the last component Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 2005 DGA and 2005 USDA MyPyramid
<b>Healthy Eating Index 2010 (HEI-2010)</b> Guenther et al. (2013) (87)	Total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, empty calories	0-5 points for fruits, vegetables, and proteins; 0-10 points for grains, dairy, fatty acids, and sodium; 0-20 for empty calories Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 2010 DGA and 2010 USDA Food Patterns

<b>Healthy Eating Index 2015 (HEI-2015)</b> Krebs-Smith et al. (2018) (88)	Total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars, SFA	0-5 points for fruits, vegetables, and proteins; 0-10 points for grains, dairy, sodium, sugar, and fats Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 2015 DGA and 2015 USDA Food Patterns
<b>Alternative Healthy Eating Index (AHEI)</b> McCullough et al. (2002) (89)	Vegetables, fruit, nuts and soy, ratio of white to red meat, cereal fiber, trans fat, PUFA to MUFA ratio, duration of multivitamin use, alcohol	0-10 points for each component except for 2.5 points for non-use of multivitamins and 7.5 points for use Total score: 2.5 (poor diet) to 87.5 (excellent diet)	Reflects adherence to 1995 DGA, 1992 Food Guide Pyramid, and macronutrient sources associated with reduced chronic disease risk
<b>Healthy Eating Index Canada (HEI-C)</b> Shatenstein et al. (2005) (90)	Grain products, vegetables and fruit, milk products, meat and meat alternatives, total fat, SFA, cholesterol, sodium, dietary variety	0-10 points for all components except 0-20 points for vegetables and fruit Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 1990 DGA, 1992 Food Guide Pyramid, 1992 CFG, and 1990 Nutritional Recommendations for Canadians
<b>Healthy Eating Index Canada 2005 (HEI-C 2005)</b> Garriguet (2009) (91)	Total fruit, whole fruit, total vegetables, dark green and orange vegetables and legumes, total grains, whole grains, milk, meat and beans, oils, SFA, sodium, calories from solid fats, alcohol, and sugar	0-5 points for fruits, vegetables, and grains, 0-10 points for milk, meat and beans, oils, SFA, and sodium, 0-20 for the last component Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 2005 DGA, 2005 MyPyramid, and 2007 CFG
<b>Healthy Eating Index Canada (HEI-C 2010)</b> Jessri et al. (2017) (92)	Total fruits and vegetables, whole fruit, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids refined grains, sodium, empty calories	0-10 points for total fruits and vegetables, whole grains, dairy, fatty acids, refined grains, and sodium; 0-5 points for whole fruit, greens and beans, total protein foods, seafood and plant proteins; 0-20 points for empty calories Total score: 0 (poor diet) to 100 (excellent diet)	Reflects adherence to 2010 DGA, 2010 USDA Food Patterns, and 2007 CFG
<b>Healthy Diet Indicator (HDI)</b>	SFA, PUFA, protein, complex carbohydrates, dietary fiber, fruits and	0–1 points for each component	Reflects adherence to 1990 WHO publication Diet,

Huijbregts et al. (1998) (93)	vegetables, pulses, nuts, and seeds, monosaccharides and disaccharides, cholesterol	Total score: 0 (poor diet) to 9 (excellent diet)	Nutrition, and the Prevention of Chronic Diseases
<b>Dietary Guidelines Index (DGI)</b> Hamack et al. (2002) (94)	Grains, vegetables, fruit, milk, meat, variety of grains, whole grains, variety of fruit, variety of vegetables, total fat, SFA, cholesterol, sweets and sugar-sweetened beverages, sodium, alcohol, and measures of physical activity and BMI	0-2 points for each major guideline Total score: 0 (poor adherence) to 18 (excellent adherence)	Reflects adherence to 2000 DGA

**Abbreviations:** AHEI, Alternative Healthy Eating Index; BMI, Body Mass Index; CFG, Canada's Food Guide; DGA, Dietary Guidelines for Americans; DGI, Dietary Guidelines Index; DQI, Diet Quality Index; DQI-I, Diet Quality Index International; DQI-R, Diet Quality Index Revised; HDI, Healthy Diet Indicator; HEI, Healthy Eating Index; HEI-C, Healthy Eating Index Canada; MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acid; SFA, Saturated Fatty Acids; USDA, United States Department of Agriculture; WHO, World Health Organization

Table 2.2. Dietary indices evaluating adherence to the Mediterranean Diet in adults

<b>Index Author (Year)</b>	<b>Index Components</b>	<b>Scoring System and Range</b>	<b>Purpose</b>
<b>Mediterranean Diet Quality Index (MDQI)</b> Gerber et al. (2000) (95)	SFA, cholesterol, meat, olive oil, fish, cereals, fruit and vegetables, cigarettes per day	0-2 points for each component Total score: 0 (excellent adherence) to 16 (poor adherence)	Reflects adherence to Mediterranean diet
<b>Mediterranean Dietary Score (MDS)</b> Trichopoulou et al. (1995) (96)	MUFA to SFA ratio, alcohol, legumes, cereals, fruit and nuts, vegetables, meat and meat products, milk and dairy products	0-1 points for each component based on sex-specific median values Total score: 0 (poor diet) to 8 (excellent diet)	Reflects adherence to Mediterranean diet
<b>Mediterranean Dietary Score adapted (MDS-adapted)</b> Haveman-Nies et al. (2002) (97)	MUFA to SFA ratio, alcohol, legumes/nuts/seeds, cereals, vegetables and fruits, meat and meat products, milk and dairy products	0-1 points for each component based on sex-specific median values Total score: 0 (poor diet) to 7 (excellent diet)	Reflects adherence to Mediterranean diet
<b>Modified Mediterranean Diet Score (MMDS)</b> Trichopoulou et al. (2003) (98)	MUFA to SFA ratio, alcohol, legumes, cereals, fruit and nuts, vegetables, meat and meat products, milk and dairy products, fish	0-1 points for each component based on sex-specific median values Total score: 0 (poor diet) to 9 (excellent diet)	Reflects adherence to Mediterranean diet
<b>A priori Mediterranean pattern</b> Martinez-Gonzalez et al. (2002) (99)	Olive oil, fiber, fruits, vegetables, fish, alcohol meat (or meat products), white bread/rice/pasta	0-1 points for each component based on dose-response relationship between consumption of food item and risk of myocardial infarction Total score: 0 (poor diet) to 8 (excellent diet)	Reflects adherence to Mediterranean diet
<b>Mediterranean Score</b> Martinez-Gonzalez et al. (2004) (100)	Olive oil, fruit, vegetables or salad, fruit and vegetables, legumes, fish, wine, meat, white bread and rice or whole-grain bread	0-1 points for each component Total score: 0 (poor diet) to 9 (excellent diet)	Reflects adherence to Mediterranean diet

<b>MedDietScore</b> Panagiotakos et al. (2006) (101)	Non-refined cereals, potatoes, fruits, vegetables, legumes, fish, red meat and products, poultry, full fat dairy products, use of olive oil in cooking, alcoholic beverages	0-5 points for each component Total score: 0 (poor diet) to 55 (excellent diet)	Reflects adherence to Mediterranean diet
<b>Relative Mediterranean Diet Score (rMED)</b> Buckland et al. (2010) (102)	Vegetables, fruit, legumes, fresh fish, cereals, olive oil, alcohol, meat, dairy products	0-2 points for each component based on sex-specific tertiles Total score: 0 (poor diet) to 18 (excellent diet)	Reflects adherence to Mediterranean diet
<b>Literature-based Adherence Score to the Mediterranean Diet (LAMD)</b> Sofi et al. (2014) (103)	Fruit, vegetables, legumes, cereals, fish, meat and meat products, dairy products, alcohol, olive oil	0-2 points for each component based on mean value of weighted medians (or means) +/- 2 SD Total score: 0 (poor diet) to 18 (excellent diet)	Reflects adherence to Mediterranean diet

**Abbreviations:** LAMD, Literature-based Adherence Score to the Mediterranean Diet; MDQI, Mediterranean Diet Quality Index; MDS, Mediterranean Dietary Score; MMDS, Modified Mediterranean Diet Score; MUFA, Monounsaturated Fatty Acid; rMED, Relative Mediterranean Diet Score; SD, Standard Deviation; SFA, Saturated Fatty Acids



### **2.4.3 Diet Quality Index International (DQI-I)**

One of the more commonly used diet quality indices in North America is the DQI and its more recent iterations. The DQI-I was developed in 2003 to facilitate cross-national comparisons of diet quality (84). It focuses on concerns related to both chronic disease and undernutrition and as a result may be used in populations that differ greatly in their economic status (84). The DQI-I's strengths include its evaluation of all four aspects of diet quality: variety (food and nutrient choice diversity), adequacy (sufficiency of intake of foods and nutrients), moderation (whether certain foods and nutrients are consumed in excess), and balance (equilibrium of food and nutrient intake), and its inclusion of both food and nutrient intake measures (84). However, the DQI-I has not been updated since its creation and was based on worldwide and national dietary guidelines that have since been updated such as the 1996 WHO Dietary Guidelines and 1992 USDA Food Guide Pyramid. The DQI-I was validated in healthy adults in the United States and China to successfully capture variability in intake of select foods (fruit and vegetable servings) and nutrients (% energy from fat and saturated fat, fibre, riboflavin, vitamin C, calcium, iron, sodium, and zinc) (all  $p < 0.0001$ ) (84). The total DQI-I scores in China and the United States were similar – 60.5 and 59.1 out of a possible 100, respectively – but the scores of each component and of the four aspects of diet quality varied significantly by country (84). This suggests that the DQI-I is an adequate tool for the assessment of diet quality in diverse populations, regardless of the particular country of origin's nutritional status and cultural dietary patterns.

### **2.4.4 Healthy Eating Index-Canada (HEI-C)**

The HEI was developed in 1995 to reflect adherence to the DGA, which provides evidence-based dietary recommendations, primarily for the prevention of chronic disease (85).

The HEI has since been revised with each iteration of the DGA every five years (86-88). The HEI-2005 and HEI-2010 have both been adapted to recommendations in Canada's Food Guide (CFG) 2007 and applied to a nationally-representative sample of participants  $\geq 2$  years of age in the 2004 CCHS-Nutrition (91, 92). The mean HEI-C 2005 score was 58.8 out of 100 and the mean HEI-C 2010 score was 50.9, which suggests a need for dietary improvement in Canada (91, 92). Both versions of the HEI-C assess two aspects of diet quality: adequacy and moderation. Neither balance, nor variety is measured in either the HEI-C 2005 or the HEI-C 2010 (91, 92), which is a limitation. Other limitations include the failure to assess micronutrients other than sodium in either of the Canadian indices and the failure to assess the quality of carbohydrate intake in the HEI-C 2005.

Both the HEI-C 2005 and 2010 have been validated in Canadian populations, through the assessment of associations between scores and certain lifestyle and socioeconomic characteristics. Participants scoring higher on the HEI-C 2005 had increased daily vegetables and fruit consumption, used vitamin and mineral supplements, and were not Aboriginal (all  $p < 0.05$ ) (91). Similarly, participants scoring higher on the HEI-C 2010 were more likely to be women, older, vitamin users, physically active, non-smokers (all  $p < 0.0001$ ), and less likely to under-report energy intake ( $p = 0.0146$ ) (92). Greater HEI-C 2010 scores were also associated with a greater consumption of beneficial micronutrients, including fiber, calcium, vitamin A, vitamin D, vitamin C, phosphorus, and magnesium density (all  $p < 0.0001$ ), among others (92). The Canadian adaptations of the HEI adequately measure diet quality in Canadian populations.

#### **2.4.5 Mediterranean Diet Score (MDS)**

The MDS was developed in 1995 to measure adherence to the traditional Mediterranean diet and contains eight components: monounsaturated-to-saturated fat ratio, alcohol, legumes,

cereals, fruits, vegetables, meat and meat products, and dairy (96). Values of 0 or 1 are assigned to each component and overall scores range from 0 to 8, with higher scores indicating greater adherence. Contrary to the HEI and DQI, the MDS' scoring system is unique to each population as the cut-off value for each component is the sex-specific median (96). Consequently, individuals' overall scores in one population may be different in another, depending on the population medians. Variations of the MDS have emerged over the years (Table 2.2) and been linked to numerous beneficial health outcomes (98). The most frequently used adaptation, the MMDS, was revised in 2003 to include fish intake, an important part of the Mediterranean diet associated with a lower risk of coronary heart disease and resulting death (98). The overall score of the MMDS ranges from 0 (minimal adherence) to 9 (maximal adherence). The MMDS, which is used extensively in epidemiological research and adapted from the seminal MDS is an important diet quality index, providing a different perspective on diet quality than those based on dietary guidelines.

## **2.5 Diet and Mental Illness**

### **2.5.1 Diet Quality as a Preventive Strategy for Mental Illness**

Diet quality indices are hypothesis-driven methods of evaluation based on existing knowledge of what characterizes a “healthy diet” (104). They quantify the extent to which individuals' diets conform to dietary recommendations. A large body of evidence exists examining overall diet quality, assessed using these composite measures, as a preventive strategy for mental illness (15-19). One cross-sectional study of 1,382 men and 3,129 women aged 35-69 in Nova Scotia, Canada found that depressed individuals were less likely to report a high quality diet, as measured by a modified HEI, with a somewhat more pronounced effect among women (OR: 0.75) than among men (OR: 0.78) (17). Depressive symptoms were measured using the

Patient Health Questionnaire, which generated a score ranging from 0 (minimum) to 27 (maximum), where a score of 10 or greater and/or current antidepressant use indicated major depression. This association was independent of a large number of potential confounders including demographic and lifestyle factors, chronic disease comorbidities, and family history of disease (17). Similarly, a prospective cohort study of 15,093 adults in the population-based Seguimiento Universidad de Navarra cohort reported inverse and significant associations between three distinct diet quality scores and depression risk among Spanish men and women over 8.5 years of follow-up (18). Better adherence to the Mediterranean Diet Score (MDS) (HR: 0.84), Pro-vegetarian Dietary Pattern (PDP) (HR: 0.74), and Alternative Healthy Eating Index-2010 (AHEI-2010) (HR: 0.60) was associated with a reduced risk of depression, which is particularly significant as each of these diet quality indices evaluates different components of diet, which differ in their vitamin, mineral, and macronutrient composition (18). Epidemiological evidence exists for an association between habitual diet quality and depression globally and across the lifespan (15-19).

Systematic reviews and meta-analyses examining diet quality as a preventive strategy for depression have provided evidence suggestive of an association, but have also highlighted the limitations to the field. A recent meta-analysis of prospective studies (n=29) found that adherence to high-quality, healthy diets – whether healthy/prudent (OR: 0.77), Mediterranean (OR: 0.75), pro-vegetarian (OR: 0.78), or Tuscan (OR: 0.64) – was associated with a lower incidence of depressive symptoms in a linear dose-response manner (overall OR: 0.77) (105). However, they noted that diet was not associated with depression incidence in studies that controlled for the severity of depression at baseline or those that used depression diagnosis as the outcome (105). Another meta-analysis examined both longitudinal and cross-sectional studies

and found evidence for an inverse association between healthy diet and depression, particularly with dietary measures evaluating adherence to a traditional Mediterranean diet (n=10; RR: 0.67 for cohort studies; 0.66 for cross-sectional studies) or lower adherence to a pro-inflammatory diet (n=9; RR: 0.76 for cohort studies; 0.64 for cross-sectional studies) (104). Studies examining HEI/AHEI score (n=7; RR: 0.76 for longitudinal studies; 0.53 for cross-sectional studies) or adherence to the Dietary Approaches to Stop Hypertension diet (n=4; RR: 0.89 for cohort studies; 0.90 for cross-sectional studies) and depression incidence are inconclusive and limited by the fewer number of studies (104). While results are predominantly consistent, all reviews highlight the limitation of heterogeneity across studies in relation to the measurement of diet quality, mental illness assessment, and study sample (104, 105). Specifically, it is difficult to compare studies that assess diet quality using a variety of diet quality indices, assess mental illness through symptom scales, self-report of physician diagnosis, linked administrative health records, or other methods, and assess the relationship in populations that differ in age, sex, and geographic locations. A number of proposed directions for future research are highlighted in these systematic reviews, namely the need for: 1) large, population-based prospective cohort studies, 2) the inclusion of all relevant confounders, and 3) investigations into mental illnesses other than depression (104, 105).

While the majority of epidemiological research has focused on diet's association with depression, a small number of studies have examined other mental health outcomes, including perceived mental health, wellbeing, and anxiety. One study of 15,546 individuals aged 19-70 from Canada's 10 provinces investigated the relationships among food insecurity, diet quality, and perceived mental health in a cross-sectional design (15). Respondents rated perceived mental health based the question "How would you say your mental health is? Excellent? Very good?

Good? Fair? Poor?” which was dichotomized as poor/fair (poor mental health) and good/very good/excellent (good mental health). An association between perceived mental health and both food insecurity (OR: 1.60) and poor diet quality (OR: 1.61) was found (15). A population-based cross-sectional study of adults aged 50-69 years in Ireland investigated diet quality and its association with self-reported wellbeing, anxiety, and depressive symptoms, assessed with the World Health Organization-5 Well Being Index (WHO-5), Hospital Anxiety and Depression Scale (HADS), and Centre for Epidemiologic Studies Depression Scale (CES-D) tools, respectively (16). While the likelihood of wellbeing was greater for those who had a high diet quality relative to those with low diet quality (OR: 1.67;  $p=0.007$ ), significant results were not found for the risk of depressive symptoms (OR: 1.06;  $p=0.80$ ) or anxiety (OR: 0.77;  $p=0.22$ ) (16). However, a cross-sectional Norwegian study of adults aged 46-49 and 70-74 years found an association between 1-SD increases in diet quality and reduced anxiety assessed with the HADS scale in women (OR: 0.77), but not in men (OR: 1.00) (19). In relation to these findings, it has been hypothesized that increased anxiety may be related to an increased adherence to dietary practices designed to protect against adverse mental health outcomes (19). Research is needed to further investigate the role of diet in the development of these mental health outcomes as well as others such as bipolar disorder, psychotic disorders, and substance use disorders, which have been studied less.

### **2.5.2 Diet Quality as a Treatment for Mental Illness**

Beyond acting as a preventive strategy for mental illness, results have emerged from randomized controlled trials (RCT) that dietary interventions, with a whole-of-diet approach, can act as treatments and result in improved depression outcomes in various clinical populations (106). A systematic review of RCT ( $n=17$ ) which investigated the role of diet in the treatment of

depression found an effect size among the positive studies for validated depression scores ranging from 0.19 to 2.02 (Cohen's  $d$ ) (106). This is an effect size comparable to that from pharmacotherapy or psychotherapy (106, 107). Existing research suggests that dietary interventions could be used as preventive strategies at the population level, thereby reducing the public health burden of mental illness.

More recently, a 12-week, parallel-group, single blind RCT, titled the Supporting the Modification of lifestyle in Lowered Emotional States trial, was conducted in Australia, to assess the treatment of moderate to severe depression (108). The intervention was personalised dietary advice and nutritional counselling support sessions with a clinical dietician (108). The control condition involved a 'befriending' protocol, with a visit schedule and length the same as the dietary intervention, but in which neutral topics of interest to the participant were discussed (108). At 12 weeks, the dietary intervention group displayed a significantly greater improvement in depressive symptoms than the control group, as measured by the Montgomery-Åsberg Depression Rating Scale (Cohen's  $d$ : -1.16), with an estimated change in the depression rating score of 7.1 points from baseline (108). The results of this trial suggest that dietary improvement may be an efficacious strategy for the treatment of depression. However, certain issues have since been highlighted by other researchers which may account for the remarkable results, namely expectation bias and difficulties with blinding (109). This trial, being the first RCT to investigate diet quality improvement as a treatment for depression, brings attention to a field that is of considerable public interest, but based on methodological concerns, conclusions regarding causality should not be drawn based on its results. Overall, diet quality as a strategy for the prevention of mental illness – whether primary, secondary, or tertiary – is promising, but in need of more methodologically rigorous studies.

### 2.5.3 Dietary Patterns and Mental Illness

Analysis of dietary patterns, which derives shared patterns in populations via data-driven statistical techniques, is another method of characterizing overall diet (71). Routinely, studies identify two or more dietary patterns, one of which reflects healthy dietary habits (typically named “prudent” or “traditional”) and another which reflects unhealthy (“western”) dietary habits (110). For instance, in the 16,744 men and women aged 35-69 years enrolled in Alberta’s Tomorrow Project (ATP) in Canada, cluster analysis based on FFQ data derived four dietary patterns for men and three dietary patterns for women (111). For men, the four clusters were labeled “dairy and sweets”, “Western”, “healthy”, and “wholemeal bread and jam”; the three clusters for women were “Western and sweets”, “healthy”, and “low fat dairy and breakfast cereal” (111). In both men and women, the healthy cluster was characterized by higher energy contributions from healthy foods, such as fruits, poultry, vegetables, and fish, and lower energy contributions from meat, sweets, soda, other bread, French fries, butter, margarine, or mayonnaise (111). For both sexes, the healthy cluster had a greater proportion of individuals with normal BMI ( $18.5 < 25 \text{ kg/m}^2$ ), smaller waist circumference, higher educational attainment and physical activity levels, in comparison with other clusters (all  $p < 0.05$ , compared separately for men and women) (111). The derived healthy, Western, and Western and sweets patterns broadly correspond to the two predominant patterns of “prudent/healthy” and “Western” that have been described in different populations (110), although have yet to be linked to any mental health outcomes in this population.

Some cross-sectional studies have found “healthy” dietary patterns to be inversely associated with depressive symptoms and “western” dietary patterns to be associated with increased depressive symptoms. In one cross-sectional study of middle-aged or older (aged 42,



48, 54, or 60 years) Finnish men, a 1-SD increase in score for the “prudent” dietary pattern involving a high intake of fresh and cooked vegetables, fruits, whole-grain bread, poultry, berries, low-fat cheese, and fish was found to be associated with a lower prevalence of elevated depressive symptoms (OR: 0.75) (112). They further found that a 1-SD increase in score for the “western” dietary pattern with a high intake of sausages, meats, sweet snacks, candies and chocolate, sweet soft drinks and juices, baked potatoes, and French fries, was associated with an increased prevalence of elevated depressive symptoms (OR: 1.41) (112). A third “mixed” pattern was not associated with depressive symptoms (OR: 1.10) (112). In a cross-sectional study of 4,180 men and 2,196 women aged 20-79 in the United States, two dietary patterns were derived: a “Western” pattern loaded with refined grains, white potatoes, tomatoes, and cheese, and a “prudent” pattern loaded with whole grains, dark green vegetables, orange vegetables, and fish and shellfish (113). No statistically significant association was found between the highest quintile of “Western” dietary pattern and depression scores in both men (OR: 0.71;  $p=0.393$ ) and women (OR: 0.80;  $p=0.375$ ) (113). The highest quintile of “healthy” dietary pattern was inversely associated with depression scores in women, after adjusting for confounders (OR: 0.60;  $p<0.001$ ), but not men (OR: 0.76;  $p=0.408$ ) (113). The studies and the larger body of research indicate that the cross-sectional relationship between dietary patterns and depression is promising but inconclusive at present.

A number of prospective studies have investigated the relationship between data-driven dietary patterns and depression. In one study of 1,358 community-dwelling older adults (67-84 years) in Québec, Canada, followed-up between one and three years, three dietary patterns were derived (114). The first, “varied diet”, was loaded with fruit, fruit and vegetable juice, other vegetables, nuts and seeds; the second, “traditional diet”, was loaded with red meat, butter and

fats, alcoholic beverages, potatoes, and soups; the third, “convenience diet” was loaded with sugar beverages, fried foods, and fast foods (114). In an unadjusted model, individuals in the highest tertile of adherence to the “varied diet” pattern were less likely to develop depression at three years follow-up relative to the lowest tertile (OR: 0.58; p=0.007), but this association was no longer significant once confounders were controlled (OR: 0.86; p=0.533) (114). Neither the “traditional diet” (OR: 0.96; p=0.876) nor the “convenience diet” (OR: 0.89; p=0.579) patterns were associated with depression in this population (114). Another prospective study following three age cohorts (20+; 40+; 60+ years) of Australian men and women over eight years displayed an association between dietary patterns and depressive symptoms, with those in the lowest intake of a “prudent” diet (OR: 1.18 in oldest cohort) or the highest intake of a “western” diet (OR: 1.14 in oldest cohort) showing increased risk of subsequent depressive symptoms (115). The “prudent” diet reflected consumption of fresh vegetables, salad, fruit and grilled fish, whereas the “western” diet was characterised by the consumption of roast meat, sausages, hamburgers, steak, chips, crisps, and soft drinks (115). Overall, as with the cross-sectional research, the prospective association between dietary patterns and depression has not been conclusively determined.

To account for the wide variability of results in research examining data-driven dietary patterns and mental illnesses, in which some studies find strong associations and others find no significant results, differences in dietary patterns have been highlighted. Diet varies between geographical regions and cultures and as a result, the dietary patterns generated via statistical techniques such as principal component analysis and cluster analysis, which allow an examination of dietary intakes in particular populations, will also differ. This distinction partially explains the inconsistency between studies. For example, while derived “healthy” dietary patterns typically contain vegetables, fruits, and fish (111, 113,115-117), country- or region-

specific “healthy” dietary patterns differ in their inclusion of certain foods, such as poultry, low-fat cheese, olive oil, legumes, and other foods (112, 117).

A number of systematic reviews have been conducted in the past decade evaluating the relationship between dietary patterns and depression. The most recent of which, published in 2017, examined 21 studies from ten countries with 117,229 participants (118). Evidence for an association between a “healthy” dietary pattern and a decreased risk of depression was found (OR: 0.64) (118). It was further found that a “western” dietary pattern was associated with an increased risk of depression (OR: 1.18) (118). To explore these relationships, subgroup analyses were conducted and it was noted that region played a particularly important role in the relationship, with Asian and “other” subjects displaying more obvious associations between dietary patterns and depression (OR: 0.59 for “healthy” patterns and 1.25 for “western” patterns), as compared to European and American subjects (OR: 0.82 for “healthy” patterns and 1.14 for “western” patterns) (118). The association was also more prominent in subjects less than 50 years of age (OR: 0.61 for “healthy” patterns and 1.31 for “western patterns), as compared to those greater than 50 years of age (OR: 0.70 for “healthy” patterns and 1.08 for “western” patterns) and in case-control studies (OR: 0.58 for “healthy” patterns and 1.25 for “western” patterns), as compared to cohort studies (OR: 0.68 for “healthy” patterns and 1.16 for “western” patterns) (118). This is evidence of a need for more prospective cohort studies, which are less susceptible to recall and selection bias than the cross-sectional studies commonly used in this field.

As with diet quality, there is less research investigating the relationship between data-driven dietary patterns and mental illnesses other than depression. One cross-sectional study, using a randomly selected population-based sample of 1,046 Australian women aged 20-93 years

utilized the SCID-IV to investigate anxiety outcomes in relation to dietary patterns (116). They found that a 1-SD increase in score for a dietary pattern characterized by a high intake of vegetables, fruit, beef, lamb, fish, and whole-grain foods, called the “traditional” dietary pattern was associated with a lower likelihood of anxiety disorders (OR: 0.68) (116). One cross-sectional study investigating dietary patterns and anxiety as measured by the HADS in a Norwegian adult population found similar results (19). In both men (OR: 1.27;  $p < 0.001$ ) and women (OR: 1.29;  $p < 0.001$ ), the “Western” dietary pattern, comprised of meat and liver, processed meats, pizza, salty snacks, and chocolates, was positively associated with anxiety, but not significant after adjusting for confounders (19). Additionally, in women, a “traditional” dietary pattern (OR: 0.77;  $p = 0.001$ ), comprised of fish and shellfish, potatoes, fruits, vegetables, butter and margarine, and eggs, along with the “healthy” dietary pattern (OR: 0.87;  $p = 0.01$ ) of vegetables, fruits, salads, and rice, demonstrated a significant inverse relationship with the likelihood of anxiety following adjustment (19). Few other high quality studies exist examining the relationship between data-driven dietary patterns and anxiety or mental illnesses other than depression. Overall, research on the association between dietary patterns and mental illness highlights the role of diet as a potential risk factor, but the heterogeneity between derived dietary patterns makes drawing conclusions about their role difficult at present.

#### **2.5.4 Theory-driven Mediterranean Diet Indices and the Prevention of Mental Illness**

Comparative studies have found the lifetime prevalence of mental illness to be lower in Mediterranean countries than in Northern European countries (119). Age-standardized suicide rates, which serve as an indirect reflection of the prevalence of severe depression, are also typically lower in Mediterranean countries (120). As a result, it has been suggested that the Mediterranean diet (MD) may be protective against depression. The MD is characterized by a

high intake of olive oil, grains, and plant foods, low intake of saturated fat, meat, and poultry, and moderate consumption of fish, dairy products, and alcohol (98). Previous research has shown the MD to be beneficial with respect to cardiovascular disease (121), multiple cancers (122), diabetes (123), metabolic syndrome (124), and overall mortality (103). The MD is considered a good model for healthy eating, and its link with anti-inflammatory effects and reduced oxidative stress support a possible pathway between diet and depression.

A meta-analysis of nine studies, of which seven were cross-sectional, examined the relationship between adherence to the MD (measured via a priori diet scores) and risk of depression (20). High adherence to the MD was consistently associated with reduced risk for depression (OR: 0.68) (20). Even moderate adherence to the MD was found to be protective against depression, although to a lesser extent than high adherence (OR: 0.77) (20). However, the cross-sectional nature of these studies does not preclude the possibility of reverse causality.

Building on the cross-sectional research, a small number of prospective studies have investigated the link between adherence to the MD and risk of depression. In a cohort of 11,800 Spanish university graduates followed-up over 8.5 years, the prospective relationship between adherence to the MD and the risk of depression was assessed (21). When adherence to the MD was appraised using an index including: 1) high ratio of monounsaturated to saturated fatty acids, 2) moderate alcohol intake, 3) high intake of legumes, 4) high intake of cereals, 5) high intake of fruits and nuts, 6) high intake of vegetables, 7) low intake of meat and meat products, 8) moderate intake of milk and dairy products, and 9) high fish intake, an association was found between the upper categories of high adherence with reductions in depression risk (HR: 0.82) (21). Recent evidence from a prospective cohort study of 2,031 women and 1,492 men in France with mean follow-up of 12.6 years supports these findings (22). In this study, higher adherence

to the MD, as measured by the relative Mediterranean diet score (rMED) at midlife was associated with a lower risk of incident depressive symptoms in men (OR: 0.91;  $p=0.04$ ), but not in women (OR: 1.01;  $p=0.75$ ) (22). Three separate indices measuring adherence to the MD were used, rMED, the “classic” MD Score (MDS) (OR: 0.82 in men and 1.03 in women), and the Literature-Based Adherence Score to the Mediterranean Diet (LAMMD) (OR: 0.86 in men and 0.98 in women), providing evidence for a protective effect of the Mediterranean diet in men – measured any number of ways – against incident depression (22).

### **2.5.5 Data-driven Measures of the Mediterranean Diet and the Prevention of Mental Illness**

Along with measuring adherence to a theoretically-defined MD, analyses have been conducted using data-driven approaches to examine the role of a Mediterranean dietary pattern and its association with depression. Research in Australian adult women aged 50-55 years, has indicated a cross-sectional inverse association between higher consumption of a Mediterranean-style dietary pattern and a lower prevalence of depressive symptoms (OR: 0.82), as well as a prospective association with lower incidence of depressive symptoms at three years follow-up (OR: 0.83) (23). Similar findings were noted in an Italian population-based cohort study of 1,362 men and women aged 18-102 years (117). A dietary pattern labelled the “typical Tuscan dietary pattern”, which was rich in vegetables, olive oil, grains, fruit, fish, and moderate in wine and red and processed meat, was observed to be inversely associated with depressive symptoms both at baseline ( $\beta$ : -2.77;  $p=0.002$ ) and at nine years follow-up ( $\beta$ : -1.78;  $p=0.013$ ) (117).

A recent systematic review explored the strength of evidence associated with the MD and depression ( $n=26$ ). Of the studies that assessed diet via data-driven measures, it was consistently shown that dietary intake characteristic of the MD was protective against depressive symptoms, whereas Western dietary patterns were not beneficial (125). However, it was suggested that the

MD may not be the only dietary pattern capable of lowering the risk of depression (125). Instead, it was proposed that dietary patterns characterized by greater intakes of plant-based foods and whole grains display similarly beneficial impacts on depressive symptoms as those of the MD (125). While research on the relationship between the MD and mental illnesses is common in Mediterranean countries such as Spain, France, and Italy, there is a significant dearth of such studies in Canada.

### **2.5.6 Mediterranean Diet as a Treatment for Mental Illness**

Relative to individuals without mental illness, those living with mental illness report less healthy lifestyle behaviours, including poorer diets, as well as less knowledge of the health risks associated with these behaviours (126). In recent years, a small number of RCT have assessed the mental health outcomes of dietary interventions for individuals with mental illness. One example of this is the secondary analysis conducted on the *Prevención con Dieta Mediterránea* trial, an RCT with the aim of assessing the effects of a Mediterranean-style diet on cardiovascular disease (126). One study made use of this trial to investigate MD and the risk of developing depression in the population of 3,923 mid-aged and senior men and women (55-80 years) in Spain (126). Two Mediterranean diets were assessed: 1) the MD supplemented with extra virgin olive oil (MD-evo), and 2) the MD supplemented with mixed nuts (MD-nuts), and were compared to a low-fat diet control group (126). The authors did not find a significant decrease in depression risk in the participants assigned either to the MD-evo (HR: 0.91; 95% CI: 0.67, 1.24) or MD-nuts (HR: 0.78; 95% CI: 0.55, 1.10) groups, although they noted a significant 40% reduction in depression risk in the MD-nuts group when the analysis was restricted to participants with diabetes mellitus type 2 (HR: 0.59; 95% CI: 0.36, 0.98) (126). In order to explain these findings, the authors note that the control group was a healthy dietary

pattern recommended by the American Health Association to prevent cardiovascular disease and that adherence to the MD would likely show a greater benefit had it been compared to the typical unhealthy Western diet (126).

More recently, an RCT was conducted in Australia to examine an MD intervention for mental health and quality of life in individuals with self-reported depression (127). Adults aged 18-65 were randomized into either a treatment group (n=47), which included food hampers and cooking workshops aligned with the MD for three months and fish oil supplements for six months or to a comparison group (n=38), which entailed social group activities for three months (127). The MD treatment group reported greater increases in their MD diet score as compared to the social comparison group from baseline to three months ( $p < 0.001$ ), which was sustained at six months. The MD treatment group displayed a 45% improvement in depression scores, as measured by the Depression Anxiety Stress Scale, which was significantly more than the comparison group ( $p = 0.027$ ) and sustained at six months (127). The conflicting results of these two RCTs highlight the heterogeneity present in this field. It is difficult to compare studies that utilize substantially different exposures, assessment of outcomes, and populations. As with research on theory-driven and data-driven measures of overall diet, measures of the MD are promising, although inconclusive at present and highlight the need for further research.

### **2.5.7 Length of Follow-up in Studies of Diet and Mental Illness**

Length of follow-up for studies investigating the relationship between diet and mental illness ranges from less than one year to over thirty years (105). Mental illnesses are known to impact dietary choices. For instance, a common symptom of depression is reduced appetite, and certain individuals with depression are more likely to consume foods high in fat and sugar (128), as well as less vegetables and fruit (129). As a result, follow-up time in prospective cohorts



needs to be of a sufficient length to preclude reverse causality. Studies with insufficient follow-up time are incapable of determining the directionality of the relationship. Specifically, it may be unclear whether diet quality acted as a risk factor for mental illness, or whether it was an outcome of the disease. Certain meta-analyses have chosen at least five years as the cut-off for follow-up time to be of sufficient length to make reverse causality unlikely in the association between diet and mental illness (104). The need for prospective cohort studies has been highlighted in a number of publications, and it is important that the follow-up period of future studies be long enough to determine directionality.

## **2.6 Other Variables in the Relationship between Diet and Mental Illness**

A number of factors interact to influence the association between dietary behaviour and mental illness (105) and as a result, many confounders in this relationship need to be adjusted for. Cross-sectional and prospective studies investigating this association take into account confounders such as baseline sociodemographic and lifestyle variables, however there is inconsistency in terms of which variables are included. Commonly controlled-for variables include age, sex, ethnicity, physical activity, BMI, and smoking status (15-19) as all are associated with both diet and mental illness. For instance, better quality diets are consumed by individuals who have greater levels of physical activity and vice versa, as healthy and unhealthy lifestyle behaviours tend to cluster together (12). Physical activity is associated with a number of mental illnesses, as it improves mood and reduces symptoms of mental illness (9). It is also important to consider the other lifestyle variables including smoking status, alcohol consumption, and BMI. Studies that have not controlled for lifestyle behaviours must be interpreted with caution, as they are not examining the independent effect of diet on mental illness, but instead an effect potentially distorted by modifiable lifestyle behaviours. Further, as

systematic reviews and meta-analyses have highlighted, comparisons between studies are difficult when each study includes differing confounders, or confounders measured in inconsistent manners (104, 105).

Diet is influenced by occupation, education, and income, indicators that comprise socioeconomic status (SES) (130). Diet, measured with diet quality indices or data-driven dietary patterns, has been demonstrated to increase with greater SES (91, 131, 132). Intake of specific foods is patterned according to SES, with high-SES individuals consuming more whole grains, lean meats, fish, and fresh vegetables and fruit (133). A socioeconomic gradient characterizes intakes of most vitamins, minerals, and fiber, with high SES individuals achieving greater intake (133). Possible causal mechanisms for the link between SES and diet include individual nutrition knowledge (134), motivation (135), access to grocery stores, transportation, and neighbourhood safety (136, 137), and financial and time requirements (138). SES is also inversely associated with the risk of mental illness. Surveys in seven countries conducted by the WHO found a greater prevalence of anxiety disorders, mood disorders, and substance-use disorders among people of lower SES (OR: 1.9-3.8 for education; 1.6-3.3 for income; 1.9-3.3 for employment) (139). In terms of depression, low SES increases both the risk of episode onset (OR: 1.24) and the risk for persistence (OR: 2.06) (140). This relationship isn't isolated to the lowest tier of SES, but is graded throughout the entire population. Possible explanations for the association between SES and mental health include avoidance of risk factors and harmful exposures such as stressful life events and poor social support (140). High SES also enables health promoting behaviours, such as abstaining from smoking and substance use (141), as well as more favorable access to health care (140). Overall, strong associations exist between SES and both mental illness and diet.

Disease comorbidities are important confounders to consider in the relationship between diet and mental illness, although few studies have taken them into account in their analyses. The likelihood of having comorbid chronic and mental illness is significantly higher than that of having mental illness in the absence of a chronic disease (142). Diet also plays a major role in the development of certain chronic diseases, and national dietary guidelines such as the DGA and CFG are targeted directly for chronic disease prevention. One study of 51,529 individuals in the United States showed that men in the highest quintile of adherence to the AHEI had a significant inverse relation with overall major chronic disease risk (composite outcome of cardiovascular disease, cancer, or death) (RR: 0.80) and a stronger association with cardiovascular disease specifically (RR: 0.61) (89). The results for women were similar, but slightly attenuated (RR: 0.89 and 0.72, respectively) (89). It is important to consider disease comorbidities in research on diet and mental illness, and one meta-analysis on this topic has suggested that future studies should stratify their results by the incidence of certain chronic diseases (105). However, it is also possible that adjusting for disease comorbidities may represent overadjustment, which may result in an underestimation of the true relationship between diet quality and mental illness.

The use of prescription medications indicated for mental illness is worth considering as a covariate although certain difficulties exist with respect to their inclusion. To our knowledge, few studies investigating diet and mental illness have included them as covariates either through self-report or linkage with administrative pharmaceutical databases (16, 143). Medications such as antidepressants, anxiolytics, and antipsychotics fit the description of confounders in the association between diet quality and mental health service utilization, such that they are related to both exposure and outcome, but not on the causal pathway. However, medications indicated

for certain mental illnesses are often prescribed for non-mental health concerns. For example, benzodiazepines, which are indicated for anxiety are also commonly prescribed for insomnia (144). Prior to including prescription medications for mental illness in studies as a confounder, researchers need to ensure that such medications were truly prescribed for mental illness purposes.

## **2.7 Thesis Objectives**

Despite the large personal, societal, and economic burden of mental illnesses, insufficient research has been conducted on their prevention. The 2012 CCHS survey brought attention to the large proportion of Canadians suffering from mental illness and estimated that overall 10.1% of Canadians 15 years of age and older met the criteria for a 12-month prevalence of major depressive disorder, bipolar disorder, generalized anxiety disorder, or substance use disorder (5). Studies estimating the prevalence of mental illness have typically focused on the number of individuals meeting symptomatic criteria and have ignored the prevalence of mental health service utilization. Given the stigma and discrimination surrounding mental illnesses, it is likely that a proportion of the Canadians expressing symptoms of mental illness are not seeking mental health care and receiving diagnoses of mental illness. At present, many of the characteristics that differ between individuals using the health care system for mental illness purposes and those who do not, are unknown.

*The first objective of this thesis is to describe in detail the factors associated with the utilization of health services for mental illness in Albertan adults.*

Research investigating the relationship between diet quality and mental illness has increased in recent years, but the directionality and strength of this association is still unclear.

Reasons for this include a reliance on cross-sectional studies, insufficient control of confounders, and the use of rating scales. First, cross-sectional studies which assess exposure and outcome simultaneously, are incapable of providing information on directionality. Prospective cohort studies, having the advantages of a clear temporal sequence and possible examination of multiple effects of a single exposure (i.e., a number of mental illnesses) are needed. Second, residual confounding has been highlighted as a possible explanation for the association between diet quality and mental illness (115). A greater number of potential covariates need to be considered and potentially adjusted for in analyses. Third, most studies in this field have used rating scales to assess caseness of mental illness. These measures evaluate the presence of symptoms, regardless of whether formal diagnostic criteria have been met. As a result, prevalence estimates of mental illnesses may be artificially inflated and the relationship between diet and mental illness may be overestimated (105). Physician administrative data provides a more accurate view of the true prevalence of mental illness in a population, although they may be underestimated for the reasons mentioned above.

*The second objective of this thesis is to assess the prospective relationship between diet quality and the number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses, while taking into account the wide range of relevant confounders.*

## **2.8 Statement of Contributions**

For this thesis, I was responsible for developing the research objectives, writing the research proposal, and planning the analysis to address the objectives. I personally conducted the literature review that formed Chapter 2. I conducted all analyses in Chapters 3 and 4, as well as interpreted all the results. All chapters in this thesis were written by myself and reviewed by my supervisory committee.

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## **Chapter 3: Sociodemographic and Lifestyle Characteristics of Albertan Adults Seeking Health Care for Mental Illness**

### **3.1 Introduction**

Mental illnesses are one of the leading causes of disability globally (1). In Canada, one in five individuals meet the criteria for a 12-month prevalence of mood, anxiety, or substance use disorders (2). Studies investigating the prevalence and risk factors for mental illness have typically focused on individuals meeting symptomatic criteria (3-5), but less is known about the health service utilization of Canadians for mental illnesses. A large proportion of individuals with mental illness do not seek health care, although early treatment may significantly improve long-term prognoses (6). For instance, the Public Health Agency of Canada found that in 2009/10, only 13.6% of Canadians aged one year and older sought health care for mental illness (7). In Alberta, the proportion of individuals receiving mental health care was slightly higher at 13.9% (7), suggesting that barriers – whether societal, environmental, or clinical – exist in terms of mental health care service utilization.

The distinction between individuals seeking mental health care and individuals meeting diagnostic criteria for a mental illness is important as they comprise separate but overlapping subgroups of the population (8). Health service utilization research captures individuals assigned diagnostic codes based on clinical assessments, although individuals may or may not have met all diagnostic criteria for a particular mental illness. However, it does not capture individuals meeting all diagnostic criteria who do not seek physician-provided care through the provincial medical system, whether due to stigma, accessibility difficulties, or other reasons.

Among the factors predisposing individuals to use health services for mental illness, sociodemographic variables are the most researched. Several studies from the United States have found middle-aged individuals to be more frequent users of mental health care relative to young adults (18-24) and seniors ( $\geq 65$ ) (9, 10). A more recent study conducted in Montreal, Canada found that older age up to 65 years was associated with increased mental health service usage (11). Females are consistently greater users of mental health services (11, 12), as are married individuals (8, 10). Greater educational achievement is also associated with increased mental health service use (8), although mental illnesses are more prevalent among individuals with less education (13).

In contrast to the sociodemographic factors, few have examined lifestyle behaviours as predisposing factors for mental health care use. Physical activity has been found to improve mood and reduce symptoms of mental illness (14). In terms of health service utilization, moderate-to-vigorous physical activity (MVPA) is associated with reduced numbers of prescriptions and unplanned hospital admissions in older adults, although it is unknown what proportion of those are related to mental health (15). The association between smoking and mental health is less clear; a number of studies have shown that individuals report smoking to ease symptoms of mental illness, stabilize mood, and alleviate stress (16, 17). Despite these perceived mental health benefits, individuals with mental illnesses who smoke are typically heavier smokers and show greater dependency (18, 19). Body mass index (BMI) is also strongly associated with mental illness. Underweight and obese status is associated with anxiety relative to normal weight status (20), and a bidirectional link exists between overweight and obesity and depression (21). Obese individuals have also been shown to have a greater number of visits to



both primary and specialty care clinics as well as have a higher number of diagnostic services (22).

Evidence is also emerging to support a link between diet and mental illness. A recent meta-analysis of prospective studies found that adherence to high-quality diets, regardless of type, was associated with lower depression incidence in a linear dose-response pattern (23). Similarly, the consumption of fish and vegetables was linked to a lower risk of depression (23). Another meta-analysis, which evaluated the relationship between dietary patterns and depression found that diets characterized by a high intake of fruit, vegetables, whole grains, fish, olive oil, low-fat dairy, and antioxidants and a low intake of animal-derived foods was associated with a decreased risk of depressive symptoms (24). However, little is known about diet or other lifestyle behaviours as predictors of mental health service utilization in adults.

It is unclear whether individuals engaging in healthy lifestyle behaviours will have lower mental health service use due to the protective effects of a healthy lifestyle, or whether mental health service use will be higher due to increased health-consciousness (i.e., healthy user bias). This study examines which sociodemographic and lifestyle behaviours are more common among mental health care users as compared to non-users.

## **3.2 Methods**

### **3.2.1 Study Population**

This research utilized data from Alberta's Tomorrow Project (ATP), a population-based prospective cohort designed to study the etiology of cancer and chronic disease. Albertan adults aged 35-69 years were considered eligible if they had no personal history of cancer other than non-melanoma skin cancer, planned to stay in Alberta for over one year, and were capable of

completing written questionnaires in English (25). A random digit dialing procedure was used for subject selection and enrollment (25). Eligible households throughout Alberta's regional health authorities were contacted beginning in 2000 and one eligible adult was selected per household (25). Participants were considered enrolled upon completion of the Health and Lifestyle Questionnaire (HLQ), a mailed questionnaire which collected information on sociodemographic, behavioural, and health-related variables. Two other questionnaires were also mailed to participants following enrollment. The Past-Year Total Physical Activity Questionnaire (PYTPAQ) assessed physical activity over the past year and the National Cancer Institute's Diet History Questionnaire, a 124-item food frequency questionnaire adapted to the Canadian context – the Canadian Diet History Questionnaire I (CDHQ-I) – provided information on past year dietary intake including supplement use (26).

Participants also consented to have their ATP survey data linked with Alberta Health (AH) administrative health records via Personal Health Numbers (25). Over 99% of ATP participants provided valid Personal Health Numbers and consented to data linkage with AH databases and other health records (25). AH collects health service utilization data concerning types of health care and services accessed, frequency of service utilization, diagnosis or purpose of sought physician care, and cost (25). Seven AH administrative datasets were linked: Ambulatory care, Inpatient, Physician/clinical service claim, Population registry, Alberta Blue Cross (ABC), Pharmaceutical Information Network (PIN), and Vital statistics (25).

From 2000 to 2008, 29,876 participants completed the HLQ and consented to data linkage (25). Following 2008, volunteer recruitment was conducted to enroll more participants, as ATP joined the Canadian Partnership of Tomorrow Project, a coalition of five cohorts in Canada (25). This study focuses on participants enrolled between 2000 and 2008, who had

completed the HLQ, PYTPAQ, and CDHQ-I, with daily caloric intake  $\geq 500$  &  $\leq 5,000$  kcal (27) and without missing dietary data ( $>10$  missing responses on the CDHQ-I). This resulted in a study sample of 25,016 ATP participants.

### **3.2.2 Mental Health Service Utilization**

ATP survey data was linked to AH administrative health datasets from 2000 to 2015, which contained records of physician visits from practitioner claims for mental illness. A participant's visit to a physician was considered if it was coded as an affective disorder, anxiety disorder, psychotic disorder, substance use disorder, or depression on physician service claims' primary, secondary, or tertiary health diagnosis fields. Affective disorders, also referred to as mood disorders, are characterized by disturbances in mood, but may also include other mental or somatic disturbances (28). Depression, one type of affective disorder, is diagnosed based on sadness, loss of interest or pleasure, and reduced functioning (28). Psychotic disorders were categorized into organic psychoses (i.e., those induced through substances or physiologic reasons, such as pain or infection) and non-organic psychoses (i.e., schizophrenia-type psychoses). All psychotic disorders are characterized by distorted thought and perception (28). Substance use disorders involve the problematic use of drugs of abuse, including alcohol, prescription medications, and illicit drugs (28). International Classification of Diseases (ICD), Ninth Revision or ICD, 10<sup>th</sup> Revision codes were used to identify physician visits for all mental illnesses. Anatomical Therapeutic Chemical Classification (ATC) codes for antidepressants or mood stabilizers from ABC pharmacy claims or PIN dispenses along with inpatient care information were additionally used to identify physician visits for depression (see Table 3.1 for ICD-9/10 and ATC codes used). Physician visits for psychotic disorders and substance use

disorders were combined into an “other mental illnesses” category due to smaller numbers of participants seeking physician care for these illnesses.

Due to the large range and overdispersion of the distribution of physician visits for mental illness, results were categorized according to the number of visits for depression, anxiety disorders, affective disorders, and other mental illnesses: 0 visits, 1-3 visits,  $\geq 4$  visits. We assessed only physician visits following cohort enrollment in order to ascertain temporality in the relationship between characteristics and mental health service utilization. Follow-up time per participant ranged from approximately six to 14 years, as participants were enrolled throughout 2000-2008 and AH administrative records covered 2000-2015.

### **3.2.3 Sociodemographic Characteristics**

From the HLQ, sociodemographic variables included were: sex, age group (35-44 years, 45-54 years, or 55-69 years), location of residence (urban or rural) based on postal code, household income ( $< \$30,000$ ;  $\$30,000-59,999$ ;  $\$60,000-99,999$ ;  $\geq \$100,000$ ), highest level of education (up to high school completion, some university, or up to post-graduate degree completion), marital status (married/not married, but living with someone or divorced/separated/widowed/single), and employment status (full-time, part-time, or other).

### **3.2.4 Lifestyle Characteristics**

Participants were provided with tape measures and instructions on the HLQ for measuring height and weight. This method has previously been tested for validity, and Spearman rank correlations between self-reported and measured height and weight were found to be high ( $r > 0.9$ ,  $p < 0.0001$ ) (29). BMI was calculated from these measures as weight in kilograms divided by height in meters squared, and categorized into underweight/normal weight ( $< 25.0 \text{ kg/m}^2$ ),

overweight (25.0-29.9 kg/m<sup>2</sup>), or obese ( $\geq$ 30.0 kg/m<sup>2</sup>) (30) according to Health Canada recommendations. Underweight and normal weight were collapsed into one category due to small numbers of participants with a BMI <18.5 kg/m<sup>2</sup> (n=171).

Participants reported the frequency, duration, and intensity of leisure-time physical activity in the previous year. Total minutes per week engaging in recreational activities at moderate (3-6 metabolic equivalent of task (MET)) or vigorous (>6 MET) intensities were categorized into quartiles and rounded to meaningful values: <70.0 minutes/week, 70.0-209.9 minutes/week, 210.0-389.9 minutes/week, or  $\geq$ 390.0 minutes/week. These cut-off values were chosen to align with the approximately 210 minutes/week recommended by the 1998 Canada's Physical Activity Guide to Healthy Active Living, which was in place during ATP recruitment (31).

Participants were asked about present and former tobacco use histories and three categories of smoking status were defined as: current smokers, former smokers, and those who had never smoked. Current smokers included individuals who smoked either daily or occasionally at the present time and former smokers included both daily and occasional smokers in the past.

The Charlson index of disease comorbidities (0, 1,  $\geq$ 2) was calculated at baseline, specifically from three years before enrollment to six months afterwards. It was derived from administrative data of a list of disorders, including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, liver disease, diabetes with and without chronic complications, hemiplegia or paraplegia, renal disease, any malignancy (except malignant skin cancer), metastatic solid tumor, and AIDS/HIV (32).

Responses to the CDHQ-I were analyzed by Diet\*Calc software (version 1.4.2; National Cancer Institute) with a data dictionary modified for the CDHQ-I, producing data for energy intake, nutrients, foods, and food groups. Daily servings of non-starchy vegetables and fruit (excluding fruit juice) were categorized according to the 2007 Canada's Food Guide (CFG) (33) based on Lieffers et al. methodology (34). Specifically, because CFG 2007 has a composite recommendation for vegetables and fruit (33), separate recommendations for vegetables and fruit were estimated from the 2015 Global Burden of Disease (GBD) Theoretical Minimum Risk Exposure (35). The recommended daily servings of dairy and whole grains were from CFG 2007, where whole grains recommendations are half the recommended servings of grain products (33). Since CFG 2007 does not provide age- and sex-specific recommendations, daily intake of nuts and seeds, red meat, processed meat, saturated fat, added sugars, and sodium recommendations from other North American organizations were used. Daily intake in grams of nuts and seeds was categorized according to the Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult, where at least 30 grams per day or approximately one serving according to CFG 2007 constituted adherence to recommendations (36). Red meat and processed meat were measured in servings per day and categorized according to the Canadian Cancer Society guidelines of no more than three 85 gram servings of red meat per week (estimated as  $\leq 0.5$  servings/day) and processed meat only at special occasions (estimated as 0.05 servings/day) (37). Saturated fat and added sugars were measured as a percentage of daily energy and categorized according to the World Health Organization (WHO) guidelines of <10% of daily energy each (38, 39). Daily milligrams of sodium were categorized according to the recommendation of <2,300 milligrams per day set

by the 2015-2020 Dietary Guidelines for Americans (39). A summary of food and nutrient recommendations is provided in Table 3.2.

Diet quality was assessed with the Diet Quality Index-International (DQI-I) score, calculated from responses on the CDHQ-I. The DQI-I is a composite index of diet comprised of four dietary components: variety, adequacy, moderation, and overall balance (40). The total index score is the sum of the scores of the four components and ranges from 0 to 100, with higher scores indicating better diet quality (40). Variety (score 0 to 20) measures diversity in food choices and protein choices. Adequacy (score 0 to 40) measures sufficient intake of food groups and nutrients. Moderation (score 0 to 30) measures whether certain foods and nutrients are consumed in excess. Overall balance (score 0 to 10) measures the equilibrium of macronutrients and fatty acids. (Appendix A details scoring criteria for DQI-I). The overall DQI-I score and its four categories were dichotomized using a cut-off of 60% of total and component scores to differentiate better versus poor quality diets (40).

The CDHQ-I also queried information about participants' alcohol consumption. Individuals reported the frequency and volume of beer, wine/wine coolers, and liquors/mixed drinks in the past year. Weekly consumption of alcoholic drinks was highly skewed and the majority of participants met the recommendations for weekly alcohol consumption set by Canada's Low-Risk Drinking Guidelines (41), specifically 88.6% of men consumed  $\leq 15$  drinks/week and 92.2% of women consumed  $\leq 10$  drinks/week. As a result, alcohol was assessed in grams of ethanol consumed per week and categorized into rounded tertiles:  $< 10.0$  grams/week,  $10.0-49.9$  grams/week, and  $\geq 50.0$  grams/week.

We assessed past-year intake of four supplements (yes/no): multivitamins, vitamin D, other nutritional supplements, and herbal supplements. Nutritional supplements are vitamins or

minerals separate from a multivitamin, and herbal supplements are herbs or plant products taken for health-related purposes (42). Other supplements included one or more of vitamin A,  $\beta$ -carotene, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>3</sub>, vitamin B<sub>6</sub>, vitamin B<sub>9</sub>, vitamin B<sub>12</sub>, vitamin C, vitamin E, calcium, magnesium, iron, zinc, copper, or selenium. Herbal supplements included one or more of aloe vera, astragalus, bilberry, cascara sagrada, cat's claw, cayenne, cranberry, dong kuai (tangkwei), echinacea, evening primrose oil, feverfew, ginko biloba, ginseng (American or Asian), goldenseal, grapeseed extract, kava kava, milk thistle, saw palmetto, Siberian ginseng, St. John's wort, or valerian. Vitamin D was assessed separately due to its association with mood (43).

### **3.2.5 Statistical Analyses**

Both 14.5 year (2000-2015) and 12 month (2014) prevalence estimates were calculated from AH data for depression, anxiety disorders, affective disorders and other mental illnesses. Prevalence was based on having one or more physician visits for the four categories of mental illness during that time period. Results are presented as number of participants and percentage of the total sample. Sociodemographic and lifestyle characteristics of ATP participants seeking mental health care 0 times, 1-3 times, and  $\geq 4$  times following enrollment were compared using chi-square tests. Descriptive statistics were presented as percentages for all variables. All analyses were conducted using the statistical software program STATA (Stata Corp LP. 2007, Release 14). Statistical significance was set at  $p < 0.05$ .

### **3.3 Results**

Approximately 1 in 3 ATP participants had one or more physician visit for depression, an anxiety disorder, or an affective disorder between 2000 and 2015, as shown in Table 3.3. In that



same time period, over 1 in 20 participants sought physician care for an other mental illness. In decreasing order, the 12 month prevalence of physician visits for mental illnesses in 2014 was depression (10%), affective disorders (8%), anxiety disorders (5%), and other mental illnesses (1%).

The distribution of the number of physician visits for mental illness from cohort enrollment to end of follow-up in 2015 ranged zero to 35 visits for depression, zero to 39 visits for anxiety disorders, zero to 34 visits for affective disorders, and zero to 33 visits for other mental illnesses. For depression, 68.9% of the population had zero physician visits from cohort enrollment to 2015, 18.7% had one to three visits, and 12.4% had four or more visits. For anxiety disorders, 71.3% of the population had zero physician visits from cohort enrollment to 2015, 23.7% had one to three visits, and 5.0% had four or more visits. For affective disorders, 71.8% of the population had zero physician visits from cohort enrollment to 2015, 17.8% had one to three visits, and 10.4% had four or more visits. For other mental illnesses, 95.1% of the population had zero physician visits from cohort enrollment to 2015, 4.2% had one to three visits, and 0.7% had four or more visits.

Compared to participants included in analyses (n=25,506), participants excluded (n=4,860) had similar age (less than 55 years of age: 68.2% vs. 66.4%), lower percentage of women (51.8 vs. 62.8 %), similar geographic distribution (rural: 24.8% vs. 23.6%), similar education (post-secondary or higher: 70.2 vs. 72.5%), and slightly higher percentage with one or more comorbidity (20.4 vs. 16.8%).

A comparison of the number of physician visits for mental illnesses according to sociodemographic characteristics is presented in Table 3.4. A greater percentage of men than women sought no mental health care for depression (79% vs 63%), anxiety disorders (78% vs

67%), and affective disorders (81% vs 66%) (all  $p < 0.001$ ). A consistent relationship was not apparent in terms of age. Older adults (55-69 years) used physician services more for fewer visits (1-3 visits throughout follow-up) relating to depression, affective disorders, and other mental illnesses as compared to those younger than them. However, the youngest category of adults (35-44 years) used physician services more for many visits ( $\geq 4$  visits throughout follow-up) relating to depression, affective disorders, and other mental illnesses relative to those older than them (all  $p < 0.001$ ). A greater percentage of individuals living in rural locations sought no physician care for depression (71% vs 68%), anxiety disorders (72% vs 71%), and affective disorders (74% vs 71%), compared to those living in urban locations (all  $p < 0.001$ ). The use of physician services for all mental illnesses was higher among those with household incomes  $< \$30,000$ , educational attainment lower than a university degree, unattached marital status, and non-full-time employment (all  $p < 0.001$ ).

Table 3.5 displays a comparison of physician visits for mental illnesses by lifestyle characteristics. Obese individuals sought physician services more often for depression, affective disorders, and other mental illnesses (all  $p < 0.001$ ), as well as fewer visits for anxiety (1-3 visits throughout follow-up) compared to under/normal weight and overweight individuals ( $p = 0.003$ ). Individuals completing  $< 70$  minutes/week MVPA had more physician visits for depression, affective disorders, and other mental illnesses (all  $p < 0.001$ ) and more anxiety-related visits ( $\geq 4$  visits throughout follow-up) relative to those exercising  $\geq 70$  minutes/week ( $p = 0.005$ ). For all mental illnesses, a greater percentage of individuals who had never smoked sought no physician care relative to former and current smokers (depression: 73% vs 67% vs 61%; anxiety disorders: 73% vs 67% vs 61%; affective disorders: 76% vs 71% vs 64%; other mental illnesses: 97% vs 95% vs 90%) (all  $p < 0.001$ ). The use of physician services for depression, affective disorders, and

other mental illnesses was higher among those with  $\geq 2$  comorbidities as measured with the Charlson index of comorbidities, as well as for fewer visits for anxiety disorders (1-3 visits throughout follow-up), as compared to those with zero or one comorbidities (all  $p < 0.001$ ).

The dietary characteristics are presented in Table 3.6. Use of physician services for depression, anxiety disorders, and affective disorders was higher for participants regularly using vitamin D supplements, other supplements, multivitamins, and herbal supplements, relative to those not regularly using them (all  $p < 0.001$ ). Individuals in the lowest category of weekly alcohol consumption ( $< 10$  grams/week) sought physician care more often for depression, anxiety disorders, and affective disorders, as well as fewer physician visits for other mental illnesses, relative to those in the two higher categories of alcohol consumption (10.0-49.9 and  $\geq 50.0$  grams/week) (all  $p < 0.001$ ). Participants adhering to the recommendations for red meat and processed meat were more often visiting physicians for depression, anxiety disorders, and affective disorders, as compared to those not adhering to the recommendations (all  $p < 0.001$ ). For all mental illnesses, a greater percentage of individuals adhering to the recommendations for added sugars as compared to those not adhering to the recommendations, sought no physician care (depression: 70% vs 67%; anxiety disorders: 72% vs 70%; affective disorders: 73% vs 70%; other mental illnesses: 96% vs 95%) ( $p = 0.004$  for anxiety disorders;  $p = 0.002$  for other mental illnesses;  $p < 0.001$  otherwise). Those who achieved a poor DQI-I score were more often seeking physician care for depression ( $p = 0.012$ ), affective disorders ( $p = 0.007$ ), and other mental illnesses ( $p = 0.001$ ), with the components adequacy ( $p = 0.001$  for depression and affective disorders;  $p = 0.003$  for other mental illnesses) and variety ( $p < 0.001$  for depression;  $p = 0.004$  for anxiety disorders;  $p = 0.005$  for affective disorders;  $p = 0.003$  for other mental illnesses) also displaying

this relationship, when compared to individuals achieving high DQI-I, adequacy, and variety scores.

### **3.4 Discussion**

In this study we described the characteristics of users and non-users of health care for mental illness in a population of adults in Alberta, Canada. Physician visits for mental illnesses were highly prevalent in this cohort, with over one third of participants seeking physician care for depression, anxiety disorders, or affective disorders in a 14.5 year period. The lifetime prevalence of mood disorders and generalized anxiety disorder were an estimated 12.6% and 8.7%, respectively, in a sample of Canadians aged 15 years and older (2). Similarly, our 12 month prevalence estimates for depression, anxiety disorders, and affective disorders are larger than those estimated by Pearson et al. (2), likely due to their use of symptom scales to assess mental illness. However, our 14.5 year and 12 month prevalence estimates for other mental illnesses – a composite category of substance use disorders and psychotic disorders – were substantially lower than the substance use disorder estimates of Pearson et al.: 6% and 1%, respectively, in the ATP cohort, as compared to 33% and 10%, respectively, in the national sample (2).

While a large focus has been placed on describing the sociodemographic predictors of health service utilization, we chose to additionally evaluate lifestyle behaviours due to their emerging role in the primary prevention of mental illness. Given that a large proportion of individuals with symptoms of mental illness do not seek physician care, the high prevalence of mental health service utilization in this population is concerning.

In terms of sociodemographic characteristics, our results are largely consistent with the literature. Previous research has demonstrated a greater propensity for women to seek mental health services (11, 12), which is consistent with the higher prevalence of past-year depression and anxiety symptoms reported among women in Canada (2). It has been suggested that men may perceive more stigma for mental illnesses and their treatment or that women may demonstrate improved abilities to identify and accept mental illness diagnoses (10, 12).

A number of studies have highlighted age as a significant predictor of mental health care seeking, with middle-aged individuals using it more frequently relative to those under 25 or over 65 years (11). Results of our study show that mental health care seeking behaviour is not homogeneous throughout middle-age. Specifically, younger adults in our population (35-44 years) consistently sought mental health care most frequently ( $\geq 4$  visits throughout follow-up), although they had the lowest prevalence of care-seeking for fewer visits (1-3 visits throughout follow-up). Younger adults may be less able to notice a need for treatment and may prefer solving their difficulties on their own (9), except in cases of more severe mental illness. It is possible that this tendency is responsible for the younger adults in our population (35-44 years) seeking mental health care less often (1-3 visits), and may also possibly represent less severe cases of mental illness. Although older adults (55-69 years) sought health care the most for few numbers of visits (1-3 visits throughout follow-up), stigma may play a role in terms of their seeking greater numbers of visits ( $\geq 4$  visits) much less relative to the younger age groups.

The association between socioeconomic variables and health service utilization has been frequently noted in the literature. We found the number of physician visits increased with each \$30,000 decrease in household income, with individuals having a household income  $< \$30,000$  to be the most frequent users of health care for all mental illnesses. While some have not found

income to be associated with mental health service use (8, 11), others, particularly those in the United States, have noted the inverse whereby low income is associated with less physician visits for mental illness (10). Financial barriers associated with accessing the health care system in the United States may explain those findings. Our results, in which mental health service utilization was patterned according to household income highlight the important of income as a predictor of physician visits for all mental illnesses in Canada, where health care is largely publicly-funded.

In contrast to previous findings, we noted that individuals with more education – completion of a university degree or more – used health care less for all mental illnesses. Those in the lowest educational attainment group did not consistently seek mental health care more than those in the middle group however. Although it has been suggested that higher education is associated with a more positive view of mental health services (8), our findings mimic the relationship between higher educational attainment and fewer symptoms of mental illness (13).

Marital separation or distress is common in the literature as a predisposing factor to more frequent use of mental health services (8, 44). It has been suggested that psychological distress, such as that from the dissolution of a relationship, may predispose individuals to seek physician care (8). Loneliness, which is associated with both unattached marital status and mental illness, may play an important role in this association as well (45). Our findings corroborate this literature such that individuals who were either married or else living with a partner had a consistently lower prevalence of health care seeking for all mental illnesses.

We found that obese, physically inactive, and currently smoking individuals, as well as those with disease comorbidities used health care more frequently. These findings are in line with the research on lifestyle and symptoms of mental illness. A recent population-representative cross-sectional study of German adults found that those who were physically active, did not

smoke, and had normal to overweight BMI, had improved mental health (46). It appears that those who are most at risk for mental illnesses, in terms of lifestyle behaviours are also seeking physician care for mental illnesses. Lifestyle behaviours tend to cluster together, suggesting that those who engage in a number of unhealthy lifestyle behaviours may be disproportionately at risk for mental illness.

All supplement users, including multivitamins, nutritional supplements, or herbal supplements, sought physician care for depression, anxiety disorders, and affective disorders more frequently than those not regularly using supplements. It is possible that ATP, a cohort in which enrollment was voluntary, may be characterized by individuals taking an active interest in their health and seeking out preventive therapies. Previous research on this cohort found that an estimated 70% are regular users of dietary supplements and that those taking all types of dietary supplements (multivitamins, specific nutrition supplements, and herbal supplements) were more likely to self-report engaging in healthy lifestyle behaviours (42). However, it is unclear whether the supplement use is related to health maintenance, disease prevention, or treatment of pre-existing disease (42).

Foods and nutrients consumed more frequently among mental health care users include: <10 grams/week alcohol,  $\leq 0.5$  servings/day red meat,  $\leq 0.05$  servings/day processed meat, and  $\geq 10\%$  daily energy from sugar. Otherwise, individual dietary components were largely not significantly linked to mental health care service utilization. In contrast, overall diet quality and its components were negatively related to physician visits for mental illnesses. Specifically, individuals consuming better quality diets utilized physician services less often. It is important to recognize that foods and nutrients are not consumed in isolation and that studying them individually ignores the complex interactions of nutrients in daily diets (47). In recent years, a

shift has occurred from investigating the relationship between specific foods or nutrients and mental illness, to investigating diet as a whole and its relationship with mental illness. It is possible that diet quality may play a more important role in the development and progression of mental illness rather than single foods or nutrients, and further research on the relationship between diet quality and health service utilization for mental illnesses is needed. Furthermore, given the clustering of healthy and unhealthy lifestyle behaviours, studies that examine the independent and concurrent effects of these behaviours could shed light on the association with health service use.

Future research would benefit from accounting for the wide range in the distribution of physician visits for mental illness. In our population, individuals had up to 39 physician visits for a particular class of mental illnesses throughout the six to 14 years of follow-up. The majority of the literature has compared predictors of mental health care use between those with no physician visits and those with one or more visits. Our results underscore the importance of accounting for the number of physician visits. We found that individuals seeking health care for mental illnesses fewer times (1-3 visits) differed in a number of their sociodemographic and lifestyle characteristics as compared to those seeking health care for mental illnesses more frequently ( $\geq 4$  visits). Future research in this area could have a significant impact in reducing the health care costs associated with mental health service utilization.

The main strengths of this study are the use of a large, population-based cohort of adults, the wide range of sociodemographic and lifestyle characteristics, and the inclusion of four categories of mental illness. However, this study is not without limitations. All characteristics with the exception of disease comorbidities were based on self-report and can be prone to social desirability bias or poor recall. We examined provincial mental health service utilization data,



and as such only individuals who sought physician care through the traditional health care system were captured. Individuals who utilized other sources of care, such as community mental health services, or who encountered barriers to accessing physician care may have been missed. Those with higher socioeconomic levels may have access to private counselling, which was not captured in this dataset. As a result, estimates of mental health service utilization may be underestimated. Further investigation of the characteristics associated with mental health care service use, particularly lifestyle behaviours is necessary.

### **3.5 Conclusions**

Our findings support and supplement the existing literature on the determinants of health service utilization for mental illness. To our knowledge, no previous study has focused on a wide range of variables, particularly those pertaining to lifestyle behaviours. Physician visits for a number of mental illnesses in Alberta were more common among those with: low household incomes, no university degrees, unattached marital status, non-full-time employment, obesity, low physical activity, current smoking status, disease comorbidities, dietary supplement use, low alcohol consumption, non-adherence to sugar recommendations, adherence to red meat and processed meat recommendations, and low diet quality, particularly adequacy and variety components. Given the link between unhealthy lifestyle behaviours and mental health service use, primary prevention strategies targeting lifestyle behaviours could have a significant impact on the economic and societal burden that mental illnesses presently pose.

Table 3.1. ICD 9/10 and ATC Codes Identifying Physician Visits for Mental Illnesses

<b>Disorder</b>	<b>ICD-9/10 and ATC codes</b>
<b>Affective disorders</b>	Claim data ICD-9: 296, 300.4, 301.1, 309.0, 309.1, 311
<b>Anxiety disorders</b>	Claim data ICD-9: 300, 309.8, excluding 300.14, 300.15, 300.16, 300.19, 300.4, 300.8, 300.81, 300.82, 300.89
<b>Depression</b>	Inpatient data ICD-9: 296.2-296.8, 300.4, 309, 311; ICD-10: F31, F32, F33, F34.1, F38.0, F38.1, F41.2, F43.1, F43.2, F43.8, F53.0, F93.0 <b>OR</b> Claim data ICD-9: 296, 309, 311 <b>OR</b> Inpatient data ICD-9: 300; ICD-10: F32.0, F34.1, F40, F41, F42, F44, F45.0, F45.1, F45.2, F48, F68.0, F99 <b>AND</b> ABC/PIN dispense data within 6 months of hospitalization ATC: N03AB02, N03AB52, N03AF01, N05AN01, N06A <b>OR</b> Claim data ICD-9: 300 <b>AND</b> ABC/PIN dispense data within 6 months of claims ATC: N03AB02, N03AB52, N03AF01, N05AN01, N06A
<b>Non-organic psychoses</b>	Claim data ICD-9: 295, 297, 298
<b>Organic psychoses</b>	Claim data ICD-9: 291, 292, 293, 294
<b>Substance use disorders</b>	Claim data ICD-9: 303, 304, 305.2-305.9

**Abbreviations:** ABC, Alberta Blue Cross; ATC, Anatomical Therapeutic Chemical Classification; ICD, International Classification of Diseases; PIN, Pharmaceutical Information Network

Table 3.2. Food and nutrient recommendations for lifestyle behaviours

<b>Food</b>	<b>Dietary recommendation</b>	<b>Source</b>
<b>Fruit, excluding fruit juice</b>	3 servings/day	CFG 2007 and GBD 2015
<b>Non-starchy vegetables</b>	Female: 4 servings/day; Male: 35-50 years: 5 servings/day, 51+ years: 4 servings/day	CFG 2007 and GBD 2015
<b>Dairy</b>	35-50 years: 2 servings/day, 51+ years 3 servings/day	CFG 2007
<b>Whole grains</b>	Female: 3 servings/day; Male: 35-50 years: 4 servings/day, 51+ years: 3 servings/day	CFG 2007
<b>Nuts and seeds</b>	1 serving/day	2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult
<b>Red meat</b>	No more than 3x85 gram servings/week (rounded to $\leq 0.5$ servings/day)	Canadian Cancer Society
<b>Processed meat</b>	Only for special occasions (assumed 0.05 servings/day)	Canadian Cancer Society and GBD 2015
<b>Saturated fat</b>	Less than 10% of energy intake	WHO
<b>Added sugar</b>	Less than 10% of energy intake	WHO
<b>Sodium</b>	Less than 2,300 milligrams per day	2015-2020 DGA

**Abbreviations:** CFG, Canada's Food Guide; DGA, Dietary Guidelines for Americans; GBD, Global Burden of Disease; WHO, World Health Organization

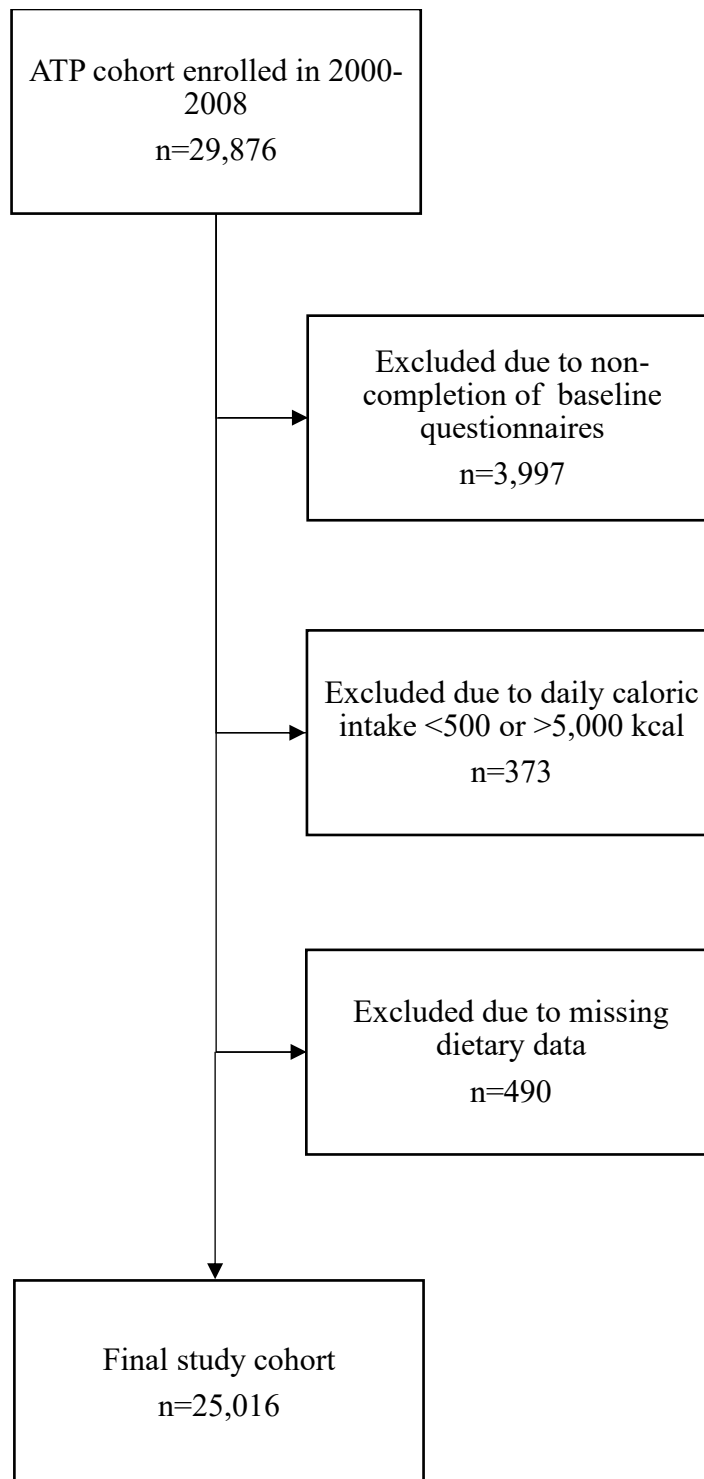


Figure 3.1. Flow chart for the inclusion and exclusion of Alberta's Tomorrow Project (ATP) cohort (2000-2008)

Table 3.3. Prevalence of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses, 14.5 year and 12 month, in the ATP cohort (n=25,016)

	<b>14.5 year prevalence (n)</b>	<b>14.5 year prevalence (%)</b>	<b>12 month prevalence (n)</b>	<b>12 month prevalence (%)</b>
<b>Depression</b>	9,162	36.62	2,582	10.32
<b>Anxiety disorders</b>	9,136	36.52	1,352	5.40
<b>Affective disorders</b>	8,708	34.81	2,013	8.05
<b>Other mental illnesses</b>	1,482	5.92	270	1.08

**Abbreviations:** ATP, Alberta's Tomorrow Project

Table 3.4. Sociodemographic characteristics of ATP participants by number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses (n=25,016)

		Depression			Anxiety disorders			Affective disorders			Other mental illnesses			
	Sample size (n)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	
<b>Sex</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			0.864			
	<b>Male</b>	9,301	79.09	13.91	7.00	77.95	19.21	2.84	81.01	13.24	5.75	95.03	4.21	0.75
	<b>Female</b>	15,715	62.81	21.57	15.62	67.34	26.34	6.33	66.39	20.42	13.19	95.18	4.11	0.71
<b>Age (years)</b>														
	<b>p-value</b>	<0.001			0.220			<0.001			<0.001			
	<b>35-44</b>	7,763	67.53	18.68	13.80	70.46	24.28	5.26	70.39	17.69	11.93	95.81	3.44	0.75
	<b>45-54</b>	8,850	68.11	18.69	13.20	71.33	23.54	5.13	70.90	17.86	11.23	95.38	3.92	0.70
	<b>55-69</b>	8,403	70.89	18.79	10.32	71.99	23.30	4.71	74.13	17.86	8.19	94.22	5.05	0.74
<b>Residence location</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			0.128			
	<b>Urban</b>	19,103	68.09	18.06	10.57	71.10	23.52	5.38	71.27	17.84	10.89	95.24	4.02	0.75
	<b>Rural</b>	5,913	71.37	18.92	12.99	71.88	24.23	3.89	73.62	17.45	8.93	94.76	4.58	0.66
<b>Household income</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			<0.001			
	<b>&lt;\$30,000</b>	3,180	58.99	22.01	18.99	65.72	27.11	7.17	62.74	21.16	16.10	90.00	7.77	2.23
	<b>\$30,000-59,999</b>	6,727	66.82	19.65	13.53	70.28	24.13	5.59	69.51	18.94	11.55	94.31	4.86	0.83
	<b>\$60,000-99,999</b>	7,973	70.40	17.96	11.64	72.47	23.02	4.52	73.47	16.83	9.70	95.96	3.56	0.48
	<b>≥\$100,000</b>	6,576	73.94	16.88	9.18	74.00	22.02	3.98	76.86	15.62	7.53	97.45	2.30	0.26
<b>Education<sup>a</sup></b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			<0.001			
	<b>High school</b>	6,877	67.56	19.83	12.61	70.09	24.68	5.23	70.64	18.95	10.41	93.92	5.18	0.90
	<b>Some university</b>	11,743	67.74	18.95	13.31	70.62	24.22	5.16	70.71	18.09	11.21	95.19	4.10	0.72
	<b>Post-graduate</b>	6,395	72.34	17.11	10.56	73.79	21.64	4.57	75.17	15.82	9.01	96.31	3.13	0.56
<b>Marital status<sup>b</sup></b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			<0.001			
	<b>Attached</b>	19,636	70.83	17.96	11.21	71.93	23.40	4.66	73.69	17.02	9.29	95.93	3.55	0.51
	<b>Unattached</b>	5,377	61.67	21.50	16.83	68.92	24.73	6.34	65.04	20.38	14.58	92.17	6.32	1.51

<b>Employment<sup>c</sup></b>													
<b>p-value</b>	<0.001			<0.001			<0.001			<0.001			
<b>Full-time</b>	14,013	71.87	17.38	10.75	73.26	22.31	4.43	74.40	16.44	9.16	96.08	3.46	0.46
<b>Part-time</b>	4,207	64.82	20.39	14.78	68.36	26.12	5.51	68.20	19.52	12.29	95.46	3.92	0.62
<b>Other</b>	6,789	65.21	20.44	14.35	69.05	25.01	5.94	68.80	19.34	11.86	92.94	5.72	1.34

**Abbreviations:** ATP, Alberta's Tomorrow Project

<sup>a</sup>High school: did not complete grade 8, completed grade 8 but not high school, completed high school; Some university: some technical school/college training completed, completed technical school/college training, some part of university degree completed; Post-graduate: completed university degree, some part of post-graduate university degree completed, completed university post-graduate degree

<sup>b</sup>Attached: married, not married but living with someone; Unattached: divorced, separated, widowed, single (never married)

<sup>c</sup>Full-time: 30 hours or more per week; Part-time: less than 30 hours per week; Other: not employed but looking for work, homemaker, student, retired, other

Table 3.5. Lifestyle characteristics of ATP participants by number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses (n=25,016)

		Depression			Anxiety disorders			Affective disorders			Other mental illnesses		
	Sample size (n)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)
<b>BMI</b>													
<b>p-value</b>		<0.001			0.003			<0.001			<0.001		
<b>Under/normal weight</b>	8,512	69.09	19.03	11.88	70.41	23.97	5.63	72.77	17.34	9.89	95.65	3.58	0.76
<b>Overweight</b>	9,783	70.94	17.81	11.25	72.20	23.16	4.64	73.54	16.96	9.51	95.44	3.91	0.64
<b>Obese</b>	6,661	65.61	19.67	14.73	71.15	24.08	4.77	68.20	19.43	12.37	94.02	5.19	0.78
<b>MVPA quartiles (minutes/week)</b>													
<b>p-value</b>		<0.001			0.005			<0.001			<0.001		
<b>&lt;70</b>	6,272	64.60	20.41	14.99	70.22	24.30	5.48	67.52	19.74	12.74	93.37	5.77	0.86
<b>70-&lt;210</b>	6,715	68.83	18.29	12.88	71.32	23.92	4.77	71.81	17.13	11.06	95.37	3.84	0.79
<b>210-&lt;390</b>	5,915	70.72	18.34	10.94	70.53	24.56	4.90	73.98	17.06	8.96	96.38	3.11	0.51
<b>≥390</b>	6,114	71.48	17.83	10.70	73.06	21.97	4.97	74.17	17.06	8.77	95.44	3.83	0.74
<b>Smoking status<sup>d</sup></b>													
<b>p-value</b>		<0.001			<0.001			<0.001			<0.001		
<b>Never</b>	11,287	72.88	16.89	10.23	73.03	22.87	4.10	75.59	15.70	8.71	97.03	2.55	0.42
<b>Former</b>	9,439	67.46	19.17	13.37	70.58	23.77	5.65	70.71	18.14	11.16	95.24	4.09	0.67
<b>Current</b>	4,286	61.36	22.59	16.05	68.22	25.66	6.11	64.37	22.31	13.32	89.85	8.47	1.68
<b>Charlson index</b>													
<b>p-value</b>		<0.001			<0.001			<0.001			<0.001		
<b>0</b>	20,823	70.75	17.89	11.36	72.41	22.91	4.68	73.56	16.78	9.65	95.74	3.63	0.63
<b>1</b>	3,579	60.44	22.16	17.41	65.86	27.38	6.76	63.82	22.24	13.94	93.01	5.98	1.01
<b>≥2</b>	614	53.91	26.87	19.22	64.82	28.50	6.68	59.61	24.27	16.12	86.48	11.07	2.44

**Abbreviations:** ATP, Alberta's Tomorrow Project; BMI, Body Mass Index; MVPA, Moderate-to-Vigorous Physical Activity

<sup>d</sup>Former smokers includes daily and occasional smokers in the past; Current smokers includes daily and occasional smokers presently



Table 3.6. Dietary characteristics of ATP participants by number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses (n=25,016)

		Depression			Anxiety disorders			Affective disorders			Other mental illnesses			
	Sample size (n)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	0 visits (%)	1-3 visits (%)	≥4 visits (%)	
<b>Vitamin D supplement</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			0.510			
	<b>Yes</b>	14,741	66.98	19.39	13.62	70.47	24.06	5.47	70.27	18.20	11.53	95.07	4.24	0.69
	<b>No</b>	10,275	71.56	17.75	10.69	72.45	23.15	4.40	74.05	17.10	8.85	95.20	4.02	0.78
<b>Other supplements</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			0.013			
	<b>Yes</b>	20,009	67.60	19.31	13.09	70.35	24.18	5.47	70.72	18.30	10.98	95.16	4.19	0.65
	<b>No</b>	5,007	73.90	16.38	9.73	75.01	21.73	3.26	76.23	15.54	8.23	94.97	3.99	1.04
<b>Multivitamin</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			0.268			
	<b>Yes</b>	12,779	66.63	19.54	13.83	70.12	24.31	5.57	70.03	18.15	11.82	94.95	4.34	0.70
	<b>No</b>	12,237	71.19	17.86	10.94	72.49	23.04	4.46	73.70	17.32	8.97	95.30	3.95	0.75
<b>Herbal supplements</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			0.066			
	<b>Yes</b>	5,569	64.72	20.60	14.69	67.52	26.20	6.28	67.39	19.90	12.71	94.54	4.69	0.77
	<b>No</b>	19,447	70.05	18.18	11.77	72.36	22.97	4.67	73.10	17.13	9.77	95.29	4.00	0.71
<b>Alcohol (grams/week)</b>														
	<b>p-value</b>	<0.001			<0.001			<0.001			<0.001			
	<b>&lt;10</b>	8,385	64.39	20.26	15.35	69.11	24.60	6.29	67.72	19.57	12.71	94.29	4.88	0.83
	<b>10.0-49.9</b>	8,868	69.76	18.34	11.91	71.39	23.93	4.68	72.58	17.31	10.12	96.15	3.43	0.42
	<b>≥50</b>	7,763	72.68	17.49	9.83	73.50	22.43	4.07	75.41	16.28	8.31	94.85	4.19	0.97
<b>Fruit (adherence to recommendations)</b>														
	<b>p-value</b>	0.116			0.035			0.052			0.034			
	<b>Yes</b>	5,403	67.74	19.23	13.03	70.00	24.49	5.52	70.61	18.80	10.59	95.45	4.09	0.46
	<b>No</b>	19,613	69.17	18.58	12.25	71.64	23.47	4.89	72.16	17.46	10.38	95.03	4.17	0.80
<b>Vegetables (adherence to recommendations)</b>														
	<b>p-value</b>	0.046			0.015			0.015			0.164			
	<b>Yes</b>	5,223	67.49	19.74	12.77	70.09	24.18	5.72	70.48	19.09	10.43	95.60	3.81	0.59

<b>No</b>	19,793	69.23	18.45	12.32	71.60	23.56	4.85	72.18	17.40	10.42	95.00	4.24	0.76
<b>Dairy (adherence to recommendations)</b>													
<b>p-value</b>			0.151			0.705			0.179			0.592	
<b>Yes</b>	5,599	68.07	18.79	13.15	71.69	23.27	5.04	71.05	17.90	11.06	95.37	3.91	0.71
<b>No</b>	19,417	69.09	18.70	12.21	71.16	23.81	5.03	72.05	17.70	10.24	95.05	4.22	0.73
<b>Whole grains (adherence to recommendations)</b>													
<b>p-value</b>			0.951			0.347			0.579			0.096	
<b>Yes</b>	776	68.43	18.81	12.41	73.45	21.52	5.03	71.52	17.01	11.47	93.81	4.90	1.29
<b>No</b>	24,240	68.88	18.72	12.41	71.21	23.76	5.03	71.84	17.77	10.39	95.17	4.13	0.71
<b>Nuts and seeds (adherence to recommendations)</b>													
<b>p-value</b>			0.876			0.259			0.560			0.141	
<b>Yes</b>	140	70.71	17.14	12.14	77.14	17.86	5.00	75.00	14.29	10.71	93.57	4.29	2.14
<b>No</b>	24,876	68.85	18.73	12.42	71.25	23.72	5.03	71.81	17.77	10.42	95.13	4.15	0.72
<b>Red meat (adherence to recommendations)</b>													
<b>p-value</b>			<0.001			<0.001			<0.001			0.158	
<b>Yes</b>	10,489	66.03	20.44	13.53	69.52	24.59	5.89	69.30	19.12	11.57	95.03	4.12	0.85
<b>No</b>	14,527	70.91	17.48	11.61	72.55	23.04	4.41	73.65	16.76	9.60	95.19	4.17	0.64
<b>Processed meat (adherence to recommendations)</b>													
<b>p-value</b>			<0.001			<0.001			<0.001			0.711	
<b>Yes</b>	5,605	65.69	20.61	13.70	69.53	24.55	5.92	68.69	19.61	11.70	94.92	4.32	0.77
<b>No</b>	19,411	69.78	18.18	12.04	71.79	23.44	4.77	72.73	17.21	10.06	95.18	4.10	0.72
<b>Saturated fat (adherence to recommendations)</b>													
<b>p-value</b>			0.404			0.001			0.751			0.013	
<b>Yes</b>	10,386	68.56	19.11	12.32	70.21	24.30	5.49	71.82	17.90	10.28	94.94	4.15	0.91
<b>No</b>	14,630	69.08	18.44	12.48	72.04	23.25	4.70	71.83	17.64	10.53	95.26	4.15	0.59
<b>Added sugars (adherence to recommendations)</b>													
<b>p-value</b>			<0.001			0.004			<0.001			0.002	
<b>Yes</b>	14,031	70.22	18.26	11.52	72.11	23.07	4.82	72.95	17.38	9.66	95.54	3.76	0.70
<b>No</b>	10,985	67.13	19.31	13.56	70.22	24.48	5.30	70.39	18.22	11.40	94.59	4.64	0.76
<b>Sodium (adherence to recommendations)</b>													
<b>p-value</b>			<0.001			0.167			<0.001			0.702	
<b>Yes</b>	9,115	67.02	19.79	13.19	70.58	24.22	5.20	70.20	18.66	11.14	95.22	4.03	0.76
<b>No</b>	15,901	69.92	18.11	11.97	71.69	23.38	4.93	72.76	17.23	10.02	95.07	4.22	0.71
<b>DQI-I</b>													
<b>p-value</b>			0.012			0.280			0.007			0.001	

<b>≥60 points</b>	14,252	69.57	18.46	11.97	70.95	23.86	5.19	72.45	17.63	9.93	95.56	3.80	0.64
<b>&lt;60 points</b>	10,764	67.93	19.06	13.01	71.72	23.46	4.82	71.01	17.91	11.08	94.55	4.61	0.85
<b>Moderation</b>													
<b>p-value</b>			0.302			0.016			0.489			0.338	
<b>≥18 points</b>	4,750	67.94	19.20	12.86	71.01	23.16	5.83	71.18	18.00	10.82	94.86	4.25	0.88
<b>&lt;18 points</b>	20,266	69.08	18.61	12.31	71.35	23.81	4.84	71.98	17.69	10.33	95.18	4.13	0.69
<b>Adequacy</b>													
<b>p-value</b>			0.001			0.137			0.001			0.003	
<b>≥24 points</b>	23,922	69.09	18.63	12.28	71.40	23.58	5.02	72.01	17.71	10.28	95.22	4.07	0.71
<b>&lt;24 points</b>	1,094	63.89	20.66	15.45	68.65	26.05	5.30	67.73	18.65	13.62	92.96	5.85	1.19
<b>Overall balance</b>													
<b>p-value</b>			0.523			0.207			0.050			0.215	
<b>≥6 points</b>	868	68.55	19.93	11.52	68.89	25.12	5.99	69.93	20.74	9.33	95.62	4.15	0.23
<b>&lt;6 points</b>	24,148	68.88	18.68	12.45	71.37	23.64	4.99	71.89	17.64	10.46	95.11	4.15	0.75
<b>Variety</b>													
<b>p-value</b>			<0.001			0.004			0.005			0.003	
<b>≥12 points</b>	21,618	69.33	18.46	12.21	71.63	23.48	4.89	72.18	17.60	10.23	95.29	4.03	0.68
<b>&lt;12 points</b>	3,398	65.92	20.36	13.71	69.10	25.01	5.89	69.60	18.72	11.68	94.06	4.89	1.06

**Abbreviations:** ATP, Alberta's Tomorrow Project; DQI-I, Diet Quality Index-International

### 3.6 References

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## **Chapter 4: Diet Quality and Health Care Utilization for Mental Illness: A Prospective Investigation of Alberta's Tomorrow Project**

### **4.1 Introduction**

Mental illnesses are the leading cause of disability, accounting for almost one quarter (22.9%) of the global burden of disease (1). An estimated 1 in 3 Canadians meet the criteria for a mental illness in their lifetime (2). As the national population grows and ages, the number of individuals suffering from mental illness is predicted to increase by 31% by 2041 (3). However, individuals with symptoms of mental illness and individuals seeking physician-provided mental health care form two separate but overlapping groups (4). Although barriers to physician care exist, such as stigma and accessibility issues, the burden of mental illnesses on the Canadian health care system is substantial.

The economic burden of mental illnesses reached \$22.6 billion in 2011 in terms of direct costs (3). These costs to the health care system only include public and private expenses associated with the services and supports of mental health treatment, and are a small fraction of the total costs to Canada's economy incurred by mental illnesses (5). The indirect costs of mental illnesses, which include disability claims, lost productivity at school and work through absenteeism or poor performance, and social and judicial services, add an additional economic burden (5). Indirect costs have been estimated to pose a burden of up to \$51.0 billion in Canada (6), and will only increase if the status quo in terms of mental illness prevention, treatment, and awareness is maintained.

In recent years, an association has emerged between diet and mental illness. Existing studies primarily focused on individual nutrients or foods in this relationship. A number of

studies identified associations between the intake of vitamin D (7, 8), B vitamins (9, 10), folate (11, 12), and fish (13, 14) with mental illnesses. However, nutrients or foods are not consumed in isolation, and studying diet individually ignores the complex interactions between dietary components (15). In more recent years, the focus has shifted to studying diet as a whole, whether through a priori-defined diet quality indices or data-driven dietary patterns.

Several systematic reviews and meta-analyses have been published in recent years attempting to elucidate the associations between diet and mental illness. A 2018 meta-analysis of prospective studies found that adherence to high-quality, healthy diets – whether healthy/prudent, Mediterranean, pro-vegetarian, or Tuscan – was linked to a lower incidence of depressive symptoms in a linear dose-response fashion (ORs 0.64-0.78) (16). However, the authors of the meta-analysis highlighted that there was no association when studies controlled for baseline depression severity or used a physician diagnosis as the outcome. The Mediterranean diet specifically has received significant attention in recent years and has been inversely linked to mental health outcomes. A systematic review supported the association between a Mediterranean dietary pattern characterised by vegetables, fruits, legumes, nuts, cereals, olive oil, and fish and reduced depressive symptoms (17).

Research examining diet and mental illness has increased rapidly in recent years, but questions around the directionality and strength of the association remain unclear. The meta-analysis by Molendijk et al. on diet quality and depression highlighted the need for large prospective investigations controlling for a wide range of relevant confounders (16). Given these concerns echoed throughout a number of recent primary studies and meta-analyses, it is important to conduct research assessing diet and mental illness using study designs that help facilitate assessment of causal and temporal relationships. The present study examined the



association between diet quality and mental illness in a large prospective cohort linked with administrative records, accounting for multiple potential confounders.

## **4.2 Methods**

### **4.2.1 Study Population**

Participants were drawn from Alberta's Tomorrow Project (ATP), a population-based prospective cohort study of cancer and chronic disease in Alberta, Canada. Eligibility criteria were ages 35-69 years, no personal history of cancer other than non-melanoma skin cancer, plans to stay in Alberta for at least one year, and able to complete written questionnaires in English (18). Recruitment to the cohort was done in two phases from Alberta's general population (18). In Phase I (2000-2008), random digit dialling mapped to Alberta Regional Health Authorities was used to select households with eligible individuals and one or two eligible residents from these households were invited to participate in ATP (18). Phase I had a 49% response rate and enrolled 29,876 participants who completed ATP questionnaires and consented to data linkage with administrative health care databases (18). In 2008, ATP joined the Canadian Partnership of Tomorrow Project, a coalition of five population-based cohorts across Canada and recruitment methods changed. In Phase II (2009-2015), in order to recruit more participants for the Canadian Partnership of Tomorrow Project, random digit dialling was replaced by volunteer recruitment through media coverage, advertising, corporate presentations, and other methods (18). This method resulted in 22,932 new Canadian Partnership of Tomorrow Project/ATP participants (18). As of March 2015, a total of 52,810 Albertan adults were enrolled into the cohort (18).

ATP data was linked to Alberta Health (AH) administrative health care databases via Personal Health Numbers and covered the years 2000 to 2015. Over 99% of ATP participants

were successfully linked after providing valid Personal Health Numbers and consenting to data linkage (18). Variables measured by AH databases include Ambulatory Care, Inpatient, Physician/Clinical Service Claims, Population Registry, Alberta Blue Cross (ABC), Pharmaceutical Information Network (PIN), and Vital Statistics (18).

This study focused on the 29,876 participants enrolled between 2000 and 2008. Participants were excluded if they had unrealistic daily caloric intakes (<500 or >5,000 kcal) (19), had missing dietary data (>10 missing responses on the CDHQ-I), or had not completed the three baseline questionnaires – the Health and Lifestyle Questionnaire (HLQ), Past-Year Total Physical Activity Questionnaire (PYTPAQ), and Canadian Diet History Questionnaire I (CDHQ-I). The final study population was 25,016 participants.

#### **4.2.2 Dietary Intake Assessment**

Past-year diet was assessed by the CDHQ-I, the National Cancer Institute's 124-item food frequency questionnaire (FFQ) of foods, beverages, and dietary supplements adapted to the Canadian context (20, 21). The CDHQ-I reflects food availability, brand names, nutrient composition, and food fortification in Canada and is representative of the foods commonly consumed by Canadian adults (22). Responses were analyzed using Diet\*Calc (version 1.4.2) software (National Cancer Institute, Bethesda, MD, USA) with a nutrient database adapted for the CDHQ-I to measure each participant's mean daily intake of energy, nutrients, foods, food groups servings and supplement use.

#### **4.2.3 Developing the HEI-C 2015**

The HEI-C 2015 is based on HEI-2015 scoring criteria (23) and adapted to Canada's Food Guide (CFG) 2007 (24). The HEI-2015, developed from the Dietary Guidelines for

Americans (DGA) 2015, expresses its components in an energy density manner with intake measured per 1,000 calories, congruent with the DGA (25). To align with CFG 2007, the HEI-C 2015 specifies food intake in sex- and age-specific CFG 2007 servings. The HEI-C 2015 score ranges 0-100, with higher scores indicating greater adherence to dietary recommendations (Appendix B details scoring criteria for HEI-2015 and HEI-C 2015).

The HEI-2015 assesses two major components of diet: adequacy and moderation. Adequacy, which measures sufficiency of intake of foods and nutrients, includes the components total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, and fatty acids in the HEI-2015. Moderation, which measures whether certain foods and nutrients are consumed in excess, includes the components refined grains, sodium, added sugars, and saturated fats in the HEI-2015. Similar to Jessri et al. who adapted the HEI-2010 to the Canadian context (26), the total fruits and total vegetables categories were combined in the HEI-C 2015 to adhere to CFG 2007 in which vegetables and fruit form one food group.

CFG 2007 serving recommendations for vegetables and fruit, milk and alternatives, and meat and alternatives formed the cut-off for the maximum scores in the HEI-C 2015 components total fruits and vegetables, dairy, and total protein foods, respectively. The cut-off for the maximum score of the HEI-C 2015 whole grains category is half the recommended number of grain products servings in CFG 2007, as it is recommended that 50% of grain products be whole grain (24). For all adequacy components other than fatty acids, the minimum score of zero is given when no servings of a particular component are consumed. Scoring criteria for fatty acids is identical to HEI-2015, in which a ratio of polyunsaturated fatty acids (PUFA) and

monounsaturated fatty acids (MUFA) to saturated fat (SFA) receives the maximum score if  $(\text{PUFA}+\text{MUFA})/\text{SFA}\geq 2.5$  and the minimum score if  $(\text{PUFA}+\text{MUFA})/\text{SFA}\leq 1.2$ .

The components of whole fruits and greens and beans from the HEI-2015 are included in the HEI-C 2015 as a percentage of the total recommended vegetables and fruit servings in CFG 2007 (27). For instance, the standard for the maximum score of greens and beans in the HEI-2015 is 10.5% of the standard for the maximum score of total fruits and total vegetables combined (i.e.,  $[0.2 \text{ greens and beans cup equivalents}/1,000\text{kcal}] / ([1.1 \text{ total vegetables cup equivalents}/1,000\text{kcal}] + [0.8 \text{ total fruit cup equivalents}/1,000\text{kcal}])$ ). To obtain the maximum score on the greens and beans component of the HEI-C 2015, 10.5% of the required total vegetables and fruit servings must be greens and beans servings, which is 0.74-0.84 servings/day depending on the age and sex group. The same calculation is done for whole fruits, of which 1.47-1.68 servings/day are required for the maximum score. Similarly, the component of seafood and plant proteins is also scored as a percentage total protein foods, calculated in the same manner as whole fruits and greens and beans.

In contrast to previous versions of the HEI, in the HEI-2015, legumes are counted in both vegetable and protein groups, including total protein foods, seafood and plant proteins, total vegetables, and greens and beans. The reasons for this change include facilitating the calculation of HEI scores, simplifying interpretation and tracking of scores over time, and highlighting protein variety (23). A further change made in the creation of the HEI-2015 relative to the previous version is the replacement of the empty calories category with added sugars and saturated fats categories, which are incorporated in the HEI-C 2015. Alcohol, which was part of the empty calories component in the HEI-2010, is no longer included as an index component.

All moderation components are reverse-scored to reward the restriction of consumption of refined grains, sodium, added sugars, and saturated fats. As CFG 2007 recommends 50% of grains consumed be whole grain (24), HEI-C 2015 gives the maximum score to refined grains consumption <50% and the minimum score to exclusive consumption of refined grains. CFG 2007 does not have quantitative recommendations for sodium, added sugars, or saturated fat intake. Sodium recommendations were taken from the Institute of Medicine (now National Academies of Science Health and Medical Division) Dietary Reference Intake. The maximum score in HEI-C 2015 was given for sodium consumption at or below the tolerable upper intake level (UL) of 2,300 mg/day (28), which is also the recommendation put forward by the DGA 2015 (25). The minimum score was given for double or more the UL. Scoring criteria for added sugars and saturated fats are identical to those in HEI-2015.

#### **4.2.4 Other Diet Quality Indices**

As a sensitivity analysis, diet quality was assessed using the Modified Mediterranean Diet Score (MMDS), which has been used extensively in assessing the diet quality of adults in Greece (29), Spain (30), and Italy (31). The MMDS has nine beneficial or detrimental components and total index score ranges from zero to nine, with higher scores indicating greater adherence to the Mediterranean diet. Each of the nine components is scored either zero or one based on the sex-specific median, with the exception of alcohol whose scoring criteria is based on set consumption values. The MMDS' components are constituents of the traditional Mediterranean diet, which is associated with a number of beneficial chronic disease outcomes (Appendix C details scoring criteria for MMDS). More detail regarding the MMDS can be found elsewhere (29).

#### **4.2.5 Assessment of Physician Visits for Mental Illness**

The number of physician visits for mental illness was obtained from AH administrative health datasets for practitioner claims between 2000 and 2015. A participant's visit with a physician was counted if it was coded as an affective disorder, anxiety disorder, psychotic disorder, substance use disorder, or depression on the primary, secondary, or tertiary health diagnosis fields of physician claims. Affective disorders, also referred to as mood disorders, are characterized by disturbances in mood, but may also include other mental or somatic disturbances (32). Depression, one type of affective disorder, is diagnosed based on sadness, loss of interest or pleasure, and reduced functioning (32). Psychotic disorders were categorized into organic psychoses (i.e., those induced through substances or physiologic reasons, such as pain or infection) and non-organic psychoses (i.e., schizophrenia-type psychoses). All psychotic disorders involve distorted thought and perception (32). Substance use disorders are characterized by the problematic use of drugs of abuse, including alcohol, prescription medications, and illicit drugs (32). International Classification of Diseases (ICD), Ninth Revision or ICD, 10<sup>th</sup> Revision codes were used to identify physician visits for all mental illnesses. For depression, additional ICD-9/10 codes were considered in combination with inpatient data and Anatomical Therapeutic Chemical Classification (ATC) codes for antidepressants or mood stabilizers from ABC pharmacy claims or PIN dispenses (see Table 4.1 for ICD-9/10 and ATC codes used). Only physician visits following participants' enrollment were considered.

#### **4.2.6 Other Covariates**

The baseline surveys collected self-report data on potential confounders. Sociodemographic variables were: sex; age; region of residence (urban or rural) determined by postal code; family history of gambling, alcohol, or drug addiction (yes/no); household income (<\$30,000, \$30,000-59,999, \$60,000-99,999, ≥\$100,000); highest level of education (high

school, some university, post-graduate); marital status (attached or unattached); employment status (full-time, part-time, other). Lifestyle factors included: body weight status (underweight/normal weight, overweight, obese); leisure time moderate-to-vigorous physical activity (MVPA) (quartiles rounded to meaningful values: <70.0 minutes/week, 70.0-209.9 minutes/week, 210.0-389.9 minutes/week,  $\geq 390.0$  minutes/week); smoking status (present, former, never); alcohol intake (g/week); use of supplements (yes/no), specifically vitamin D and other (vitamin A, beta carotene, vitamin E, vitamin C, thiamin, riboflavin, niacin, folic acid, calcium, magnesium, iron, zinc, copper, selenium). The Charlson comorbidity index (0, 1,  $\geq 2$  comorbidities) was calculated at baseline, specifically from three years prior to enrollment and six months afterwards, using AH records and the ICD-9/10 coding algorithm for administrative healthcare data. (33).

#### **4.2.7 Statistical Analyses**

Descriptive statistics are presented as means and standard deviations for continuous variables and percentages for categorical variables. Given the overdispersion of physician visits for mental illness, the associations between diet quality and mental illness physician visits were calculated using Negative Binomial Regression Models (NBM) for count data. Unadjusted, parsimonious, and fully adjusted NBMs were constructed. Parsimonious models were adjusted for potential confounding covariates identified in the literature: age, sex, annual household income, educational attainment, physical activity, BMI, and energy intake. Fully adjusted models were adjusted for potential confounding covariates based on statistics, using the purposeful selection method: age, sex, living in rural/urban areas, annual household income, educational attainment, marital status, family history of addiction, physical activity, BMI, smoking status, chronic disease comorbidities, vitamin d supplement use, other supplement use, alcohol

consumption, and energy intake. Missing values for confounding variables were treated as separate covariate categories in the multivariable NBMs, but their estimates are not presented. Analyses of the associations are reported as rate ratios, 95% confidence intervals, and corresponding p-values.

Four washout periods were used to account for mental illness occurring before enrollment in the ATP cohort, including three washout periods of fixed length and one of variable length. Due to the nature of the data linkage, AH health care records were not available prior to 2000. To assess the temporal relationship between diet quality and mental health service utilization, participants were excluded for:

- 1) Having a physician visit for mental illness in the *six months* prior to cohort enrollment or enrolling in the cohort between October 2000 and April 2001 (n=2,597)
- 2) Having a physician visit for mental illness in the *one year* prior to cohort enrollment or enrolling in the cohort between October 2000 and October 2001 (n=5,391)
- 3) Having a physician visit for mental illness in the *two years* prior to cohort enrollment or enrolling in the cohort between October 2000 and October 2002 (n=12,657)
- 4) Having a physician visit for mental illness *any time* after October 2000 and prior to cohort enrollment (n=7,681)

To account for potential increased health-consciousness immediately following enrollment in the ATP cohort, a second sensitivity analysis was conducted. The association between diet quality and the number of physician visits for mental illness was examined, with physician visits in the three months following enrollment not considered.



All analyses were conducted using STATA statistical software (Stata Corp LP. 2007, Release 14). Statistical significance was set at  $p < 0.05$ .

## **4.3 Results**

### **4.3.1 Characteristics of Study Participants**

A total of 25,016 participants (15,715 women and 9,301 men) were included in this analysis. Baseline characteristics of ATP participants are presented in Table 4.2. In this subset of the ATP cohort, 62.8% of participants were female and 65.7% were overweight or obese. Based on FFQ data, the mean HEI-C 2015 score was  $61.56 \pm 11.02$  and scores ranged from 19.81-96.07 (maximum range 0-100) (Table 4.3). The mean total MMDS score was  $4.28 \pm 1.70$ , ranging 0-9, which is the maximum score range. Of the 25,016 participants included in the analysis, 7,789 (31.14%) saw a physician for depression following enrollment, 7,184 (28.72%) for anxiety, 7,048 (28.17%) for an affective disorder, and 1,220 (4.88%) for an other mental illness.

Compared to participants included in analyses ( $n=25,506$ ), participants excluded ( $n=4,860$ ) had similar age (48.0 vs. 50.4 years), lower percentage of women (51.8 vs. 62.8 %), similar geographic distribution (rural: 24.8% vs. 23.6%), similar education (post-secondary or higher: 70.2 vs. 72.5%), and slightly higher percentage with one or more comorbidity (20.4 vs. 16.8%).

### **4.3.2 Diet Quality and Physician Visits for Mental Illness**

Table 4.4 presents the estimated reduction in the number of physician visits for depressive, anxiety, affective, and other mental illnesses for every 10-unit increase in HEI-C 2015 and component scores. After adjusting for all confounders, every 10-unit increase in HEI-C 2015 scores was associated with 4.79%, 5.92%, and 12.08% fewer physician visits for

depression, affective disorders, and other mental illnesses (RRs of 0.95, 0.94, and 0.88, respectively). Dietary adequacy was also negatively associated with physician visits, leading to 9.15%, 11.23%, and 17.44% fewer visits for depression, affective disorders, and other mental illnesses (RRs of 0.91, 0.89, and 0.83, respectively). For each 1-unit increase in MMDS score, there was a 2.48% and 2.22% reduction in the number of physician visits for depression and affective disorders, respectively (RR: 0.98 for both) (Table 4.5). Parsimonious and fully adjusted models displayed similar results for analyses measuring diet quality either as HEI-C 2015 or MMDS.

### **4.3.3 Controlling for Baseline Mental Illness**

When exclusion periods of six months, one year, two years, and variable length were considered, sample sizes were 22,419, 19,625, 12,359, and 17,335, respectively. A similar reduction in the number of physician visits for mental illness to models with no washout period was observed with washout periods of six months, one year, and variable length. In fully adjusted models with the six-month washout period, a 10-unit increase in HEI-C 2015 scores was negatively associated with depression (RR: 0.94 [95% CI: 0.91, 0.98]), affective disorders (RR: 0.93 [95% CI: 0.90, 0.97]), and other mental illnesses (RR: 0.90 [95% CI: 0.82, 0.98]). Similar results were observed for the adequacy component of the HEI-C 2015 for depression (RR: 0.91 [95% CI: 0.85, 0.96]), affective disorders (RR: 0.88 [95% CI: 0.83, 0.94]), and other mental illnesses (RR: 0.85 [95% CI: 0.73, 0.98]) (Table 4.6). Considering a one-year washout period, a 10-unit increase in HEI-C 2015 scores was associated with fewer physician visits: 5.52% for depression and 7.04% for affective disorders (RRs of 0.94 and 0.93, respectively). Similarly, following the one-year washout period, a 10-unit increase in adequacy scores was associated with 8.43% fewer visits for depression, 11.61% fewer visits for affective disorders,

and 16.45% fewer visits for other mental illnesses (RR: 0.92, 0.88, and 0.84, respectively) (Table 4.7). Considering the variable-length washout period, each 10-unit increase in HEI-C 2015 score was associated with fewer physician visits for depression (RR: 0.91 [95% CI: 0.87, 0.96]), affective disorders (RR: 0.90 [95% CI: 0.86, 0.95]), and other mental illnesses (RR: 0.87 [95% CI: 0.77, 0.98]) (Table 4.9).

Table 4.10 presents the results of the sensitivity analysis where physician visits in the three months immediately following cohort enrollment were not considered. Results are similar to those where no physician visits following enrollment were excluded (Table 4.4).

#### **4.4 Discussion**

This study examined the association between two diet quality indices, the HEI-C 2015 and the MMDS, and physician visits for four categories of mental illness in a sample of Albertan adults aged 35-69 years. The HEI-C 2015 and its components were inversely associated with mental health care use for depression, affective disorders, and other mental illnesses. Results with the MMDS were largely similar, with an inverse association displayed between MMDS scores and physician visits for depression and affective disorders. This suggests that adherence to healthy diets, whether those promoted by national dietary guidelines or in line with the Mediterranean diet, may be effective in reducing the health care burden of mental illnesses.

No associations were observed between diet quality, measured with any diet quality index, and anxiety. Previous studies have found similar results and have proposed reverse causality as a potential explanation (34). It is possible that pre-clinical anxiety may manifest through “healthy” dietary practices, resulting in the non-significant results found in this study and in others (34).

Our observation that diet quality was inversely associated with physician visits for other mental illnesses is novel. The 20% decrease in the number of physician visits associated with each 10-unit increase in HEI-C 2015 score and 8% decrease associated with each 1-unit increase in MMDS score are encouraging although the results with the MMDS did not remain significant following adjustment. To our knowledge, other mental illnesses, which was a composite category of psychotic disorders and substance use disorders, have not been investigated in relation to primary prevention via diet. In terms of tertiary prevention, a meta-analysis of 18 randomized trials of vitamin and mineral supplement use, found that vitamin B interventions were more effective than placebo treatments at reducing psychiatric symptoms for schizophrenia (35). It is possible that diet may play a protective and beneficial role for other mental illnesses, but given the dearth of research on the primary prevention of these other mental illnesses, we recommend further research to confirm these associations and determine which illnesses are driving the relationship.

It is difficult to situate this thesis in the body of literature as most studies on diet and mental illness have utilized symptom scales to measure mental illness outcomes. Symptom scales evaluate the presence of mental illness symptoms, regardless of whether formal diagnostic criteria are fulfilled. Promising results have emerged from research with this type of outcome measure. For example, the association between diet quality indices and depression in adults was recently summarized in a meta-analysis of 41 observational studies (36). Three cohort studies and four cross-sectional studies assessed diet using a version of the HEI or Alternative Healthy Eating Index (AHEI) (36). The cohort studies demonstrated a lower risk of incident depressive symptoms with high adherence to the diet quality index (0.76; 95% CI: 0.57, 1.02), as did the cross-sectional studies (0.53; 95% CI: 0.38, 0.75) (36). With regards to studies assessing

adherence to the Mediterranean diet, cohort studies displayed an inverse association between the highest degree of adherence and incident depressive symptoms (0.67; 95% CI: 0.55, 0.82), although the results of the cross-sectional studies were inconsistent (36). However, individuals with symptoms of mental illness and individuals seeking physician-provided mental health care form two separate but overlapping groups (4). Our study fills an important gap in examining whether the association between diet quality and symptoms of mental illness extends to individuals seeking health care for mental illness and contributes to our understanding of the potential of using dietary approaches to reduce the health care utilization burden.

Our results in which the adequacy component of the HEI-C 2015 remained significant following adjustment for confounders, but the moderation component did not are interesting and corroborate existing literature. A 2018 meta-analysis of 29 prospective studies found that adherence to high-quality diets – whether healthy/prudent, Mediterranean, pro-vegetarian, or Tuscan – was associated with a lower incidence of depression (16). However, unhealthy dietary patterns and food groups were not associated with incident depression (16). Taken together, these findings suggest that a diet sufficient in beneficial foods and nutrients may be more important than a diet restrictive in foods and nutrients recommended to be consumed in moderation. To our knowledge, other studies that have used versions of the HEI to investigate the relationship between diet quality and mental illness have not examined or reported the components of adequacy or moderation.

As a result of the ATP study design, in which participants were enrolled between 2000 and 2008 and linked to their administrative health care records from 2000 to 2015, we were unable to assess *incident* mental illness. Given the chronic and episodic nature of mental illness, our use of washout periods sought to exclude participants with mental health care utilization

prior to cohort enrollment. It is compelling that our results remained significant with the washout periods of six months (n=22,419), one year (n=19,625), and all visits between 2000 and cohort enrollment (n=17,335). Although our results were no longer significant with the two-year washout, either adjusted or crude, this is likely due to excluding all participants enrolled in the first two years of ATP. This resulted in a substantial reduction of study sample (12,359/25,016 or approximately half) and therefore loss of statistical power. Furthermore, as suggested by Molendijk et al., the correction for mental illness status at baseline may negate the cumulative effects of lifestyle behaviours in the years before the study (16).

The results of our study suggest that diet may have a significant impact on the health care burden of mental illness. The primary prevention of mental illness has received less attention than secondary and tertiary prevention. Recently, a 12-week randomized controlled trial titled the Supporting the Modification of lifestyle in Lowered Emotional States trial was conducted in Australia, to assess the treatment of moderate to severe depression (37). The intervention group, which received personalised dietary advice and nutritional counselling from a clinical dietician, displayed a significant improvement in depressive symptoms compared to the control group (37). However, it has been noted that selection bias and loss of blinding may have contributed to the large effects (38). Other dietary interventions have been conducted in recent years and lend support to our findings that dietary intake impacts mental health (14, 39, 40).

Certain limitations should be considered in the interpretation of this study. Although we included a wide range of relevant confounders, the possibility of residual confounding via unmeasured or imprecisely measured variables remains. The exposures of interest and confounders, with the exclusion of disease comorbidities, were based on self-report. Social desirability bias may be present, such that participants may have under- or over-reported certain

foods or nutrients, overestimated physical activity, and underestimated weight. Questionnaires were only completed at baseline, meaning we were unable to include time-varying variables in our models. Although a link has been posited between underweight and anxiety, we had to collapse the fields of underweight and normal weight in our analyses due to a small number of participants with a BMI classified as underweight (n=171). Our outcome measure was mental health service utilization, meaning we only included participants who had sought out and received physician care for a mental illness. Those who encountered barriers to care or received care outside of the medical system (e.g., psychological counselling through community mental health services) were not included, underestimating mental illness burden. Additionally, individuals of higher SES may have chosen to seek mental health support through private services, which were also not included. While the longitudinal design with years of follow-up was a significant strength, it is a limitation that not all participants were followed-up for the same length of time. Specifically, follow-up time ranged from six to 14 years, depending on the date of participants' enrollment. Other strengths of this study include the large sample size, the use of multiple measures of diet quality, and the inclusion of four categories of mental illnesses.

#### **4.5 Conclusions**

The present study contributes to the literature investigating the relationship between diet quality and mental illness. Findings from this study indicate that healthy, high-quality diets contribute to a reduced mental health service utilization burden, independent of SES, other lifestyle behaviours, and disease comorbidities. Given that the diet quality of many Canadians is of poor quality and either stagnating or declining (41, 42), interventions to improve the diets of Canadians at the population level could have a significant public health impact. Future studies

investigating the longitudinal association between diet and mental health care utilization are important to strengthen the prospective findings of this study.



Table 4.1. ICD 9/10 and ATC Codes Identifying Physician Visits for Mental Illnesses

<b>Disorder</b>	<b>ICD-9/10 and ATC codes</b>
<b>Affective disorders</b>	Claim data ICD-9: 296, 300.4, 301.1, 309.0, 309.1, 311
<b>Anxiety disorders</b>	Claim data ICD-9: 300, 309.8, excluding 300.14, 300.15, 300.16, 300.19, 300.4, 300.8, 300.81, 300.82, 300.89
<b>Depression</b>	Inpatient data ICD-9: 296.2-296.8, 300.4, 309, 311; ICD-10: F31, F32, F33, F34.1, F38.0, F38.1, F41.2, F43.1, F43.2, F43.8, F53.0, F93.0 <b>OR</b> Claim data ICD-9: 296, 309, 311 <b>OR</b> Inpatient data ICD-9: 300; ICD-10: F32.0, F34.1, F40, F41, F42, F44, F45.0, F45.1, F45.2, F48, F68.0, F99 <b>AND</b> ABC/PIN dispense data within 6 months of hospitalization ATC: N03AB02, N03AB52, N03AF01, N05AN01, N06A <b>OR</b> Claim data ICD-9: 300 <b>AND</b> ABC/PIN dispense data within 6 months of claims ATC: N03AB02, N03AB52, N03AF01, N05AN01, N06A
<b>Non-organic psychoses</b>	Claim data ICD-9: 295, 297, 298
<b>Organic psychoses</b>	Claim data ICD-9: 291, 292, 293, 294
<b>Substance use disorders</b>	Claim data ICD-9: 303, 304, 305.2-305.9

**Abbreviations:** ABC, Alberta Blue Cross; ATC, Anatomical Therapeutic Chemical Classification; ICD, International Classification of Diseases; PIN, Pharmaceutical Information Network

Table 4.2. Sample characteristics at baseline of ATP participants (n=25,016)

<b>Characteristic</b>	<b>% or Mean (SD)</b>
<b>Age</b>	
Years	50.39 (9.17)
<b>Sex</b>	
Male	37.18%
Female	62.82%
<b>BMI (kg/m<sup>2</sup>)</b>	
Underweight/normal weight ( $\leq 24.9$ )	34.03%
Overweight (25.0-29.9)	39.11%
Obese ( $\geq 30.0$ )	26.63%
<b>Location</b>	
Rural	23.64%
Urban	76.36%
<b>Family alcohol, drug, or gambling problem</b>	
True	22.77%
False	77.15%
<b>Leisure time MVPA</b>	
0-69.9 minutes/week	25.07%
70-209.9 minutes/week	26.84%
210-389.9 minutes/week	23.64%
$\geq 390$ minutes/week	24.44%
<b>Smoking status</b>	
Never	45.12%
Former	37.73%
Current	17.13%
<b>Household income</b>	
<\$30,000	12.71%
\$30,000-59,999	26.89%
\$60,000-99,999	31.87%
$\geq$ \$100,000	26.29%
<b>Highest level of education</b>	
High school	27.49%
Some university	46.94%
Post-graduate	25.56%
<b>Marital status</b>	
Attached	78.49%
Unattached	21.49%
<b>Employment status</b>	
Full-time	56.02%
Part-time	16.82%
Other	27.14%
<b>Alcohol</b>	
Grams/week	63.03 (137.37)
<b>Charlson comorbidity index</b>	
0	83.24%
1	14.31%
2+	2.45%
<b>Vitamin D use</b>	
Yes	58.93%

<b>No</b>	41.07%
<b>Other supplements use</b>	
<b>Yes</b>	79.98%
<b>No</b>	20.02%
<b>Energy intake</b>	
<b>Kcal/day</b>	1,826.81 (730.92)

**Abbreviations:** ATP Alberta's Tomorrow Project; BMI, Body Mass Index; MVPA, Moderate-to-Vigorous Physical Activity; SD, Standard Deviation

Table 4.3. Average Healthy Eating Index-Canada 2015 (HEI-C 2015) and component scores of ATP participants (n=25,016)

<b>Category/component</b>	<b>Possible range</b>	<b>Mean (SD)</b>
<b>Overall HEI-C 2015</b>	0-100	61.56 (11.02)
<b>Adequacy</b>	0-60	34.93 (8.88)
<b>Total fruits and vegetables</b>	0-10	8.02 (2.28)
<b>Whole fruits</b>	0-5	4.04 (1.40)
<b>Greens and beans</b>	0-5	2.53 (1.65)
<b>Whole grains</b>	0-10	3.64 (2.30)
<b>Dairy</b>	0-10	5.86 (3.14)
<b>Total protein foods</b>	0-5	3.43 (1.26)
<b>Seafood and plant proteins</b>	0-5	2.42 (1.44)
<b>Fatty acids</b>	0-10	4.98 (2.78)
<b>Moderation</b>	0-40	26.64 (6.33)
<b>Refined grains</b>	0-10	5.29 (2.33)
<b>Sodium</b>	0-10	7.08 (3.39)
<b>Added sugars</b>	0-10	7.86 (2.37)
<b>Saturated fats</b>	0-10	6.42 (2.90)

**Abbreviations:** ATP, Alberta's Tomorrow Project; HEI-C 2015, Health Eating Index-Canada 2015; SD, Standard Deviation

Table 4.4. Rate ratios and percent reductions for the association of **10-unit increases** in HEI-C 2015 and component scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses (n=25,016)

	Unadjusted			Parsimonious <sup>a</sup>			Fully Adjusted <sup>b</sup>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
HEI-C 2015	<b>0.96 (0.94, 0.99)</b>	<b>3.68%</b>	<b>0.010</b>	<b>0.95 (0.92, 0.98)</b>	<b>5.12%</b>	<b>0.001</b>	<b>0.95 (0.92, 0.98)</b>	<b>4.68%</b>	<b>0.002</b>
Moderation	<b>0.94 (0.89, 0.99)</b>	<b>6.03%</b>	<b>0.016</b>	<b>0.93 (0.88, 0.99)</b>	<b>6.55%</b>	<b>0.034</b>	0.96 (0.89, 1.02)	4.48%	0.172
Adequacy	0.97 (0.94, 1.01)	2.75%	0.122	<b>0.92 (0.88, 0.96)</b>	<b>8.10%</b>	<b>&lt;0.001</b>	<b>0.91 (0.87,0.96)</b>	<b>8.78%</b>	<b>&lt;0.001</b>
<b>Anxiety disorders</b>									
HEI-C 2015	1.02 (0.99, 1.04)	-1.77%	0.180	0.98 (0.96, 1.01)	1.50%	0.291	0.99 (0.96, 1.01)	1.44%	0.323
Moderation	1.02 (0.97, 1.06)	-1.72%	0.463	0.98 (0.92, 1.04)	2.04%	0.490	0.99 (0.93, 1.05)	1.39%	0.654
Adequacy	1.02 (0.99, 1.05)	-1.89%	0.250	0.98 (0.94, 1.02)	2.32%	0.277	0.97 (0.93, 1.02)	2.70%	0.230
<b>Affective disorders</b>									
HEI-C 2015	<b>0.95 (0.92, 0.98)</b>	<b>4.95%</b>	<b>0.001</b>	<b>0.94 (0.91, 0.97)</b>	<b>6.27%</b>	<b>&lt;0.001</b>	<b>0.94 (0.91, 0.97)</b>	<b>5.76%</b>	<b>&lt;0.001</b>
Moderation	<b>0.93 (0.88, 0.98)</b>	<b>7.38%</b>	<b>0.005</b>	<b>0.92 (0.86, 0.98)</b>	<b>8.00%</b>	<b>0.013</b>	0.94 (0.88, 1.01)	5.86%	0.088
Adequacy	<b>0.96 (0.92, 1.00)</b>	<b>4.12%</b>	<b>0.028</b>	<b>0.90 (0.86, 0.95)</b>	<b>9.98%</b>	<b>&lt;0.001</b>	<b>0.89 (0.85, 0.94)</b>	<b>10.68%</b>	<b>&lt;0.001</b>
<b>Other mental illnesses</b>									
HEI-C 2015	<b>0.82 (0.77, 0.88)</b>	<b>18.13%</b>	<b>&lt;0.001</b>	<b>0.83 (0.77, 0.89)</b>	<b>16.81%</b>	<b>&lt;0.001</b>	<b>0.89 (0.82, 0.95)</b>	<b>11.45%</b>	<b>0.001</b>
Moderation	<b>0.77 (0.69, 0.87)</b>	<b>22.66%</b>	<b>&lt;0.001</b>	0.88 (0.76, 1.02)	11.88%	0.085	<b>0.80 (0.68, 0.94)</b>	<b>19.90%</b>	<b>0.006</b>
Adequacy	<b>0.84 (0.77, 0.91)</b>	<b>16.00%</b>	<b>&lt;0.001</b>	<b>0.71 (0.64, 0.79)</b>	<b>28.69%</b>	<b>&lt;0.001</b>	<b>0.84 (0.75, 0.94)</b>	<b>16.13%</b>	<b>0.003</b>

**Abbreviations:** 95% CI, 95% Confidence Interval; HEI-C 2015, Health Eating Index-Canada 2015; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake

Table 4.5. Rate ratios and percent reductions for the association of **1-unit increases** in MMDS scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses (n=25,016)

	Crude			Parsimonious <sup>a</sup>			Fully Adjusted <sup>b</sup>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
MMDS	<b>0.94 (0.92, 0.96)</b>	<b>5.76%</b>	<b>&lt;0.001</b>	<b>0.97 (0.95, 0.99)</b>	<b>2.75%</b>	<b>0.004</b>	<b>0.98 (0.96, 0.99)</b>	<b>2.48%</b>	<b>0.010</b>
<b>Anxiety disorders</b>									
MMDS	1.00 (0.98, 1.02)	-0.14%	0.868	1.02 (1.00, 1.03)	-1.51%	0.085	1.01 (1.00, 1.03)	-1.36%	0.121
<b>Affective disorders</b>									
MMDS	<b>0.94 (0.92, 0.96)</b>	<b>6.07%</b>	<b>&lt;0.001</b>	<b>0.97 (0.95, 0.99)</b>	<b>2.67%</b>	<b>0.008</b>	<b>0.98 (0.96, 1.00)</b>	<b>2.22%</b>	<b>0.029</b>
<b>Other mental illnesses</b>									
MMDS	<b>0.92 (0.88, 0.97)</b>	<b>7.72%</b>	<b>0.001</b>	<b>0.94 (0.90, 0.99)</b>	<b>5.62%</b>	<b>0.018</b>	0.97 (0.93, 1.02)	3.23%	0.170

**Abbreviations:** 95% CI, 95% Confidence Interval; MMDS, Modified Mediterranean Diet Score; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake

Table 4.6. Rate ratios and percent reductions for the association of **10-unit increases** in HEI-C 2015 and component scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses with six-month washout (n=22,419)

	<b>Crude</b>			<b>Parsimonious<sup>a</sup></b>			<b>Fully Adjusted<sup>b</sup></b>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
HEI-C 2015	<b>0.96 (0.93, 1.00)</b>	<b>3.58%</b>	<b>0.025</b>	<b>0.94 (0.91, 0.98)</b>	<b>5.60%</b>	<b>0.001</b>	<b>0.95 (0.91, 0.98)</b>	<b>5.39%</b>	<b>0.002</b>
Moderation	<b>0.94 (0.89, 1.00)</b>	<b>5.85%</b>	<b>0.033</b>	<b>0.92 (0.86, 0.99)</b>	<b>7.69%</b>	<b>0.026</b>	0.93 (0.86, 1.00)	7.00%	0.056
Adequacy	0.97 (0.94, 1.01)	2.53%	0.202	<b>0.92 (0.87, 0.96)</b>	<b>8.36%</b>	<b>0.001</b>	<b>0.91 (0.86, 0.96)</b>	<b>8.98%</b>	<b>0.001</b>
<b>Anxiety disorders</b>									
HEI-C 2015	1.02 (0.99, 1.05)	-1.97%	0.163	0.98 (0.95, 1.01)	1.92%	0.206	0.99 (0.96, 1.02)	1.47%	0.348
Moderation	1.01 (0.97, 1.06)	-1.45%	0.559	0.97 (0.91, 1.03)	3.16%	0.318	0.99 (0.92, 1.05)	1.49%	0.657
Adequacy	1.02 (0.99, 1.06)	-2.32%	0.187	0.97 (0.93, 1.02)	2.66%	0.239	0.97 (0.93, 1.02)	2.69%	0.261
<b>Affective disorders</b>									
HEI-C 2015	<b>0.95 (0.92, 0.99)</b>	<b>4.60%</b>	<b>0.006</b>	<b>0.93 (0.90, 0.97)</b>	<b>6.66%</b>	<b>&lt;0.001</b>	<b>0.94 (0.90, 0.97)</b>	<b>6.43%</b>	<b>&lt;0.001</b>
Moderation	<b>0.93 (0.88, 0.99)</b>	<b>6.57%</b>	<b>0.024</b>	<b>0.92 (0.86, 0.99)</b>	<b>7.77%</b>	<b>0.034</b>	0.92 (0.85, 1.00)	7.59%	0.050
Adequacy	0.96 (0.92, 1.00)	3.81%	0.069	<b>0.89 (0.85, 0.94)</b>	<b>10.68%</b>	<b>&lt;0.001</b>	<b>0.89 (0.84, 0.94)</b>	<b>11.12%</b>	<b>&lt;0.001</b>
<b>Other mental illnesses</b>									
HEI-C 2015	<b>0.82 (0.76, 0.88)</b>	<b>18.45%</b>	<b>&lt;0.001</b>	<b>0.82 (0.76, 0.89)</b>	<b>17.64%</b>	<b>&lt;0.001</b>	<b>0.90 (0.83, 0.98)</b>	<b>9.62%</b>	<b>0.017</b>
Moderation	<b>0.81 (0.72, 0.92)</b>	<b>18.61%</b>	<b>0.001</b>	0.93 (0.79, 1.09)	6.97%	0.378	0.84 (0.70, 1.00)	16.22%	0.053
Adequacy	<b>0.83 (0.75, 0.91)</b>	<b>17.31%</b>	<b>&lt;0.001</b>	<b>0.69 (0.61, 0.77)</b>	<b>31.22%</b>	<b>&lt;0.001</b>	<b>0.86 (0.76, 0.98)</b>	<b>13.78%</b>	<b>0.023</b>

**Abbreviations:** 95% CI, 95% Confidence Interval; HEI-C 2015, Health Eating Index-Canada 2015; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake

Table 4.7. Rate ratios and percent reductions for the association of **10-unit increases** in HEI-C 2015 and component scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses with one-year washout (n=19,625)

	Crude			Parsimonious <sup>a</sup>			Fully Adjusted <sup>b</sup>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
HEI-C 2015	<b>0.96 (0.93, 0.99)</b>	<b>4.07%</b>	<b>0.023</b>	<b>0.94 (0.91, 0.98)</b>	<b>5.85%</b>	<b>0.002</b>	<b>0.95 (0.91, 0.98)</b>	<b>5.38%</b>	<b>0.006</b>
Moderation	<b>0.92 (0.86, 0.98)</b>	<b>8.35%</b>	<b>0.006</b>	<b>0.91 (0.84, 0.98)</b>	<b>9.21%</b>	<b>0.017</b>	<b>0.92 (0.84, 1.00)</b>	<b>8.50%</b>	<b>0.039</b>
Adequacy	0.98 (0.94, 1.03)	1.91%	0.395	<b>0.92 (0.87, 0.97)</b>	<b>7.96%</b>	<b>0.004</b>	<b>0.92 (0.86, 0.98)</b>	<b>8.12%</b>	<b>0.006</b>
<b>Anxiety disorders</b>									
HEI-C 2015	1.01 (0.98, 1.05)	-1.41%	0.364	0.98 (0.95, 1.01)	2.24%	0.181	0.98 (0.95, 1.02)	1.87%	0.278
Moderation	1.01 (0.95, 1.06)	-0.69%	0.799	0.96 (0.89, 1.03)	4.28%	0.219	0.97 (0.90, 1.04)	2.97%	0.420
Adequacy	1.02 (0.98, 1.06)	-1.84%	0.343	0.97 (0.93, 1.02)	2.77%	0.264	0.97 (0.92, 1.02)	2.87%	0.276
<b>Affective disorders</b>									
HEI-C 2015	<b>0.95 (0.91, 0.98)</b>	<b>5.20%</b>	<b>0.006</b>	<b>0.93 (0.89, 0.97)</b>	<b>7.24%</b>	<b>&lt;0.001</b>	<b>0.93 (0.89, 0.97)</b>	<b>6.82%</b>	<b>0.001</b>
Moderation	<b>0.91 (0.85, 0.97)</b>	<b>8.79%</b>	<b>0.006</b>	<b>0.91 (0.83, 0.99)</b>	<b>9.35%</b>	<b>0.023</b>	<b>0.91 (0.83, 0.99)</b>	<b>9.32%</b>	<b>0.032</b>
Adequacy	0.96 (0.92, 1.01)	3.57%	0.133	<b>0.89 (0.84, 0.95)</b>	<b>10.87%</b>	<b>&lt;0.001</b>	<b>0.89 (0.83, 0.95)</b>	<b>11.03%</b>	<b>&lt;0.001</b>
<b>Other mental illnesses</b>									
HEI-C 2015	<b>0.81 (0.74, 0.88)</b>	<b>18.98%</b>	<b>&lt;0.001</b>	<b>0.84 (0.77, 0.92)</b>	<b>15.72%</b>	<b>&lt;0.001</b>	0.93 (0.84, 1.02)	7.45%	0.102
Moderation	0.87 (0.76, 1.00)	12.79%	0.058	1.12 (0.93, 1.34)	-11.74%	0.230	0.97 (0.79, 1.18)	3.01%	0.764
Adequacy	<b>0.79 (0.71, 0.87)</b>	<b>21.49%</b>	<b>&lt;0.001</b>	<b>0.67 (0.59, 0.76)</b>	<b>33.37%</b>	<b>&lt;0.001</b>	<b>0.85 (0.74, 0.98)</b>	<b>15.28%</b>	<b>0.022</b>

**Abbreviations:** 95% CI, 95% Confidence Interval; HEI-C 2015, Health Eating Index-Canada 2015; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake



Table 4.8. Rate ratios and percent reductions for the association of **10-unit increases** in HEI-C 2015 and component scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses with two-year washout (n=12,359)

	Crude			Parsimonious <sup>a</sup>			Fully Adjusted <sup>b</sup>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
HEI-C 2015	0.99 (0.94, 1.03)	1.50%	0.537	0.96 (0.91, 1.01)	4.39%	0.088	0.98 (0.93, 1.03)	2.14%	0.426
Moderation	0.94 (0.86, 1.02)	6.12%	0.144	<b>0.89 (0.80, 0.99)</b>	<b>11.03%</b>	<b>0.035</b>	0.94 (0.84, 1.05)	6.05%	0.278
Adequacy	1.01 (0.95, 1.07)	-0.78%	0.796	0.96 (0.89, 1.04)	4.11%	0.290	0.98 (0.90, 1.07)	1.83%	0.660
<b>Anxiety disorders</b>									
HEI-C 2015	1.02 (0.98, 1.07)	-2.29%	0.283	0.99 (0.95, 1.04)	0.67%	0.772	1.00 (0.95, 1.05)	0.18%	0.940
Moderation	1.02 (0.95, 1.10)	-1.83%	0.632	0.96 (0.87, 1.05)	4.40%	0.362	0.95 (0.86, 1.05)	5.21%	0.298
Adequacy	1.03 (0.98, 1.08)	-2.59%	0.322	1.01 (0.94, 1.08)	-0.70%	0.837	1.02 (0.95, 1.10)	-2.24%	0.538
<b>Affective disorders</b>									
HEI-C 2015	0.98 (0.93, 1.03)	1.68%	0.515	<b>0.94 (0.89, 1.00)</b>	<b>5.83%</b>	<b>0.034</b>	0.97 (0.91, 1.03)	3.19%	0.269
Moderation	0.94 (0.86, 1.03)	5.86%	0.192	0.89 (0.79, 1.00)	10.73%	0.056	0.96 (0.85, 1.08)	4.43%	0.464
Adequacy	1.00 (0.94, 1.07)	-0.34%	0.916	0.92 (0.85, 1.01)	7.58%	0.067	0.95 (0.87, 1.04)	5.25%	0.237
<b>Other mental illnesses</b>									
HEI-C 2015	<b>0.77 (0.68, 0.87)</b>	<b>23.05%</b>	<b>&lt;0.001</b>	<b>0.83 (0.73, 0.95)</b>	<b>16.71%</b>	<b>0.006</b>	0.96 (0.84, 1.10)	3.80%	0.578
Moderation	0.83 (0.67, 1.02)	17.14%	0.078	1.00 (0.76, 1.31)	0.49%	0.972	1.14 (0.85, 1.53)	-14.08%	0.378
Adequacy	<b>0.73 (0.62, 0.85)</b>	<b>26.97%</b>	<b>&lt;0.001</b>	<b>0.68 (0.56, 0.82)</b>	<b>32.23%</b>	<b>&lt;0.001</b>	0.85 (0.69, 1.05)	14.72%	0.137

**Abbreviations:** 95% CI, 95% Confidence Interval; HEI-C 2015, Health Eating Index-Canada 2015; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake

Table 4.9. Rate ratios and percent reductions for the association of **10-unit increases** in HEI-C 2015 and component scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses with variable-length washout (n=17,335)

	Crude			Parsimonious <sup>a</sup>			Fully Adjusted <sup>b</sup>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
HEI-C 2015	<b>0.92 (0.89, 0.96)</b>	<b>7.61%</b>	<b>&lt;0.001</b>	<b>0.91 (0.87, 0.95)</b>	<b>9.17%</b>	<b>&lt;0.001</b>	<b>0.92 (0.88, 0.96)</b>	<b>8.34%</b>	<b>&lt;0.001</b>
Moderation	<b>0.88 (0.82, 0.94)</b>	<b>11.87%</b>	<b>&lt;0.001</b>	<b>0.87 (0.79, 0.95)</b>	<b>13.45%</b>	<b>0.002</b>	<b>0.87 (0.79, 0.96)</b>	<b>12.85%</b>	<b>0.005</b>
Adequacy	<b>0.94 (0.90, 0.99)</b>	<b>5.74%</b>	<b>0.022</b>	<b>0.87 (0.81, 0.93)</b>	<b>13.04%</b>	<b>&lt;0.001</b>	<b>0.87 (0.81, 0.93)</b>	<b>12.76%</b>	<b>&lt;0.001</b>
<b>Anxiety disorders</b>									
HEI-C 2015	1.01 (0.97, 1.04)	-0.52%	0.757	0.96 (0.93, 1.00)	3.52%	0.052	0.97 (0.93, 1.00)	3.17%	0.088
Moderation	0.99 (0.94, 1.05)	0.88%	0.763	0.94 (0.87, 1.01)	6.04%	0.103	0.96 (0.88, 1.03)	4.33%	0.270
Adequacy	1.01 (0.97, 1.06)	-1.28%	0.546	0.95 (0.90, 1.01)	4.69%	0.083	0.95 (0.89, 1.00)	5.24%	0.065
<b>Affective disorders</b>									
HEI-C 2015	<b>0.92 (0.88, 0.95)</b>	<b>8.47%</b>	<b>&lt;0.001</b>	<b>0.90 (0.86, 0.94)</b>	<b>9.95%</b>	<b>&lt;0.001</b>	<b>0.91 (0.87, 0.95)</b>	<b>9.31%</b>	<b>&lt;0.001</b>
Moderation	<b>0.87 (0.81, 0.94)</b>	<b>12.67%</b>	<b>&lt;0.001</b>	<b>0.87 (0.79, 0.96)</b>	<b>13.07%</b>	<b>0.004</b>	<b>0.87 (0.78, 0.96)</b>	<b>13.32%</b>	<b>0.005</b>
Adequacy	<b>0.93 (0.88, 0.98)</b>	<b>6.84%</b>	<b>0.009</b>	<b>0.85 (0.79, 0.91)</b>	<b>14.92%</b>	<b>&lt;0.001</b>	<b>0.85 (0.79, 0.92)</b>	<b>14.74%</b>	<b>&lt;0.001</b>
<b>Other mental illnesses</b>									
HEI-C 2015	<b>0.80 (0.73, 0.88)</b>	<b>19.68%</b>	<b>&lt;0.001</b>	<b>0.81 (0.73, 0.90)</b>	<b>19.01%</b>	<b>&lt;0.001</b>	<b>0.88 (0.79, 0.98)</b>	<b>12.05%</b>	<b>0.016</b>
Moderation	<b>0.75 (0.65, 0.88)</b>	<b>24.66%</b>	<b>&lt;0.001</b>	0.87 (0.71, 1.07)	12.61%	0.191	<b>0.76 (0.61, 0.95)</b>	<b>24.24%</b>	<b>0.015</b>
Adequacy	<b>0.85 (0.76, 0.95)</b>	<b>14.75%</b>	<b>0.005</b>	<b>0.70 (0.61, 0.81)</b>	<b>29.97%</b>	<b>&lt;0.001</b>	0.85 (0.73, 1.00)	14.60%	0.051

**Abbreviations:** 95% CI, 95% Confidence Interval; HEI-C 2015, Health Eating Index-Canada 2015; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake

Table 4.10. Rate ratios and percent reductions for the association of **10-unit increases** in HEI-C 2015 and component scores with number of physician visits for depression, anxiety disorders, affective disorders, and other mental illnesses from three months after cohort enrollment (n=25,016)

	<b>Crude</b>			<b>Parsimonious<sup>a</sup></b>			<b>Fully Adjusted<sup>b</sup></b>		
	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value	RR (95% CI)	(1-RR)%	p-value
<b>Depression</b>									
HEI-C 2015	<b>0.96 (0.94, 0.99)</b>	<b>3.75%</b>	<b>0.009</b>	<b>0.95 (0.92, 0.98)</b>	<b>5.08%</b>	<b>0.001</b>	<b>0.95 (0.92, 0.98)</b>	<b>4.68%</b>	<b>0.002</b>
Moderation	<b>0.94 (0.89, 0.99)</b>	<b>6.11%</b>	<b>0.015</b>	<b>0.94 (0.88, 1.00)</b>	<b>6.41%</b>	<b>0.039</b>	0.96 (0.89, 1.02)	4.48%	0.172
Adequacy	0.97 (0.94, 1.01)	2.81%	0.115	<b>0.92 (0.88, 0.96)</b>	<b>8.06%</b>	<b>&lt;0.001</b>	<b>0.91 (0.87, 0.96)</b>	<b>8.78%</b>	<b>&lt;0.001</b>
<b>Anxiety disorders</b>									
HEI-C 2015	1.01 (0.98, 1.04)	-1.44%	0.280	0.98 (0.95, 1.01)	1.87%	0.194	0.98 (0.95, 1.01)	1.83%	0.214
Moderation	1.01 (0.97, 1.06)	-1.39%	0.555	0.98 (0.92, 1.03)	2.50%	0.402	0.98 (0.92, 1.04)	1.96%	0.530
Adequacy	1.02 (0.98, 1.05)	-1.54%	0.353	0.97 (0.93, 1.01)	2.90%	0.178	0.97 (0.92, 1.01)	3.32%	0.142
<b>Affective disorders</b>									
HEI-C 2015	<b>0.95 (0.92, 0.98)</b>	<b>5.00%</b>	<b>0.001</b>	<b>0.94 (0.91, 0.97)</b>	<b>6.18%</b>	<b>&lt;0.001</b>	<b>0.94 (0.91, 0.97)</b>	<b>5.67%</b>	<b>&lt;0.001</b>
Moderation	<b>0.93 (0.88, 0.98)</b>	<b>7.36%</b>	<b>0.006</b>	<b>0.92 (0.86, 0.99)</b>	<b>7.74%</b>	<b>0.018</b>	0.94 (0.88, 1.01)	5.54%	0.109
Adequacy	<b>0.95 (0.92, 0.99)</b>	<b>4.20%</b>	<b>0.026</b>	<b>0.90 (0.86, 0.95)</b>	<b>9.91%</b>	<b>&lt;0.001</b>	<b>0.89 (0.85, 0.94)</b>	<b>10.61%</b>	<b>&lt;0.001</b>
<b>Other mental illnesses</b>									
HEI-C 2015	<b>0.82 (0.76, 0.87)</b>	<b>18.31%</b>	<b>&lt;0.001</b>	<b>0.83 (0.77, 0.89)</b>	<b>16.90%</b>	<b>&lt;0.001</b>	<b>0.88 (0.82, 0.95)</b>	<b>11.61%</b>	<b>0.001</b>
Moderation	<b>0.77 (0.69, 0.86)</b>	<b>23.06%</b>	<b>&lt;0.001</b>	0.88 (0.76, 1.01)	12.19%	0.078	<b>0.80 (0.68, 0.93)</b>	<b>20.34%</b>	<b>0.005</b>
Adequacy	<b>0.84 (0.77, 0.91)</b>	<b>16.10%</b>	<b>&lt;0.001</b>	<b>0.71 (0.64, 0.79)</b>	<b>28.80%</b>	<b>&lt;0.001</b>	<b>0.84 (0.75, 0.94)</b>	<b>16.30%</b>	<b>0.002</b>

**Abbreviations:** 95% CI, 95% Confidence Interval; HEI-C 2015, Health Eating Index-Canada 2015; RR, rate ratio

<sup>a</sup>Adjusted for sex, age, BMI, leisure time MVPA, household income, educational attainment, caloric intake

<sup>b</sup>Adjusted for sex, age, BMI, urban/rural location, family history of addiction, leisure time MVPA, smoking status, household income, educational attainment, marital status, employment status, chronic disease comorbidities, use of vitamin D supplements, use of other supplements, weekly alcohol intake, caloric intake

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## **Chapter 5: General Discussion and Conclusions**

### **5.1 Overview**

Mental illnesses are highly prevalent both globally (1) and in Canada (2), however not all individuals with symptoms of mental illness seek medical care (3). Contemporary treatments for mental illness such as psychopharmacology and psychosocial treatments are only effective in a proportion of cases and recurrence is common (4, 5). Despite the need for effective and novel interventions, our knowledge base remains limited. The primary prevention of mental illness through diet has emerged as a potential strategy to address the rising numbers of individuals with mental illness. In this thesis, I examined mental health service utilization in a population of Albertan adults, and focused on diet quality as a potential risk factor. I began with a literature review on mental illness in adults and the role of diet, and identified the challenges inherent to these fields.

### **5.2 Summary of Key Findings**

The objective of the first manuscript was *to describe in detail the factors associated with the utilization of health services for mental illness in Albertan adults*. Prior research has focused primarily on the sociodemographic characteristics, while neglecting lifestyle characteristics that may predict mental health service utilization. We confirmed the sociodemographic characteristics of mental health care users; specifically, those with female gender, low household income, unattached (i.e., not married or living with a partner) marital status, and non-full-time employment, were seeking physician-provided health care for mental illness more often.

In terms of lifestyle characteristics, we found that physician visits for mental illness were more common among those with low physical activity, current smoking status, obesity, disease

comorbidities, use of dietary supplements, low alcohol consumption, non-adherence to sugar recommendations, adherence to red and processed meat recommendations, and adherence to the Diet Quality Index-International (DQI-I). The link between “unhealthy” lifestyle behaviours and more frequent use of health care services for mental illness is not surprising, given the research on associations between diet, physical activity, and smoking and mental illness symptoms (6-10). However, the use of mental health care in individuals regularly using vitamins and/or dietary supplements, consuming low amounts of alcohol, and meeting recommendations for red and processed meat is unexpected. It is possible that Alberta’s Tomorrow Project (ATP), a cohort in which enrollment was voluntary, may be characterized by individuals taking an active interest in their health and seeking out preventive therapies, i.e., the healthy user effect.

The objective of the second manuscript was *to assess the prospective relationship between diet quality and the number of physician visits for mental illness, while taking into account the wide range of relevant confounders*. Adherence to a healthy diet, measured by the Healthy Eating Index-Canada 2015 (HEI-C 2015), was associated with a significant reduction in physician visits for depression, affective disorders, and other mental illnesses. When diet quality was assessed using the Modified Mediterranean Diet Score (MMDS), adherence was associated with a significant reduction in physician visits for depression and affective disorders. Associations were unattenuated after adjustment for numerous potential confounders, including sociodemographic variables, lifestyle variables, and disease comorbidities. Significant results also persisted when varying washout periods for mental health care utilization prior to cohort enrollment were tested. This suggests that adherence to healthy diets, whether those promoted by national dietary guidelines or in line with the Mediterranean diet, may reduce the burden of mental illness on the health care system.



We did not find an association between diet quality, measured via any diet quality index, and anxiety in this thesis. This is in line with previous research, which has hypothesized reverse causality as a potential explanation (8). It is possible that pre-clinical anxiety may manifest through increased adherence to dietary recommendations, resulting in the non-significant results found in this thesis and in other studies (8).

## **5.3 Contribution to the Literature**

### **5.3.1 Directionality**

The majority of the literature on diet and mental illness has utilized cross-sectional study designs, from which directionality cannot be determined (11, 12). A common outcome of mental illness is reduced-quality diets (13, 14), meaning that cross-sectional designs cannot differentiate between diet quality as a risk factor for mental illness or as an outcome. In this thesis, we utilized a prospective cohort study design with up to 15 years of follow-up time to assess the longitudinal relationship between diet quality and mental illness, specifically to ascertain the role of diet quality as a *predictor* of future mental illness.

Our persisting significant results with three washout periods and attenuated results with the two year washout period in Chapter 4 highlight the debate surrounding correction for baseline mental illness in this field. The association between diet and depression has recently been summarized in a systematic review of prospective studies, but the association was largely found to disappear when analyses controlled for baseline symptoms (11). Due to the relatively unchanging nature of dietary habits in adulthood, it was suggested that baseline correction could cancel out the effects of diet in the years prior to cohort entry (11). We did not have access to physician records prior to 2000 such that even with our most stringent washout periods, it is

possible that participants with prior physician visits for mental illness were included in our analyses. As a result, we were unable to calculate true incidence in this population. The Negative Binomial Regression Models in Chapter 4 calculate the Rate Ratio of physician visits for mental illness associated with diet quality, as opposed to an Incidence Rate Ratio. However, this thesis and the growing body of literature support directionality whereby improved diet quality reduces the risk of mental illness.

### **5.3.2 Health Service Utilization**

Administrative health data from Alberta Health (AH) was used to calculate the number of physician visits for mental illness in this thesis. Individuals with symptoms of mental illness and individuals seeking physician-provided mental health care form two separate but overlapping groups (15). Meta-analyses and systematic reviews have shown that the majority of research on the relationship between diet and mental illness has relied on symptom scales such as the Center for Epidemiologic Studies Depression scale (CES-D) or the Hospital Anxiety and Depression Scale (HADS), which evaluate the presence of mental illness symptoms, regardless of whether formal diagnostic criteria are fulfilled (11, 12). Symptoms scales may indicate the presence of a mental illness or else the presence of another disease with shared symptoms, such as metabolic disease (11). Furthermore, not all individuals with symptoms of mental illness seek health care (3). As a result, symptoms scales may overestimate the association between diet and mental illness. Studies that use physician-defined mental illness have typically relied on self-report such as through the question “Have you ever been diagnosed as having depression by a medical doctor?” on baseline questionnaires (16). The use of such self-report outcome measure may underestimate the prevalence of mental illness due to stigma. Furthermore, a physician visit for mental illness does not necessarily entail a diagnosis. The use of administrative health data in

this thesis circumvents these concerns and provides crucial information on the health care burden of mental illness.

### **5.3.3 Covariates**

A recent systematic review on diet and depression in children and adolescents by Khalid et al. highlighted the inadequate and inconsistent controlling for confounders in this field of research (12). We chose to create two models: 1) a parsimonious model with potential confounders informed by the literature and 2) a fully-adjusted model with potential confounders informed both by statistical methods and the literature. Although the fully-adjusted model included a number of more potential confounders, results of the two models were similar for all analyses. Overall, we included: age, sex, living in rural/urban areas, annual household income, educational attainment, marital status, family history of addiction, physical activity, body mass index (BMI), smoking status, disease comorbidities, vitamin d supplement use, other supplement use, alcohol consumption, and energy intake. Information on all confounders other than disease comorbidities was obtained from the baseline surveys completed between 2000 and 2008.

Variables of socioeconomic status (SES) including occupational status, educational achievement, and household income are important confounders in the relationship between diet quality and mental illness. Individuals with lower educational attainment, no full-time employment, and lower income are more likely to have worse mental health (17, 18). Further, improved diet quality or “healthy” dietary patterns are associated with higher SES (19, 20). The consumption of specific foods is patterned according to SES, with high-SES individuals consuming greater intakes of whole grains, lean meats, fish, vegetables and fruit (21). It is imperative that SES variables be included in analyses of the relationship between diet and mental health as all are associated with mental health status and dietary intakes.

As “healthy” and “unhealthy” lifestyle behaviours tend to cluster together (10), variables such as physical activity, smoking status, and alcohol consumption must be controlled for. A number of studies have been conducted displaying independent associations between each of these variables and mental illnesses (9, 10, 22). In fact, recent studies have found stronger associations between lifestyle behaviours and mental illness when examined concurrently (23). For instance, a recent study of 10- and 11-year old adolescents in Nova Scotia, Canada found that meeting an additional established lifestyle recommendation was associated with a reduction in physician visits for mental illness (23). To our knowledge, these results have not been replicated in adults. In our analysis in Chapter 3, we found that seeking mental health care was more common among those displaying certain unhealthy lifestyle behaviours: obesity, low physical activity, smoking, disease comorbidities, and poor diet quality. Given our results in Chapter 4, in which diet quality was independently associated with a reduced number of physician visits for depression, affective disorders, and other mental illnesses, it is likely that independent inverse associations exist between BMI, physical activity, smoking status, and disease comorbidities with the number of physician visits for certain mental illnesses. Further, the clustered nature of lifestyle variables suggests that the effect of these behaviours may be cumulative with respect to mental health service utilization in adults.

Disease comorbidities are rarely controlled for in the mental health literature, although some frequently co-occur with mental illnesses. We included as a covariate the Charlson comorbidity index, comprised of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, liver disease, diabetes with and without chronic complications, hemiplegia or paraplegia, renal disease, any malignancy (except malignant skin cancer),

metastatic solid tumor, and AIDS/HIV (24). Diet has been linked to a number of these diseases, however metabolic health has been highlighted as particularly important in the relationship between diet and mental illness (11). It is hypothesized that metabolic health may be on the causal pathway between diet and mental illness such that certain dietary habits predispose to metabolic health status which may increase the risk of mental illness (11). In this thesis, we controlled for disease comorbidities to ensure that they did not distort the true relationship between diet and mental illness and did not expand further on metabolic health. It is possible that because certain chronic diseases relating to metabolic health may be intermediaries in the association between diet quality and mental health service utilization, that adjustment for the Charlson index may represent overadjustment. Future research on the relationships between diet quality, mental illness, and chronic disease comorbidities is required.

It is also important to adjust for total energy intake when self-report dietary data comes from FFQ (25). In order to assess the association between diet quality and mental illness independent of energy intake, we adjusted for this variable in all multivariate models (25).

Although we included a wider range of confounders than is typical in the literature, the possibility of residual confounding remains. Observational studies with secondary data are limited by the data previously collected. It is possible that variables distorting the relationship between diet quality and mental illness exist and were not controlled for or were not sufficiently controlled for in the analyses. We suggest that future research examine other potential confounders that may be associated with both diet quality and mental health service utilization. Specifically, additional sociodemographic variables that could be investigated include race/ethnicity and recent immigration status. We included weekly alcohol intake as a covariate, but additional substance use such as cannabis could be an important confounder. Certain

psychosocial variables such as social exclusion and perceived health may be linked to both diet and mental health service utilization. We were unable to assess whether participants had a family doctor or regularly took medications either indicated for mental illness or indicated for other diseases but occasionally prescribed for mental illness. These variables are worth exploring and the question of how the use of medications should be controlled for requires further research. Finally, as highlighted above, metabolic health may play an important role in the relationship between diet quality and mental health service utilization. The meta-analysis by Molendijk et al. suggests that future analyses stratify results by changes in metabolic health (i.e., incident obesity, incident diabetes) (11). We support this idea, which would shed light on the extent to which a relationship between diet and mental health is moderated by metabolic health. However, it is worth noting that the inclusion of more confounders is not necessarily better and that overadjustment is a possibility.

#### **5.3.4 Diet**

Early research on diet and mental illness focused on specific nutrients or foods, such as vitamin D (26, 27), B vitamins (28, 29), folate (30, 31), and fish (32, 33). More recently, the focus has shifted to assessing diet as a whole, whether through diet quality indices or data-driven dietary patterns. In this thesis, diet was assessed in a number of ways, as adherence to food and nutrient recommendations and the DQI-I in Chapter 3 and as the HEI-C 2015 and MMDS in Chapter 4.

We examined a variety of food and nutrient recommendations and their distribution among users of physician services for mental illness in Chapter 3. We included dietary recommendations set by the government of Canada and other reputable North American organizations, specifically, Canada's Food Guide (CFG) 2007 (34), the 2015 Global Burden of

Disease Theoretical Minimum Risk Exposure (35), the Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult (36), the Canadian Cancer Society (37), the World Health Organization (38), and the 2015-2020 Dietary Guidelines for Americans (39). The largely non-significant results with respect to specific foods or nutrients predicting mental health service utilization in Chapter 3 suggest that no individual dietary component may be responsible for the primary prevention or increased risk of mental illness. Specifically, it is likely that diet as a whole is more significant in the development of mental illness, as evidenced by the association between DQI-I and component adherence with physician visits for mental illness.

In Chapter 4, we adapted the HEI-C 2015 from the HEI-2015 (40) using recommendations from CFG 2007 (34) and to our knowledge, were the first to do so. Previous versions of the HEI and the MMDS have been linked with symptoms and diagnoses of mental illness (16, 41-43). However, the existing literature evaluating the relationship between these particular indices and others, with mental illness has been inconsistent. For example, while the meta-analysis by Molendijk et al. found that high-quality diets were associated with a decreased risk of depression, this association was not apparent with low quality diets and food groups (11). Multiple systematic reviews and meta-analyses have been conducted in an attempt to assess whether adherence to various dietary guidelines or traditional dietary patterns is associated with symptoms or diagnoses of mental illness, most often depression (11, 12). Although these reviews tend to suggest an overall positive effect of high-quality diets on mental illness, these reviews have also highlighted the heterogeneity among measurement methods, which makes drawing conclusions difficult (11, 12).

In the ATP cohort, food frequency questionnaire (FFQ) was used to assess dietary intake. FFQ are used in approximately two-thirds of epidemiologic studies of diet and mental illness (11, 44). Other methods used less often include 24-hour dietary recall, diet records (DR), and single questions relating to the amount and portion size of a specific food or food group consumed (11, 44). One significant limitation of the 24-hour recall, DR, and single questions is that they focus on short term intake. Diet, which has underlying consistency, varies significantly from day to day. When investigating mental illnesses, it is long-term dietary exposure that is of interest. As a result, FFQ is the more relevant tool for measuring diet when investigating the relationship between diet quality and mental illness.

#### **5.4 Public Health and Clinical Implications**

Our results indicate that diet may positively impact mental health in adults and as a result, there are a number of public health and policy implications. The use of diet quality indices, which measure diet as a whole and produce a single, easy-to-interpret, and objective score, are easily translated for relevant knowledge users. The findings are interpretable by a wide-range of audiences including policy-makers, health promotion experts, academics, and educators. Furthermore, the results suggest that adherence to national government guidelines for nutrition have benefits beyond reducing chronic disease risk. Adherence to CFG 2007 may not only reduce an individual's risk of cardiovascular disease and cancer, but may also reduce the risk of certain mental illnesses. The way nutritional recommendations are presented could be reconsidered to include the demonstrated mental health benefits from the literature. For instance, CFG, which was most recently updated in 2019 contains no mentions of the mental health benefits of a healthy diet, even in the policy documents for health professionals (45). As diet is a



modifiable behaviour, primary prevention strategies for mental illness based on diet quality may have a significant impact, reducing the public health burden of these illnesses.

As this thesis used administrative health data to measure the outcome, there are clinical implications as well. With a high prevalence of mental illness in Alberta and throughout Canada (2), effective strategies to manage mental illnesses are greatly needed. In this thesis, it was demonstrated that adherence to a high-quality diet is associated with a reduced number of physician visits for certain mental illnesses, providing evidence for a positive impact on the health care system as a result of improved dietary practices. There are economic benefits to promoting dietary improvement via policy or education. Improving population-level nutrition will reduce health care costs not only for mental illness but also for all nutrition-related chronic diseases. It will reduce costs of mental illness-related absenteeism and presenteeism, social and judicial services, and disability claims. Overall, the results of this thesis have large implications for health service use and economics.

Future research is needed to confirm and expand upon the literature examining diet and mental illness. Specifically, 1) little research has been conducted beyond depression and anxiety as outcomes in this field, and the promising results concerning diet as a primary prevention tool for depression suggest that diet may be associated with other mental illnesses. The results of this thesis demonstrate an association between diet and affective disorders and other mental illnesses, and studies focusing on these individual mental illnesses are needed to confirm the association. 2) The majority of the research on diet and mental illness has been cross-sectional, meaning that the temporal sequence between exposure and outcome is unknown. The field would benefit from more large population-based cohort studies that can assess the directionality of the relationship. 3) It is not yet clear whether baseline mental illness should be controlled for in analyses. Greater

investigation into this issue, whether through washout periods or otherwise is required. As we were unable to discuss incident mental illness in this cohort due to administrative health data constraints, studies that follow our methodology with only incident cases of mental illness (i.e., washout period of all cases prior to cohort enrollment) would shed light on this debate. 4) Few randomized controlled trials have been conducted to examine diet as a primary prevention tool for mental illness. Although costly and time-consuming, these would provide stronger evidence than observational trials are capable of providing.

## **5.5 Strengths and Limitations**

A major strength of this thesis was the use of linked population-based cohort data and administrative health data. ATP is a research platform investigating the risk factors for chronic disease and cancer (46). AH administrative health data encompasses routinely collected records on healthcare services, frequency of service utilization, diagnoses, medications, and costs. The combination of two separate data sources, which differ in objective and function, maximizes the research potential of both the ATP and the administrative health data.

The large sample size of the ATP was a significant strength. This population includes both genders and a wide range of ages (35-69 years of age) randomly selected from Alberta's general population (46). However, as enrollment in the ATP was voluntary, there is the possibility of healthy user bias with health-conscious individuals enrolling in greater numbers than those with less interest in their health. This population may not necessarily be representative of the wider Canadian population, which may limit generalizability of results.

We comprehensively assessed diet using a variety of measures: adherence to various established North American dietary guidelines, the DQI-I, the HEI-C 2015, and the MMDS.

These measures are based on different concepts of a “healthy” diet and include dietary components distinct from one another, providing contrasting assessments of diet quality. To our knowledge, this is the first study to develop the HEI-C 2015 by adapting CFG 2007’s recommendations to the HEI-2015 for use in the Canadian context.

There are limitations to this thesis that should be acknowledged. As with all observational studies, there is the possibility of residual confounding via unmeasured or imprecisely measured variables. As we included a wider range of covariates than is typical, and included variables that have been highlighted as important, such as SES components, we believe that residual confounding is not a likely explanation for the observed associations.

In terms of study design, exposure was assessed at a single time period between 2000 and 2008, and participants were followed-up until 2015. Repeated measures of the exposure and covariates throughout follow-up would confirm the longitudinal association of diet and mental illness. Furthermore, due to the nature of the study design, all participants differed in the number of years of health records included before and after enrollment. Follow-up time ranged from approximately six to 14 years, which is a significant strength. In fact, previous research has highlighted the need for prospective cohort studies with long follow-up periods (11, 12). The longitudinal cohort design allowed for temporality between exposures and outcome.

The use of self-report data from FFQ to measure dietary exposures and covariates, instead of dietary biomarkers is a further limitation. Frequent underreporting occurs with foods recommended to be consumed in moderation, such as those high in sugar (47) or fat (48) when dietary intake is self-reported. Specific practices including the addition of salt during meal preparation or snacking behaviours may not accurately be captured by self-report FFQ (49). The CDHQ-I has been validated for Canadian adult populations and is representative of the foods

most commonly consumed by Canadians (50), however measurement error via underreporting is a potential limitation.

The assessment of all other covariates, with the exception of comorbidities, was also based on self-report and as a result may also involve a degree of error. Participants may have reported higher physical activity, lower weights, less smoking, and increased income, for example, due to social desirability bias. There is also the possibility of poor recall affecting any of the self-report data.

Reverse causation, wherein mental illness could affect the diet quality rather than vice versa, remains a possible interpretation of the observed results. We tested four washout periods to address this concern and found similar results between diet quality and mental illness with three of the washout periods. However, a two-year washout period, in which participants were excluded for having a physician visit for mental illness in the two years prior to ATP enrollment, was found to attenuate the results such that they were no longer significant. Molendijk et al. has highlighted the problem of controlling for baseline mental illness status, which may cancel out the effects of diet in the years prior (11).

## **5.6 Conclusions**

As the prevalence of mental illness is predicted to rise in Canada with a growing and aging population (2), urgent solutions are needed. Diet has been highlighted as a potential risk factor, impacting the development and progression of mental illness. This thesis evaluated diet quality as a correlate of mental illness, and findings suggest that diet quality may be an important risk factor to consider when examining physician visits for depression, affective disorders, and other mental illnesses in this age group. The modifiable nature of diet makes it an important

target in population-level primary prevention interventions of mental illness. Future research should build on these results to address gaps in the research and inform public health interventions on dietary improvement.

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## Appendix A: Scoring Criteria for the Diet Quality Index-International (DQI-I)

Score	Component	Scoring Criteria
<b>0-20</b>	<b><i>Variety</i></b>	
<b>0-15</b>	Overall food group variety (meat/poultry/fish/eggs; dairy/beans; grains; fruit; vegetables)	$\geq 1$ serving from each food group/day = 15 Any 1 food group missing/day = 12 Any 2 food groups missing/day = 9 Any 3 food groups missing/day = 6 $\geq 4$ food groups missing/day = 3 None from any food groups = 0
<b>0-5</b>	Within-group variety for protein source (meat; poultry; fish; dairy; beans; eggs)	$\geq 3$ different sources/day = 5 2 different sources/day = 3 1 source/day = 1 None = 0
<b>0-40</b>	<b><i>Adequacy</i></b>	
<b>0-5</b>	Vegetable group	$\geq 3$ -5 servings/day = 5 Proportionately scored in between 0 servings/day = 0
<b>0-5</b>	Fruit group	$\geq 2$ -4 servings/day = 5 Proportionately scored in between 0 servings/day = 0
<b>0-5</b>	Grain group	$\geq 6$ -11 servings/day = 5 Proportionately scored in between 0 servings/day = 0
<b>0-5</b>	Fiber	$\geq 20$ -30 grams/day = 5 Proportionately scored in between 0 grams/day = 0
<b>0-5</b>	Protein	$\geq 10\%$ of energy/day = 5 Proportionately scored in between 0% of energy/day = 0
<b>0-5</b>	Iron	$\geq 100\%$ RDA (AI)/day = 5 Proportionately scored in between 0% RDA (AI)/day = 0
<b>0-5</b>	Calcium	$\geq 100\%$ AI/day = 5 Proportionately scored in between 0% AI/day = 0
<b>0-5</b>	Vitamin C	$\geq 100\%$ RDA (RNI)/day = 5 Proportionately scored in between 0% RDA (RNI)/day = 0
<b>0-30</b>	<b><i>Moderation</i></b>	
<b>0-6</b>	Total fat	$\leq 20\%$ total energy/day = 6 $> 20$ -30% total energy/day = 3 $> 30\%$ total energy/day = 0
<b>0-6</b>	Saturated fat	$\leq 7\%$ total energy/day = 6 $> 7$ -10% total energy/day = 3

		>10% total energy/day = 0
<b>0-6</b>	Cholesterol	≤300 milligrams/day = 6 >300-400 milligrams/day = 3 >400 milligrams/day = 0
<b>0-6</b>	Sodium	≤2400 milligrams/day = 6 >2400-3400 milligrams/day = 3 >3400 milligrams/day = 0
<b>0-6</b>	Empty calorie foods	≤3% total energy/day = 6 >3-10% total energy/day = 3 >10% total energy/day = 0
<b>0-10</b>	<i>Overall balance</i>	
<b>0-6</b>	Macronutrient ratio (carbohydrate:protein:fat)	55-65:10-15:15-25 = 6 52-68:9-16:13-27 = 4 50-70:8-17:12-30 = 2 Otherwise = 0
<b>0-4</b>	Fatty acid ratio (PUFA:MUFA:SFA)	PUFA/SFA = 1-1.5 and MUFA/SFA = 1-1.5 = 4 Else if PUFA/SFA = 0.8-1.7 and MUFA/SFA = 0.8-1.7 = 2 Otherwise = 0

**Abbreviations:** AI, Adequate Intake; DQI-I, Diet Quality Index International; MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; RDA, Recommended Dietary Allowance; RNI, Recommended Nutrient Intake; SFA, Saturated Fatty Acids

**Appendix B: Scoring Criteria for the Healthy Eating Index-Canada 2015 (HEI-C 2015)**

	Maximum Points	Component	Standard for Maximum Points		Standard for Minimum Score of Zero	
			HEI-2015	HEI-C 2015	HEI 2015	HEI-C 2015
<b>Adequacy</b>	5	Total Fruits	≥0.8 cup eq. per 1,000 kcal		No Fruits	
	5	Total Vegetables	≥1.1 cup eq. per 1,000 kcal		No Vegetables	
	10	Total Fruits and Vegetables		7-8 servings		No Fruits and Vegetables
	5	Whole Fruits	≥0.4 cup eq. per 1,000 kcal	1.47-1.68 servings		No Whole Fruits
	5	Greens & Beans	≥0.2 cup eq. per 1,000 kcal	0.74-0.84 servings		No Dark Green Vegetables or Legumes
	10	Whole Grains	≥1.5 oz eq. per 1,000 kcal	3-4 servings		No Whole Grains
	10	Dairy	≥1.3 cup eq. per 1,000 kcal	2-3 servings		No Dairy
	5	Total Protein Foods	≥2.5 oz eq. per 1,000 kcal	2-3 servings		No Protein Foods
	5	Seafood & Plant Proteins	≥0.8 oz eq. per 1,000 kcal	0.64-0.96 servings		No Seafood or Plant Proteins
	10	Fatty Acids		(PUFA + MUFA)/SFA ≥ 2.5		(PUFA + MUFA)/SFA ≤ 1.2
<b>Moderation</b>	10	Refined Grains	≤1.8 oz eq. per 1,000 kcal	<50% of grains refined	≥4.3 oz eq. per 1,000 kcal	100% of grains refined
	10	Sodium	≤1.1 gram per 1,000 kcal	≤UL	≥2.0 grams per 1,000 kcal	≥2x UL
	10	Added Sugars		≤6.5% of energy		≥26% of energy
	10	Saturated Fats		≤8% of energy		≥16% of energy

**Abbreviations:** HEI-2015, Healthy Eating Index 2015; HEI-C 2015, Healthy Eating Index Canada 2015; MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; SFA, Saturated Fatty Acids; UL, Tolerable Upper Intake Level



### Appendix C: Scoring Criteria for the Modified Mediterranean Diet Score (MMDS)

<b>Max Points</b>	<b>Component</b>	<b>Standard for Maximum Points</b>	<b>Standard for Minimum Score of Zero</b>
1	Vegetables	≥sex-specific median	<sex-specific median
1	Legumes	≥sex-specific median	<sex-specific median
1	Fruits and nuts	≥sex-specific median	<sex-specific median
1	Cereal	≥sex-specific median	<sex-specific median
1	Fish	≥sex-specific median	<sex-specific median
1	Meat and meat products	<sex-specific median	≥sex-specific median
1	Dairy	<sex-specific median	≥sex-specific median
1	Alcohol	10-50g/day for men 5-25 g/day for women	otherwise
1	MUFA: SFA ratio	≥sex-specific median	<sex-specific median

**Abbreviations:** MMDS, Modified Mediterranean Diet Score; MUFA, Monounsaturated Fatty Acids; SFA, Saturated Fatty Acids