Dietary patterns and their impacts on colorectal cancer in Newfoundland and Labrador

by

© Zhi Chen

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Abstract

Dietary habits have long been regarded as an important environmental factor which may contribute to or prevent chronic health conditions, such as colorectal cancer (CRC). This thesis aims to derive the major dietary patterns and explore the association with CRC in the Newfoundland and Labrador (NL) population using two existing databases. It is presented in a manuscript format that includes three complementary papers focusing on the topic of dietary patterns and CRC. The first paper examines the dietary patterns in the general NL population and the assessment of whether these patterns vary according to demographic characteristics. The second paper relates the derived dietary patterns with CRC risk in this population. The third paper assesses the reliability of the identified dietary patterns by comparing them with those from another study several years later using identical methods in the NL population. Overall, findings from this thesis suggest a four-factor dietary pattern (i.e., Meat pattern, Vegetables/Fruits pattern, Fish pattern, Grain pattern). Further, results suggest that the Meat-diet and the Sugary-diet increased the risk of CRC with corresponding odds ratios (ORs) of 1.84 (95% CI: 1.19-2.86) and 2.26 (95% CI: 1.39-3.66) for people in the highest intake quintile compared to those in the lowest. Whereas plant-based diet pattern decreased the risk of CRC with a corresponding OR of 0.55 (95% CI: 0.35-0.87). The reliability study suggests that the identified NL dietary patterns are reasonably stable overtime and across studies. This thesis provides more evidence to support healthy eating for the primary prevention of CRC in the NL population.

Key Words colorectal cancer, dietary pattern, nutritional epidemiology, exploratory factor

analysis, reproducibility, Newfoundland and Labrador population

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Table of Contents

Abbreviations

BMI	Body Mass Index
BTS	Bartlett's Test of Sphericity
CCHS	Canadian Community Health Survey
CCS	case control study
CHD	coronary heart disease
CRC	colorectal cancer
CTCC	Colorectal Cancer Interdisciplinary Health Research team in Colorectal Cancer
EFA	exploratory factor analysis
ESHA	Elizabeth Stewart Hands and Associations
FAP	familial adenomatous polyposis
FFQVP	food frequency questionnaire validation project
FFQ	food frequency questionnaire
FHQ	family history questionnaire
HRT	hormone replacement therapy
HRU	Health Research Unit
HREA	Health Research Ethical Approval
HREB	Health Research Ethics Board
ICD	International Classification of Disease
KMO	Kaiser-Meyer-Olkin
METs	metabolic equivalent hours
NFCCR	Newfoundland familial colorectal cancer registry
NLCAHR	Newfoundland and Labrador Center for Applied Health Research

NL	Newfoundland and Labrador
NSAIDs	non-steroidal anti-inflammatory drugs
ON	Ontario
OR	odds ratios
PCA	principal component analysis
PHQ	personal history questionnaire
95% CI	95% confidence interval
SAS	Statistical Analysis System
SPSS	Statistical Package for Social Science

List of Tables

List of Figures

Candidate's Contribution to the Work

This project used secondary data recruited by Newfoundland Familial Colorectal Cancer Registry (NFCCR) and Health Research Unit from Memorial University. Dr. Peizhong Peter Wang and the candidate conceptualized and designed the specific research projects presented in this thesis. Then, the candidate conducted the literature review, wrote project proposal, and compiled the secondary data for further analysis. Finally, the candidate conducted all statistical analyses using the SAS and SPSS software, then presented and interpreted the study findings, and completed final thesis.

To date, Chapter 4, *Paper 1. Four major dietary patterns identified for a target-population of adults residing in Newfoundland and Labrador, Canada*, is published by BioMed Central Public Health [1]; Chapter 5: *Paper 2. Dietary patterns and colorectal cancer: results from a Canadian population-based study*, has been published online by Nutrition Journal [2]. They are open access articles and published online. All of the co-authors made contributions to revise the papers so that they meet the standards of publication. Detailed information were listed in separated cover page in every experimental paper.

Chapter 1: Introduction

1.1 Background & Rationale

In Canada, colorectal cancer (CRC) is the second leading cause of death from cancer with approximate 22,500 newly diagnosed cases and 9,100 deaths in 2010 [3]. The statistics remain increasing; an estimated 24,400 new cases and 9,300 deaths were reported in 2014 [4, 5]. Newfoundland and Labrador (NL) has been reported to have the highest age-standardized incidence rate in Canada with a rate of 88 per 100,000 for men and 52 per 100,000 for women in 2010 [6]. Even though exact causes are unknown, dietary factors have been widely considered as one of the most important factors in causing or preventing CRC [7-9]. Two major approaches were applied to explore the association between diet and CRC in nutritional epidemiological studies: the single nutrient/food approach and dietary pattern analysis.

The single nutrient/food approach was the traditional one used in previous nutritional epidemiology and abundantly valuable associations were found. However, because people do not eat isolated nutrients and foods, there are several limitations to this traditional approach. The single-nutrient approach fails to take into consideration the complicated interactions among nutrients, potential confounding effects of an individual's eating habit, and the increased false positives due to multiple comparisons [10]. To address these limitations, dietary pattern analysis is proposed and used with increasing popularity. It takes advantage of considering the joint effect of nutrients and foods which are consumed

in combination in the real world. It may provide a more accurate and comprehensive description of actual dietary exposure and be used as a more practical way to explain the relationship between dietary habits and CRC.

This thesis aims to explore the dietary patterns in the NL population and their association with demographic and socioeconomic factors, as well as the risk of CRC incidence. A better understanding of diet and chronic disease can allow for enhanced public education and awareness on nutrition, enhanced support, policy development, and ideally the improvement of the dietary habits of communities. This thesis comprises three studies, which were independently conducted on two time-separated study samples from the same population. Detailed rationale and a brief introduction of the three studies are listed in the following paragraphs.

Due partly to geographic isolation, people always believe that dietary and cultural differences exist between NL and the rest of Canada [11]. Because the 2004 Canadian Community Health Survey (CCHS Cycle 2.2, Nutrition Focus) [12] did not contain some foods commonly found in the NL diet, such as, pickled meat and cloudberry (bake-apples), it may not have portrayed an accurate representation of this population's unique dietary intakes. Even though single nutrient/food consumptions and their relationships with CRC incidence have been extensively discussed in NL, very limited epidemiological study on this topic was conducted from the perspective of dietary pattern [13-19]. In order to know more about the true food consumption patterns of NL residents, there is a need to assess dietary patterns of this population. The first study of this thesis project was

conducted on a general adult NL population, aged from 35-70 years, recruited between February 2011 and May 2012. Dietary information was evaluated using a self-administrated food-frequency questionnaire (FFQ), while demographic information was collected through telephone interviews. After exclusion, a total of 192 respondents were entered into the final analysis.

Previous studies have explored the relationships between dietary patterns and CRC risk in different populations [20-23]. Due to the effects of individual dietary habits, geographic factors, and cultural differences, however, the dietary pattern approach is population-dependent, which may limit the external validity of existing findings [24]. Therefore, it is necessary to elucidate the relationship between certain dietary patterns and CRC risk of the general NL population. The second study of this project is a case-control study conducted among CRC cases diagnosed during 1999-2003 and population controls recruited during 2001-2005. After exclusion, a total of 1179 participants (cases and controls) remained for final analysis. Dietary exposure data was collected using a self-administered FFQ, and demographic and medical information was collected using a personal history questionnaire (PHQ).

People's diet habits usually change only when they experience dramatic changes in their personal circumstances, including getting married, moving to another country, or being warned by a doctor that their current diet will have a significant and negative impact on their health. Researchers summarized several factors which may influence individual and population-based food choices: family income, food prices, individual preferences and

religion reliefs, cultural traditions and customs, as well as other geographic and environmental factors [8, 25]. While dietary patterns are often believed to be stable in a population, there is limited research assessing its reliability. This study derived and compared major dietary patterns defined by factor analysis. Dietary data was collected with a food-frequency questionnaire (FFQ) in two projects conducted in the NL population: a population-based case-control study (CCS) from 2001 to 2005 and a food-frequency questionnaire validation project (FFQVP) in 2012. The third study firstly derived major dietary pattern for the 554 from the CCS (controls) and the 192 participant from FFQVP and then compared their dietary patterns to discuss the reliability of the dietary pattern analysis approach used in this study.

1.2 Study objectives

The study objectives of the thesis projects are:

1. To identify the major dietary patterns for the general NL population and to assess whether these patterns vary according to demographic characteristics.
2. To determine the associations between the derived dietary patterns and CRC risk in this population.
3. To assess the reliability of dietary patterns in the NL population by comparing dietary patterns identified from two studies conducted in different times using identical method in the same population.

1.3 Organization

This thesis is divided into seven chapters. Chapter 1 is an overall introduction to this

thesis. Chapter 2 reviews the epidemiologic description and risk factors of CRC, and describes the new approach of dietary pattern analysis. Chapter 3 presents in detail the data sources and methods on information collection employed in this study. Chapter 4 to 6 presents three papers in manuscript format, each including its own introduction, methods, results, discussion and conclusion. They are distinct but related. Some repetition of methods was not avoidable. Chapter 7 summarizes the key findings, and discusses the implications of the study results and suggests future research.

Chapter 2: Literature review

People get essential nutrients from food which is responsible for body's energy, growth, repair, and regulation; therefore, diet is considered a determinant of health. A healthy diet plays an important role in immune system health, maintaining a healthy weight, and avoiding general illness [26]. Epidemiological studies have demonstrated the effects of dietary factors on contributing to and preventing from many diseases, including cancer, coronary heart disease, and diabetes [7-9]. Even though the perspective of this study is broad, the literature review section is confined to two areas that are directly related to the study purposes: 1) epidemiology of colorectal cancer; 2) dietary patterns.

2.1 Epidemiology of colorectal cancer

CRC is considered to be caused by adenomatous polyps (adenomas), and about 1-10% of adenomas are likely to develop into invasive cancer [27]. This disease is age-related; half of patients are diagnosed at age 60 years or higher [28]. Generally, this disease is diagnosed by colonoscopy. It is usually treated through surgery, sometimes, after treated by chemotherapy.

2.1.1 Incidence and mortality of CRC

The distribution of CRC significantly varies over the world [29, 30]. In general, the rates in developed countries are very high, where consumed very high quantities of meat, including North America, northern and western Europe, Australia, and New Zealand [31,

32]. Conversely, with a high consumption of fiber-rich vegetables and starchy carbohydrate, the lowest rates in the world are found in Asia, Africa, and most of Latin America [31, 32]. For example, in the time period 1998 to 2002, the incidence rate among males in India was 4.1 per 100,000 while the rate was 59.1 per 100,000 in Czech; among females, the rate in India was 3.6 per 100,000 versus 39.5 per 100,000 in New Zealand [32]. In total, there are about 655, 000 deaths worldwide per year due to CRC; it is the second leading cause of death from cancer in men and women combined [3, 33, 34].

In Canada, 22,500 diagnoses and 9,100 deaths were from CRC in 2010 [3]. In 2014, an estimated 24,400 new cases will be diagnosed and more than 9,300 patients will die of this disease in Canada [4, 5]. In 2010, the estimated age-standardized incidence rates of CRC were 62 per 100,000 among men and 41 per 100,000 among women, and the estimated age-standardized mortality rates were 26 per 100,000 men and 16 per 100,000 women [3]. The Canadian Cancer Statistics shows the trend of CRC incidence rate during 1984 to 2013, which declined from the mid-1980s until the mid-1990s; the incidence rate only rose through 2000 then declined significantly thereafter [35].

The inter-provincial CRC incidence rates vary markedly in Canada. NL has the highest rates of CRC in Canada, with a rate of 88 per 100,000 for men and 52 per 100,000 for women in 2010 [6], followed by Prince Edward Island, Nova Scotia. British Columbia has the lowest rates for both genders. Rates in Ontario (ON) lies in the middle place among the ten Canadian provinces/territories, with rates of 60 per 100,000 among men and 41 per 100,000 among women [6].

2.1.2 Risk factors associated with CRC

2.1.2.1 General risk factors associated with CRC

Even though the exact causes of CRC are unknown, there are certain known risk factors. These risk factors could be roughly grouped into 2 categorizes: inherent risk factors and lifestyle-related risk factors; the former cannot be changed while the latter links to habits that are modifiable [36].

In the literature are reported a series of inherent risk factors of CRC, including age (i.e., risk gets higher as one gets older) [37]; gender (males are at higher risk) [38]; race or ethnic background (e.g., being African American or Ashkenazi) [39, 40]; history of polyps or ulcerative colitis or Crohn's disease [41-43]; history of type 2 diabetes [44, 45]; family history of CRC [46-48]; inherited family syndromes (e.g., familial adenomatous polyposis (FAP) or hereditary non-polyposis colon cancer (HNPCC)) [49]. Approximately 5%-10% of familial CRC cases result from hereditary genetic mutations, and mainly consist of FAP and HNPCC [50, 51]. FAP accounts for less than 1% of all CRC patients [52], while HNPCC accounts for 1% - 6% of all colorectal cancers [53-55]. The high CRC incidence in NL may be attributed to high prevalence of familial hereditary colon cancer [56]. However, hereditary genetic mutations can only explain part of high CRC incidence in NL.

Some lifestyle-related factors have been also related to a higher risk of CRC, including dietary habits [57-59], less physical activity [60, 61], obesity [62-64], and environmental factors (e.g., occupation) [65, 66]. One study reported that 70% of CRC incidence can be

prevented by changes in diet and lifestyle [67]. The considerable difference in worldwide incidence (about thirty-fold between developed and developing countries) may be attributed to the role of dietary factors in inducing this cancer. Researchers summarized that risk factors, including meat consumption, dietary fat intake, tobacco and alcohol use, and smoking**,** may be associated with higher incidence rate of CRC [32, 36, 68]. Similar epidemiologic studies have suggested that increased intake of dietary fiber (e.g., grains, vegetables and fruits, etc.) is associated with a decreased risk of CRC [69]. Dietary factor will be considered emphatically in the following paragraphs.

2.1.2.2 Dietary risk factors associated with CRC

Dietary factors have been strongly associated with the incidence of CRC in many studies [48, 70]. Hence, interest in diet as well as associations between dietary factors and CRC has been raised for a while. From the perspective of methodologies, there are two major approaches in nutritional epidemiological studies on this topic: the single-nutrient approach and dietary pattern analysis. Therefore, similarly, specific nutrients or foods and certain dietary patterns are the two commonly used approaches to study dietary risk factors associated with CRC.

The single-nutrient approach, which typically examines the associations between diseases and one or more nutrients or foods, has been widely used in nutritional epidemiology for decades. Results from this traditional approach can help people understand the possible mechanism since it explores associations between certain nutrients with CRC. For example, results showed that higher consumptions of animal fat and/or protein (e.g., meat,

red meat) are associated with higher risk of CRC while higher intakes of fruits and vegetables are related to lower risk of CRC [71, 72]. Higher consumption of animal fat and protein can be related to overweight and obesity, which previous studies have found to be important risk factors for CRC [73-75]. While one possible mechanism of protective effects of vegetables and fruits against CRC is that they are good sources of vitamins A, C, and E, fibers, minerals, selenium, and carotenoids which could help to bind and dilute carcinogens, enhance anti-oxidant effects, and promote healthy physical environment in colonic flora [76-78].

Dietary pattern analysis was also applied in a large body of studies in the past decade to investigate the associations between dietary factors and CRC [21, 79-87]. Dietary patterns take overall effect of one's dietary exposure into consideration which would more approach to the real world [10]. Generally, according to the literature, the patterns that were labelled as "healthy" or "prudent", mainly characterized by a higher consumption of fruits, vegetables, and grains, and lower consumption of sweets, red meat, and processed meat, were associated with a lower risk of colorectal cancer; conversely, those defined as "western", which entail higher intakes of meat, highly processed food, potatoes, and refined carbohydrates, as well as lower intakes of greens and dietary fiber, have been associated with an increased CRC risk [20-22].

However, critical conceptual and methodological concerns of the traditional single-nutrient approach have been raised. Specifically, the specific effect of a single nutrient or food is likely to be confounded by others because people do not consume foods or

nutrients in isolation [88] [89, 90]. Therefore, dietary pattern analysis, which described a more comprehensive and accurate dietary exposure of a population, have been proposed and used in nutritional epidemiology with increasing popularity. This thesis project was conducted through dietary pattern analysis and a detailed introduction of this approach will be outlined below.

2.2 Dietary patterns

Dietary pattern analysis has been used widely as an alternative and complementary approach to describe the dietary habits of individuals and populations. Different from traditional single-nutrient approach, dietary pattern analysis examines the effects of overall food- and nutrient-consumptions, which resembles more closely the real world. Because dietary patterns conceptually describe a more comprehensive and real diet, it may be more predictive of disease risk compared to isolated foods or nutrients [10].

2.2.1 The single-nutrient approach versus dietary pattern analysis

2.2.1.1 Strengths & limitations of the single-nutrient approach

The single-nutrient approach explored the associations between a specific nutrient/food and health outcomes; results from this approach are obvious and can help people better understand the possible mechanism. It is quite valuable for translating knowledge into public health guidance. However, the conceptual and methodological limitations were proposed.

First of all, the single-nutrient approach is likely to be confounded by the effect of an

individual's dietary patterns because of the common associations between nutrient intakes and particular dietary patterns [91, 92]. For example, an association between lower dietary fat and higher consumption of vegetables, fruits, and whole grains was reported by Ursin et al [93]. Because the so-called "prudent" pattern, characterized by higher intakes of vegetables, fruits, and whole grains, has been reported to be protective against coronary heart disease (CHD) [94, 95], these dietary components are likely to confound the relationship between dietary fat and CHD. Therefore, the simple single-nutrient analysis needs to be adjusted for the possible confounding factors; however, it may not be possible to remove all the confounding effects because of the interactions among them.

Secondly, the single-nutrient approach may fail to take into account the complicated interactions among nutrients when conducting studies in free-living populations [96]. The combined nutrients people ingest from meals that consist of a variety of foods may have an interactive or synergistic relationship [96]. Intake of a particular food or nutrient may occur at the expense of other foods or nutrients [97]. For example, the presence of vitamin C will significantly increase iron absorption [98]. Therefore, in studies conducted on free-living people, it is hard to determine harmful or protective effects of some components on certain diseases even if very strong associations with these diseases are detected.

Thirdly, given that strict inter-correlation may exist among some nutrients, it is difficult to determine their separate effects of one or several nutrients when they are simultaneously entered into a logistic regression equation [97]. For example, the degree of independent

variation of potassium and magnesium would be considerably reduced when they are introduced into a model together [99]. Also, because of the complicated inter-correlations among various nutrients or foods, rate of false positives may be increased when conducting multiple comparisons [97].

Finally, because most dietary components are related to total energy intake, components of a diet are considered to be correlated with a disease when an association between total energy intake and the disease is found [100]. However, not every component shows the same association with the disease as the total energy intake. In this case, an inverse or wrong relationship may be explored if a conclusion is made simply based on the relationship between total energy intake and a disease [97].

2.2.1.2 Strengths & limitations of dietary pattern analysis

Dietary pattern analysis was suggested to overcome the limitations of the traditional single-nutrient approach. Different from this traditional method, it explores the effects of overall diet instead of analyzing the effect of each food or nutrient. This new direction considers the joint effects of combined nutrients and foods and takes advantage of the collinearity of nutrients and foods, therefore representing a comprehensive and accurate picture of dietary exposure, and thus may be more predictive of disease risk than the traditional single-nutrient focus [10].

However, this approach was criticized by its arbitrary decision-making regarding the assignment of foods to food groups, the number of retained factors, the method of rotation,

and the labels of retained components [101]. While factor analysis using predefined food groups is widely accepted in nutritional epidemiological research [24, 102, 103], we have not noticed published studies that compare differences using predefined food groups and the raw food items. As part of a sensitivity analysis, in the first study of this thesis, we did factor analysis based on the 169 original food items in the FFQ and discussed its reliability through two time-separated studies in the NL population.

2.2.2 Major dietary patterns identified from previous studies

Although dietary patterns are not consistent among different populations, there are two typical dietary patterns derived by a large quantity of studies. The healthier one is often labeled as the "Prudent or Healthy" pattern or "Mediterranean" pattern, and generally characterized by a high consumption of fruits and vegetables [104-108], and particularly, by whole grains in some Western populations[83, 84, 109, 110], by soya foods in Asian countries [111-116], and by seafood in both western and Asian countries [111, 113, 116]. The less healthy one is often named as the "Western" pattern, characterized by high intakes of meat, highly processed meat, sweets and desserts, French fries, and refined grains; it has been identified in many previous studies in both Asian populations [111-117] and Western countries [39, 58, 79, 83, 84, 109, 110, 118, 119].

2.2.3 Dietary patterns and demographic factors

Demographic and socioeconomic factors have been associated with dietary patterns [120, 121]. Studies have shown that women more likely follow healthier dietary patterns than men [102, 121-124], and older populations are associated with healthier dietary patterns;

for example, several studies reported that age was found to have a negative relationship with the Western diet and a positive association with vegetable-based patterns [125, 126]. Additionally, the associations between healthy dietary patterns and high income as well as high educational level have been consistently reported in many studies [111, 114, 121, 124, 127]. For example, a study by Park [125] showed that individuals with higher scores for a healthy dietary pattern tend to be more educated than those scoring lower. Furthermore, dietary patterns may be influenced by marital status: in a study, Barker et al [128] reported that those married or living with a partner are more likely to choose the healthy dietary pattern than those who are single, divorced, or widowed. As for demographic factors, the number of household members has been associated with some dietary patterns. For example, a study conducted in Tehran reported a positive association between larger housing size per person and a healthy dietary pattern [124]. Moreover, according to studies conducted in Asian populations, smokers are less likely to choose the healthy dietary pattern [86, 111, 114]. Individuals who prefer a healthy dietary pattern are more likely to report weekly physical exercise in several studies [86, 114].

2.2.4 Dietary pattern and health outcomes

Diet is one of the most important modifiable risk factors for chronic diseases [129]. Because of the methodological limitations of traditional nutritional epidemiology, dietary pattern analysis helps explore the effect of overall diet on risk of disease and suggest strategy for disease prevention and treatment [10, 130]. Using this approach, the Western pattern has been associated with many adverse health outcomes and the Prudent or Healthy pattern has been associated with protective effects on same adverse health

outcomes in many studies. For example, a reduced risk for all-cause mortality has been reported to be associated with a prudent/healthful dietary pattern in some studies [131-133]; conversely, the Western diet has been associated with an increased risk of all-cause mortality in one study [132]. Also, many epidemiological studies reported associations between dietary patterns and the risk of CHD [94, 95, 134, 135], type 2 diabetes [136, 137], Parkinson's disease [138, 139], and breast [140-143], renal [144-148], gastric [112, 149-151] and colorectal cancers [88, 152-155]. The association between dietary patterns and CRC will be individually discussed in this thesis.

2.2.5 Dietary pattern and colorectal cancer

Dietary exposures may play an important role in CRC risk. A large body of epidemiologic, clinical metabolic, and experimental studies conducted in a wide variety of populations suggest a protective effect of a "healthy" dietary pattern (that is, a diet high in dietary fibers, vegetables, grains, and fruits.) on the risk of CRC [152-154] as well as an association between an "unhealthy" dietary pattern (that is, a diet high in calories and fat, and low in fiber, cereals, fruits, and vegetables) and increased CRC risk [88, 155]. However, results from analytical epidemiological studies have been inconsistent, especially in Asian populations.

A community-based case-control study conducted in a Japanese population suggested a statistically significant protective association between the Prudent dietary pattern and the risk of distal colon cancer, but not that of either proximal colon or rectal cancer [86].

However, another study conducted in Japan reported that the “healthy” dietary pattern was unrelated to CRC risk [111]. A prospective study conducted in another Asian population, Singapore Chinese, observed no association between the healthier dietary pattern (that is, a vegetable-fruit-soy pattern) and CRC risk [114]. In Western countries, a protective association between the prudent or healthy dietary pattern and CRC has been reported in several studies [39, 58, 109, 118, 119], but not in others [79, 83, 84, 110, 156].

Kurotani et al suggested that there was no association between the high-fat dietary pattern and CRC risk in the Japanese population, while Kim et al reported a positive association of the Western dietary pattern with colon cancer risk in females [86, 111]. Butler et al concluded that the meat-dim sum pattern, characterized by a high consumption of red meat and dairy food, did not appear to explain the increased risk of CRC among the Singaporean Chinese population.

Chapter 3: Data sources & information collection

3.1 Data source

Data source used in the thesis project includes two parts. One part is from a large case-control study (CCS) which occurred within the *Colorectal Cancer Interdisciplinary Health Research team in Colorectal Cancer* (CTCC) established in 2001. Detailed description of the methods of the CTCC has been published previously and will be introduced briefly below [56, 157-159]. Only information of CRC cases and population controls participating in the Newfoundland Familial Colorectal Cancer Registry (NFCCR) was used in this thesis study. The other part of the data source is from a broader *Food-Frequency Questionnaire Validation Project* (FFQVP) conducted by the Health Research Unit (HRU) of Memorial University [160].

Ethics approval for this project study has been obtained from the Health Research Ethical Approval (HREA), Faculty of Medicine, Memorial University, with a reference number of 14.098.

3.1.1 Case ascertainment in NFCCR

NFCCR recruited the colon or rectal cancer patients newly diagnosed and included in the Provincial cancer registry (that is, the Newfoundland Cancer Treatment and Research Foundation, NCTRF). Inclusion criteria for cases were:

1) Incident primary invasive colon or rectal cancer identified by International Classification of Diseases 9th revision codes (ICD-9 codes): 153.0-153.9, 154.1-154.3 and 154.8; or ICD-10 codes: 18.0-18.7, 19.9, 20.9.
2) Diagnosed between January 1999 and December 2003.
3) Diagnosed at ages between 20 and 74 years old (20 and 74 years old included)
4) Residents of NL at time of diagnosis.

Participants who agreed to take part in the study were sent a survey package, in sequence, that contained a written consent form, personal history questionnaire (PHQ), food frequency questionnaire (FFQ).

3.1.2 Control ascertainment in NFCCR

Population controls were a random sample of NL residents, aged from 20-74 years old. Due to the frequency matched case-control study design, controls were selected so that they had the same distribution of sex and age as the cases. Controls were identified by random digit dialing. Initially, a list with total of 192,000 possible residential telephone numbers was generated and arranged for recruiting controls used in this project [161].

The eligible household members who were willing to participate this study were contacted for an initial screening interview. A survey package was then forwarded to each potential participant once a verbal consent for participation was obtained during the phone interview. The package was comprised of an information pamphlet that introduced the general information about the study, a written consent form, a PHQ, a FFQ, and a self-

addressed stamped envelope.

3.1.3 Participants ascertainment in FFQVP

Participant recruitment and data collection for FFQVP were conducted by the HRU of Memorial University. Due to the sample size calculated based on the mean and standard deviation for various nutrients derived from the FFQ data of the on-going CRC project [13, 162-164] and the generally acceptable correlation coefficient value of 0.6 [165], and an expected 30% attrition rate per step of the validation study, an initial random sample of 450 participants from the general population was recruited by telephone. The trained HRU telephone interviewers made initially contacted participants using a list of landline numbers provided by Info Canada. The objectives and procedure of this project were introduced to the household member if she/he was between 35 and 70 years old. The baseline demographic information was gathered once a participant made the verbal consent. Also, the survey package including a written consent form and a FFQ was sent out.

The inclusion criteria of an eligible participant as follows:

1) A non-institutionalized adult resident of NL who had lived in NL for at least two years at the time of the study;

2) 35-70 years of age;

3) Able to speak and read English at the 8^{th} grade level; and

4) Without cognitive impairment identified, psychological challenges, or pregnancy.

3.1.4 Response rates and counts

As of July 2006, 1159 out of 1175 eligible cases identified through NCTRF were contacted. 1126 cases consented to take part in this study. Finally, 705 cases (63%) returned the PHQ and 608 cases (54%) returned FFQ. For the controls, a total of 2168 individuals were contacted though random digit dialing and 1603 persons had consented to participate in the study. 720 controls (45%) returned the PHQ and 687 controls (43%) returned the FFQ (Figure 3.1).

Between February 2011 and May 2012, using a list of landline numbers provided by Info Canada, an initial random sample of 450 participants from the general population was recruited by telephone. A total of 306 persons were identified as eligible respondents and were sent the survey packages. 205 individuals participated in the survey, giving a response rate of 67% (figure 3.2).

We excluded those who did not provide sufficient dietary information at baseline or failed to provide information on potential risk factors at baseline, or those who reported energy intakes outside the range of 500-5000 kcal [166]. This led to 1179 subjects (506 cases and 673 controls) from NFCCR and 192 subjects from FFQVP in the final analysis.

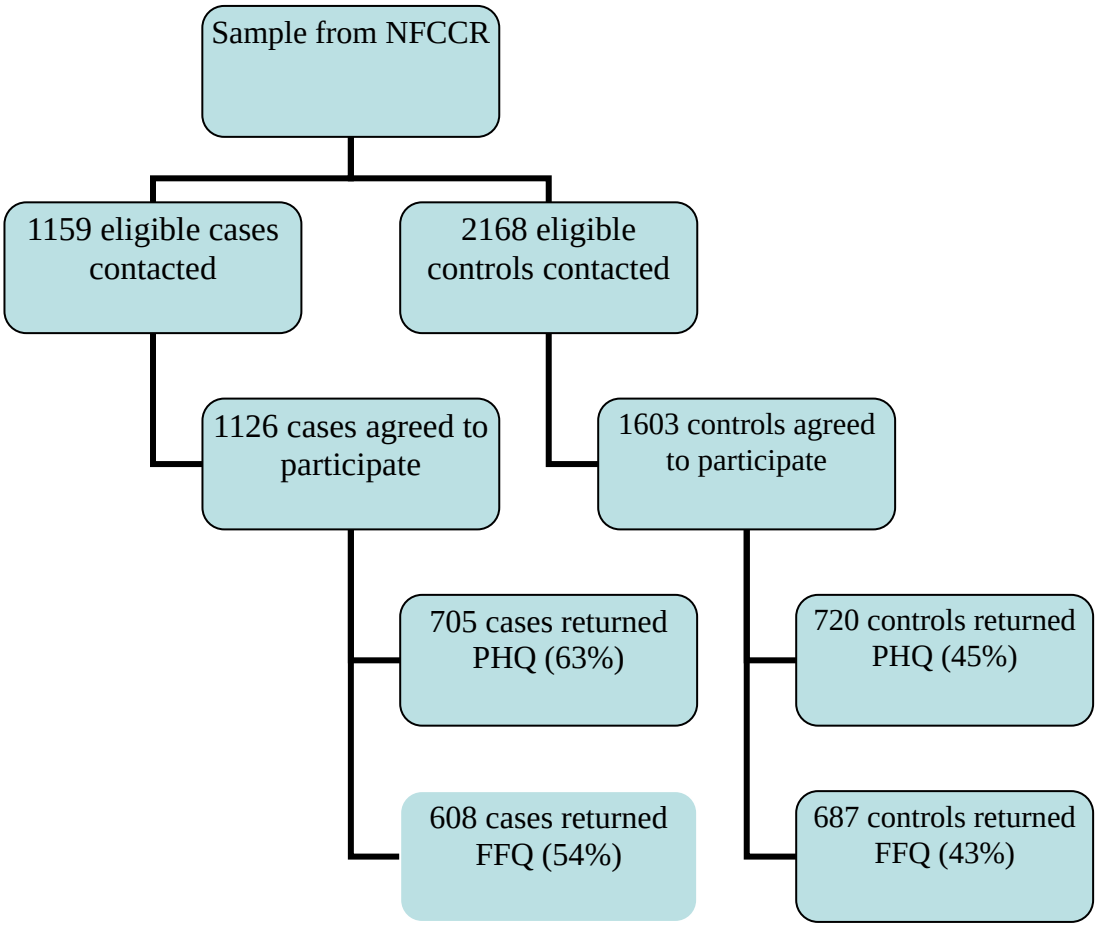

Figure 3.1 Sample size and response rates of sample from NFCCR

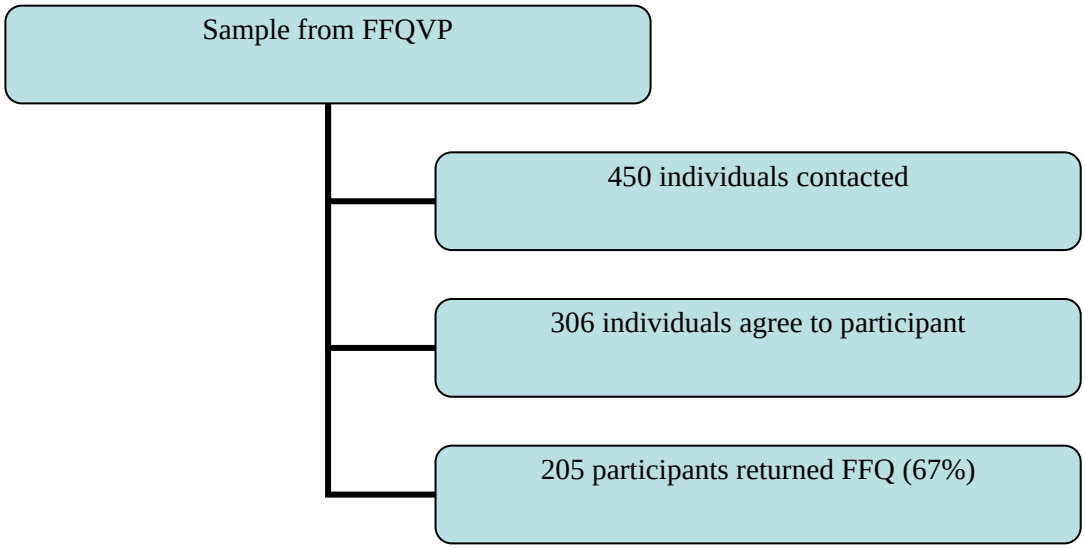

Figure 3.2 Sample size and response rates of sample from FFQVP

3.2 Information collection

3.2.1 Dietary information

A self-administrated FFQ (Appendix A) was applied to gather dietary information in both NFCCR and FFQVP. Detailed introduction of FFQ is described in Chapter 4.

Nutrient intakes were computed by multiplying the frequency of consumption of each food item by the nutrient content of portion size based on the 2005 Canadian Nutrient File (NFCCR) or through using the Elizabeth Stewart Hands and Associations (ESHA) Food Processor database software (FFQVP) [167].

3.2.2 Epidemiologic information

3.2.2.1 Epidemiologic information collection for NFCCR

The self-administered PHQ (Appendix B) was used in NFCCR to collect demographic information such as sex, age, date of birth, and marital status, and other possible risk factors for CRC, including medical history, bowel screening history, diet, medication use, physical activity, alcohol and tobacco use and socio-demographic measures such as education and income. For female participants there were additional questions relating to reproductive factors, including ages at menarche, first birth, and menopause, parity, hysterectomy, menopausal status, and reason for menopause.

Specifically, for example, physical activity was reported by each participant, including : the frequency and duration of walking, jogging, running, bicycling, swimming, tennis, squash/racquetball, calisthenics, aerobics, vigorous dance, football, soccer/rugby,

basketball and subjects' self-reported participation in other sports when a participant was between the ages of 20-30, 30-50, and 50 or older. A family CRC history means that one or more members of one's family had suffered from CRC. Subjects were defined as smokers or non-smokers based on the answer to the question of "Have you ever smoked one cigarette per day for three months or more?" Alcohol users were those who consumed any alcoholic beverages at least once a week for six months or longer, while non-users were those who did not drink ever. Medications were investigated through the question "Have you ever taken any of the following medications regularly (at least twice a week for more than a month)". Use of nonsteroid anti-inflammatory drugs (including ibuprofen and aspirin use), multivitamin supplements (such as One-A Day -, Theragram, Centrum, Unicap) were collected for final analysis. HRT was assessed only for females through the question: "Have you ever taken HRT prescribed by a doctor and in the form of a pill or a patch (i.e. progestin/estrogen)".

3.2.2.2 Epidemiologic information collection for FFQVP

Very limited demographic information was collected by telephone interview (Appendix C) for the FFQVP and included: age, gender, size of the participant's community, marital status, employment status, level of education, smoking habits.

Respondents in this project were categorized into four age groups for further analyses: 35-40, 41-50, 51-60 and 61-70 years. According to the population living in each community, their residential areas were defined as 'rural community' (< 10,000 people in the community) or 'urban community' (≥10,000 people living in the community).

Information on education attainment was obtained through asking the question: “What is the highest level of education that you completed?” and responses were divided into three classes: some school but no high school certificate, high school certificate, and post-secondary education. The responses to the question “What is your marital status?” were used to determine the marital status (single, separated/divorced, widowed, married/living together). The response to the question “Are you currently employed” were used to determine current employment status. Among those who responded “yes”, further information of job type (part-time, full-time, or seasonal) was collected. Among those who responded “no”, to the current employment status question, retirement status was further collected by the question “are you retired”. Additionally, participants were also asked about their current or past occupations. According to the responses to the question “Do you currently or ever smoke cigarettes daily”, all subjects were classified as smoker, former smokers or non-smokers.

Chapter 4: Paper 1. Four major dietary patterns identified for a target-population of adults residing in Newfoundland and Labrador, Canada

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AUTHOR'S CONTRIBUTION

PPW contributed to the conception and design of this manuscript. ZC analyzed the data and drafted the first version of the manuscript. PPW, BR, AR, JC, JY, and NB subsequently revised the manuscript. ZC and LL were responsible for the collection and had full access to the data. All the authors provided final approval.

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4.1 Introduction

Traditional approaches to nutritional epidemiology have focused on the associations of diseases with one or a small number of specific nutrients or foods [102, 103]. Given that people eat a variety of foods with a complex combination of nutrients, the single-nutrient approach may fail to take into consideration the complicated interaction among nutrients, the potential confounding by an individual's eating pattern, and the increased false positive rate due to multiple comparisons [10]. In order to overcome these limitations, an increasing number of researchers have begun to use food consumption patterns to characterize a population's dietary intake and to examine potential relationships of these patterns with health [168-171]. Such an analysis of dietary patterns may provide a more accurate and comprehensive description of actual dietary exposure. Several studies have identified the modern "Western" dietary pattern, characterized by high intake of meat, highly processed foods, and sweets [102, 105, 172-174]. In contrast, a healthier pattern referred to as "Healthy or Prudent", is characterized by higher intake of fruits, vegetables, legumes, whole grains, poultry, and fish [105]. These two major dietary patterns are not only associated with health outcomes, but have also been shown to be related to age, gender, living area, educational attainment, and other baseline demographic characteristics. For example, studies by Park SY et al [125] and Schulze MB et al [126], which were conducted in Hawaii, Los Angeles and some European populations, showed that older residents are more likely to practice the vegetable-based dietary intake pattern over the Western pattern. Another study conducted in the US reported that, urbanites tend to choose the healthier dietary pattern than rural residents and women have a healthier dietary pattern than men [175].

It is widely believed that dietary and cultural differences exist between Newfoundland and Labrador (NL) and the rest of Canada due partly to geographic isolation [11]. The life expectancy is lower [176] and the rates of death due to such chronic illnesses as cardiovascular disease and diabetes mellitus are higher than in any of the other ten Canadian provinces [177, 178]. However, limited nutritional epidemiological research has been conducted to examine unique characteristics of the NL diet. Additionally, because the 2004 Canadian Community Health Survey (CCHS Cycle 2.2, Nutrition Focus) [12] did not collect information of some foods commonly found in the NL diet, such as, pickled meat and cloudberries (bake-apples), it may not have portrayed an accurate representation of this population's dietary intake. It could be that dietary intakes of this population were not well estimated by analysis of CCHS data. Therefore, there is a need to investigate the dietary patterns of NL residents, in order to know more about the true current food consumption patterns of this population and to see if such dietary patterns can provide insight into the elevated rates of illness experienced in the province.

Realizing the potential value of studying this particular population with its somewhat unique dietary characteristics and the higher rates of certain illnesses (e.g., diabetes, CRC), our research group has recently developed and validated a food-frequency questionnaire (FFQ) for use with this population [160]. The objectives of this study are to proceed with the next step of a larger investigation of this population by using this tool to make a preliminary evaluation of the dietary patterns in one subgroup of the NL population, the adult, and to assess whether these patterns vary according to demographic

characteristics.

4. 2 Method

Dietary data used in this study were collected in the Canadian province of NL between February 2011 and May 2012.

4.2.1 Study participants

According to the 2011 Census Information and Statistics [179], the population of NL is approximately 514,536, with over 57% rural residents. A stratified random digit dialing [161] with proportional allocation sampling methodology was adopted for this study. Geographically, the survey covered the whole of NL, including both the urban and rural areas.

With the intention of measuring food intake for the general adult population of NL, the following inclusion criteria were used. An eligible participant was required to be:

1) A non-institutionalized adult resident of NL who had lived in NL for at least two years at the time of the study;

2) 35-70 years of age;

3) Able to speak and read English at the 8^{th} grade level; and

4) Without cognitive impairment, psychological challenges, or pregnancy.

Therefore, using a list of landline telephone numbers provided by Info Canada, an initial random sample of 450 participants from the general population was recruited by telephone. A total of 306 persons were identified as eligible respondents and were sent the survey packages. Two hundred five (205) individuals participated in the survey, giving a

response rate of 67.0%.

4.2.2 Data collection

A self-administered food-frequency questionnaire (FFQ) was used to collect food consumption information among the NL adult population. The FFQ was modified from the Hawaii FFQ to account for the unique food consumption habits in NL. The original Hawaii FFQ was designed to assess the typical food intake of individual males and females in a multi-ethnic Hawaiian/Southern Californian population [180-183]. In the adapted NL FFQ, food items considered unusual in NL (for example, tamales and ham hocks) were deleted or altered while some items commonly consumed in NL (for example, moose meat and pickled meat) were added. The NL FFQ consists of 169 food items and includes a number of composite dishes that may contain multiple ingredients [160]. The foods listed in the FFQ are categorized into nine major groups: (1) beverages (other than liquid milk), (2) dairy products, (3) mixed dishes, (4) vegetables, (5) meat and fish, (6) cereals and grains, (7) fruits, (8) desserts and sweets, and (9) miscellaneous.

Participants were required to recall the frequency with which they usually consumed each item, choosing only one from the following options provided for each food/beverage item: (1) serving per day, (2) serving per week, (3) serving per month, or (4) rarely or never. In addition, subjects were requested to indicate the number of servings habitually consumed at a single sitting. An “average” portion, a standard serving expressed in household measures or grams, was provided for each food item or beverage in the FFQ. Respondents who consumed an amount different than the “average” portion provided were given the

option of choosing “smaller” or “larger” portion sizes. A smaller size was defined as a portion approximately 75% or less of the average portion size, while a larger one was approximately 125% or more of the average size.

If a food item was consumed on a seasonal basis, the respondent was not only asked to estimate the frequency of the food item consumed during its season, expressed as times per day/week/month, or never/rarely, but also to indicate the length of the particular food’s season (for example, consuming cloudberry 2 times per week for 3 months only).

Demographic information--age, gender, size of community, marital status, employment status, level of education, and smoking habits--was collected by telephone interview. The current study involved the secondary analysis of data collected for FFQ validation. Thus, certain potential confounding factors of interest were not available to us.

4.2.3 Statistical analyses

According to the nutritional characteristics and the usual frequency of consumption in this population, the 169 food items in the FFQ were grouped into 39 predefined categories based on the role of each food in the diet. Several foods (for example, eggs, beer, jam, and pies) comprised their own groups since they were considered inappropriate for combination. Nutrient intakes for individuals were calculated using the Elizabeth Stewart Hands and Associations (ESHA) Food Processor database software [167], and were adjusted for total energy intake with the use of the residual method [166] to obtain factors uncorrelated with total energy intake. If a participant reported consuming food that was

not present in the database, the most appropriate alternative was chosen through a discussion with the research team or by consultation with academic nutrition experts.

Exploratory factor analysis of the reported number of servings of the various food groups was used to define the food consumption patterns within this population. The terms ‘Principal component analysis’ and ‘exploratory factor analysis’ are used interchangeably in much of the literature. To be consistent with our previous work, only the term—‘exploratory factor analysis’ was used in this study. Bartlett’s Test of Sphericity (BTS) and the Kaiser-Meyer-Olkin (KMO) measurement of sample adequacy were used to verify the appropriateness of factor analysis. Exploratory factor analysis was used for factor extraction. Factors were also orthogonally rotated (Varimax option) to achieve simpler structure with greater interpretability. Factors were retained based on the following criteria: factor eigenvalue>1.35, identification of a break point in the scree plot, the proportion of variance explained, and factor interpretability [184]. The strength and direction of the associations between the patterns and food groups were described through a rotated factor loading matrix. Items were considered to load on a factor if they had a factor loading >0.5 [185]. Each individual received a factor score calculated for his/her dietary pattern to indicate the extent to which the diet corresponded to that pattern.

Univariate analyses and multivariable linear regression models were used to assess the associations between participants’ dietary patterns and demographic variables, with factor scores of each dietary pattern being the dependent variable. Because four dietary patterns were derived for this sample, four linear regression models were fitted to explore the

associations. Those demographic factors were coded and entered into linear regression models as independent variables. Details are as following: age in years (1: 35-40, 2: 41-50, 3: 51-60, 4: 61-70), gender (1: female, 2: male), size of the participant's community (1: less than 10,000, rural area; 2: more than 10,000, urban area), education attainment (1: some school but no high school certificate, 2: high school certificate, 3: post-secondary education), marital status (1: single, 2: separated/divorced, 3: widowed, 4: married/living together), and current smoker (1: yes, 2: no).

Pearson's correlation coefficients were calculated between the factor scores of each pattern and energy-adjusted nutrient intakes so that the correlation between dietary patterns and specific nutrient intakes could be studied. Statistical analyses were performed using the Statistical Analysis System (SAS, version 9.2) software and the Statistical Package for Social Science (SPSS, version 10.5). Differences with *p*-value <0.05 were considered to be statistically significant.

4.3 Results

Out of a total of 205 questionnaires received by June 2012, we excluded participants who had left over 20 continuous items blank on the FFQ (n=5) and those who reported energy intakes outside the range of 500-5000 kcal (n=8). The latter exclusion matches the exclusionary rules for food-frequency questionnaire data used by Willett [166]. The remaining 192 respondents were involved in all further analyses. Comparison of selected demographic characteristics between respondents and non-respondents were made, with the only significant difference being the age profile of responders (35 to 40 years, 9%; 41

to 50 years, 24%; 51 to 60 years, 41%; 61 to 70 years, 26%) and non-responders (35 to 40 years, 16%; 41 to 50 years, 34%; 51 to 60 years, 32%; 61 to 70 years, 18%), p=0.0032. Based on these differences we conducted a separate factor analysis with respondent data weighted to the age profile of the NL population. Results demonstrated no meaningful difference between weighted and un-weighted analysis.

Table 4.1 presents the social and demographic characteristics of the study sample. The sample consisted of 43 men and 149 women, aged 35 to 70 years, with a mean age of 55.0±8.7 years. Most participants were non-smokers (82.8%) and had completed post-secondary education (59.4%). When stratified by gender, no significant differences in demographic characteristics were found between groups (data not shown).

The observed KMO was 0.602 and therefore the sample was considered to be adequate for factor analysis. The BTS was significant ($p<0.001$), indicating homogeneity of variance by the food consumed. Figure 4.1 shows the scree plot of eigenvalues for each factor. The first four eigenvalues, which were 3.53, 3.25, 1.85, and 1.44 respectively, dropped substantially. After the fifth factor (1.29), the values remained more consistent (1.28 for the sixth and 1.02 for the seventh factor). As a result, a 4-factor solution was selected. These four factors accounted for 63% of the variability of food consumption within the sample. Some studies have found that factor solutions differ by gender [103, 186]. Therefore, we conducted factor analyses separately for men and women. We found no difference in the number of food consumption patterns between genders (data not

shown).

The four retained factors were identified as four dietary patterns and were labelled Meat, Vegetable/fruit, Fish and Grain, according to the results obtained from the factor loading matrix (Table 4.2), where a higher factor loading of a given food group indicates a greater contribution of that food group to the specific pattern. We named the first pattern Meat, since it is characterized by a high consumption of red meat, cured/processed meat, and cured/processed red meat. Conversely, the Vegetable/fruit pattern has an emphasis on several vegetable/fruit groups, including greens, tomato sauce, berries, and other vegetables. The Fish pattern indicates a preference for fish and processed fish. The final pattern was labeled as Grain because of the high positive loadings in whole grains, cereals, and grains, and negative loadings in the groups containing beer, white wine, and coffee.

The results from the multivariate regression analysis shown in Table 4.3 indicated that the overall models, which included all demographic information, were significant for the Meat (F=3.28), Fish (F=2.42), and Grain (F=6.81) patterns, while the model fitted for Vegetable/fruit pattern (F=2.10) is not significant. Older people are more likely to choose Grain pattern but less likely to have a Meat pattern. Male participants are more likely to exhibit the Meat and Fish patterns. Current smokers and those married/living together prefer the Grain pattern. The rest of the demographic factors were not related to the scores for any pattern.

The association of the factor scores for each dietary pattern with total energy and energy-

adjusted nutrient intakes are illustrated in Table 4.4. Scores of the Meat pattern have positive significant association with total energy, fat, sodium, cholesterol, and calcium intakes, as well as significant negative associations with carbohydrate and fiber intakes. The Vegetable/fruit pattern scores were positively correlated with total energy, fiber, and sodium. With the Fish pattern, the higher the factor scores, the higher the protein intake and the lower the fat intake. The grain pattern was characterized by high intakes of total energy, carbohydrates, and calcium, but with low intakes of sodium, fat, and cholesterol. Pearson's correlation coefficients between factor scores of each dietary pattern and absolute nutrient intakes were also calculated. According to the results, correlations between factor scores of each dietary pattern and absolute nutrient intakes are similar in magnitude to those between factor scores and energy-adjusted nutrient intakes.

4.4 DISCUSSION

Although the NL diet is known to be unique and is suspected to play an important role in the high incidence for several diseases, there have been no studies that systematically assess NL dietary patterns. Results from the present study added new knowledge that contributes to future nutritional epidemiological research. We identified four major dietary patterns, Meat, Vegetable/fruit, Fish, and Grain, from a sample of the adult population of NL. The total variance explained by the four aforementioned food patterns was 63%, with the largest variance, 22%, being explained by the Meat pattern. After fitting two linear regression models to explore the associations between factor scores of dietary patterns and demographic factors, no main effect of the demographic factors on the Meat pattern was found. Associations between education attainment and

Vegetable/fruit, gender and fish, age/marital status and Grain pattern were found.

The Meat pattern, with a high consumption of red meat, processed/cured meat, and processed/cured red meat, is similar to the set of food items referred to as the Western pattern in many previous studies [187, 188]. This pattern has been reported to have associations with adverse outcomes such as cancer [22], cardiovascular diseases [175, 189], and obesity [102]. The second pattern identified in the current study, Vegetable/fruit, is comparable to the Prudent and Vegetable/fruit patterns described in other studies [125, 187, 190]. This pattern consists mainly of vegetables, tomato sauce, and fruits. Studies describe this pattern as the most desirable or healthy diet for a population, since it has been shown to be associated with a decreased risk of coronary heart disease [191], type 2 diabetes [187], colorectal cancer [86], and mortality for all groups who follow this dietary pattern. The Fish pattern, characterized by high consumption of fish and processed fish, seems to be unique to the NL population and is unlike any pattern described in other research. This phenomenon may be attributed to geographic isolation and the historical importance of the cod fishery in NL [192]. The final pattern, Grains, shares common elements with the “cereals” or “cereal-based” patterns discussed in several previous publications [126, 193].

According to the results of linear regression analysis, the factor scores were associated with several demographic factors, including age, sex, marital status and current smoking status. Consistent with previous studies [125, 126], age was found to have a negative relationship with the Western diet and a positive association with vegetable-based patterns.

Older respondents in this study were less likely to follow the Meat pattern and more likely to follow the Fish pattern. However, no significant effect of age on the Vegetable/fruit pattern was observed. Previous studies have reported that women and urban residents tend to have higher loadings on healthy dietary patterns [125, 126, 175]. Our results showed that women are likely to have lower scores for the Fish patterns. Moreover, our findings indicated that living in urban or rural areas and attaining a high level of formal education are not associated with individuals' dietary patterns. This is inconsistent with Park's [125] results, which suggest that individuals with higher scores for a healthy dietary pattern tend to be more educated than those scoring lower. The results from our study pertaining to marital status support a hypothesis that dietary patterns may be influenced by marital status [128]. Those who self-reported as being married and/or living together were more likely to choose the Grain pattern than those who were single and/or divorced, or widowed. No significant correlation was found between marital status and other food patterns. Finally, current daily smoking daily was positively associated with the Grain pattern in our study. This contrasts with the results of some other studies [125, 126].

Dietary pattern analysis has been criticized by some due to predefined food groups and self-labeling factors based on an investigator's own interpretation of the data. The present study attempted to further characterize such factors and explain the labeling by calculating the correlation of the patterns' scores with total energy and energy-adjusted nutrient intakes. Similar to the results of the majority of studies which have investigated dietary patterns, the Meat pattern (similar to the Western pattern proposed in other studies)

was associated with higher energy, fat, cholesterol, and sodium, as well as lower carbohydrate and fiber. Our Vegetable/fruit pattern was very similar to the Prudent pattern described in other research and correlated with high fiber intake [125, 187, 190, 194].

There are some limitations to the present study. The use of factor analysis requires some arbitrary decision-making regarding the assignment of foods to food groups, the number of retained factors, the method of rotation, and the labels of components [101]. While factor analysis using predefined food groups is commonly used in nutritional epidemiological research [24, 102, 103], it is potentially useful to compare differences when using predefined food groups versus the raw food items. As part of a sensitivity analysis, we also conducted factor analysis based on the 169 original food items in the FFQ, which only explains 16% of total variation. Thus, we believe the predefined food group approach is both more practically meaningful and statistically advantageous. Secondly, the FFQ, although a useful tool to measure dietary exposures, requires participants to recall their past dietary habits, often one or two years prior to the investigation. Consequently recall bias and social desirability bias are unavoidable. Thirdly, while aids were provided, participants were asked to self-report their eating habits. Information bias may have resulted especially when estimate of quantities of foods consumed are considered. Potential selection bias may exist because people who agree to participate in diet-health study are more likely to have an interest in healthy lifestyles and to practice healthier eating behaviours. As for any cross-sectional study, the researchers do not know how well findings, in this case dietary patterns, reflect population bahaviours of the past or future. Additionally, this study was based on secondary data analyses and so

we were constrained from exploring the association between some potentially important demographic factors and factor scores, such as obesity. Use of secondary data also means that the researchers did not conduct sample size calculations and power analysis for this study.

The fast growth of mobile phone only users in the past two decades poses a great challenge to the traditional random-digital-dialing recruitment approach. Because our study participants were recruited through land-line phones, mobile phone only users would have been missed. According to Statistics Canada, 56% of all Canadian households used landline phones in 2013 [195]. Phone use is strongly patterned by age. Among households with members under 35 years of age, the percentage using cell phones only is much lower than among those households with members aged over 55 (60.6% vs. 6.4%) [195]. Given the study participants were aged 35 to 70 years, it might therefore be expected that the lower proportion of younger participants compared to the NL population might be due to both non-response in this age group as well as patterns of phone ownership.

Although we were faced with challenges, our study has several strengths. First, our subjects belongs to an understudied group with unique experiences/characteristics which when studied could potentially contribute to the understanding of that important association between dietary intakes and health status. Not only did we have access to this group of respondents but we had access to a tool developed specifically for use with the NL adult population and this tool, a FFQ, has been pretested to have a moderate measure

of relative validity. In addition, few studies have considered gender differences as they pertain to food consumption patterns. We conducted factor analyses stratified for different genders, though no significant difference was found. Finally, we not only labelled the retained four factors but also explained the correlations between specific nutrient intakes and factor scores behind the labels that are emphasized by Slattery [89].

This study is an initial attempt to utilize our newly developed FFQ with a population subgroup at a higher risk of ill health in many regards as compared to other Canadian adults. This preliminary investigation has identified food patterns which characterize the consumption pattern of adult residents of NL. Future research is required to verify that these patterns truly represent the larger population of the province. Comparison of these dietary patterns with those practiced in other regions of the country could be informative. Further investigations into the unique Fish pattern identified by this study could also prove to be valuable.

4.5 CONCLUSION

In conclusion, the present study provides an initial investigation into the dietary patterns practically adult residents of NL, a subgroup of the Canadian population with comparatively high rates of such diseases as cardiovascular disease and diabetes mellitus. We identified four major food consumption patterns in this population: Meat, Vegetable/fruit, Grain, and Fish, the latter of which has not yet been identified in studies of dietary intake patterns in other geographic areas.

Table 4.2 Demographic characteristics of the study participants from Newfoundland and Labrador general adult population (n=192)

Characteristics	n (%)
Age Range (years)	
35-40	15 (7.9%)
41-50	42 (22.0%)
51-60	81 (40.3%)
61-70	49 (29.8%)
Gender	
Males	43 (22.4%)
Females	149 (77.6%)
Living Area	
Rural area	111 (57.8%)
Urban area	81 (42.2%)
Education Attainment	
Some school but no high school certificate	27 (14.0%)
High school certificate	51 (26.6%)
Post-secondary education	114 (59.4%)
Marital Status	
Single	15 (7.8%)
Separated/Divorced	18 (9.4%)
Widowed	8 (4.2%)
Married/Living together	151 (78.6%)
Current Employment	
Part-time	16 (8.3%)
Full-time	74 (38.5%)
Seasonal	15 (7.8%)
Not employed	84 (43.8%)
Retired	61 (31.8%)
Not retired	21 (11.0%)
No answer provided	2 (1%)
Unusable data	3 (1.6%)
Currently Smoking Daily	
Smoker	33 (17.2%)
No	159 (82.8%)
Previous Smoking Daily	
Yes	84 (43.8%)
No	75 (39.0%)
N/A	33 (17.2%)

Figure 4.1 Scree plot test in factor extraction (exploratory factor analysis)

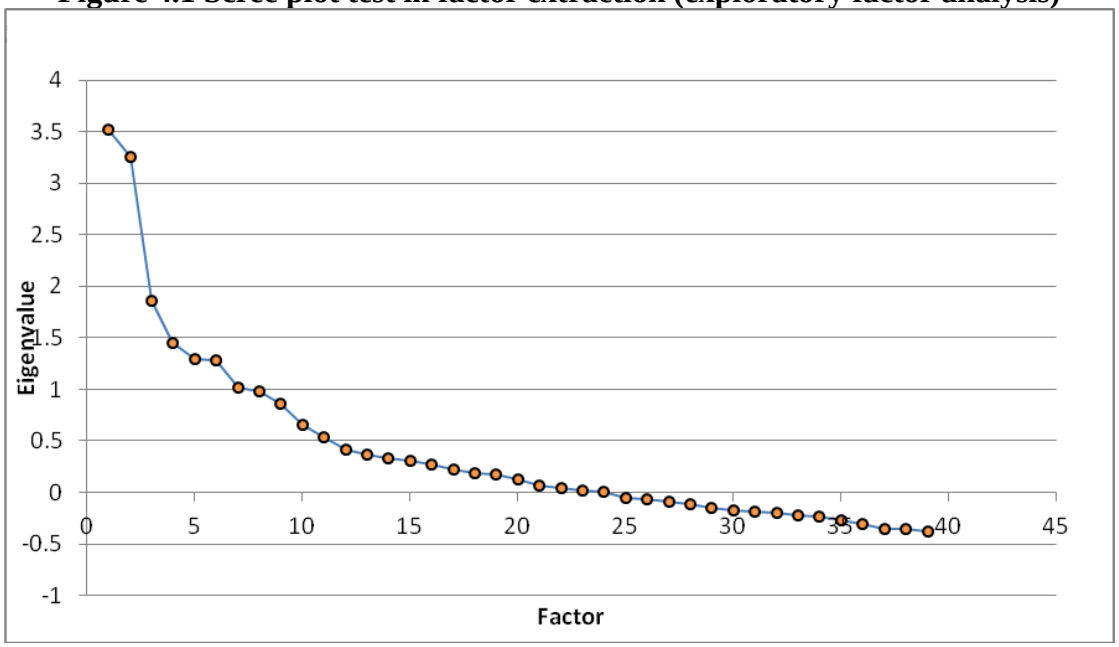

Table 4.3 Factor loadings and explained variances for the four major dietary patterns identified in an adult Newfoundland and Labrador population, using an exploratory factor analysis [a]

Food Groups	Servings/week (mean ± standard deviation)	Factor loading			
		Meat	Vegetable/fruit	Fish	Grain
Milk	1.08±1.09	-0.16		0.18	0.43
Yogurt	0.68±0.85		0.30		0.32
Coffee	1.40±1.65		0.18		-0.31
Tea	1.56±1.71			0.17	0.19
Sugar	1.25±2.25				
Soft drinks	0.73±1.16	0.42		-0.15	-0.20
Egg	0.48±0.76	0.16			
Cheese	0.50±0.62		0.25		
Mixed dishes	0.35±0.29	0.32			
Red meat	0.93±0.59	**0.83**			
Game	0.08±0.13			0.21	
Cured/processed red meat	0.41±0.37	**0.90**			
Cured /processed meat	0.64±0.46	**0.93**		0.20	
Poultry	0.30±0.21	0.21	0.32		
Fish	0.27±0.24	0.22	0.16	**0.78**	
Processed fish	0.11±0.14	0.31		**0.70**	
Fruit juice	0.89±1.46		-0.25		0.38
Other fruits	1.51±1.14		0.34		0.30
Root vegetables	1.40±0.99		0.31	0.37	
Cruciferous vegetables	0.47±0.59		0.33	0.22	
Other greens	0.45±0.68		**0.68**		
Beans, peas	0.31±0.31		0.29	0.45	
Tomato sauce	0.71±0.57	0.16	**0.60**		
Other vegetables	1.26±0.96		**0.75**	0.23	
Total cereals and grains	3.52±2.13	0.16	0.17		**0.55**
Whole grains	0.97±1.17		0.30		**0.52**
Desserts and sweets	1.03±1.01	0.22			0.21
Vegetable juice	0.07±0.30			0.34	0.26
Beer	0.11±0.30				-0.24
White wine	0.06±0.14				-0.26
Red wine	0.08±0.19	-0.18	0.26		
Liquor	0.14±0.44				
Citrus	0.34±0.38		0.20	0.17	0.20
Berries	0.36±0.47	-0.15	**0.50**		
Dried fruit	0.14±0.41		0.39		

Canned fruit	0.11±0.24	0.16			0.34
Pies, tarts	0.07±0.19				
Jam, jelly	0.39±0.55				0.30
Pickled vegetables	0.10±0.20				017
Proportion of VAR explained (%)		22%	20%	12%	9%
Cumulative VAR explained (%)		22%	42%	54%	63%

[a] Absolute values less than 0.15 were not listed and those above 0.50 indicated in bold to visually emphasize strength of association.
VAR: variance

Table 4.3 Association between various pattern scores and selected demographic characteristics in this study population as assessed by multivariate linear regression analysis

	Meat‡	Vegetable/Fruit	Fish‡	Grain‡
Age	-0.15*	0.10	0.15	0.16*
Gender	0.18*	-0.12	0.18*	-0.12
Living area	-0.13	0.06	0.05	-0.07
Education attainment	-0.05	0.16	-0.11	-0.07
Marital status	-0.06	0.02	0.02	-0.33*
Currently Smoking Daily	-0.11	0.11	-0.01	0.22*

* β are significant at $p<0.05$.

ǂ indicates significant multivariate model ($p<0.05$) included all the demographic information.

Table 4.4 Pearson's correlation coefficients of dietary pattern scores with total energy and energy-adjusted nutrient intakes

	Meat	Vegetable/fruit	Fish	Grain
Energy	0.39**	0.38**	0.28**	0.55**
Protein (g)	0.12	0.12	0.31**	0.09
Carbohydrate (g)	-0.26**	-0.10	0.10	0.40**
Fiber (g)	-0.29**	0.59**	0.23**	0.10
Fat (g)	0.18*	0.05	-0.24**	-0.32**
Na (mg)	0.36**	0.22**	0.27**	-0.10
Cholesterol (mg)	0.22**	-0.05	0.11	-0.05
Calcium (mg)	-0.36**	0.04	0.03	0.32**

Correlation is significant at * $p<0.05$ and ** $p<0.01$

Chapter 5: Paper 2. Dietary patterns and colorectal cancer: results from a Canadian population-based study

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AUTHOR'S CONTRIBUTION

P.P.W. contributed to the conception and design of this manuscript. Z.C. conducted the research, analyzed the data and wrote the paper. P.P.W., B.R., J.W., Y.Z., J.M. and P.P. subsequently revised the manuscript. All authors read and approved the final manuscript.

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5.1 Introduction

Studies on diet and chronic diseases suggest that lifestyle factors, especially dietary habits and physical activities, play major roles in causing or preventing colorectal cancer (CRC) [7, 8]. There has been an increased interest in associations between dietary factors and CRC for a while; several articles on this subject have been published by our research group, a large and diverse multidisciplinary team of more than 40 researchers from Newfoundland and Labrador (NL) and Ontario (ON) [14, 18, 163, 196]. Most previous researchers have focused on the effects of a single food or nutrient; for example, Sun et al [14, 163] reported that selected micronutrients(e.g., calcium, vitamin D, vitamin C, folate) are associated with a lower risk of incident CRC, while diets high in macronutrients (i.e., protein, fiber, and carbohydrate) may reduce the risk of the disease. However, studies of single food items or groups in relation to CRC may not be valid because they assume that each single food or nutrient has an isolated effect [118, 197, 198]. The dietary pattern approach, which has been increasingly used in nutritional epidemiology, could capture and assess the overall dietary experience through considering simultaneous effects of dietary exposures potentially interacting with each other [24]. Zhu et al [196] explored the effects of dietary patterns on CRC patients' survival and suggested that the processed meat pattern, which is characterized by higher intake of red meat, cured/processed meat, fish and processed fish, is associated with a decreased disease-free survival after CRC diagnosis.

Even though considerable differences exist between population characteristics, study designs, and the methodologies used for conducting dietary pattern analysis, the results

pertaining to the relationship between diet and CRC from previous studies applying this approach were nearly consistent [20, 199]. Generally, the patterns that were labelled as "healthy" or "prudent", mainly characterized by higher consumption of fruits, vegetables, and grains, and lower consumption of sweets, red meat, and processed meat, were associated with a lower risk of CRC. Conversely, diets defined as "western", which indicate higher intakes of meat, highly processed food, potatoes, and refined carbohydrates, as well as lower intakes of greens and dietary fiber, have been associated with an increased CRC risk [20-23].

However, due to the effects of individual dietary habits, geographic factors and cultural differences, the dietary pattern approach is population-dependent, which may limit the external validity of existing findings [24]. Therefore, in order to translate this knowledge into dietary recommendation for different populations, population-specific studies using this methodology are needed. The present study aims to identify the association between dietary patterns and CRC in a Canadian population, from the province of NL.

5.2 Methods

5.2.1 Study design

A case-control study was conducted for the investigation of dietary patterns and CRC in the NL population. This study uses existing data that were collected by the Newfoundland Familial Colorectal Cancer Registry (NFCCR).

5.2.2 Study participants

A detailed description of study participants can be found elsewhere [13, 18, 161, 163]. Briefly, eligible cases were newly diagnosed CRC patients identified from the NFCCR during 1999-2003, between the ages of 20-74 years. Incident CRC diagnosis was identified through International Classification of Diseases 9th revision codes (ICD-9 codes): 153.0-153.9, 154.1-154.3 and 154.8; or ICD-10 codes: 18.0-18.7, 19.9, 20.9. Controls were selected from the NL population through random-digit dialing using telephone numbers provided by Aliant (a local telephone company in NL). They were frequency-matched with cases, also aged 20-74 years, by sex and age on 5-year strata [13, 161]. Both cases and controls were residents of NL at time of diagnosis or interview.

A written consent form, personal history questionnaire (PHQ), and food frequency questionnaire (FFQ) were sent to each case and control who agreed to participant in this survey. Based on PHQ returning, the analytical sample sizes for the present study were 703 cases and 717 controls. However, only those participants who completed both PHQ and FFQ were entered into final analysis. Hence, the total sample size s 1204 (518 cases and 686 controls) [13].

5.2.3 Data collection

Dietary intake data was gathered using a modified FFQ, based on the validated Hawaii FFQ, that was adapted to include foods particular to NL (e.g. cloudberries, game, and pickled/smoked fish). The modified version of the FFQ has been validated by our team and was widely used in the province of NL [160]. Diet assessment in this FFQ was

carried out one to two years prior to diagnosis or interview. Herein, interview indicates this survey on PHQ and FFQ. The 169 food items listed in the FFQ were categorized into nine major groups: beverages; dairy products; mixed dishes; vegetables; meat and fish; cereals and grains; fruits; desserts and sweets; and miscellaneous. Participants were required to recall the frequency of food intake and their usual portion size from the choices “smaller”, “average”, and “larger”, based on food photographs indicating examples of portion sizes. A “smaller” size means 75% of an “average” size while a “larger” size is defined as 125% of an “average” size. Total energy intakes were calculated based on the composition values from the 2005 Canadian Nutrient file, by multiplying the frequency of each food item by the calories contained in each portion [163].

The PHQ was applied to gather socio-demographic information, such as age, sex, date of birth, marital status, educational attainment, medical history, bowel screening history, medication use, physical activity, reproductive factors (females only), alcohol and tobacco use.

In this analysis, we excluded those who did not provide sufficient dietary information at baseline, or failed to provide information on potential risk factors at baseline. In addition, those who reported energy intakes outside the range 500-5000 calories/day were excluded [166]. After the exclusion, 1179 participants (506 cases and 673controls), who completed both the PHQ and FFQ, remained for further analysis.

5.2.4 Statistical analysis

The 169 food items in the FFQ were divided into 39 food groups based on the roles of food in diet and nutritional characteristics. Several foods that could not be appropriately combined with others were defined as their own groups; for example, eggs, jams, beer, and fruit pies. Exploratory common factor analysis was used to identify major dietary patterns for both cases and controls recruited from the NL population, based on the 39 predefined food groups. These factors were rotated by a varimax rotation (orthogonal) procedure for greater interpretability, uncorrelated components and greatest amount of variance explained. Factors were retained according to the following criteria: factor eigenvalue greater than 1.15; the break point of the scree plot; the proportion of variance explained; and factor interpretability [200]. Patterns were labelled based on food groups with absolute rotated factor loadings equal to or greater than 0.35. A factor score calculated for each dietary pattern (factor) by loading matrix was assigned to each participant, indicating the extent to which their diet corresponded to that pattern. In other words, an individual with a higher factor score has a stronger adherence to that pattern.

Two unconditional logistic models were used to calculate the odds ratios (OR) and the corresponding 95% confidence intervals (CI) that were used to interpret the associations between dietary patterns and CRC risk. The original models were adjusted only for age and total energy intake. The multivariate regression analyses were used to further adjust for additional confounding factors. They included sex, body mass index (BMI), marital status, educational attainment, household income status; use of alcohol, tobacco, non-steroidal anti-inflammatory drugs (NSAIDs); family history of CRC; history of polyps,

diabetes, colon screening procedures, high cholesterol, Crohns disease or colitis; multivitamin supplement use; and physical activities. Generally, potential confounding factors were selected into models according to the results of the literature review or biological plausibility. Additionally, in order for a factor to be selected there must be a 10% or more change in the regression coefficient of the primary predictors after addition of the factors and the model must have a p-value <0.05 when the covariate is entered. Factor scores assigned to each participant were categorized into quintiles and entered into each model as independent variables, with the lowest quintile as the reference group; the outcome variable is the status of each participant (CRC patient or control) [14]. P values for trend were calculated by Mantel-Haeszel Chi-Square Test to assess dose-response relationships.

Statistical analyses were carried out using Statistical Analysis System (SAS, version 9.2) software. All statistical tests were two-sided, and p-values<0.05 were considered statistically significant.

5.3 Results

The socio-demographic, lifestyle and medical characteristics of the 506 cases and 673 controls are shown in Table 5.1. Due to frequency-matched design, the gender distribution is similar in cases and controls (p>0.05). Cases (62.5±9.2) are significantly older than controls (60.5±9.5) (p=0.0003). Difference in mean of total energy intake between the case (2444.3±890.9) and control (2259.2±784.6) group is significant (p=0.0003). Compared to controls, cases tended to be less educated; more obese (BMI≥30); either

physically inactive (0~7.4 hours/week) or extremely physically active (>53.0 hours/week); more likely to have a history of polyp, diabetes and smoking; and less colon screening procedure and NSAIDs use ($p<0.05$). No significant difference was found in other baseline factors between the two groups.

Three major dietary patterns were derived using common factor analysis and factor labelling; the three patterns are shown in Table 5.2. These three dietary patterns explained 74% of variance. A predefined food group was considered as being loaded on a specific pattern when its absolute factor loading was ≥ 0.35. The first pattern was defined as Meat-diet pattern, which is characterized by high loadings for red meat, cured/processed red meat, fish, and processed fish. The second pattern, which loaded heavily on root vegetables, tomato sauce, total cereals and grains, berries, dried fruits, other fruits, other green vegetables, and other vegetables, was labelled as Plant-based diet pattern. The final pattern was named Sugary-diet pattern because it has high loadings of pies, tarts, desserts, and sweets.

Table 5.3 presents the ORs and their 95% CIs for CRC by the quintiles of factor scores for each dietary pattern. After adjusting for potential covariates, the higher risk of CRC is associated with the Meat-diet pattern (highest vs. the lowest quintiles: OR=1.84; 95% CI=1.19~2.86), and the Sugary-diet pattern (highest vs. the lowest quintiles: OR=2.26; 95% CI=1.39~3.66). The factor scores for the Plant-based diet pattern are reversely related to the risk of CRC (highest vs. the lowest quintiles: OR=0.55; 95% CI=0.35~0.87).

In order to further clarify the effects of the three dietary patterns, logistic regression models were fitted by proximal colon cancer, distal colon cancer and rectal cancer, respectively (Table 5.4). After adjusting for potential confounders, no significant effects of the Meat-diet and Plant-based diet pattern on proximal colon cancer were detected. However, the Sugary-diet pattern is associated with higher risk of proximal colon pattern (highest vs. the lowest quintiles: OR=2.90; 95% CI=1.54~5.45). As for distal colon cancer, higher risk is significantly associated with the Meat-diet pattern (highest vs. the lowest quintiles: OR=2.29; 95% CI=1.16~4.53) and the Sugary-diet pattern (highest vs. the lowest quintiles: OR=2.40; 95% CI=1.20~4.81), and non-significantly inversely related to the Plant-based diet pattern (highest vs. the lowest quintiles: OR=0.72; 95% CI=0.35~1.45). Additionally, the Meat-diet (highest vs. the lowest quintiles: OR=2.01; 95% CI=1.06~3.80) and Plant-based diet pattern (highest vs. the lowest quintiles: OR=2.01; 95% CI=1.01~4.00) are significantly associated with higher risk of rectum cancer. However, the Plant-based diet pattern is inversely related to the risk of rectum cancer (highest vs. the lowest quintiles: OR=0.46; 95% CI=0.23~0.90).

5.4 Discussion

Three major dietary patterns were derived for the NL population, including the Meat-diet, Plant-based diet and Sugary-diet pattern, which are highly consistent with another project conducted by our team for exploring the association between dietary pattern and CRC survival [196]. This case-control study further suggested that the Plant-based diet pattern conferred a protective effect against CRC, while the Meat-diet pattern and the Sugary-diet pattern were associated with a greater risk of CRC. After analyzing by proximal colon

cancer, distal colon cancer, and rectum cancer, even though ORs were not always statistically significant, similar associations were found.

Our findings regarding less healthy patterns, such as the Meat-diet pattern and the Sugary-diet pattern, are largely in an agreement with those of other comparable studies that used factor analysis to derive dietary patterns. A study conducted in a US population [83] indicated that the Western pattern characterized by a high consumption of sweets and desserts, red and processed meats, refined grains, and French fries was associated with increased CRC risk. Slattery et al [58] conducted a factor analysis in a multicenter US population and identified a Western pattern characterized by higher intakes of red meat, processed meat, and sugar-containing food, that is related to an increased risk of colon cancer in both genders. From a case-control study conducted in Western New York, Randall et al [87] identified a Traditional pattern of meat and baked goods that was associated with a higher risk of colon cancer. Furthermore, the overall conclusions from two recent systematic reviews addressing this topic are compatible with our results. In one of the reviews, the less healthy pattern with higher intakes of red and processed meat, potatoes and refined carbohydrates was associated with a higher risk of CRC [199]. Another review supposed that the self-labelling diet as “Western” was related to an increased risk of CRC with ORs ranging from 1.18 to 11.7 [20].

A healthier pattern with vegetables, fruits and other healthy foods which has been generally considered protective against the incidence and development of CRC was identified from previous studies [39, 58]. According to Fung et al’s [83] study in a US

population, a prudent pattern of vegetables, fruits, legumes, fish, poultry and whole grains was reported to be inversely, but not significantly, associated with colon cancer. Another US population-based case-control study reported a similar and significant association between a prudent pattern, which is characterized by higher intakes of vegetables and fruits, and a reduced risk of colon cancer in both genders [58]. Randall et al [87] suggested a significant association between the healthier pattern (that is, salad vegetables) and a decreased risk of colon cancer in women, but insignificant one in men. Additionally, other studies conducted in different populations, including Asian people, have also suggested that a diet with higher intakes of fruits, vegetables, cereals, legumes and low fat dairy products would be protective against CRC [39, 117, 186].

We hypothesized that the Plant-based diet pattern would be associated with a reduced risk of CRC, but there was no strong significant evidence of this in this NL population, after analyzing by proximal colon cancer, distal colon cancer, and rectum cancer. Through fitting multivariable logistic regression models, only a significantly inverse association between the Plant-based diet pattern and rectum cancer was found. However, this healthier pattern is non-significantly inversely related to the risk of proximal and distal colon cancer. Even though the direction of this association is similar to the findings from other studies, it is not significant [39, 58, 87, 117, 186].

High consumption of red meat, processed meat, sweets and processed sugar, which are typical characteristics of the Meat-diet and Sugary-diet patterns, might determine these patterns' relationship with CRC. The causal mechanism could involve overweight and

obesity, which previous studies have found to be important risk factors for CRC [73-75]. From a study conducted among Hispanic women, an association between an animal protein pattern and a greater than three-fold increased risk of obesity was reported [201]. Murtaugh et al [202] conducted a cross-sectional study in an Iranian population and suggested that a western pattern with a higher intake of sweets and desserts, and red and processed meat was positively associated with obesity. Another possible mechanism is that heme, sodium nitrate, nitrite and N-nitro compounds, which were found in lots of red meat and processed meat, have been associated with higher CRC risk [203-206].

In this study, fruits, vegetables and whole grains were loaded to the factor labelled as the Plant-based diet pattern. One possible mechanism of their protective effects against CRC is that they are good sources of vitamins A, C, and E, fibers, minerals, selenium, and carotenoids [76, 77]. These nutrients could have the effect of binding and diluting carcinogens as well as an anti-oxidant effect to change the physical environment for colonic flora, thereby affecting the incidence and development of CRC [76, 78].

Based on existing literature, this appears to be the first study that focuses on the relationships between dietary pattern and CRC in a Canadian population and provides updated information that may be applied to guide public health action for primary prevention of CRC. This study has a number of strengths. First of all, this study was conducted on a large sample which increases the likelihood of observing associations that would be impossible to detect in smaller studies. Secondly, instead of single nutrient/food approach, we used common factor analysis to derive new non-correlated variables to

explain the variation in dietary habits, thereby allowing us to obtain a more comprehensive and accurate picture of dietary exposures in this population. Thirdly, the FFQ used for this study, modified from the Hawaii FFQ, has been adapted to include regional foods consumed in NL and has been validated by our team [160].When exploring the relationships of dietary patterns and CRC risk, multivariate logistic regression models that controlled for a wide range of potential confounding factors were fitted. Finally, two logistic regression models were adjusted for total energy intake. Between-person variation generated by over-reporting or under-reporting of food intakes were reduced by this adjustment [100].

The methodological limitations of case-control studies in general, and specifically shortcomings on the design and data analysis choices of this study, which may have influenced the observed associations, should be discussed. First of all, selection and recall bias are possible as in most case-control studies. Because exposure information was collected after diagnosis, differential recall between cases and controls could bias the results. Specifically, cases may recall their diets differently than controls because of their disease status [207]. In addition, controls who agreed to join this study may have done so because of an interest in health and may therefore have healthier dietary and physical activity habits. The differences in dietary pattern between the selected controls and cases may be larger than with truly comparable controls. Second, related to the design, cases and controls had similar sex distribution but not well-comparable age groups. Third, the factors retained, self-labelling and interpretation of the dietary patterns is somewhat arbitrary; however, the patterns derived for this study population have emerged repeatedly

across studies that applied factor analysis or cluster analysis to determine dietary patterns in different populations [39, 58, 83, 87, 117, 186].

5.5 Conclusion

The present study demonstrated that diets that are characterized by a high consumption of red meat, processed meat, fish and processed fish (labelled as the Meat-diet pattern) or with a high consumption of fruit pies, tarts, desserts and sweets (labelled as the Sugary-diet pattern) are associated with an increased risk of CRC in a Canadian population. However, the Plant-based diet pattern of fruits, vegetables and whole grains has a protective effect against CRC. In addition, the diet-disease relationships investigated here could be used to develop targeted interventions aimed at promoting healthy eating habits, with the goal of preventing CRC in Canada, and particularly in the NL population.

Table 5.1 Characteristics of case and control groups

Variables	Cases (n=506) n (%)	Controls (n=673) n (%)	p-value
Gender			
Male	306 (60.47%)	400 (59.44%)	
Female	200 (39.53%)	273 (40.56%)	
Level of education			
Less than 11 years	246 (48.71%)	210 (31.44%)	
High school graduate	75 (14.85%)	103 (15.42%)	<0.0001
Vocational or technical school/college	141 (27.92%)	247 (36.98%)	
Bachelor/graduate degree	43 (8.51%)	108 (16.17%)	
Marital status			
Single/never married	30 (5.93%)	22 (3.27%)	
Separated, divorced or widowed	80 (15.81%)	100 (14.86%)	
Currently married or living as married	396 (78.26%)	548 (81.43%)	
Household income(per year)			
Less than $12,000	40 (8.59%)	43 (7.20%)	
$12,000-$19,999	181(40.49%)	185 (30.99%)	<0.0001
$30,000-$49,000	132 (29.53%)	163 (27.30%)	
More than $50,000	94 (21.03%)	206 (34.51%)	
Body mass index (kg/m^2)			
15-18.5	7 (1.42%)	2 (0.30%)	
18.5-25	135 (27.38%)	205 (31.20%)	0.004
25-30	206 (41.78%)	306 (46.58%)	
More than 30	145 (29.41%)	144 (21.96%)	
Physical activity (hours/week)			
0-7.4	140 (27.72%)	166 (25.08%)	
7.4-22.4	90 (17.82%)	148 (22.36%)	0.037
22.4-53.0	96 (19.01%)	151 (22.81%)	
More than 53.0	179 (35.45%)	197 (29.76%)	
Family history of colorectal cancer	54 (10.67%)	55 (8.18%)	
Polyp	240 (48.29%)	85 (12.98%)	<0.0001
Diabetes	107 (21.15%)	89 (13.40%)	0.0004
High cholesterol/triglycerides	169 (33.47%)	258 (38.39%)	
Crohns disease or colitis	12 (2.42%)	13 (2.00%)	
Any colon screening procedure	65 (12.85%)	145 (21.55%)	0.0001
Smoking status	367 (72.53%)	422 (62.70%)	0.0004
Alcohol use	301 (59.49%)	379 (56.32%)	
Multivitamin use	101 (20.08%)	146 (21.82%)	
Non-steroidal anti-inflammatory drug use	167 (33.07%)	260 (38.75%)	0.045

Significant level at 0.05; non-significant p-values are not shown

Table 5.2 Factor loadings and explained variances for the three major dietary patterns identified in an adult NL population, using an exploratory factor analysis [a]

Food Groups	Dietary pattern		
	Meat-diet	Plant-based diet	Sugary-diet
Milk		0.19	
Yogurt		0.31	
Coffee	0.18		
Tea			0.17
Sugar		-0.19	0.20
Soft drinks	0.19		
Egg	0.21		0.16
Cheese	0.15	0.21	
Mixed dishes	0.31	0.17	0.24
Red meat	**0.68**		0.18
Game	0.24		
Cured /processed red meat	**0.72**		0.21
Cured /processed meat	**0.93**		
Poultry	0.22	0.27	
Fish	**0.59**	0.31	-0.21
Processed fish	**0.51**	0.24	
Fruit juice		0.24	0.24
Other fruits		**0.59**	
Root vegetables	0.28		0.15
Cruciferous vegetables		**0.54**	
Other greens		**0.60**	-0.22
Beans, peas	0.15	0.25	
Tomato sauce		**0.50**	
Other vegetables	0.22	**0.54**	
Total cereals and grains	0.23	**0.38**	0.28
Whole grains		0.33	
Desserts and sweets	0.31		**0.63**
Vegetable juice		0.17	
Beer	0.19		
White wine			
Red wine			
Liquor	0.15		
Citrus		0.34	
Berries		**0.45**	
Dried fruit		**0.39**	
Canned fruit		0.20	0.24
Pies, tarts	0.15		**0.54**
Jam, jelly			0.26

Pickled vegetables	0.15	0.26	0.14
Proportion of VAR explained (%)	40%	23%	11%
Cumulative VAR explained (%)	40%	63%	74%

[a]Absolute values less than 0.15 were not listed and those above 0.35 indicated in bold to visually emphasize strength of association

VAR: variance

Table 5.3 Odds ratios and 95% CI of colorectal cancer according to the three major dietary patterns in a NL population

Dietary pattern	quintiles								
	Q1	Q2		Q3		Q4		Q5	P for trend
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	
Meat-diet pattern										
†original	1.00	1.52	**1.04, 2.23**	1.37	0.94, 2.03	1.86	**1.27, 2.72**	2.14	**1.41, 3.24**	0.0002
‡multivariate	1.00	1.44	0.91, 2.30	1.32	0.88, 1.97	1.64	**1.09, 2.46**	1.84	**1.19, 2.86**	0.6442
Plant-based diet pattern										
†original	1.00	1.04	0.72, 1.51	0.73	0.50, 1.06	0.69	**0.47, 0.99**	0.46	**0.31, 0.69**	<0.0001
‡multivariate	1.00	1.09	0.74, 1.60	0.78	0.53, 1.17	0.77	0.51, 1.16	0.55	**0.35, 0.87**	0.3065
Sugary-diet pattern										
†original	1.00	1.69	**1.15, 2.48**	1.55	**1.06, 2.27**	2.20	**1.48, 3.27**	2.51	**1.64, 3.84**	<0.0001
‡multivariate	1.00	1.47	0.96, 2.26	1.46	0.94, 2,25	1.92	**1.23, 3.01**	2.26	**1.39, 3.66**	0.4024

† Adjusted for age and total energy intake;

‡ Adjusted for: sex, body mass index, marital status, education attainment, household income status, use of alcohol/tobacco/non-steroid anti-inflammatory drug (NSAID), family history of CRC, history of diabetes/colon screening procedure/ high cholesterol, reported hormone replacement therapy (females only), multivitamin supplements, and physical activities;

Significant 95%CI are in bold;

P for trend was calculated by Mantel-Haenszel Chi-Square Test.

Table 5.4 Odds ratios and 95%CI for cancer of the proximal colon, distal colon and rectum according to the three major dietary patterns in a NL population

Dietary pattern	quintiles									
	Q1	Q2		Q3		Q4		Q5		P for trend
		OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	
Proximal colon cancer										
Meat-diet pattern										
†original	1.00	1.42	0.84, 2.41	1.43	0.85, 2.40	1.57	0.93, 2.65	1.30	0.72, 2.33	0.2501
‡multivariate	1.00	1.45	0.85, 2.50	1.50	0.88, 2.57	1.61	0.94, 2.78	1.34	0.72, 2.47	0.3182
Plant-based diet pattern										
†original	1.00	1.34	0.80, 2.24	0.91	0.53, 1.55	0.83	0.48, 1.43	0.70	0.40, 1.24	0.1287
‡multivariate	1.00	1.31	0.77, 2.24	0.88	0.48, 1.45	0.78	0.44, 1.38	0.64	0.34, 1.19	0.4062
Sugary-diet pattern										
†original	1.00	1.52	0.86, 2.69	1.72	0.99, 3.00	2.23	**1.27, 3.93**	2.75	**1.51, 5.03**	0.0009
‡multivariate	1.00	1.70	0.95, 3.04	1.69	0.96, 2.99	2.39	**1.32, 4.33**	2.90	**1.54, 5.45**	0.1144
Distal colon cancer										
Meat-diet pattern										
†original	1.00	1.63	0.87, 3.05	1.55	0.83, 2.90	1.68	0.89, 3.17	2.87	**1.51, 5.44**	0.0035
‡multivariate	1.00	1.55	0.81, 2.97	1.33	0.69, 2.55	1.43	0.74, 2.80	2.29	**1.16, 4.53**	0.0035
Plant-based diet pattern										
†original	1.00	1.14	0.64, 2.03	0.80	0.44, 1.45	0.82	0.45, 1.47	0.54	0.28, 1.02	0.0534
‡multivariate	1.00	1.27	0.69, 2.32	0.90	0.48, 1.68	0.99	0.53, 1.87	0.72	0.35, 1.45	0.6609
Sugary-diet pattern										
†original	1.00	1.63	0.86, 3.09	1.52	0.81, 2.88	2.28	**1.21, 4.28**	2.78	**1.44, 5.40**	0.0024
‡multivariate	1.00	1.56	0.81, 3.01	1.55	0.80, 3.01	2.14	**1.11, 4.14**	2.40	**1.20, 4.81**	0.0797
Rectum cancer										
Meat-diet pattern										
†original	1.00	1.65	0.92, 2.94	1.18	0.65, 2.17	2.39	**1.37, 4.18**	2.78	**1.54, 5.03**	0.0005
‡multivariate	1.00	1.61	0.88, 2.97	1.02	0.54, 1.93	2.11	**1.16, 3.84**	2.01	**1.06, 3.80**	0.0183
Plant-based diet pattern										
†original	1.00	1.14	0.49, 1.34	0.57	**0.34, 0.96**	0.55	**0.33, 0.92**	0.27	**0.15, 0.49**	<0.0001

‡multivariate	1.00	0.93	0.54, 1.59	0.72	0.41, 1.27	0.85	0.48, 1.51	0.46	**0.23, 0.90**	0.1316
Sugary-diet pattern										
†original	1.00	1.90	**1.09, 3.31**	1.39	0.78, 2.47	2.06	**1.17, 3.64**	1.99	**1.08, 3.69**	0.0304
‡multivariate	1.00	1.97	**1.08 3.58**	1.29	0.69, 2.41	1.96	**1.04, 3.69**	2.01	**1.01, 4.00**	0.6538

† Adjusted for age and total energy intake;

‡ Adjusted for: sex, body mass index, marital status, education attainment, household income status, use of alcohol/tobacco/non-steroid anti-inflammatory drug (NSAID), family history of CRC, history of diabetes/colon screening procedure/ high cholesterol, reported hormone replacement therapy (females only), multivitamin supplements, and physical activities;

Significant 95%CI are in bold;

P for trend was calculated by Mantel-Haenszel Chi-Square Test.

Chapter 6: Paper 3. Reliability of dietary patterns assessed with a food-frequency questionnaire

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AUTHOR'S CONTRIBUTION

P.P.W. contributed to the conception and design of this manuscript. Z.C. conducted the research, data analysis and paper writing. P.P.W., L.S., Y.Z., L.L., J.W., Z.G. and R.B. subsequently revised the manuscript. All authors have read and approved the final manuscript.

NOTE

This paper is now under-review by BioMed Central Nutrition Journal. Part of results in this paper has been reported by the first published paper (Chapter 4).

6.1 Introduction

Most previous nutritional epidemiological literature uses nutrients or individual food items to assess the association between diet and health. There are several limitations of the single-nutrient approach: people eat meals consisting of a variety of foods rather than isolated nutrients; single-nutrient analysis fails to take into account complicated interactions among nutrients [208]; and, due to high level of inter-correlation among some nutrients (for example, potassium and magnesium), the effects of nutrients are difficult to be examined separately by single-nutrient analysis [99]. Moreover, single-nutrient analysis may be confounded by each individual's dietary pattern which is commonly associated with nutrient intakes [91, 92]. In order to overcome these limitations, an emerging approach in nutritional epidemiology is to use dietary patterns rather than isolated nutrients. Compared to the traditional approaches used in previous nutritional epidemiology, dietary pattern analysis considers how food and nutrients are consumed in combination and then provides a more accurate and comprehensive description of dietary exposure in a certain population [92, 209, 210].

Dietary pattern analysis has been widely used for describing the diet habits of individuals or populations. Eating habits will usually change only when people experience dramatic changes in their personal circumstances, such as: getting married; changing geographic location; or being warned by a doctor that their current diets have significant and negative impacts on their health. Researchers summarized several factors that may influence individuals and populations' food choice, comprising of family income, food prices, individual preferences and religious beliefs, cultural traditions and customs, as well as

geographic and environment factors [8, 25]. While a dietary pattern is often believed to be stable in a population, there is limited research assessing its reliability. Objectives of this study were 1) to identify the major dietary pattern from two time-separated studies using identical methods in the NL populations 2) to examine if the dietary pattern identified in one study can be replicated in another similar study conducted several years afterwards.

Along with the increasing research interest in diet, as well as association between diet and health, our team, a large and diverse multidisciplinary group of more than 40 researchers from Ontario (ON) and NL, published several journal articles on diet in the NL population using both nutrients and dietary pattern methods [14, 163, 196, 211, 212]. Using factor analysis, this study derived and compared major dietary patterns from dietary data collected by the food-frequency questionnaire (FFQ) in two projects conducted in NL population: population-based case-control study (CCS) from 2001 to 2005 and food-frequency questionnaire validation project (FFQVP) in 2012. The purpose of this study was to assess the reliability of dietary pattern analysis approach used in this study.

6.2 Methods

6.2.1 Study participants

The CCS was conducted from 2001 to 2005, occurred within the Colorectal Cancer Interdisciplinary Health Research team. Participants used for the present study were part of the population controls from the CCS project, aged from 35-70 years. A detailed description of the selection of the population controls cohort can be found elsewhere

[161]. Controls were identified through random digit dialing using telephone numbers provided by a local phone company (Aliant). By July 2005, a total of 2168 eligible controls were contacted for further survey and 1603 controls agreed to participate. Those persons who agreed to participate were sent a survey package, comprising a written consent form, personal history questionnaire (PHQ), and food-frequency questionnaire (FFQ). Of them, 717 participants completed and returned the survey package; the response rate was 44.7%.

The FFQVP was conducted between February 2011 and May 2012, by the Health Research Unit of Memorial University. This study population was sampled by stratified random digit dialing with proportional allocation methodology. Participants were recruited in the same manner as were the CCS. Specifically, non-institutionalized adult residents of NL, aged from 35-70 years. Residence in NL was defined as having lived in NL for at least two years at the time of the study. Other inclusion criteria included an 8^{th} grade level of English speaking and reading skills and no cognitive impairment, psychological conditions, or pregnancy. From a list of landline numbers from Info Canada, an initial sample of 450 persons was recruited randomly by telephone. After exclusion, 306 participants were identified as respondents, and after giving oral consent were sent the survey package, including a written consent form and a FFQ. Finally, 205 individuals completed and returned the survey package, giving a response rate of 67%.

Those participants with 20 continuous blanks on the FFQ or energy intakes reported outside the range of 500-5000 kcal were excluded [166]. After exclusion, a total of 554

participants of the former population and 192 participants of the current population remained and entered into further analysis.

6.2.2 Data collection

For both studies, a modified FFQ, based on the well-known Hawaii FFQ, was used to gather dietary intake data. The original Hawaii FFQ was used in Hawaii/Southern California to assess the general food intake of a multi-ethnic population [183]. It has been validated and widely used in the United States [180-182]. In our new version of the FFQ, some unusual food items (for example, tamales and ham hocks) were deleted or altered, and some items commonly consumed in NL (for example, cloudberries/bakedapples, game, and pickled/smoked fish) were added in order to adapt it to specific food consumption habits among the NL population. The food items listed in the NL FFQ, which has been validated by our team [160], include nine major categories: beverages; dairy products; mixed dishes; vegetables; meat and fish; cereals and grains; fruits; desserts and sweets; and miscellaneous.

Dietary assessment of participants using this FFQ was carried out one or two years prior to interview. Each participant was required to recall the frequency of each food item they consumed, the number of servings, and portions habitually consumed at a single sitting. The units of frequency ranged from per day, per week, per month to rarely or never, and the portion sizes include average, smaller, and larger sizes. An average size indicates a standard serving, expressed in common household measures or grams, which is specified for each food item or beverage in the FFQ. The smaller portion size is 75% or less of an

average size while the larger size is 125% or more of an average one. Participants can choose their usual portion size based on supplied food photographs.

The study sample from CCS was administered a PHQ to collect socio-demographic and medical information, comprising age, sex, date of birth, marital status, educational attainment, medical history (for example, history of diabetes or high cholesterol), bowel screening history, medication use (for example, multivitamins and nonsteroidal anti-inflammatory drugs), physical activity, reproductive factors, alcohol and tobacco use, and other information.

Very limited socio-demographic information was gathered for the study population for FFQVP by phone interview, such as age, sex, size of community, marital status, employment status, level of education, and smoking habits.

6.2.3 Statistical analyses

Except for several independent food items, the 169 food items were categorized into 39 predefined food groups, based on their nutritional characteristics and their role in the diet (Table 6.1). Those independent food items comprised their own groups, given the fact that they could not be appropriately combined with others, for example, eggs, beer, jam, and fruit pies. Total energy and nutrient intakes for individuals were calculated according to the composition values from the 2005 Canadian Nutrients file or by using the Elizabeth Stewart Hands and Associations (ESHA) Food Processor database software [167].

The appropriateness of factor analysis for each study sample was verified by Bartlett's Test of Sphericity (BTS) and the Kaiser-Meyer-Olkin (KMO) measurement. Exploratory factor analysis was used for factor extraction, and orthogonal rotation (varimax option) was used for simpler structures with greater interpretability. A factor was retained when it met the following criteria: factor eigenvalue>1.50, identification of a break point in the scree plot (that is, the difference between each two points becomes small suddenly), the proportion of variance explained (at least 50% of variance in this study), and factor interpretability (that is, the fewer the factors, the greater the interpretability). A rotated loading matrix described the strength and direction of the associations between the retained factors and food groups. If a food group had a factor loading ≥0.5 (for the current population) or ≥0.35 (for the former population), it was loaded on a factor. We also retained food groups that had negative correlations (≤-0.2) to incorporate the valuable information concerning infrequently consumed foods within each factor [186]. According to the characteristics of food groups loaded on a retained factor, this factor will be given a name which is called dietary pattern.

After stratification by age group and gender, differences in demographic information between the two study populations were detected by t-tests. Statistical analyses were performed using the Statistical Analysis System (SAS, version 9.2) software. Differences with p-value <0.05 were considered to be statistically significant.

6.3 Results

In total, the study sample was comprised of 554 participants from the CCS samples and

192 participants from the FFQVP samples. The gender distributions between the two populations were significantly different ($p<0.0001$): the percentage of males in the study population of CCS (58.1%) was much higher than in the FFQVP study population (22.4%). All of the study participants were aged from 35-70 years; individuals from the CCS (58.7±7.7) are significantly older than those from the FFQVP (56.2±8.7). Because of very limited demographic information collected for the FFQVP sample, description and comparison in other baseline information are not shown in the present study.

The observed KMOs for the two populations are 0.68 for the CCS and 0.60 for the FFQVP; therefore, the two samples from different populations are adequate for factor analysis. P values from the BTS are <0.0001, suggesting homogeneity of variance across the samples. Figure 6.1 shows the scree plots for both study populations. For the CCS sample, the first three eigenvalues, which are 3.73, 3.24, and 1.56, drop substantially. After the fourth eigenvalue (1.43), the values remain more consistent (1.39 for the fifth, and 0.89 for the sixth). As a result, the third point is considered a break point. As for the FFQVP sample, differences between each two eigenvalues change to gentle from sharp after the fourth value; accordingly, the fourth point is regarded as a break point on this plot. All eigenvalues before each break point are greater than 1.50. Combined with total variance explained and factor interpretability, a 3-factor solution was selected for the study population from CCS; this explained 54% of variance. The first four factors were retained for the study population from FFQVP, and this explained 63% of variance (Table 6.2).

According to the results obtained from the factor loading matrix shown in Table 6.2, the retained factors were labelled, depending on the given food groups loaded on them. A factor loading ≥ 0.35 of a certain food group indicates a greater contribution of that food group to the specific pattern for the CCS population. The three retained factors were identified as three dietary patterns and were labelled Meat, Plant-based diet, and Fish. The first pattern was defined as the Meat pattern, and characterized by high loadings for red meat, cured/processed red meat, cured/processed meat, and mixed dishes. The second pattern, which loaded heavily on fruits, cruciferous vegetables, other green vegetables, beans, peas, other vegetables, tomato sauce, total cereals and grains, and whole grains, was labelled the Plant-based diet pattern. The final pattern was named Fish pattern because it has high loadings of fish, processed fish, berries and other fruits and negative loadings in the food groups of cheese.

The four retained factors were identified as four dietary patterns for the FFQVP population and were labelled Meat, Vegetables/fruits, Fish, and Grains. The four-factor dietary pattern was identified based on the results retained from the factor loading matrix (Table 6.2), where a higher factor loading of a given food group indicates a greater contribution of that food group to the specific pattern. The first pattern was labelled because of a high intake of red meat, cured/processed meat, and cured/processed red meat. The Vegetables/fruits pattern indicates a preference for several vegetable/fruit groups, including greens, tomato sauce, berries, and other vegetables. The Fish pattern has an emphasis on fish and processed fish. We named the final pattern Grains, since it is characterized by a high consumption of whole grains, cereals, and grains, and a low

consumption of beer, white wine, and coffee.

6.4 Discussion

Even though dietary pattern analysis has emerged as a possible approach to examine diet-disease relations, few data are available on the reliability of this approach. In this study, we assessed the reliability of major dietary patterns derived for two time-separated NL populations assessed with a self-administered comprehensive FFQ.

The present study derived a three-factor dietary pattern for the CCS and a four-factor dietary pattern for the FFQVP. We observed both similarities and differences in dietary patterns between the two studies. The total variances explained for the CCS and FFQVP studies were similar, 54% and 63%, respectively. Both identified meat and plant-based food as top two major factors, which in combination explain almost equal amount of variation (42% and 44%). According to the factor loading matrix, the patterns labelled Meat pattern and Fish pattern derived for the CCS are largely the same to those two derived from the FFQVP. The meat pattern is similar to the food items (for example, red meat, processed meat, other high-fat food) referred to as the Western pattern in many previous studies [187, 188], which has been associated with cancer [22], cardiovascular diseases [175, 189], and obesity [102]. The Fish pattern, which is characterized by high intakes of fish and processed fish, seems to be different from any pattern described in other research. Geographic isolation and the historical importance of the cod fishery in NL may be the leading cause of this unique phenomenon[192].The Plant-based diet pattern derived for CCS is a combination of the Vegetable/fruit and Grains pattern in the

FFQVP. This pattern is comparable to the Prudent and/or Vegetable/fruit patterns described in other studies, with a high consumption of vegetables, fruits, and other plant-based diet[125, 187, 190], which has been reported a protective effect against coronary heart disease [191], type 2 diabetes [187], CRC [86]. Also, the main food items of whole grain, cereals and grains from the Grains pattern contain fiber which has been proven to be beneficial to health, especially by decreasing the risk of chronic diseases such as CRC [39, 117, 186].

According to findings obtained from the FFQVP and the CCS, we can make a conclusion that dietary patterns using factor analysis derived for those two studies are almost the same, except the number of factors retained and total variance explained by the retained patterns. These minor differences should be attributed to several points. First of all, the sample size may be too small to be representative of the whole population; there are only 554 study participants from CCS and 192 from FFQVP. Secondly, distributions of sex and age between the two study populations are significantly different. There were much more males from CCS than from FFQVP. According to previous studies, dietary patterns are likely to vary according to sex. For example, an association between women and higher loadings on healthy dietary patterns has been reported by many previous studies [125, 126, 175]. However, small sample size (stratified by sex) is not appropriate and adequate to conduct factor analysis in this study. Additionally, study participants from CCS are controls to CRC cases, who are more likely to be families of CRC cases or persons who are interested in cancer and or nutrition. Those individual may not be able to represent general population. However, study participants for FFQVP were randomly recruited

from general population. Further, information bias may exist because study participants were required to recall their diet habits one or two years prior to the interview or survey. Moreover, dietary information collected for CCS was in July 2005, while that for FFQVP was during 2011 and 2012. It is possible that some people's dietary habits changed over time so that minor difference exists in dietary patterns derived from the two time-separated studies.

All in all, this study is the first nutritional epidemiological research conducted in the NL population to identify the reliability of dietary pattern analysis. This result will provide an overall picture indicating the dietary exposure for the NL populations and update the current dietary-habit-related information previously published in this province. In addition to this, this study could provide guidance and reference to future researchers to conduct related studies on this topic, through an improved method and study design.

6.5 Conclusion

After comparison in dietary patterns derived for study participants of the FFQVP and the CCS project, no considerable difference was found between the two studies. Therefore, we can conclude that the dietary patterns derived for the NL population are reasonably stable overtime and across studies. However, due to issues of methodology and study design, further research to determine the reproducibility and validity of dietary pattern analysis assessed by FFQs should be conducted in other populations.

Table 6.1 Food groups used in the dietary pattern analysis

Food group	Food items
Milk	Whole milk, 2% milk, skim milk, milk shake
Yogurt	Yogurt drink, yogurt (regular/light, plain/fruit/frozen)
Coffee	Coffee (regular/decaffeinated)
Tea	Tea (regular/herbal)
Sugar	Sugar (in tea/coffee)
Soft drinks	Cola, Pepsi, diet/other soft drinks
Egg	Egg (boiled/fried)
Cheese	Cream cheese(regular fat), cheese(regular fat, light, ultra light), cottage, ricotta cheese
Mixed dishes	Soups(creamed), pasta(with meat sauce), mixed dishes (with cheese), pizza (with meat), meat stew with vegetables, chili with meat
Red meat	Ground beef(regular/medium/lean), roast beef, steak, pork chop, roast pork, baked ham, bacon, veal, lamb, hot dog, wiener, sausage, corned beef, cold cuts
Game	Sea-bird, seal, caribou, moose, partridge, other wild birds
Cured/processed red meat	Baked ham, bacon, hot dog, wiener, corned beef, cold cuts, salted/dried meat, pickled meat
Cured/processed meat	Baked ham, bacon, hot dog, wiener, corned beef, cold cuts, fried chicken, salted/dried meat, pickled meat, fried/canned/smoked/salted/dried/pickled fish
Poultry	Fried chicken, chicken(roasted or stewed/skin removed)
Fish	Shellfish, fish (baked or broiled), fried/canned/smoked/salted/dried/pickled fish
Processed fish	canned/smoked/salted/dried/pickled fish
Fruit juice	Orange/grapefruit/apple/grape/other fruit juice, fruit drinks/lemonade, iced tea
Other fruit	Apple, pear, grape, banana, beach, plum, nectarine, apricot, cantaloupe, watermelon, honeydew melon, mango, papaya, apple sauce, all other fruit
Root vegetables	Potatoes (mashed, baked), fried potatoes/French fries, carrots (raw or cooked)
Cruciferous vegetables	Broccoli, cabbage, coleslaw, cauliflower, asparagus or brussel sprouts
Other green	Spinach/other green-leaf vegetables, green salad
Beans, peas	Peas, lima beans, green/yellow beans, beans/lentils, pea soup
Tomato sauce	Tomatoes (fresh/canned), ketchup

Other vegetables	Corn, cucumber, onions, beets, yellow squash, zucchini or eggplant, sweet pepper, bean sprout, avocado, other vegetables
Total cereals and grains	Bran or granola cereal, whole wheat cereals, cereals (not sugar coated), hot cereals, sugar coated cereals, other breakfast cereals, sugar on cereal, 100% whole grain/dark bread, 60% whole grain/light rye, white bread, white bread rolls, whole wheat rolls, crackers, bran/oat muffin, other muffins, pancake, waffles, macaroni, spaghetti, noodles, rice, crisp snacks
Whole grains	Whole wheat cereals, 100% whole grain/dark bread, 60% whole/light rye, whole wheat rolls
Dessert and sweet	Cakes, pies and tarts, donuts and sweet rolls, cookies, iced cream, light or diet ice cream, pudding, diet or light pudding, jell-o, popsicles, freezies, candy (with/without chocolate)
Vegetable juice	Vegetable juice
Beer	Beer, ale
Whiter wine	White wine
Red wine	Red wine, sherry
Liquor	Liquor
Citrus	Citrus fruits
Berries	Berries
Dried fruits	Dried fruits
Canned fruits	Canned fruits
Pies, tarts	Pies, tarts
Jam, jelly	Jam, jelly, honey syrup
Pickled vegetables	Pickles, relish

Figure 6.1 Scree plot for eigenvalues from factor extraction in two separated studies

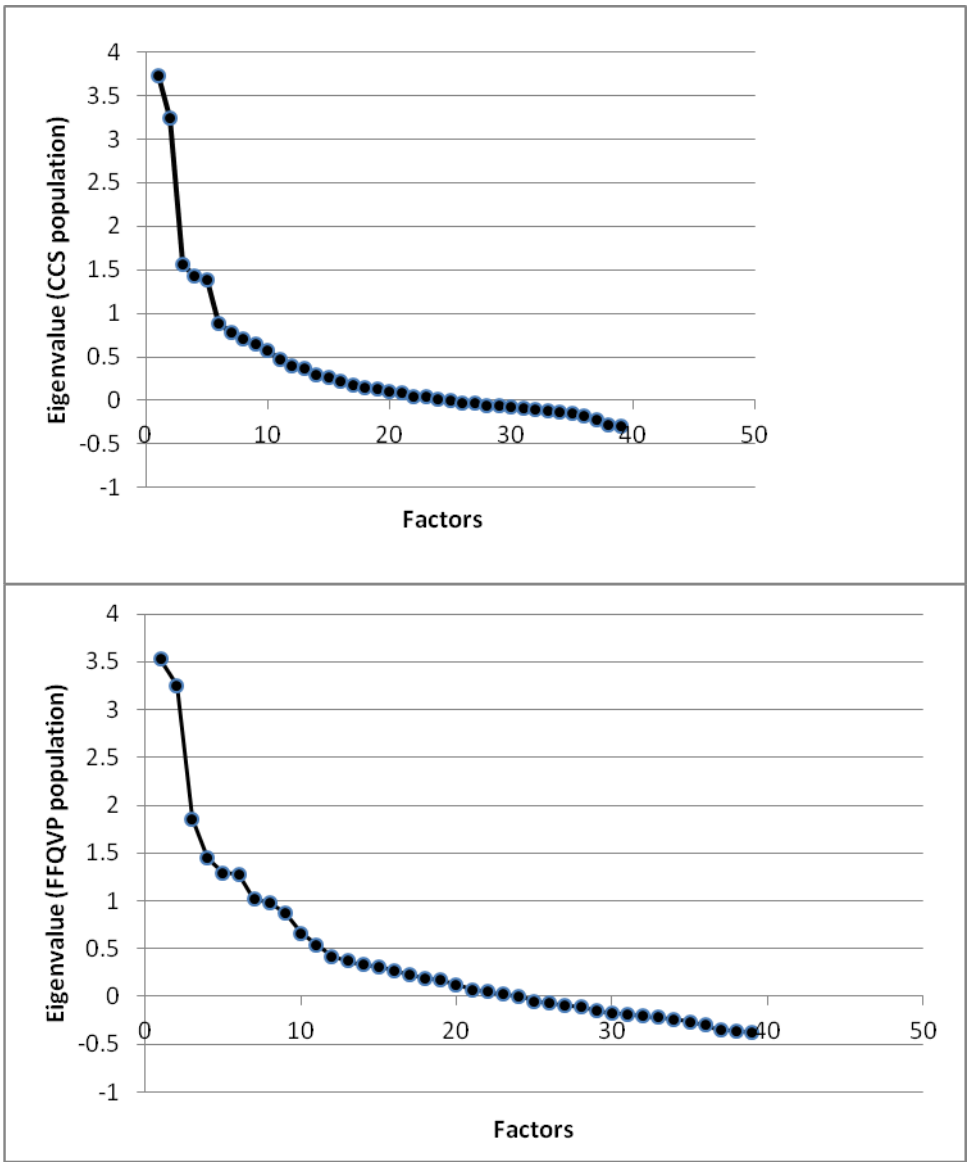

Table 6.2 Factor loadings and explained variances of the major dietary patterns identified in two studies, using an exploratory factor analysis

Food groups	Factor loadings*						
	FFQVP population				CCS population		
	Meat	Vegetables /Fruits	Fish	Grain	Meat	Plant-based diet	Fish
Milk							
Yogurt							
Coffee				-0.31			
Tea							
Sugar							
Soft drinks				-0.20			
Egg							
Cheese							-0.24
Mixed dishes					0.43		
Red meat	0.83				0.88		
Game							
Cured/processed red meat	0.90				0.91		
Cured /processed meat	0.93				0.92		
Poultry							
Fish			0.78				0.73
Processed fish			0.70				0.68
Fruit juice		-0.25					
Other fruits						0.42	0.48
Root vegetables							
Cruciferous vegetables						0.58	
Other greens		0.68				0.50	
Beans, peas						0.52	
Tomato sauce		0.60				0.41	
Other vegetables		0.75				0.57	
Total cereals and grains				0.55		0.38	
Whole grains				0.52		0.36	
Desserts and sweets							
Vegetable juice							
Beer				-0.24			
White wine				-0.26			
Red wine							
Liquor							
Citrus							
Berries		0.50					0.49
Dried fruit							

Canned fruit Pies, tarts Jam, jelly Pickled vegetables									
Proportion of explained (%)	VAR	22%	20%	12%	9%	24%	20%	10%	
Cumulative explained (%)	VAR	22%	42%	54%	63%	24%	44%	54%	

* Factor loadings ≥ 0.5 will be loaded on a factor in FFQVP population while factor loadings ≥ 0.35 will be loaded on a factor in CCS population; negative loading ≤ -0.20 will be retained; other loadings are not shown in the table.

VAR: variance

Chapter 7: Summary

7.1 Summary of key findings

The primary goals of this thesis are to: 1) derive the major dietary patterns for the NL populations, 2) explore their associations with CRC risk, 3) and assess the reliability of dietary patterns derived for the NL population. These objectives were pursued through three separated studies. In this chapter, I will summarize the key findings from the three studies, discuss the implications of these findings, and propose future studies.

The first component of this thesis identified four major dietary patterns for the NL population; all participants of this study were from the subjects recruited for FFQVP. The first pattern, Meat, is characterized by a high consumption of red meat, cured/processed meat, and cured/processed red meat. Conversely, the Vegetables/Fruits pattern has an emphasis on several vegetable/fruit groups, including greens, tomato sauce, berries, and other vegetables. The Fish pattern indicates a preference for fish and processed fish. The final pattern was labeled as Grains due to the high positive loadings in whole grains, cereals, and grains, and negative loadings in the groups containing beer, white wine, and coffee. Except the Fish pattern which is unique compared to other patterns derived for other populations, the other three dietary patterns remain consistent with existing similar studies.

The second study of this thesis derived three-factor dietary pattern (Meat-diet pattern,

Plant-based diet pattern, Sugary-diet pattern) for the NL population; participants were from cases and controls recruited for CCS. It suggested that the Meat-diet pattern and the Sugary-diet pattern increase the risk of CRC with corresponding ORs of 1.84 (95% CI: 1.19-2.86) and 2.26 (95% CI: 1.39-3.66) for people in the highest intake quintile compared to those in the lowest. In contrast, the Plant-based diet pattern decreased the risk of CRC with a corresponding OR of 0.55 (95% CI: 0.35-0.87). Even though ORs were not always statistically significant, largely similar associations across three cancer sites were found: the proximal colon, the distal colon, and the rectum.

The third project of this thesis derived a four-factor dietary pattern (Meat, Vegetables/fruits, Fish, and Grains) for FFQVP and a three-factor dietary pattern (Meat, Plant-based diet, and Fish) for CCS (only controls). According to factor loading matrix, dietary patterns derived for those two studies largely remain consistent, except the number of factor retained and total variance explained by the retained patterns. Those minor differences may be attributed to small sample size, significant difference in gender distribution, participant recruitment, information bias and time separation of these two studies. All in all, a conclusion could be made that the dietary patterns in the NL population are reasonably stable overtime and across studies.

7.2 Implications of these findings

First of all, these findings can probably update dietary-habit-related information previously published for this province, in addition to existing information on isolated nutrients and foods consumption. For example, the first study derived a unique dietary

pattern “Fish” for this population, which has not been reported yet before. This may be attributed to this province’s flourishing cod fishery and unique dietary culture [192]. Secondly, dietary pattern plays an important role in describing the total effect of overall diet so that it could be more predictive of disease risk [10]. Therefore, the findings on dietary patterns could also contribute to further research into the association between dietary practices and health. Additionally, findings from this study emphasize the importance of exploring the relationship between dietary habits and CRC by dietary pattern analysis. The diet-disease relationships investigated here could be used to develop targeted interventions aimed at promoting healthy eating habits, with the goal of preventing CRC in the NL population. For example, findings from the second study suggest that the Meat and Sugary-diet pattern is associated with an increased risk of CRC while the plant-based diet pattern is associated with a decreased risk of CRC. According to the findings, people could purposely improve their current eating patterns so that they can modify the dietary risk factor to CRC incidence and development as possible. The third piece of this thesis is a pilot study to discuss the reliability of dietary patterns derived for this population. Findings from this study indicate that dietary patterns always remain stable except dramatic changes experienced, which is consistent with literature. Also, it will provide guidance and reference to future researchers to conduct further studies to explore the reproducibility and validity of dietary pattern analysis, through an improved method and study design.

7.3 Future research

Results from other similar epidemiological studies indicated that obesity has been

associated with dietary patterns. Generally, the traditional diet (e.g., higher consumptions of rice and beans) was associated with decreased risk of overweight (BMI=25 to 29.9 Kg/m^2) or obesity (BMI $\geq$ 30 Kg/m^2), compared to the western diet (e.g., higher consumptions of fat and sugar) [213, 214]. However, because the subjects in this study were originally recruited for FFQ validated purpose, we were constrained from exploring the association between BMI and factor scores. Future research should carefully design the questionnaire or the telephone interview transcript to collect potentially important demographic information to verify the associations between the baseline factors and dietary patterns in this NL population.

The second paper explored important associations between dietary patterns and CRC risk. However, due to methodological limitations of case-control studies (e.g., recall and selection bias), the observed associations may be biased. Future studies could be conducted through prospective study design to verify the associations in this population.

Findings from the third paper indicate that the dietary patterns derived for this population remain largely consistent from two separated studies. Then a conclusion was made from the pilot study that the reliability of dietary patterns derived for the NL population were reasonably stable over time and cross studies. The future study should further explore the precise reproducibility and validity of dietary pattern analysis by recruiting a sample of participants to complete two FFQs (one year apart) and two one-week diet record (about 7 months apart). Pearson correlation coefficients between factor scores of dietary patterns derived from 2 FFQs and diet records would be calculated to evaluate the reproducibility

and validity [215].

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Appendixes

Appendix A. Personal History Questionnaire

Please write in your answers where space is provided, or place tick marks in circles O

What date are you filling out this questionnaire? _____/_____/_____
Day Month Year

Identifying information

1. Are you male or female?
O male
O female

2. What is your date of birth?
___ ___ years
O don't know

2. What is your age?
day ___ ___
month ___ ___
year ___ ___
O don't know day
O don't know month
O don't know year

3. Are you a twin or triplet?
O yes, a twin
O yes, other multiple (triplet, quadruplet, etc.): _____
Please specify
O no
O don't know

If yes, please read the following statement and answer the question.

Non-identical twins are no more alike than ordinary brothers and sisters. Genetically identical twins, on the other hand, look so much alike *that is, they have a strong resemblance to each other in height, colouring, features of the face, etc.) that people often mistake one for the other, especially during their childhood.

Do you have a genetically identical twin or triplet?
O yes
O no
O don't know

5. What is your marital status?
O currently married or living as married
O separated
O divorced
O widowed
O single or never married
O don't know

Bowel Screening and Health

6. Have you ever had a test for blood in your stool, called a smear test or a hemoccult? This test is frequently done as part of a routine physical examination, or it can be done at home.

O yes
O no → Please go to # 7
O don't know → Please go to # 7

6a. When did you first have this test?

age when first tested ___ ___
or
year of first test ___ ___ ___ ___
O don't know

6b. What were the reasons for your first test? Please tick all that apply.

O to investigate a new problem
O family history of colorectal cancer
O routine/yearly examination or check-up
O follow up of previous problem
O don't know

6c. How many times have you had a hemoccult test?

___ number of hemoccult tests
O don't know

6d. If you have had a hemoccult test more than once, when did you last have this test?

age when last tested ___ ___
or
year of last test ___ ___ ___ ___
O don't know

8. Have you ever had a colonoscopy? colonoscopy is an examination of the entire large bowel using a long flexible instrument. This examination is usually done under sedation.

O yes
O no → Please go to # 9

7. Have you ever had a sigmoidoscopy? sigmoidoscopy involves looking inside the lower bowel and rectum with a lighted instrument. This examination is usually done in a doctor's office without anesthesia.

O yes
O no → Please go to # 8
O don't know → Please go to # 8

7a. When did you first have this test?

age when first tested ___ ___
or
year of first test ___ ___ ___ ___
O don't know

7b. What were the reasons for your first sigmoidoscopy? Please tick all that apply.

O to investigate a new problem
O family history of colorectal cancer
O routine/yearly examination or check-up
O follow up of previous problem
O don't know

7c. How many times have you had a sigmoidoscopy?

___ number of sigmoidoscopies
O don't know

7d. If you have had a sigmoidoscopy more than once, when did you last have this test?

age when last tested ___ ___
or
year of last test ___ ___ ___ ___
O don't know

9. Has a doctor ever told you that you had polyps in your large bowel or colon or rectum? Polyps are growths in the lining of the colon which vary in size from a tiny dot several inches.

O yes
O no → Please go to # 10

O don't know → Please go to # 9

8a. When did you first have this test?

age when first tested ___ ___
or
year of first test ___ ___ ___ ___
O don't know

8b. What were the reasons for your first colonoscopy? Please tick all that apply.

O to investigate a new problem
O family history of colorectal cancer
O routine/yearly examination or check-up
O follow up of previous problem
O other: _____
Please specify
O don't know

8c. How many times have you had a colonoscopy?

___ number of colonoscopies
O don't know

8d. If you have had a colonoscopy more than once, when did you last have this test?

age when last tested ___ ___
or
year of last test ___ ___ ___ ___
O don't know

O don't know → Please go to # 10

9a. When did your doctor first tell you that you have had polyps?

age when first tested ___ ___
or
year of first test ___ ___ ___ ___
O don't know

9b. Have you been told more than once that you had polyps?

O yes
O no
O don't know

9c. When did you your doctor last tell you that you had polyps?

age at last diagnosis ___ ___
or
year of last diagnosis ___ ___ ___ ___
O don't know

9d. Do you know what kind of polyps they were?

O benign
O adenomatous (pre-cancerous)
O hyperplastic
O other: _____
Please specify
O don't know

9e. Did you have the polyps removed (by a procedure called a polypectomy)? (This can be done during a sigmoidoscopy or colonoscopy.)

O yes
O no → Please go to # 10
O don't know → Please go to # 10

9f. When did you first have polyps removed?

age at first polypectomy ___ ___
or
year of first polypectomy ___ ___ ___ ___
O don't know

11. Has a doctor ever told you that you had Crohn's disease? This is where you have an inflammation that extends into the deeper layers of the intestinal wall. It may also affect other parts of the digestive tract, including the mouth, esophagus, stomach, and small intestine.

O yes
O no → Please go to # 12
O don't know → Please go to # 12

11a. When did your doctor first tell you that you had Crohn's disease?

age when first tested ___ ___

9g. Have you had polyps removed more than once?

O yes
O no
O don't know

9h. If you have had polyps removed more than once, when did you last have polyps removed?

age at first polypectomy ___ ___
or
year of first polypectomy ___ ___ ___ ___
O don't know

10. Has a doctor ever told you that you had familial adenmotaous polyposis, known also as FAP? This is a condition, sometimes occurring in families, in which numerous polyps line the inside of the large bowel or colon.

O yes
O no → Please go to # 11
O don't know → Please go to # 11

10a. When did your doctor first tell you that you had FAP?
age at first diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

or
year of first test ___ ___ ___ ___
O don't know

12. Has a doctor ever told you that you had ulcerative colitis? This is an inflammation and ulceration of the lining of the bowel (colon) & rectum. It is not a stomach ulcer.

O yes
O no → Please go to # 13
O don't know → Please go to # 13

12a. When did your doctor first tell you that you had ulcerative colitis?

age at first diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

13. Has a doctor ever told you that you had irritable bowel syndrome? This is a disorder of the bowels leading to cramping, gassiness, bloating and alternating diarrhea and constipation. It is sometimes called IBS, or spastic colon.

O yes
O no → Please go to # 14
O don't know → Please go to # 14

13a. When did your doctor first tell you that you had irritable bowel syndrome?

age at first diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

14. Has a doctor ever told you that you had diverticular disease? This may also be called diverticulosis or diverticulitis. It's a condition in which the bowel may become infected, and can lead to pain and chronic problems with bowel habits. and small intestine.

15b. Have you had more than one surgery to remove your bowel or colon?

O yes
O no → Please go to # 16
O don't know → Please go to # 16

15c. When did you last have any of your bowel or colon removed?

age at last operation ___ ___
or
year of last operation ___ ___ ___ ___
O don't know

16. Have you had your gallbladder removed?

O yes
O no → Please go to # 15
O don't know → Please go to # 15

14a. When did your doctor first tell you that you had diverticular disease?

age at first diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

15. Have you ever had any of your large bowel or colon removed?

O yes
O no → Please go to # 16
O don't know → Please go to # 16

Was it completed removed, or was only part of it removed?
O completed removed
O partly removed
O don't know

15a. When did you first have any of your bowel or colon removed?

age at first operation ___ ___
Or
year of first operation ___ ___ ___ ___
O don't know

O yes
O no → Please go to # 17
O don't know → Please go to # 17

16a. When did you have your gallbladder removed?

age at operation ___ ___
or
year of operation ___ ___ ___ ___
O don't know

17. Has a doctor ever told you that you had diabetes, also known as diabetes mellitus? Please do not include diabetes which you had only during pregnancy.

O yes
O no → Please go to # 14
O don't know → Please go to # 14

17a. When did your doctor first tell you that you had diabetes?

age at first diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

17b. Did you ever take medication to control your diabetes?

O yes
O no → Please go to # 18
O don't know → Please go to # 18

17c. What type of medication did you use, pill or insulin injections?

O pills
O insulin injections
O both
O don't know → Please go to # 18

17d. How often did you usually take it? Please choose the most appropriate

18. Has a doctor ever told you that you had high cholesterol? If your doctor told you it borderline, please tick no.

O yes
O no → Please go to # 19
O don't know → Please go to # 19

18a. When did your doctor tell you that you had high cholesterol?

age at diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

18b. How you ever take medication to control

category.

	Pills	Insulin
times per day or	___ ___	___ ___
times per week or	___ ___	___ ___
times per month or	___ ___	___ ___
times per year	___ ___	___ ___
don't know	O	O

17e. About one year before your recent cancer diagnosis, were you taking it?

	Pills	Insulin
O yes	O	O
O no	O	O
O don't know	O	O

17f. How long, in total, have you taken this medication?

	Pills	Insulin
number of moths or	___ ___	___ ___
number of years	___ ___	___ ___
don't know	O	O

your high cholesterol?

O yes
O no → Please go to # 19
O don't know → Please go to # 19

18c. How often did you usually take it? Please choose the most appropriate category.

___ ___ times per day or
___ ___ times per week or
___ ___ times per month or
___ ___ times per year or
O don't know

18d. About one year before your recent cancer diagnosis, were you taking it?

O yes
O no
O don't know

18e. How long, in total, have you taken this medication?

___ ___ number of months or
___ ___ number of years
O don't know

19. Has a doctor ever told you that you had high levels of fat (other than cholesterol) in your blood, also called high triglycerides? If your doctor told you it was borderline, Please tick no.

O yes
O no → Please go to # 20
O don't know → Please go to # 20

19a. What did your doctor first tell you that you had high triglycerides?

age at diagnosis
or
year of diagnosis
don't know

19b. Did you ever take medication to control the high levels of fat in your blood?

20. Has a doctor ever told you that you had any type of cancer?

O yes
O no → Please go to # 24
O don't know → Please go to # 24

20a. What type of cancer was it?
_____ cancer

20b. When did your doctor tell you that you had this type of cancer?

age at diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

20c. Were you treated with radiation therapy (radiotherapy) for this cancer?

O yes
O no → Please go to # 20
O don't know → Please go to # 20

19c. How often did you usually take it? Please choose the most appropriate category.

___ ___ times per day or
___ ___ times per week or
___ ___ times per month or
___ ___ times per year or
O don't know

19d. About one year before your recent cancer diagnosis, were you taking it?

O yes
O no
O don't know

19e. How long, in total, have you taken this medication?

___ ___ number of months or
___ ___ number of years
O don't know

O yes
O no
O don't know

21. Has a doctor ever told you that you had any other cancer?

O yes
O no → Please go to # 24
O don't know → Please go to # 24

21a. What type of cancer was it?
_____ cancer

21b. When did your doctor tell you that you had this type of cancer?

age at diagnosis ___ ___
or
year of diagnosis ___ ___ ___ ___
O don't know

21c. Were you treated with radiation therapy (radiotherapy) for this cancer?

O yes
O no
O don't know

19. Has a doctor ever told you that you had any cancer?

O yes
O no → Please go to # 24
O don't know → Please go to # 24

22a. What type of cancer was it?

_____cancer

22b. When did your doctor first tell you that you had this type of cancer?

age at diagnosis
or
year of diagnosis
don't know

22c. Were you treated with radiation therapy (radiotherapy) for this cancer?

Medications

Have you ever taken any of the following medications regular (at least twice a week for more than a month)?

24. Aspirin (such as Anacin, Bufferin, Bayer, Excedrin, Ecotrin)

O yes
O no → Please go to # 25
O don't know → Please go to # 25

O yes
O no
O don't know

23. Has a doctor ever told you that you had any other cancer?

O yes
O no → Please go to # 24
O don't know → Please go to # 24

22a. What type of cancer was it?

_____cancer

23b. When did your doctor first tell you that you had this type of cancer?

age at diagnosis
or
year of diagnosis
don't know

23c. Were you treated with radiation therapy (radiotherapy) for this cancer?

O yes
O no
O don't know

24a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month)? __ Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

24b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

24c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

Have you ever taken any of the following medications regularly (at least twice a week for more than a month)? (continued)

25. Acetaminophen (such as Tylenod, Anacin-3, Panadol)

O yes
O no → Please go to # 26
O don't know → Please go to # 26

25a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month?

26. Ibuprofen medications (such as Advil, Motrin, Medipren, Indocid, Naprosyn, NSAIDS (NSAIDS are non-steroidal anti-inflammatory drugs)

O yes
O no → Please go to # 27
O don't know → Please go to # 27

26a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month?

Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

25b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

25c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

26b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

26c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

Have you ever taken any of the following medications regularly (at least twice a week for more than a month)? (continued)

27. Bulk-forming laxatives (such as Metamucil, Citrucel, FiberCon. Serutan, psyllium)

O yes
O no → Please go to # 28
O don't know → Please go to # 28

27a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month? Please choose one of the following.

___ ___ times per day or

28. Other laxatives (such as Ex-Lax, Correctol, Dulcolax, Senokot, Colace, castor, cod liver oil, mineral oil, milk of magnesia, lactulose, Epsom salts)

O yes
O no → Please go to # 29
O don't know → Please go to # 29

28a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month? Please choose one of the following.

___ ___ times per day or

___ ___ times per week
O don't know

27b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

27c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

___ ___ times per week
O don't know

28b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

28c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

Have you ever taken any of the following medications regularly (at least twice a week for more than a month)? (continued)

29. Multivitamin supplements (such as One-A-Day, Theragram, Centrum, Unicap) (not individual vitamins)

O yes
O no → Please go to # 28
O don't know → Please go to # 28

29a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month? Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

30. Folic acid or folate pills or tablets

O yes
O no → Please go to # 31
O don't know → Please go to # 31

30a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month? Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

29b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

29c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

30b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes
O no
O don't know

30c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

Have you ever taken any of the following medications regularly (at least twice a week for more than a month)? (continued)

31. Calcium pills or tablets

O yes
O no → Please go to # 32
O don't know → Please go to # 32

29a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month? Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

29b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes

32. Calcium-based antacids (such as Tums, Rolaids, Extra-strength Rolaids, Alka-Mints, Chooz Antacid gum)

O yes
O no → If female, Please go to # 33 If male. Please go to # 44
O don't know → If female, Please go to # 33 If male. Please go to # 44

32a. How often did you usually take it when you were taking it regularly (that is, at least twice a week for more than a month? Please choose one of the following.

___ ___ times per day or
___ ___ times per week
O don't know

32b. About one year before your recent cancer diagnosis, were you taking it regularly?

O yes

O no
O don't know

29c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

O no
O don't know

32c. How long, in total, have you taken this medication regularly? If you started and stopped and then started again, please _ count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

Men: please go to #44 on page 17
Women: please continue with #33 on page 13

Menstruation, Pregnancy, and Menopause

33. How old were you when you had your first menstrual period?

___ ___ years of age
O don't know
O never had a menstrual period

34. Have you ever been pregnant?

O yes
O no → Please go to # 35
O don't know → Please go to # 35
>How many times have you been pregnant? Please include miscarriages, stillbirths, tubal pregnancies and abortions.

___ ___ number of pregnancies
O don't know

34a. How many times were you pregnant with more than one baby (twins, triplets or ___ more)? If you are pregnant now, please do not include your current pregnancy. _

O never
___ ___ number of pregnancies with more than one baby
O don't know

34c. How many of your pregnancies resulted in live births?

O never
___ ___ number of pregnancies with live-born children
O don't know

34d. How old were you at the first live birth?

age at first birth ___ ___ or
year of first birth ___ ___ ___ ___
O don't know

34e. How old were you at the last live birth?

age at last birth ___ ___ or
year of last birth ___ ___ ___ ___
O don't know

35. Have you ever used birth control pills or other hormonal contraceptives (implants or injections) for at least one year?

O yes
O no → Please go to # 36
O don't know → Please go to # 36
>How old were you when you first used Any of these hormonal contraceptives?

age at first use ___ ___ or

year of first use ___ ___ ___ ___
O don't know

34b. How many of your pregnancies lasted 6 months or longer? (Pregnancy usually lasts 9 months. Six months is about the earliest a baby could survive.) If you are pregnant now, please do not include your current _ pregnancy.

O never
___ ___ number of pregnancies lasting 6 months or longer
O don't know

35a. Were you still using hormonal contraceptives about one year before your recent cancer diagnosis?

O yes
O no
O don't know

35b. In total, how long did you take these hormonal contraceptives? If you started and stopped and then started again, please count only the time you were taking these contraceptives.

___ ___ number of years
O don't know

36. Have you had a menstrual period in the last 12 months? Please include only menstrual bleeding, not bleeding that results from hormonal replacement therapy (HRT) or progesterones, progesttins or withdrawal bleeding.

O yes → Please go to #42
O no
O don't know → Please go to #42

Have your periods stopped permanently or only temporarily due to pregnancy, breast-feeding, or other conditions?

O permanently
O temporarily → Please go to #42

37. How old were you when your periods stopped permanently?

age they stopped ___ ___ or
year they stopped ___ ___ ___ ___
O don't know

Please complete the next few questions which ask about surgeries you may have had.

39. Hysterectomy (only the uterus or womb Removed)

O yes
O no
O don't know
>age when removed ___ ___ or
years when removed ___ ___ ___ ___
O don't know

39a. Hysterectomy with one ovary or part of an Ovary removed)

O yes
O no
O don't know
>age when removed ___ ___ or
years when removed ___ ___ ___ ___
O don't know

39b. Hysterectomy with both ovaries removed

O yes
O no
O don't know
>age when removed ___ ___ or
years when removed ___ ___ ___ ___
O don't know

38. Why did your menstrual periods stop permanently? Please tick all that apply.

O natural menopause
O surgery
O radiation or chemotherapy
O other reason
Please specify: _____
O Don't know

39c. One ovary removed, completely or partly, without hysterectomy

O yes
O no
O don't know
>age when removed ___ ___ or
years when removed ___ ___ ___ ___
O don't know

39d. Both ovaries removed without hysterectomy

O yes
O no
O don't know
>age when removed ___ ___ or
years when removed ___ ___ ___ ___
O don't know

40. If you had radiation or chemotherapy, when did you first have it?

O had radiation or chemotherapy
>age when this was given ___ ___ or
year when this was given ___ ___ ___ _
O don't know
O never had radiation or chemotherapy

41. if your periods stopped permanently for any reason other than surgery, radiation or chemotherapy, when did you this occur?

O other reason
Please specify: _____
>age when occurred ___ ___ or
year when occurred ___ ___ ___ ___
O don't know
O not applicable

42. Doctors prescribe hormonal replacement therapy for many reasons, including menopausal symptoms, surgical removal of the ovaries, osteoporosis, and heart disease prevention. (Menopausal symptoms include hot flashes, sweating, and depression.)

Have you ever taken hormonal replacement therapy prescribed by a doctor and in the form of a pill or a patch?

Please do not include hormonal therapy that

42a. Were you still having menstrual periods when you first took these hormones?

O yes
O no
O don't know

42b. Were you prescribed either an estrogen-only pill or patch (such as Premarin) for hormone replacement therapy?

O yes
O no
O don't know
>How old were you when you first took estrogen-only medication?

age when first taken ___ ___ or
years when first taken _____ ___ _
O don't know

42c. Were you still using estrogen-only medication for hormone replacement therapy about one year before your recent cancer diagnosis?

O yes
O no
O don't know

42d. In total, how long did you take estrogen-

was prescribed for birth control, infertility, hormone therapy delivered by injections, vagina creams or vaginal suppositories, or herbal or soy products.

O yes
O no → Please go to #43
O don't know → Please go to #43

42e. Progesterone or progestin is frequently prescribed by doctors together with estrogen for hormone replacement therapy. One common brand name is Provera. Another one is Prometrium. Have you ever taken progesterone or progestin together with estrogens for hormone replacement therapy?

O yes
O no → Please go to #43
O don't know → Please go to #43

>How old were you when you first took progesterone or progestin together with estrogens?

age when first taken ___ ___ or
year when first taken ___ ___ ___ ___
O don't know

42f. Were you still using progesterone or progestin medication about one year before your recent cancer diagnosis?

O yes
O no
O don't know

42g. In total, how long did you take progesterone or progestin together with estrogens? If you started and stopped and then started again, please count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

43. Have you ever taken tamoxifen, raloxifene, or other anti-estrogen medication (such as Lupron or Depo-Provera)?

O yes
O no → Please go to #44
O possibly – I have participated in a clinical trial for tamoxifen or other anti-estrogen medication

O don't know

>What anti-estrogen medication did you take? Please tick all that apply.

O tamoxifen
O raloxifene
O other: _____
Please specify

43a. How old were you when you first took tamoxifen, raloxifene or other anti-estrogen medication?

age when first taken ___ ___ or
year when first taken ___ ___ ___ ___
O don't know

43b. Were you still using tamoxifen, raloxifene or other anti- estrogen medication about one year before your recent cancer diagnosis?

O yes
O no
O don't know

43c. In total, how long did you take tamoxifen, raloxifene or other anti-estrogen medication? If you started and stopped and then started again, please count only the time you were taking this medication.

___ ___ number of months or
___ ___ number of years
O don't know

___ ___ number of months or
___ ___ number of years
O don't know

Diet

44. About one year before your recent cancer diagnosis, on average, how often did you eat a piece serving of fruit?
(A serving of fruit is: 1 medium-sized fresh fruit; ½ cup of chopped, cooked or canned fruit; ¼ cup of dried fruit; 6 ounces of fruit juice (50%-100% pure juice).) Please choose one of the following.

___ ___ servings per day or
___ ___ servings per week or
___ ___ servings per month
O don't know

45. About one year before your recent cancer diagnosis, on average, how often did you eat a piece serving of vegetables?
(A serving of vegetables is: 1 medium-sized fresh vegetables; ½ cup of chopped, cooked or chopped vegetables; 6 ounces of vegetable juice (50%-100% pure juice).) Please choose one of the following.

___ ___ servings per day or
___ ___ servings per week or
___ ___ servings per month
O don't know

46. About one year before your recent cancer diagnosis, on average, how often did you eat a serving of red meat (not chicken or fish)?

(A serving of red meat is: 2-3 ounces of red meat (a piece of meat about the size of a deck of cards). Red meats include: beef, steak, hamburger, prime rib, ribs, beef hot dogs, beef-based processed meat, veal, pork, bacon, pork sausage, ham, lamb, venison.)

___ ___ servings per day or
___ ___ servings per week or
___ ___ servings per month
O don't eat red meat → Please go to #47
O don't know

46a. About one year before your recent cancer diagnosis, on average, how often did you eat a serving of red meat that was cooked by broiling, grilling, barbecueing or pan-frying (not stir-fried or deep-fried)? Please choose one of the following.

___ ___ servings per day or
___ ___ servings per week or
___ ___ servings per month
O don't eat red meat that was cooked by these methods → Please go to #47

O don’t know

46b. On average, when you ate red meat cooked by these methods, which of the following best describes its appearance?

What was its outside appearance?	What was its inside appearance? (how well done it was)?
O lightly browned	O red (rare)
O medium browned	O pink (medium)
O heavily browned or blackened	O brown (well-done)
O don’t know	O don’t know

47. About one year before your recent cancer diagnosis, on average, how often did you eat a serving of chicken? Please do not include turkey or any other bird.
(A serving of chicken is: 2-3 ounces of chicken meat; 1 drumstick; 1 thigh; half a breast; 2 wings; 3 nuggets.) Please choose one of the following.

___ ___ servings per day or
___ ___ servings per week or
___ ___ servings per month
O don’t eat red meat that was cooked by these methods → Please go to #48
O don’t know

47a. About one year before your recent cancer diagnosis, on average, how often did you eat a serving of chicken that was cooked by broiling, grilling, barbecueing or pan-frying (not stir-fried or deep-fried)? Please choose one of the following.

___ ___ servings per day or
___ ___ servings per week or
___ ___ servings per month
O don’t eat chicken that was cooked by these methods → Please go to #48
O don’t know

47b. On average, when you ate chicken cooked by these methods, which of the following best describes its appearance?

What was its outside appearance?

O lightly browned
O medium browned
O heavily browned or blackened
O don’t know

We would like you to think back to when you were in your 20s and remember the physical activities you participated in then.

48. In your 20s, did you participate regularly in physical activity for a total of at least 30 minutes a week? Please describe your activities below.

		For how many years?	During those years, for many months per year?	During those months, on average, for how many minutes or hours per week?
Walking	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Jogging (running slower than a mile in 10 minutes)	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Running (running faster than a mile in 10 minutes)	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Bicycling (including using an exercise bicycle	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Swimming laps	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Tennis, squash racquetball	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Calisthenics, aerobics, vigorous dance (including ballet), using a rowing machine, lifting weights	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Football, soccer rugby, basketball	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Heavy household work (examples: using a non-power mower, shoveling, moving heavy loads, scrubbing floors)	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week

In your 20s, did you do any other strenuous activities? Strenuous activity means something that really increased your heart rate, make you hot, and caused you to sweat. Some examples are: skiing, skating, hockey, hunting, shedding or tobogganing, water-skiing.

Activity Please specify		For how many years?	During those years, for many months per year?	During those months, on average, for how many minutes or hours per week?
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
		___ ___ years	___ ___ months	__ minutes per week / __hours per week

49. When you were in your 20s, what was your usual occupation? (When mean what you did for the longest time, including any paid or unpaid employment, such as being a student or housewife of being unemployed.)

_____ occupation

O don't know

If you are younger than 31, please go to the next section (Alcohol Consumption) on page 25. Otherwise, please continue with #50.

Now, please think back to your 30s and 40s.

50. In your 30 and 40s, did you participate regularly in physical activity for a total of at least 30 minutes a week? Please describe your activities below.

		For how many years?	During those years, for many months per year?	During those months, on average, for how many minutes or hours per week?
Walking	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Jogging (running slower than a mile in 10 minutes)	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Running (running faster than a mile in 10 minutes)	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Bicycling (including using an exercise bicycle	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Swimming laps	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Tennis, squash racquetball	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Calisthenics, aerobics, vigorous dance (including ballet), using a rowing machine, lifting weights	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Football, soccer rugby, basketball	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Heavy household work (examples: using a non-power mower, shoveling, moving heavy loads, scrubbing	O yes → O no	___ ___ years	___ ___ months	__ minutes per week / __hours per week

floors)

In your 30s and 40s, did you do any other strenuous activities? Strenuous activity means something that really increased your heart rate, make you hot, and caused you to sweat. Some examples are: skiing, skating, hockey, hunting, shedding or tobogganing, water-skiing.

Activity Please specify		For how many years?	During those years, for many months per year?	During those months, on average, for how many minutes or hours per week?
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
		___ ___ years	___ ___ months	__ minutes per week / __hours per week

51. When you were in your 30s and 40s, what was your usual occupation? (When mean what you did for the longest time, including any paid or unpaid employment, such as being a student or housewife of being unemployed.)

_____ occupation

O don't know

If you are younger than 31, please go to the next section (Alcohol Consumption) on page 25. Otherwise, please continue with #50.

Now, please think back to since you turned 50s.

52. In your 50s, did you participate regularly in physical activity for a total of at least 30 minutes a week? Please describe your activities below.

		For how many years?	During those years, for many months per year?	During those months, on average, for how many minutes or hours per week?
Walking	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Jogging (running slower than a mile in 10 minutes)	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Running (running faster than a mile in 10 minutes)	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Bicycling (including using an exercise bicycle	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Swimming laps	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Tennis, squash racquetball	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Calisthenics, aerobics, vigorous dance (including ballet), using a rowing machine, lifting weights	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Football, soccer rugby, basketball	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week
Heavy household work (examples: using a non-power mower, shoveling, moving heavy loads, scrubbing floors)	O yes → O no →	___ ___ years	___ ___ months	__ minutes per week / __hours per week

In your 50s, did you do any other strenuous activities? Strenuous activity means something that really increased your heart rate, make you hot, and caused you to sweat. Some examples are: skiing, skating, hockey, hunting, shedding or tobogganing, water-skiing.

Activity Please specify		For how many years?	During those years, for many months per year?	During those months, on average, for how many minutes or hours per week?
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
_____	→	___ ___ years	___ ___ months	__ minutes per week / __hours per week
		___ ___ years	___ ___ months	__ minutes per week / __hours per week

53. When you were in your 50s, what was your usual occupation? (When mean what you did for the longest time, including any paid or unpaid employment, such as being a student or housewife of being unemployed.)

_____ occupation

O don't know

We would like you to think back to when you were in your 20s.

54. In your 20s, did you ever consume any alcoholic beverages at least once a week for 6 months or longer? Please describe your consumption below.

		For how many years?	During those years, how much did you typically consume?
Beer, hard cider (at least 3% alcohol)	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 12 ounce cans or bottles O per day O per week O don't know
Wine	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 4 ounce glasses of wine O per day O per week O don't know
Sake, sherry, port	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 1 ounce servings O per day O per week O don't know
Spirits, liquor mixed drinks, brandy, liqueurs	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 1 ounce shots liquor or spirits O per day O per week O don't know

55. When you were in your 20s, how many years in total did you consume at least one alcoholic beverage (of any type) a week?

___ ___ years consumed
O never consumed alcohol

56. On average, how many alcoholic beverages a week did you consume during those years? That is, how many 4 ounce glasses of wine or 12 ounce cans or bottles of beer or hard cider, or 1 ounce servings of sake, sherry, port, or spirits, mixed drinks and cocktails.

___ ___ years consumed
O never consumed alcohol

If you are younger than age 31, please go to the next section (Smoking) on page 28.
Otherwise, please continue with #57.

Now, please think back to your 30s and 40s.

57. In your 30s and 40s, did you ever consume any alcoholic beverages at least once a week for 6 months or longer? Please describe your consumption below.

		For how many years?	During those years, how much did you typically consume?
Beer, hard cider (at least 3% alcohol)	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 12 ounce cans or bottles O per day O per week O don't know
Wine	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 4 ounce glasses of wine O per day O per week O don't know
Sake, sherry, port	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 1 ounce servings O per day O per week O don't know
Spirits, liquor mixed drinks, brandy, liqueurs	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 1 ounce shots liquor or spirits O per day O per week O don't know

58. When you were in your 30s and 40s, how many years in total did you consume at least one alcoholic beverage (of any type) a week?

___ ___ years consumed
O never consumed alcohol

56. On average, how many alcoholic beverages a week did you consume during those years? That is, how many 4 ounce glasses of wine or 12 ounce cans or bottles of beer or hard cider, or 1 ounce servings of sake, sherry, port, or spirits, mixed drinks and cocktails.

___ ___ years consumed
O never consumed alcohol

If you are younger than age 51, please go to the next section (Smoking) on page 28.
Otherwise, please continue with #60.

Now, please think back to since you turned 50s.

60. In your 50s, did you ever consume any alcoholic beverages at least once a week for 6 months or longer? Please describe your consumption below.

		For how many years?	During those years, how much did you typically consume?
Beer, hard cider (at least 3% alcohol)	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 12 ounce cans or bottles O per day O per week O don't know
Wine	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 4 ounce glasses of wine O per day O per week O don't know
Sake, sherry, port	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 1 ounce servings O per day O per week O don't know
Spirits, liquor mixed drinks, brandy, liqueurs	O yes → O no O don't know	___ ___ years consumed	___ ___ number of 1 ounce shots liquor or spirits O per day O per week O don't know

61. When you were in your 30s and 40s, how many years in total did you consume at least one alcoholic beverage (of any type) a week?

___ ___ years consumed
O never consumed alcohol

62. On average, how many alcoholic beverages a week did you consume during those years? That is, how many 4 ounce glasses of wine or 12 ounce cans or bottles of beer or hard cider, or 1 ounce servings of sake, sherry, port, or spirits, mixed drinks and cocktails.

___ ___ years consumed
O never consumed alcohol

Smoking

64. Have you ever smoked at least one

63. Have you ever smoked at least one cigarette a day for 3 months or longer?

O yes
O no → Please go to #64
O don't know → Please go to #64

63a. When did you first start smoking at least one cigarette a day?

age at first use ___ ___ or
year of first use ___ ___ ___ ___
O don't know

63b. During periods when you smoked regularly, how many cigarettes did you typically smoke in a day?

___ ___ ___ ___ cigarettes per day
O don't know

63c. About one year before your recent cancer diagnosis, were you still smoking at least one cigarette a day?

O yes
O no
O don't know

63d. Do you still smoke at least one cigarette a day?

O yes
O no → Please go to #63f
O don't know → Please go to #63f

63e. When did you stop smoking at least one cigarette a day (we mean stop smoking permanently)?

age at first use ___ ___ or
year of first use ___ ___ ___ ___
O don't know

63f. How many years, in total, did you smoke at least one cigarette a day for 3 months or longer? (If you have stopped and restarted at least once, count only the time when you were smoking.)

___ ___ ___ ___ total number of years
O don't know

cigar a month for at least 3 months?

O yes
O no → Please go to #65
O don't know → Please go to #65

64a. When did you first start smoking at least one cigar a month?

age at first use ___ ___ or
year of first use ___ ___ ___ ___
O don't know

64b. During periods when you smoked regularly, how many cigar did you typically smoke in a month?

___ ___ ___ ___ cigarettes per month
O don't know

64c. About one year before your recent cancer diagnosis, were you still smoking at least one cigar a month?

O yes
O no
O don't know

64d. Do you still smoke at least one cigar a month?

O yes
O no → Please go to #64f
O don't know → Please go to #64f

64e. When did you stop smoking at least one cigar a month (we mean stop smoking permanently)?

age at first use ___ ___ or
year of first use ___ ___ ___ ___
O don't know

64f. How many years, in total, did you smoke at least one cigar a month for 3 months or longer? (If you have stopped and restarted at least once, count only the time when you were smoking.)

___ ___ ___ ___ total number of years
O don't know

65. Have you ever smoked at least one pipe a month for at least 3 months?

O yes
O no → Please go to #66
O don't know → Please go to #66

65a. When did you first start smoking at least one pipe a month?

age at first use ___ ___ or
year of first use ___ ___ ___ ___
O don't know

65b. During periods when you smoked regularly, how many pipe did you typically smoke in a month?

___ ___ ___ ___ pipe per month
O don't know

65c. About one year before your recent cancer diagnosis, were you still smoking at least one pipe a month?

O yes
O no
O don't know

65d. Do you still smoke at least one pipe a month?

O yes
O no → Please go to #65f
O don't know → Please go to #65f

65e. When did you stop smoking at least one pipe a month (we mean stop smoking smoking permanently)?

age at first use ___ ___ or
year of first use ___ ___ ___ ___
O don't know

65f. How many years, in total, did you smoke at least one pipe a month for 3 months or longer? (If you have stopped and restarted at least once, count only the time when you were smoking.)

___ ___ ___ ___ total number of years
O don't know

Height and Weight

66. About how tall are you, without your shoes on?

___ feet ___ ___ inches
or
___ ___ ___ centimeters
O don't know

67. How much did you weigh about one year before your recent cancer diagnosis?

___ pounds
Or
___ ___ ___ kilograms
O don't know

Additional Information

69. Previous to this study, have you and your relatives ever taken part in any family health studies?

O yes
O no
O don't know

Background Information

70. What is the highest level of education that you completed?

O less than 8 years
O 8 to 11 years
O high school graduate
O vocational or technical school
O some college or university
O bachelor's degree
O graduate degree
O don't know

71. Country of birth sometimes affects disease risk. Please fill in country of birth for yourself, you parents and your grandparents.

In addition, scientists have found that some genetic traits are more common or less common among Jewish people of different ethnic backgrounds. Please answer the questions about Jewish descent for each person.

	Country of birth	Is this person of Jewish descent?	Ashkenazi (East European)	Sephardic	Other	Don't know
You	_____	O yes O no O don't know	O	O	O	O
Your mother	_____	O yes O no O don't know	O	O	O	O
Your father	_____	O yes O no O don't know	O	O	O	O
Your mother's mother	_____	O yes O no O don't know	O	O	O	O
Your mother's father	_____	O yes O no O don't know	O	O	O	O
Your father's mother	_____	O yes O no O don't know	O	O	O	O
Your father's	_____	O yes O no	O	O	O	O

father O don’t know

72. How many years have you lived in Canada?

O all my life
___ ___ number of years
O don’t know

73. Ethnicity and race sometimes affect disease risk. Scientists have found that some genetic traits are more common or less common among people of different backgrounds. We would like to know if this is true for genes associated with colorectal cancer.

Please fill in the background for yourself, your parents and your grandparents.
Please tick all that apply.

	You	Your mother	Your father	Your Mother’s mother	Your Mother’s father	Your Father’s mother	Your Father’s Father
Black, From Africa	O	O	O	O	O	O	O
Black, from Caribbean (Trinidad, Jamaica, Haiti)	O	O	O	O	O	O	O
Black from North America	O	O	O	O	O	O	O
Black, other	O	O	O	O	O	O	O
White	O	O	O	O	O	O	O
First Nations (Indian, Inuit)	O	O	O	O	O	O	O
North African (Egyptian)	O	O	O	O	O	O	O
Middle East (Iranian)	O	O	O	O	O	O	O
Filipino	O	O	O	O	O	O	O
Japanese	O	O	O	O	O	O	O
Korean	O	O	O	O	O	O	O
Chinese	O	O	O	O	O	O	O
Other South East Asian (Vietnamese)	O	O	O	O	O	O	O
South Asian (East Indian, Pakistani)	O	O	O	O	O	O	O
Other:							

Please specify	_____	_____	_____	_____	_____	_____	_____
Don't know	O	O	O	O	O	O	O

74. Which of the following categories best describes your total annual household income about one year before your recent diagnosis?

O no income
O less than $6,000
O $6,000 - $11,999
O $12,000 - $19,999
O $20,000 - $29,999
O $30,000 - $39,999
O $40,000 - $49,999
O $50,000 - $59,999
O $60,000 - $69,999
O $70,000 - $79,999
O $80,000 +
O don't know

75. In case we need to contact you in the future and you have moved, could we have the name of someone who is not living with you to whom we might write or call for your new address?

Name of relative or friend: _____
His or her address: _____
_____
His or her telephone number: (___ ___ ___) ___ ___ ___ - ___ ___ ___ ___

Thank you very much for taking the time to fill out this questionnaire.
We appreciate your participation.

Please mail this completed questionnaire in the return envelope provided.

Appendix B. Food Frequency Questionnaire

Canadian Study of Diet and Health

Memorial University of Newfoundland

SAMUEL LUNENFELD RESEARCH INSTITUTE
MOUNT SINAI HOSPITAL
Today's science. Tomorrow's medicine

Who this questionnaire is for and what it asks about:

This questionnaire is to be completed by the person taking part in this study:

Part I asks about the foods you ate about **one year before your diagnosis**.

Part II asks about vitamins and other dietary supplements that you may have used.

If possible, please return this questionnaire within two weeks.

The completed questionnaire should be sealed in the pre-paid envelope and mailed back to:

CRC-IHRT,
Room 1758E, Level 1, Health Science Centre,
300 Prince Phillip Drive,
St. John's, NL, Canada, A1B 9Z9.

If you have any questions about this form or the study, call our toll-free number, **1-888-908-4988.**

The information given to us in this questionnaire will be kept confidential.

Thank you for your time and assistance.

1

HOW TO COMPLETE THIS QUESTIONNAIRE

We would like to know how often you ate certain foods **about one year before diagnosis,** and their amounts.

Section A ***(lists foods and portion sizes)***
Amounts are described in various ways, including the number of:

cups, teaspoons (tsp), ounces (oz), inches ("), pieces (e.g., 1 apple)
grams (gm), tablespoons (tbsp), millilitres (ml), centimetres (cm).

We want to know the ***Portion Size*** of your **USUAL SERVING.** We have given an example of an average portion size. If your portion size was different than the average, you can indicate this by putting an **X** or ✓in the circles for ***Smaller*** or ***Larger*** portion sizes. ***Smaller*** than average is about 25% or less than the average portion size, while ***Larger*** than average is about 25% or more than the average size. Leave the circle blank if your typical portion size was average.

Included with this questionnaire is a ***FOOD PHOTOGRAPH PAGE*** that shows small, medium and large portion sizes for vegetables, meat and chicken. Some questions ask you to refer to the photo page to help you choose your usual portion size.

Section B ***(asks about how often you ate certain foods one year before diagnosis)***
For each food item listed, choose **one** column (Per Day, Per Week, Per Month, or Never / Rarely) that best describes ***HOW OFTEN*** you ate or drank that item. For example, if you ate CREAM CHEESE 3 times a month during the year of interest, you would write (3) in the *PER MONTH* column. If you ate SWEET POTATOES only 2 times during the year of interest, you can place a checkmark (✓) in *the NEVER OR RARELY* column.

Section C ***(To be completed only for seasonal foods)***
Some foods (for example fresh fruit and vegetables) are not available throughout the year. **For foods that you do not eat all year round** (i.e. in season only), indicate the number of months of the year that you ate them.

Please complete each question as best you can. We know that it is difficult to recall exactly how often you ate something. If you are not certain, try to give your best estimate.

EXAMPLE

		Section A			Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food in Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
1	CREAM CHEESE	2 tbs/ 30 ml/ 1 oz	O	O			3		
2	CANTELOUPE	1/8 or 1 slice	O	O		1			4
3	SWEET POTATOES	1 medium/ ½ cup	O	O				√	

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
	Dairy Products								
24	EGG (boiled, poached)	1 egg	O	O					
25	EGG (fried, scrambled, omelette)	1 egg	O	O					
26	CREAM CHEESE, Regular fat	2 tbs/ 30 ml/ 1 oz	O	O					
27	CHEESE, Regular fat (such as cheddar, Swiss, processed)	1 slice/ 30 g/ 1oz	O	O					
28	CHEESE, Light (6-15% fat, such as cream cheese, cheddar)	1 slice/ 30 g/ 1oz	O	O					
29	CHEESE, Ultra Light (5% fat or less, such as cheddar)	1 slice/ 30 g/ 1oz	O	O					
30	COTTAGE or RICOTTA CHEESE	125 ml/ ½ cup	O	O					
31	CREAM (coffee, whipping, sour or regular)	1 tbs/ 15 ml	O	O					
32	CREAM (half and half, light sour cream)	1 tbs/ 15 ml	O	O					
33	COFFEE WHITENER (non-dairy)	1 tbs/ 15 ml	O	O					
34	YOGURT, Regular (plain, 2.4% fat or more)	¾ cup/ 175 ml	O	O					
35	YOGURT, Light (plain, less than 2.4% fat)	¾ cup/ 175 ml	O	O					
36	YOGURT, Regular (fruit flavoured or frozen, 2.4% fat or more)	¾ cup/ 175 ml	O	O					
37	YOGURT, Light (fruit flavoured or frozen, less than 2.4% fat)	¾ cup/ 175 ml	O	O					
	Mixed Dishes								
38	SOUPS (creamed)	1 cup/ 250 ml	O	O					
39	SOUPS (non-creamed)	1 cup/ 250 ml	O	O					
40	PEA SOUP	1 cup/ 250 ml	O	O					
41	PASTA with meat sauce (spaghetti, lasagna)	1 cup/ 250 ml	O	O					
42	PASTA with tomato sauce (spaghetti)	1 cup/ 250 ml	O	O					
43	MIXED DISHES with cheese or cheese sauce (macaroni and cheese)	1 cup/ 250 ml	O	O					
44	PIZZA with meat	1 Medium slice	O	O					
45	PIZZA with vegetable only	1 Medium slice	O	O					

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
46	MEAT STEW with carrots, other vegetables	1 cup/ 250 ml/ photo A, medium	O	O					
47	CHILI with meat or Con Carne	1 cup/ 250 ml	O	O					
	Vegetables								
48	POTATOES (mashed, boiled, baked etc)	1 medium/ ½ cup/ 125 ml	O	O					
49	FRENCH FRIES or FRIED POTATOES	1 cup/ 250 ml	O	O					
50	CARROTS (raw or cooked)	1 medium/ ½ cup /125 ml	O	O					
51	BROCCOLI	1 cup/ 250 ml	O	O					
52	CABBAGE, COLESLAW	½ cup/ 125 ml	O	O					
53	CAULIFLOWER	½ cup/125 ml	O	O					
54	CORN	1 ear / ½ cup	O	O					
55	PEAS or LIMA BEANS	½ cup/125 ml	O	O					
56	GREEN or YELLOW BEANS	½ cup/125 ml	O	O					
57	BEANS or LENTILS (baked or boiled beans, kidney beans, chickpeas)	½ cup/125 ml cooked	O	O					
58	SPINACH and other green leafy vegetables (greens, collards, kale, mustard greens etc)	½ cup/125 ml cooked or 1 cup raw	O	O					
59	GREEN SALAD (with lettuce)	1 cup/ 250 ml	O	O					
60	CUCUMBER	½ cup/ 125 ml sliced	O	O					
61	TOMATOES (fresh)	1 medium/ ½ cup/ 125 ml	O	O					
62	TOMATOES (canned, pureed or sauce)	½ cup/125 ml	O	O					
63	ONIONS (raw or cooked)	½ cup/125 ml	O	O					
64	BEETS (boiled or pickled)	½ cup/125 ml	O	O					
65	TURNIPS or RUTABAGAS	1 medium/ ½ cup/125 ml	O	O					
66	OTHER ROOT VEGETABLES (sweet potatoes, yams, radish, etc)	½ cup/125 ml	O	O					
67	YELLOW SQUASH (winter type)	½ cup/125 ml	O	O					

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
90	LIVER	85 g/ 3 oz	O	O					
91	FRIED CHICKEN	photo C, medium	O	O					
92	CHICKEN / TURKEY (roasted or stewed)	photo C, medium	O	O					
93	CHICKEN / TURKEY, SKIN REMOVED	photo C, medium	O	O					
94	SALTED/ DRIED MEAT	photo C, small	O	O					
95	PICKLED MEAT (brined)	photo C, small	O	O					
96	SHELLFISH (shrimp, lobster, crab)	85 g/ 3 oz/ photo C, small	O	O					
97	FRIED FISH	175 g/ 6 oz/ photo B, medium	O	O					
98	FISH (baked or broiled)	175 g/ 6 oz/ photo B, medium	O	O					
99	CANNED FISH (tuna, salmon)	½ can/ 48 ml/ 1.7 oz	O	O					
100	SMOKED FISH or LOX	85 g/ 3 oz/ photo C, small	O	O					
101	SALTED/ DRIED FISH	85 g/ 3 oz/ photo C, small	O	O					
102	PICKLED FISH	85 g/ 3 oz/ photo C, small	O	O					
103	SEA-BIRDS, SEAL	85 g/ 3 oz/ photo C, small	O	O					
104	CARIBOU, MOOSE	85 g/ 3 oz/ photo C, small	O	O					
105	PARTRIDGE, OTHER WILD BIRDS	85 g/ 3 oz/ photo C, small	O	O					
	Cereals and Grains								
106	BRAN or GRANOLA CEREALS (including All Bran)	½ cup/ 125 ml	O	O					
107	WHOLE WHEAT CEREALS (such as shredded wheat)	½ cup/ 125 ml/ 1 biscuit	O	O					
108	CEREALS, NOT SUGAR COATED (such as Special K)	½ cup/ 125 ml	O	O					
109	HOT CEREALS (for example: oatmeal)	½ cup/ 125 ml	O	O					
110	SUGAR COATED CEREALS	½ cup/ 125 ml	O	O					
111	OTHER BREAKFAST CEREALS	½ cup/ 125 ml	O	O					
112	SUGAR ON CEREAL	1 tsp	O	O					

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
90	LIVER	85 g/ 3 oz	O	O					
91	FRIED CHICKEN	photo C, medium	O	O					
92	CHICKEN / TURKEY (roasted or stewed)	photo C, medium	O	O					
93	CHICKEN / TURKEY, SKIN REMOVED	photo C, medium	O	O					
94	SALTED/ DRIED MEAT	photo C, small	O	O					
95	PICKLED MEAT (brined)	photo C, small	O	O					
96	SHELLFISH (shrimp, lobster, crab)	85 g/ 3 oz/ photo C, small	O	O					
97	FRIED FISH	175 g/ 6 oz/ photo B, medium	O	O					
98	FISH (baked or broiled)	175 g/ 6 oz/ photo B, medium	O	O					
99	CANNED FISH (tuna, salmon)	½ can/ 48 ml/ 1.7 oz	O	O					
100	SMOKED FISH or LOX	85 g/ 3 oz/ photo C, small	O	O					
101	SALTED/ DRIED FISH	85 g/ 3 oz/ photo C, small	O	O					
102	PICKLED FISH	85 g/ 3 oz/ photo C, small	O	O					
103	SEA-BIRDS, SEAL	85 g/ 3 oz/ photo C, small	O	O					
104	CARIBOU, MOOSE	85 g/ 3 oz/ photo C, small	O	O					
105	PARTRIDGE, OTHER WILD BIRDS	85 g/ 3 oz/ photo C, small	O	O					
	Cereals and Grains								
106	BRAN or GRANOLA CEREALS (including All Bran)	½ cup/ 125 ml	O	O					
107	WHOLE WHEAT CEREALS (such as shredded wheat)	½ cup/ 125 ml/ 1 biscuit	O	O					
108	CEREALS, NOT SUGAR COATED (such as Special K)	½ cup/ 125 ml	O	O					
109	HOT CEREALS (for example: oatmeal)	½ cup/ 125 ml	O	O					
110	SUGAR COATED CEREALS	½ cup/ 125 ml	O	O					
111	OTHER BREAKFAST CEREALS	½ cup/ 125 ml	O	O					
112	SUGAR ON CEREAL	1 tsp	O	O					

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
113	100% WHOLE GRAIN or DARK BREAD	1 slice	O	O					
114	60% WHOLE GRAIN, LIGHT RYE	1 slice	O	O					
115	WHITE BREAD	1 slice	O	O					
116	WHITE BREAD ROLLS (including hot dog buns etc)	1 roll	O	O					
117	WHOLE WHEAT ROLLS	1 roll	O	O					
118	CRACKERS (snack or soda type)	2	O	O					
119	BRAN/OAT MUFFIN	1 medium, ½ extra large	O	O					
120	OTHER MUFFIN (plain cake, with berries)	1 medium, ½ extra large	O	O					
121	PANCAKES, WAFFLES	1	O	O					
122	MACARONI, SPAGHETTI, NOODLES (plain)	1 cup cooked/ 250 ml	O	O					
123	RICE	½ cup cooked/ 125 ml	O	O					
124	CRISP SNACKS (potato chips, popcorn, pretzels etc)	small bag or 1 cup	O	O					
	Fruits								
125	APPLE, PEAR	1	O	O					
126	CITRUS FRUITS (orange, grapefruit)	1 orange, ½ grapefruit	O	O					
127	BERRIES (strawberries, blueberries, bakeapples)	½ cup/ 125 ml	O	O					
128	GRAPES	½ cup/ 125 ml	O	O					
129	BANANA	1	O	O					
130	PEACH, PLUM, NECTARINE, APRICOT	1	O	O					
131	CANTALOUPE	1/8 or 1 slice	O	O					
132	WATERMELON	1 wedge, 3" base	O	O					
133	HONEYDEW MELON	1/8 or 1 slice	O	O					
134	MANGO	1	O	O					
135	PAPAYA	1	O	O					
136	APPLESAUCE	½ cup/ 125 ml	O	O					

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
137	DRIED FRUITS (raisins, dates, prunes)	2 tbsp/ 2 dates	O	O					
138	CANNED FRUIT (all kinds)	½ cup/ 125 ml	O	O					
139	ALL OTHER FRUIT (fresh kiwi, pomegranate, etc.)	1	O	O					
	Desserts and Sweets								
140	CAKES	1 slice, 2" x 4" x 1"	O	O					
141	PIES and TARTS	1 slice	O	O					
142	DONUTS and SWEET ROLLS	1	O	O					
143	COOKIES	1	O	O					
144	ICE CREAM	½ cup/ 125 ml	O	O					
145	LIGHT or DIET ICE CREAM	½ cup/ 125 ml	O	O					
146	PUDDING	½ cup/ 125 ml	O	O					
147	DIET or LIGHT PUDDING	½ cup/ 125 ml	O	O					
148	JELLO	½ cup/ 125 ml	O	O					
149	POPSICLES, FREEZIES	1	O	O					
150	CHOCOLATE BAR and CHOCOLATE CANDY	1 bar / 50g or 5 candy size	O	O					
151	CANDY (without chocolate)	1 caramel	O	O					
	Miscellaneous								
152	TOFU, TEMPEH	½ cup, 2" x 2" x 1" piece	O	O					
153	KETCHUP	1 tbs	O	O					
154	MAYONNAISE/ MIRACLE WHIP, Regular fat (on bread, salad, meat, etc)	1 tbs	O	O					
155	MAYONNAISE/ MIRACLE WHIP, Light (on bread, salad, meat, etc)	1 tbs	O	O					
156	SALAD DRESSING, Regular fat (French, Italian etc)	1 tbs	O	O					
157	OIL (in cooking)	1 tsp	O	O					

Section A					Section B YEAR BEFORE DIAGNOSIS				Section C
	FOOD	Average Portion Size	Your Portion Size, if NOT Average		HOW OFTEN? (Complete one column only)				If Ate Food In Season Only
			Smaller	Larger	per DAY (enter a number)	per WEEK (enter a number)	per MONTH (enter a number)	NEVER or RARELY (check)	enter Months per Year
158	BUTTER (on vegetables or bread; exclude use in baked and mixed dishes)	1 pat/ 1 tsp	O	O					
159	MARGARINE (on vegetables or bread; exclude use in baked or mixed dishes)	1 pat/ 1 tsp	O	O					
160	PEANUT BUTTER	1 tbs	O	O					
161	PEANUTS	30g/ 1 oz	O	O					
162	OTHER NUTS	30g /1 oz	O	O					
163	JAM, JELLY, HONEY, SYRUP	1 tbs	O	O					
164	GRAVY	4 tbs	O	O					
165	CHOCOLATE or STRAWBERRY SYRUP	1 tbs	O	O					
166	CHOCOLATE SPREADS	1 tbs	O	O					
167	SAUCES (white, cream, Mornay)	30 ml/ 1oz/ 2 tbs	O	O					
168	WHEAT BRAN	1 tbs	O	O					
169	WHEAT GERM	1 tbs	O	O					

Continue on next page ⟶

Now we would like to ask you a few questions about how you prepared certain foods ABOUT ONE YEAR BEFORE DIAGNOSIS and whether you followed any special diets. For the following questions, please check the circle or fill in the appropriate answer:

1. About 1 year before diagnosis, how much of the visible fat on your meat did you eat?

- O Most of it.
- O Some of it.
- O As little as possible.
- O Do not eat meat

2. About 1 year before diagnosis, how often did you eat the skin on chicken?

- O Most of it.
- O Some of it.
- O As little as possible.
- O Do not eat chicken

3. About 1 year before diagnosis, what kind of fat did you usually use for stir/pan frying?

- O Vegetable oil
- O Vegetable shortening
- O Lard/ pork fat
- O Butter
- O Margarine
- O Do not add fat or oil
- O Other, please specify _____

4. About 1 year before diagnosis, what kind of fat did you usually use for deep frying?

- O Vegetable oil
- O Vegetable shortening
- O Lard/ pork fat
- O Butter
- O Margarine
- O Do not fry
- O Other, please specify _____

5. About 1 year before diagnosis, what kind of fat did you usually use for baking?

- O Butter
- O Margarine
- O Vegetable Oil
- O Vegetable shortening
- O Lard/ pork fat
- O Do not bake

6. About 1 year before diagnosis, what type of oil did you use in other preparations (for example, in salad dressings)?

_____

7. About 1 year before diagnosis, what type of the following items did you usually use? *Please check one box per line.*

Mayonnaise/Miracle Whip
O regular O light O both O none

Cream cheese
O regular O light O both O none

8. About 1 year before diagnosis, were you a (*please check one box only*):

- O Non-vegetarian (eats all meat, chicken, fowl)
- O Partly non-vegetarian (eats chicken, fish, no meat)
- O Vegan (eats no dairy, no eggs, no meat)
- O Lacto-vegetarian (eats dairy, no eggs, no meat)
- O Lacto-ovo vegetarian (eats dairy & eggs, no meat)

9. About 1 year before diagnosis, were you on a special diet?

O No O Yes

If yes, what type of diet?

- O To lose Weight
- O To lower cholesterol
- O Diabetes
- O Heart disease
- O Hypertension
- O Gastric ulcer
- O Bowel disease
- O Low fat
- O High fibre
- O Other type: _____

If yes, how long were you on the special diet?

_____

PART 2 - USE OF VITAMINS AND DIETARY SUPPLEMENTS

Now we would like to know about your use of vitamins and dietary supplements.
ABOUT ONE YEAR BEFORE DIAGNOSIS, did you take any of the following? If *Yes*, then specify usual brand and amount and how long you took them.

Vitamin and Amount – if used, ⇨	How many pills did you take per week?	How long had you taken them?
Vitamin C EXAMPLE O None O Below 500 Ø 500-1000 O above 1000 mg	0 5 per week	2 4 months
Multivitamins that include minerals ⇨ O No O Yes If yes, usual brand _____	per week	months
Multivitamins, no minerals O No O Yes If yes, usual brand _____	per week	months
B Complex vitamins O No O Yes If yes, usual brand _____	per week	months
In the following items, DO NOT INCLUDE use of the above MULTIVITAMINS		
Vitamin A O None O Below 10000 O 10000-15000 O above 15000 IU	per week	months
Vitamin C O None O Below 500 O 500-1000 O above 1000 mg	per week	months
Vitamin E O None O Below 400 O 400-800 O above 800 IU	per week	months
Beta-carotene O None O Below 10000 O 10000-15000 O above 15000 IU	per week	months
Folic acid O None O Below 1.0 O 1.0 mg O above 1.0 mg*	per week	months
Calcium O None O Below 250 O 250-500 O above 500 mg	per week	months
Iron O None O Below 100 O 100-200 O above 200 mg	per week	months
Other dietary supplements (e.g., yeast, cod liver oil, etc) O No O Yes, specify type: _____ _____	per week per week	months months

* 1 mg = 1000 micrograms

We welcome any other information or comments that you would like to give us:

_____

_____

_____

THANK YOU VERY MUCH for your assistance in this research!

For Office Use Only

Study #: _____

Interviewer: _____

Date completed (D/M/Y): _____

Appendix C. Demographic Survey Questionnaire

Food-frequency questionnaire validation study
Demographic Survey (telephone interview)

1. In what year were you born? 19_ _
2. What is your sex?
    - Female
    - Male
3. What is your highest level of education? Please stop me when I get to the correct level.
    - Some school but high school certificate
    - High school certificate
    - Post-secondary education
4. How many people live in your community?
    - Less than 10,000 people
    - More than 10,000 people
5. What is your marital status?
    - Single
    - Separated/Divorced
    - Married/Living together
    - Widowed
6. Are you currently employed?
    - Yes
        - Part-time
        - Full-time
        - Seasonal
    - No

    6a. Are you retired?
    - Yes
    - No

    What is/was your occupation?_____
7. Do you currently smoke cigarettes daily?
    - Yes
    - No

    7a. Did you ever smoke cigarettes daily?
    - Yes
    - No

This completes our survey. Thank you very much for your time and comments!