PHYSICAL ACTIVITY, THE DIRECT AND INDIRECT EFFECT OF SOCIOECONOMIC STATUS ON RISK FACTORS OF COLORECTAL CANCER IN CANADA

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Physical activity, the direct and indirect effect of socioeconomic status on risk factors of colorectal cancer in Canada

by

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A thesis submitted to the School of Graduate Studies
in partial fulfillment of the requirements for the degree of

Master of Science in Medicine

Division of Community Health and Humanities

Faculty of Medicine

Memorial University of Newfoundland

October 2012

St. John’s

Newfoundland and Labrador
Abstract

The objective of this thesis was to examine the determinants of colorectal cancer (CRC) from two perspectives: 1) the associations between recreational physical activity and the risk of CRC; 2) the direct and indirect effect of socioeconomic status on the risk of CRC.

Higher levels of physical activity have been consistently associated with lower risk of CRC in previous studies. Nevertheless, the specific mode, intensity, frequency, and duration of physical activity required for CRC prevention are not well known and remain controversial. The first objective of this study is to examine the associations of walking, non-walking exercise, and total recreational physical activity on colorectal cancer development. The study used the data collected from the existing population-based case-control study of Ontario (ON) and Newfoundland and Labrador (NL), in which personal history, lifestyle and dietary information were collected using the Personal History Questionnaire (PHQ), Food Frequency Questionnaire (FFQ) and Family History Questionnaire (FHQ). Multivariable logistic regression analysis was used to estimate odds ratios (OR) and 95% confidence interval (95%CI) after adjusting potential confounding covariates. Pooled analysis in both ON and NL was also conducted. Results from this study showed that the highest quintile of walking was associated with increased colorectal cancer risk for both males and females in both provinces (highest VS lowest: ON: OR=1.51, 95%CI=1.07-2.13; NL: OR=2.01, 95%CI=1.25-3.22; pooled analysis: OR=1.70, 95%CI=1.09-2.66). However, this result could be biased because a higher proportion of cases responded to this item than controls. Non-walking exercise was insignificantly associated with a reduced risk of colorectal cancer for both sexes and provinces. These findings suggested that increasing amounts of neither walking nor non-walking exercise was associated with reducing the risk of colorectal cancer. More specified prospective studies on physical activity are needed to evaluate effective frequency, duration and intensity of physical activity in relation to colon and rectal cancer prevention.
Existing epidemiologic studies have not investigated how risk factors work together to increase the incidence of CRC; therefore, the true effect of each factor could be under- or over-estimated. The second component of this thesis was to explore how socio-economic status (SES) directly influences the risk of developing CRC and its mediated effect on CRC risk through diet while adjusting for possible risk factors of alcohol intake, smoking, physical inactivity, and obesity. Using the data from just the NL province, measurement and structural modeling was used to test conceptual models. Exploratory factor analysis was used to identify dietary patterns measured by 39 food groups. Next, the direct and intermediate effects of risk factors were examined using structural equation modeling. The results from multivariable regression analysis indicated that age (OR=1.03), SES (OR=0.89), processed meat intake (OR=1.08), non-screening (OR=2.67), smoking (OR=1.44, 1.85 (ever, current)), and family history score of CRC (OR=1.06), were significantly associated with the risk of CRC. SES (β=0.05) has a direct effect on the risk of CRC and the indirect effect (β=0.06) of SES on the risk of CRC also appeared to exist through processed meat intake (β=0.01), lower vegetable intake (β=0.01), lower screening frequency (β=0.02), and smoking (β=0.02). This study indicated that the NL population has three major dietary patterns. Also, structural equation modeling used in this study, a relatively new approach in epidemiology studies, provided unique information of the direct effect of SES on the development of CRC and its indirect effects through a set of candidate CRC risk factors.

KEY WORDS
Colorectal cancer, physical activity, socioeconomic status, diet pattern, direct effect, indirect effect.
Acknowledgement

With the support and contribution of many people, this research project has been made possible. First, I would like to express my gratitude to my supervisor, Dr. Peter Wang, who was abundantly helpful and offered invaluable assistance, support and guidance through the duration of my studies. I appreciate his vast knowledge and skill in many areas, and his assistance in writing reports (i.e., scholarship applications, manuscripts and this thesis). In addition to his contribution in my study, I am deeply impressed by his sound personalities that guide me to develop my characteristics. Moreover, I would like to appreciate members of co-supervisor committee: Dr. Barbara Roebothan, Dr. Qilong Yi, and Dr. Peter T. Cambpell for their assistance that they provided at all levels of the research project.

I would like express my many thanks to all the faculty, staff and students in the division of Community Health and Humanities for their generous advice, encouragement, help and motivation during my master’s training.

Many sincere thanks to my family members!

I would appreciate the Beatrice Hunter Cancer Research Institute with funds provided by The Terry Fox Foundation Strategic Health Research Training Program in Cancer Research at CIHR for offering me a trainee award for my graduate study.

Special thanks to the participants in both Ontario and Newfoundland and Labrador who contributed vast of their time and effort in the various components of this work.
Glossary

Comparative Fit Index (CFI): also known as the Bentler Comparative Fit Index. CFI is considered as improvement in noncentrality (from the null to the hypothesized model) to the noncentrality of the null model in which assumes that no interrelationships among any of the variables (independence model or null model). A recommended value of CFI is 0.9 or above [1, 2].

Direct Effects: the effect that goes directly from one variable to a second variable [3].

Exploratory Factor Analysis (EFA): it is a statistical method used to explore the dimensionality (factors-latent variables) of a measurement model by finding the smallest number of interpretable factors to explain the correlation among a set of variables [4].

Factor Loading: The correlation of the measured variable and its factor, with higher loadings make the variable representative of the factor. Factor loadings greater than 0.3 are considered to meet the minimal level; loadings of 0.4 are considered more important; and if the loadings are 0.5 and greater, they are considered practically significant [5].

Goodness of Fit: How well a hypothesized or theoretical model, a distribution, or an equation fits actual data [6].

Goodness of Fit Index: a measure of the proportion of variance and covariance that the hypothesized or theoretical model is able to explain [6, 7].

Indicators: also called observed variables, measured variables, or manifest variables. Actual measured value for a specific item or question, obtained either from respondents in response to questions or from observations by a researcher, which can be directly measured. Indicators are represented by squares or rectangles. By convention, indicators should have pattern coefficients (factor loadings) of 0.3 or higher on their latent factors.

Indirect Effects: the effects between two variables that are mediated by one more mediating
variables [3].

**Latent Variables:** also called *factors, constructs* or *unobserved variables*. The main characteristic of latent variables is that they cannot be directly observed or measured; it hypothetically exists in a study to explain variables that can be observed or measured. They are measured by a set of observed variables. Latent variables are represented by circles or ovals [8].

**Mediating Variable:** A variable occurs in a casual pathway from an independent to a dependent variable. It causes variation in the dependent variables but also it is influenced by the variation of the independent variables. Synonyms are intervening variable, mediator variable, intermediate variable, and contingent variable [9].

**Normed Fit Index (NFI) or Non-normed fit index (NNFI):** also known as Tucker-Lewis Index, the chi-square value of the null model is compared to that of a proposed model. A recommended value of NFI and NNFI is 0.9 or higher [1, 2].

**Root Mean Square Error of Approximation (RMSEA):** a measure of the discrepancy per degree of freedom in the model. Values less than 0.05 or 0.06 indicate reasonable fit [1, 2].

**Structural Equation Modeling (SEM):** Structural equation modeling is a multivariate technique incorporating multiple regression (examining dependence relationships) and factor analysis (representing observed (measured) and unobserved (latent factors) variables) to estimate the direct and indirect relationships of measured variables and latent factors [10].

**Weighted Root Mean Square Residual (WRMR):** This is a relatively new fit index that is believed to be better suite categorical data. WRMR values less than 1.0 depict a good fitting model [1, 2].
<table>
<thead>
<tr>
<th>Abbreviation</th>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<td>CFA</td>
<td>Confirmatory Factor Analysis</td>
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<td>CFI</td>
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<td>CI</td>
<td>Confidence Interval</td>
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<td>CRC</td>
<td>Colorectal Cancer</td>
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<td>EFA</td>
<td>Exploratory Factor Analysis</td>
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<td>FFQ</td>
<td>Food Frequency Questionnaire</td>
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<td>FHQ</td>
<td>Family History Questionnaire</td>
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<td>HRT</td>
<td>Hormone Replacement Therapy</td>
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<td>ICD</td>
<td>International Classification of Disease</td>
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<td>NFCCCR</td>
<td>Newfoundland Familial Colorectal Cancer Registry</td>
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<td>NFI</td>
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<td>NL</td>
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<td>NNFI</td>
<td>Non-normed Fit Index</td>
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<td>NOCS</td>
<td>Newfoundland and Ontario Colorectal Cancer Study</td>
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<td>NSAID</td>
<td>Nonsteroidal Anti-inflammatory Drug</td>
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<td>OFCCR</td>
<td>Ontario Familial Colorectal Cancer Registry</td>
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Chapter 1 Introduction

1.1 Background

Colorectal cancer (CRC) has become a health problem of increasing significance in Canada, with an estimated 22,500 new cases and 9,100 deaths in 2010 [11]. CRC is the third most common type of cancer among Canadian males and females [11]. The province of Newfoundland and Labrador (NL) has the highest age-standardized incidence rate of CRC in Canada at 86/100,000 [11]; indeed, this is one of the highest incidence rates of CRC in the world. Ontario experiences the average Canadian incidence rate at 51/100,000 [11].

Physical activity has long been considered an effective strategy for cancer prevention [12]. Comprehensive reviews found that increased physical activity is a substantial protective factor against colon or colorectal cancer [13-16]. Numerous prospective [17-20] and case-control [21, 22] studies have found statistically significant associations between physical activity and colon cancer, especially for men. Few studies of rectal cancer indicated no associations [23-25]. The measurement of physical activity in these studies varied and was based upon limited types of activity. The type, frequency, duration and intensity of physical activity are all important to reduce risk of colorectal cancer [12, 26]; however, this kind of information is limited. In Canada, few studies have focused on examining the relationships between specific physical activity and colorectal cancer risk, especially in a large population.

Epidemiological research to date has suggested that a wide range of environmental and lifestyle factors such as dietary factors, physical inactivity, smoking, alcohol consumption and socioeconomic status may contribute to the increased incidence of CRC; however, most of the results have been inconsistent [27-36]. The World Cancer Research Fund (WCRF) and the American Institute of Cancer Research (AICR) second expert report classified risk factors
into four major groups according to the strength of the evidence. Physical activity,
consumption of red meat, or processed meat, excessive alcohol drinking (above 30g/day),
body and abdominal fatness, and adult attained height are convincing risk factors of CRC;
intakes of dietary fibre, garlic, milk and calcium probably reduce CRC risk; non-starchy
vegetables, fruits, folate, selenium, fish and vitamin D have limited suggestive evidence of
declining CRC risk; while intakes of iron, cheese, food containing animal fat, and sugars
have limited but inconclusive evidence of raising CRC risk.

A large number of epidemiological studies have focused on examining major risk factors
of interest while controlling for other covariates. This oversimplifies the complicated,
interdependent relationships among various factors of interest [37]. Consequently, most
reported studies have been unable to specify how variables work together to give rise to CRC
and tend to under-estimate the true effect of each factor [38-40]. Therefore, studies that are
able to delineate and test how various factors are interrelated and jointly affect outcomes
would be expected to provide important insights into CRC etiology. Although the
inter-dependent relationships among socioeconomic status (SES), lifestyles, diet, and health
are well recognized [41-43], their complex inter-relationships in relevance to CRC have not
been examined. We hypothesized that lower SES predisposes people to certain risk factors
(e.g. poor dietary intake, smoking, alcohol consumption and obesity), which in turn may
interact with genetic factors and lead to the development of colorectal cancer. A large
population-based Newfoundland and Ontario Colorectal cancer Study (NOCS) was expected
to provide valuable insights on the risk factors of CRC and potential prevention strategies for
this disease.
1.2 Objectives

The objective of the first component of this thesis was to examine the association between colorectal cancer risk and several types of physical activity (walking, non-walking exercise and total physical activity).

The second component of this thesis was to achieve the following specific objectives: 1) explore the potential association among risk factors of colorectal cancer; 2) posit a conceptual model that delineates the inter-relationships with respect to how SES, dietary factors, and lifestyle factors work together to give rise to CRC; 3) operationalize the proposed conceptual model using the database of Newfoundland and Ontario Colorectal-cancer Study (NOCS). It is important to note that only the NL data was used in the second component of this thesis.

1.3 Organization

This thesis is divided into six chapters. Chapter 1 is an overall introduction to this study. Chapter 2 reviews the epidemiologic description and associated risk factors of CRC. Chapter 3 presents the research methods employed in this study. Chapters 4 and 5 are both results sections, which are written in a manuscript format, including its own introduction, methods, results, and discussion. Some repetition of methods was unavoidable. Chapter 6 summaries the key findings and discusses implications of the study results.
Chapter 2 Literature Review

2.1 Colorectal Cancer

Colorectal cancer (CRC) encompasses malignancies originating from the epithelial cells of gastrointestinal tract, which includes the colon, rectum and appendix [44]. The colon is the first four to five feet of the large intestine, which consists of the cecum, the ascending colon, the transverse colon, the descending colon, and the sigmoid colon (Figure 2.1). The main function of the colon is to remove water and nutrients from the food mass and convert the rest into waste [45]. The rectum is made up of the last several inches of the digestive tract [45]. Its major function is to store waste material prior to excretion.

Figure 2.1: The colon and rectum polyp and cancer

CRC usually begins as a noncancerous polyp which may eventually become a cancerous growth. This process may vary from several years to decades. Initiation and progression through the adenoma-carcinoma sequence is linked with accumulated defects in tumor suppressor genes, oncogenes, and DNA repair genes [46]. The tumor genesis may be started by external agents and/or inherited genetic factors [47].
2.2 Epidemiology of Colorectal Cancer

2.21 Worldwide Burden

CRC is one of the most common cause of cancer deaths each year in men (663,000 cases, 10.0% of the total) and the second in women (571,000 cases, 9.4% of the total) worldwide [48]. The majority (60%) of the cases occur in developed regions, which includes Australia/New Zealand and Western Europe [49]. On the other hand the fewest cases occur in Africa (except Southern Africa) and South-Central Asia [49]. Men usually have higher incidence rates than women (overall sex ratio 1.4:1) [49]. The worldwide estimated deaths from colorectal cancer are about 608,000 deaths per year; Central and Eastern Europe experience the highest mortality rates in both sexes estimated as 20.1 per 100,000 for males and 12.2 per 100,000 for females. Middle Africa experiences the lowest male and female mortality rates of 3.5 and 2.7 respectively [49].

2.22 Canadian Incidence and Mortality

In Canada, 22,500 diagnoses and 9,100 deaths were expected from colorectal cancer in 2010 [11]. CRC is the fourth most common malignancy and the second leading cause of death from cancer in men and women combined [11]. In 2010, the age-standardized incidence rate of CRC was 62 per 100,000 among men and 41 per 100,000 among women, and the age-standardized mortality rate was 25 per 100,000 men and 16 per 100,000 women [11]. More than 50 percent of newly diagnosed colorectal cancer cases will occur among people aged 70 years or older [11]. Although the age-standardized rates are higher in men, the number of prevalent cases and deaths is approximately equal between the sexes because of the tendency of women to live longer than men.

The 2010 Canadian Cancer Statistics reported the fluctuation of CRC incidence: the
incidence rose between 1980 and 1985; next, the incidence declined to the mid-1990s (more strongly in females than in males), then rose through 2000, only to decline significantly thereafter [11]. Recent declines in mortality rates in both sexes may be due to high screening rates, improved controls and/or treatments.

Interprovincial variations for colorectal incidence and mortality rates are obvious [11]. Newfoundland and Labrador typically has the highest rates of colorectal cancer in Canada at a rate of 88 per 100,000 for men and 52 per 100,000 for women in 2010. Ontario ranks in the middle among Canadian provinces at a rate of 59 per 100,000 for men and 40 per 100,000 for women in 2010. British Columbia has the lowest incidence with a rate of 54 per 100,000 for men and 37 per 100,000 for women. The high colorectal incidence in Newfoundland and Labrador may be partly explained by a high prevalence of families with a predisposition to hereditary colon cancer [50]. However, environmental factors are also an important component to the CRC risk.

2.3 Risk Factors Associated with CRC

The exact causes of colorectal cancer are unknown [45]. While family history is a strong risk factor for CRC, inherited familial CRC is responsible for 10%-15% of all CRC cases [51-53] and the majority of CRC cases are a result of gene-environment interactions [52, 54, 55]. Lifestyle and dietary factors play an important role. About 75 to 85 percent of CRC are sporadic, suggesting that modifiable factors are of public health importance and etiology. Important modifiable risk factors for CRC include tobacco use, unhealthy diet, physical inactivity and the consumption of alcohol [47].

2.3.1 Hereditary Factors

Those with a family history of CRC or adenomatous polyps in any first-degree relative younger than age 60, or in two or more first-degree relatives at any age are considered at increased risk for the disease. Among familial cases, approximately 5%-10% of CRC are a consequence of hereditary genetic mutations, which mainly consist of familial adenomatous polyposis (FAP), and hereditary non-polyposis CRC (HNPCC) [56, 57].

Patients who have FAP typically develop hundreds of polyps in their colon and rectum during the ages of 5 to 40 years. FAP is commonly caused by mutations of the adenomatous polyposis coli gene, which result in inoperative tumor cell growth and finally leads to the growth of hundreds of polyps in the colon and rectum. Over time, gene mutations in the cells of the polyps cause the polyps to become cancerous [58]. FAP accounts for less than 1% of all CRC patients [59].

HNPCC accounts for 1% - 6% of all CRCs [60-62]. This syndrome also develops when people are relatively young. Patients with HNPCC have fewer polyps, unlike hundreds of polyps as is seen in patients with FAP. HNPCC syndrome is characterized by early onset of CRC with microsatellite instability. Microsatellite instability of the cancer tumor is a molecular marker for DNA mismatch repair deficiency. Mutations in mismatch repair genes are detected among 85% of HNPCC patients [58].

2.3.2 Environmental Factors

Existing studies show that immigrants rapidly acquire the incidence rates of their host country, suggesting that environmental factors play a crucial role in CRC development.
As mentioned in Chapter 1, the WCRF and AICR second expert report classified risk factors into four major groups according to the strength of the evidence. Evidence linking physical activity to CRC is convincing as well as red meat, processed meat, excessive alcohol drinking (above 30g/day), body and abdominal fatness, and adult attained height (the difference between current weight and weight at their age of 20s); intakes of dietary fibre, garlic, milk and calcium probably reduce CRC risk; intakes of non-starchy vegetables, fruits, folate, selenium, fish and vitamin D have limited suggestive evidence of declining CRC risk; intakes of iron, cheese, food containing animal fat, and sugars are limited but inconclusive evidence of raising CRC risk. This expert report also suggested CRC is mostly preventable by appropriate diets and associated factors.

2.3.2.1 Socio-economic Status (SES)

There are great geographic variations in incidence rates. Rates have been shown to be higher in the western countries and lower in developing countries. Countries with high incomes have been shown to have higher colorectal cancer incidence rates than those with lower incomes [66]. This may be partly explained by the fact that residents in the developed countries have a “westernized” dietary pattern with less physical activity associated with both occupation and transportation due to industrialisation. Findings from several studies suggested that the risk of developing CRC increased with a higher education level and social class [67, 68]. On the other hand, low SES predisposes people to certain risk factors (e.g. poor dietary intake and obesity), which in turn may interact with genetic factors and lead to the occurrence of colorectal cancer. There are different social class correlates for colon and rectal cancer [67]. The two sites should not be combined in studies considering lifestyle factors in the aetiology of these neoplasms [67].
2.3.2.2 Dietary Factors

Dietary factors have been regarded as strongly associated with the incidence of CRC [53, 69], particularly when an unhealthy diet is intermingled with obesity, weight gain, physical inactivity, smoking or excessive alcohol consumption [18, 34, 70-74]. One study has indicated that about 70% of CRC can be prevented by changes in diet and lifestyle [73], but estimates vary widely [53]. Although epidemiologic studies and/or clinical trials have attempted to examine the associations among specific foods, nutrients and CRC, the results produced are inconsistent and unconvincing.

The ‘Western’ diet, known to be high in animal fat, red and processed meats but low in fruit, vegetable and fibre content, has been linked to an increased risk of CRC. This type of diet is common for people who live in Japan, North America, Northwestern Europe and Australia.

2.3.2.2.1 Total Energy

The 2007 World Cancer Research Fund and the American Institute for Cancer Research expert report concluded that total energy has no simple relation with CRC risk. Data are inconsistent for carbohydrates, proteins and cholesterol [75]. Several studies have suggested that total energy intake is positively associated with CRC risk [76-78]. High energy intakes could cause a glycemic overload, a compensatory increase of serum insulin, and related insulin growth factor-1 (IGF-1), leading to an increased cell proliferation, reduced apoptosis, and thereby increase the risk of tumorigenesis [79-82]. This may help to explain why patients with non-insulin dependent diabetes have increased CRC risk [81, 83-86]. In addition, the effects of hyperinsulinemia and type 2 diabetes have been shown to be associated with increased risk of proximal rather than distal colon cancer [84, 87]. Patients with type 2 diabetes are predisposed to lower survival rates and higher recurrence rates. Another possible
explanation could be that people with CRC and type 2 diabetes share similar unhealthy lifestyles [84].

2.3.2.2 Fruit, Vegetables and Fibre

Ever since Burkitt proposed that a lower CRC mortality in blacks compared to the whites was attributable to dietary fibre intake, the risk of colorectal cancer in relationship to fruit, vegetables and fibre has been examined by hundreds of epidemiologic studies [56]. The 1997 WCRF/AICR expert panel reviewed 21 case-control and four cohort case-control studies and concluded that vegetable consumption convincingly reduces the risk of colorectal cancer but the evidence supporting fruit consumption was limited [88]. Subsequently, the 2003 IARC evaluated 27 case-control and 13 cohort studies and suggested that higher intakes of vegetable probably declines the CRC risk and higher intakes of fruits possibly reduces risk [49]. The latest 2007 WCRF/AICR expert report indicated that fibre is probably associated with CRC risk reduction and that non-starchy vegetables and fruits have limited suggestive evidence of declining risk [56].

Overall, case-control studies showed that fibre provided approximately a 40%-50% of reduction in the risk for colon cancer while prospective cohort studies indicated a weak association between dietary fibre intake and colon cancer [32]. One meta-analysis showed that an increase of 10 g fibre per day was responsible for a 10% reduction in CRC risk (RR: 0.90 and 95% CI: 0.84-0.97) [56]. With this being said, some studies suggest that the effects of fruit, vegetables and fibre may only be evident for a person who has low baseline intake levels [32].

Many fruits, vegetables and grains are rich in fibre. Fruits and vegetables are sources of
dietary fibre, carotenoids, folate, selenium, glucosinolates, vitamins and minerals [56]. The precise mechanisms explaining the beneficial role of fibre, fruits and vegetables are not clearly understood. The protective effect of fibre may be linked with the fact that fibre dilutes fecal contents, decreases transit time and increases stool weight [32, 89], which helps to reduce the time of exposure to carcinogens or tumor promoters in the intestinal lumen [90]. The beneficial effect of fruits and vegetables may be attributed to the combined influences of constituents on several carcinogenesis pathways. Antioxidants contained in the fruits and vegetables could protect against oxidation damage through trapping free radicals and reactive oxygen molecules [32, 56]. Short-chain fatty acids produced in the fermentation process might induce apoptosis; therefore also possibly contributing to their beneficial role [32].

2.3.2.3 Meat and Fat

For the purpose of this thesis, the term “red meat” refers to beef, pork, lamb and goat from domesticated animals and “processed meat” refers to meats preserved by smoking, curing, or salting or by the addition of preservatives [56]. Red and processed meat has been postulated to increase CRC risk through several mechanisms such as the production of heterocyclic amines and polycyclic aromatic hydrocarbons with high temperature cooking method such as frying, grilling, and barbecuing [91, 92]; increased exposure to mutagenic nitrites, nitrates, N-nitroso compounds and salts [93]; stimulation of endogenous insulin which can cause cell proliferation [32]; or increased iron intake, which is considered an emerging carcinogen that may increase the formation of oxygen species and consequently lead to DNA and chromosome damage [27, 94].

The expert panel conducted a meta-analysis of 16 cohort studies which indicated that a daily increase in the consumption of 50 gram of red meat was associated with a 15% increase
in CRC risk [56]. The panel also showed that a daily 50 gram increase in the consumption of processed meat was linked with a 21% increase in CRC risk [56]. Therefore, the panel concluded that the evidence linking red and processed meat consumption with risk of CRC is convincing.

Dietary meat alternatives including fish and poultry have been associated with deceased CRC risk in most, but not all studies [33, 35, 56, 95, 96]. The mechanism is not clear. It has been proposed that n-3 polyunsaturated fatty acids in fish protect against CRC by reducing inflammation and regulating DNA methylation [97-102]. Animal trials have indicated that fish oil supplements decrease the number of colon tumors [103]. Long-chain n-3 PUFAs in fish oils can inhibit tumor cell proliferation by modifying signaling pathways [104, 105]. The evidence to support that fish and poultry intakes are associated with a reduction of CRC risk is limited [56]. The EPIC study suggested that the consumption of red and processed meat increases colorectal cancer risk while the intake of fish decreases it [98].

Meat is a major source of dietary fat, especially of saturated fat [32]. Some studies have shown that an increased risk of CRC is associated with an increased intake of total saturated fat while intakes of monounsaturated and polyunsaturated fats have been found to be associated with a reduced risk [106, 107]. A diet high in animal fats reflects higher consumption of meats and a lower consumption of vegetables and fruits. Such energy-dense diets have been directly linked with increased CRC risk or mediated through obesity. However, the women’s health study [108] and a prospective cohort study of male health professionals [79] showed that diets low in fat had no effect on CRC risk reduction. There is limited evidence suggesting that dietary animal fat is associated with risk of CRC.
2.3.2.4 Minerals and Vitamins

Calcium, selenium, vitamin D, vitamin B complexes, beta carotene and antioxidants have anti-carcinogenic effects and thus decrease CRC risk [109-111], whereas iron has been shown to increase the risk [112]. One of the most well studied minerals in CRC prevention is calcium, which is mainly found in dairy products and supplements. Calcium is known to bind secondary bile acids and ionized fatty acids in the colon lumen to form insoluble calcium soaps, preventing bile acids and fatty acids from damaging the mucosa of the intestinal lumen by inhibiting their proliferative effects [113]. Calcium may also function by reducing cell proliferation, stimulating differentiation, inducing apoptosis, and regulating the cell-cycle of normal and tumor colorectal cells [114-117]. The roles of dietary calcium and vitamin D are highly correlated because both participate in cell growth restraining, differentiation and apoptosis in intestinal cells and vitamin D regulates the absorption of calcium. Some of the effects of dairy intake on CRC risk reduction is mediated through calcium, although other bioactive constituents may have potential effects as well.

The vitamin B complexes are linked with carcinogenesis through DNA synthesis, repair and methylation [111, 118, 119]. High intake of folate and its cofactors (vitamins B6 and B12) are associated with a 30% reduction in CRC risk [111, 120-122]. One meta-analysis has suggested that folate found in naturally in foods rather than folate in the form of supplements has a beneficial effect. This might suggest that folate combined with other constituents, or in its certain active form, is truly effective in CRC prevention [32, 123].

Antioxidants, including carotene; vitamins A, C, and E; and selenium may protect against CRC through their antioxidant or anti-inflammatory characteristics [122]. Findings of observational studies, meta-analyses and placebo trials are not consistent as they pertain to
the protective effect of anti-oxidants, either as single agents or in combination with other antioxidants [124-127].

2.3.2.2.5 Dietary Patterns

Most available studies in nutritional epidemiology have investigated the effect of individual foods and nutrients [32]. Although diet and colon cancer relationships have been studied extensively, the impact of many dietary factors on colon carcinogenesis remains unresolved [27, 79, 90, 128-138]. Foods are often consumed together and similar nutrients can come from different foods; therefore, examination of the specific effect of each food is likely to be confounded by other foods consumed throughout the diet [139, 140]. Consequently, an increasing number of studies in the past decade have examined the associations between dietary patterns and CRC [36, 71, 141-148]. A number of food patterns have been identified [56], such as Asian, plant-based, Mediterranean and westernized diets. Nevertheless, overall the evidence is meager and heterogeneity of dividing food groups exists.

2.3.2.3 Physical Activity

Physical activity includes activities that are associated with occupation (at work), home, recreation (leisure) and transportation (such as walking, riding, and cycling). Engaging in physical activity has long been considered an effective strategy for CRC prevention [12]. Undertaking 150 minutes of moderate physical activity each week can reduce the risk of breast and colon cancers. In industrialized countries with high incomes, sedentary life is normal with occupational and household physical activities being dramatically reduced in recent decades- 31% of the world's population is not physically active [56, 149].
Systematic reviews have found that increased physical activity is a substantial protective factor against colon or colorectal cancer [13-16]. Numerous prospective [17-20] and case-control [21, 22] studies have found statistically significant associations between physical activity and colorectal cancer, particularly in men. However, a few studies have not found significant associations [23-25]. The beneficial role of physical activity in prevention of colon and/or rectal cancer varied in sub-sites and sex [17, 21, 25, 26, 150-153]. The WCRF and AICR [154] summarized 24 cohort studies and found that all but two of these studies have reported decreased risk. Higher levels of recreational activity were found to help protect against colon cancer in both men and women with a significant inverse trend being reported in six of 24 cohort studies. Physical activity was not associated with decreased risk of cancer of the rectum.

A few previous studies have indicated that intense physical activities have a greater CRC risk reduction. Researchers have demonstrated that a lack of lifetime vigorous leisure-time activity was associated with increased risk of colon cancer for both men and women [155].

2.3.2.4 Smoking

Tobacco use is the single most important risk factor for cancer [47]. This may be explained by the carcinogens that are released through smoking [32, 156]. Higher smoking prevalence in Atlantic Canada is associated with higher rates of lung cancer in this region [11]. Tobacco use has been associated with colorectal adenoma and cancer; however, the association has been observed to be stronger for rectal cancer [72, 157] and proximal colon cancer relative to the distal colon cancer [158, 159]. Higher levels of daily cigarette consumption and longer duration of smoking (pack-years), often associated with an earlier age of initiation, were associated with higher CRC risk. This suggests the presence of a
strong dose-response relationship between smoking and increasing CRC risk [72]. Past smokers appear to have a higher incidence of CRC as compared to current smokers; however, this may be confounded by the early damage caused by early initiation of smoking [32].

2.3.2.5 Alcohol Consumption

Most studies, but not all, indicate that alcohol consumption increases CRC risk. Meta-analysis of cohort data suggested that a 10 g daily ethanol intakes increase CRC risk by 9% [56]. Alcohol may mediate prostaglandin production, increase lipid peroxidation and oxidative species, and consequently result in increased carcinogenesis through the mechanisms of abnormal DNA methylation and/or activation of cytochrome p450 enzymes [56, 160, 161]. Alcohol is predicted to have the function of acting as a solvent for carcinogenic molecules in mucosal cells [56].

2.3.2.6 Obesity and Abdominal Fatness

Obesity (Body Mass Index ≥ 30kg/m²) and abdominal fatness (measured by waist circumference > 102cm in men and >88 cm in women or waist to hip ratio of >0.9 for men and >0.85 for women) are convincingly associated with CRC risk [56]. The association was stronger for men compared to women and for the colon relative to rectum [32, 162]. The 2007 WCRF/AICR expert report shows a 15% increased CRC risk per 5 kg/m² BMI increase and 5% increased risk per inch of waist circumference [56]. Several biological mechanisms have been proposed to understand the associations. Obesity results in insulin resistance, which leads to cancer pathogenesis mediated by the mitogenic property of insulin and hyperinsulinemia. Insulin stimulates increased free insulin growth factors which promote carcinogenesis [163-165]. Obesity and abdominal fatness also have relationship with
oestrogens, leptin, and chronic inflammation, which are all associated with increased CRC risk [166-170].

2.3.2.7 Medications

Clinical trials, cohort and case-control studies have shown that the use of aspirin and non-aspirin non-steroidal anti-inflammatory drugs (NSAIDs) was associated with decreased CRC risks [171-173]. The anti-cancer effects of NSAIDs and aspirin may be exerted through the inhibition of cyclooxygenase and lipoxygenase enzymes [173], inhibition nuclear factor-Kb [174], induction of apoptosis by activation of kinase [175], and polyamines catabolism [176]. All of these factors play key roles in the function of various cellular metabolisms.
Chapter 3 Research Methods

3.1 Data Sources

The U.S. National Cancer Institute established the Ontario Familial Colorectal Cancer Registry (OFCCR) as one of six international sites in the consortium of Colon Cancer Familial Registries (CCFR) in 1997 [177, 178]. The *CIHR Team in Colorectal Cancer* (CTCC) aimed to improve the knowledge of the determinants, impact, and control of colorectal cancer as a result this team established the Newfoundland Familial Colorectal Cancer Registry (NFCCR), which was modeled on OFCCR (details on the project can be found at: http://www.mshri.on.ca/colorectalcancer/). The study addressed by this thesis used the database of a population-based Newfoundland and Ontario Colorectal Cancer Study (NOCS). Ethics approval was obtained from the Research Ethics board of Memorial University.

The original data-base cleaning involved checking and verifying missing data, conducting range and value checks, and conducting logic and reverse logic checks [31]. The data base cleaning process involved the conversion of cell values, variable names, variable types, variable lengths, and column widths in the original data, which has all been done by previous OFCCR and NFCCR research team members. However, for this thesis study, additional variables required for analysis were derived and variable names were adapted for specific software requirements.

3.2 Study Design

Both Ontario and NL colorectal cancer studies used a population-based case-control study design to collect necessary information. Case control studies can identify risk factors of disease, especially for rare diseases, by comparing the odds of given risk factors between
cases and controls. The incidence rate of CRC in Canada meets this criterion for a rare disease; consequently, a case-control study design makes sense for the study. All eligible cases identified through the Ontario Cancer Registry and the Newfoundland Cancer Treatment and Research Foundation were invited to participate in this interdisciplinary CRC study. Controls were five-year age group and sex matched to cases. The detailed description of inclusion criteria would be outlined in the next section: study population.

3.3 Study Population

3.3.1 Cases

The Ontario Cancer Registry and the Newfoundland Cancer Treatment and Research Foundation were used to identify newly diagnosed cases of colon or rectal cancer; and cases were recruited into the OFCCR and NFCCR. Pathologists in the study confirmed the pathology reports of cases. Inclusion criteria for cases [179]:

1) Incident primary invasive colon or rectal cancer [pathology confirmed International Classification of Diseases 9th revision codes: 153.0-153.9, 154.1-154.3 and 154.8 (ON & NL); or ICD-10 codes: 18.0-18.7, 19.9, 20.9 (NL only)];

2) Diagnosed between July 1997 and June 2000 (phase one) or January 2003 and April 2006 (phase two) in ON. Diagnosed between January 1999 and December 2003 in NL;

3) Diagnosed at ages of 20 to 74 years old (phase one) or ages of 20 to 50 years (phase two) in Ontario; and

4) Residents of ON and NL at the time of diagnosis.

The pathologists of this study identified eligible cases by viewing pathology reports generated by the Ontario Cancer Registry and the Newfoundland Cancer Treatment and
Research Foundation. Initial contact was made through the surgeon/physician identified on the pathology report. A letter was sent to the physician that described the study and requested permission to contact the patient. Once physician consent was obtained, individuals were then contacted by researchers to inform them of the study. Participants who indicated their willingness to participate the study were sent, in sequence, a written consent form, Family History Questionnaire (FHQ). Then, cases were categorized into high, intermediate, and low risk of CRC (based mostly on family history). Subsequently, 100% of high and intermediate, and only 25% of the sporadic cases were invited to fill in Personal History Questionnaire (PHQ), Food Frequency Questionnaire (FFQ). In NL only, the original study packet also contained a blood requisition form.

If a participant did not return finished questionnaires within three weeks, and a follow-up telephone call was made to ensure the study package had been received. In certain circumstances, a telephone interview or assistance was offered, especially when illiteracy or physical disability was a concern. Subjects were provided with a toll-free telephone number as a way to contact study staff if they had questions regarding any of the items on questionnaire or procedures required for the study. Multiple telephone follow-ups were conducted if eligible participants did not respond to survey questionnaires. If a subject made any indication of not wanting to participate in the study, the interviewer attempted to determine and record the reason. No further contact was made with these subjects. Family history questionnaires were used to classify families as high, intermediate or low risk for genetic counseling. In NL where blood samples were collected, the samples were sent directly from the laboratory closest to the participant to a central laboratory for investigation of genetic markers.
3.3.2 Controls

Controls recruited by the OFCCR and NFCCR were comprised of a random sample of residents aged 20-74 years in each province. Within a frequency matched case-control study, controls were 5-year age group and sex matched with the colorectal cancer cases. In Ontario, controls were identified through a list of residential phone numbers provided by Bell Canada during 1999 and 2000. Info-direct, a service from Bell Canada, provided information pertaining to potential control subjects, which included their names, telephone numbers, and addresses. Households were randomly selected from this list and telephoned to obtain a census of household members (age and sex) as a method to identify eligible persons. One eligible person within each household was randomly selected and invited to participate in the OFCCR. To increase the sample size and match the case to control ratio was 1:2; therefore, additional controls were identified from population-based assessment rolls (owners and occupants) provided by the provincial government during 2001 and 2002. The detailed description of controls selection can be found within other publications of this interdisciplinary CRC study [180, 181].

In NL, controls were identified through random digit dialing [182]. Initially, a set of 192,000 possible residential telephone numbers were generated and randomly arranged. A research assistant with prior experience in telephone surveying made the initial contacts by dialing those numbers in a sequential order until the desired number of controls was reached. A screening interview was conducted among potential control subjects to identify if there was an eligible household member based on their sex and age and whether that person was willing to receive a mailed family history questionnaire.

In both provinces, once verbal consent for participation was obtained through telephone
contact, a survey package was forwarded to each potential participant. The package included an information pamphlet with general information concerning the study, a consent form, Personal History Questionnaire (PHQ), Food Frequency Questionnaire (FFQ), Family History Questionnaire (FHQ), as well as a self-addressed stamped envelope. If a participant did not return complete questionnaires within three weeks, a follow-up telephone call was made to ensure that the study package had been received. A telephone interview or assistance was offered when illiteracy or physical disability was a concern.

3.4 Response Rates

3.4.1 Response Rates in Ontario

During phase-one of the OFCCR (1997-2000), a total of 3776 eligible CRC cases were identified in Ontario. After the initial contact with the physicians and eligible CRC cases, 1593 were willing and able to participate in the registry out of which 1187 cases (75%) completed the PHQ and 1143 cases (72%) completed the FFQ.

Phase two of the OFCCR was initiated in January 2003 and scheduled to continue to the end of 2006. Consequently, phase two data which were available up to April 2006 were used in this thesis. During this period, among the 1263 eligible patients that were contacted, 727 of which agreed to participate in the registry. PHQs were returned by 641 (88%) cases and FFQ were returned by 279 (38%).

Population controls in Ontario were contacted via telephone calls. A total of 2736 control subjects from Ontario agreed to participate in the study, of which 1957 (72%) completed all three questionnaires (FHQ, PHQ, and FFQ).
3.4.2 Response Rates in Newfoundland and Labrador

In total, among 1126 eligible NL CRC cases, 705 (63%) participated and returned the PHQ, and 608 (54%) returned the FFQ. Population controls in Newfoundland and Labrador were contacted through random digit dialing. The total number of telephone calls made was not recorded. In July 2005, 1,603 controls had agreed to participate in the study in some form. 720 controls (45%) returned the PHQ and 687 controls (43%) returned the FFQ.
Figure 3.2. NL population sample size and response rates (adapted from Sun [183])

![Diagram of population sample size and response rates]

3.5 Data Measurement

All participants in the interdisciplinary CRC study were asked to complete self-administered mailed epidemiologic questionnaires, which include the Personal History Questionnaire (PHQ), the Food Frequency Questionnaire (FFQ), and the Family History Questionnaire (FHQ). OFCCR and NFCCR used the same PHQ and FHQ but the FFQ between ON and NL had some are differences.

3.5.1 Personal History Questionnaire (PHQ)

The PHQ was designed to investigate 74 items of information pertaining to participants, addressing detailed identifying information: demographic characteristics (age, sex and marital status), bowel screening history (hemoccult test, sigmoidoscopy, colonoscopy, and endoscopy
test) and health history (diabetes, high cholesterol, high triglyceride, etc), medication use (non-steroidal anti-inflammatory drugs, bulk-forming laxatives, other laxatives), physical activity (specific activities such as walking, jogging, and running during their 20’s, 30-40’s, and 50’s), alcohol consumption (beer, wine, sake, liqueurs during their 20’s, 30-40’s, and 50’s), tobacco use, socio-demographic factors (education, income and residence) and anthropometric measures (height, body mass index). Among female participants, additional questions addressing menstruation; pregnancy; ages at menarche; first birth; and menopause; parity; hysterectomy; oophorectomy; menopausal status; and reason for menopause were surveyed. This questionnaire can be found in Appendix 1.

3.5.2 Food Frequency Questionnaire (FFQ)

The FFQ administered in the ON population was originally developed for the Hawaiian and Californian populations by the Epidemiology Program of the Cancer Research Center of Hawaii, which has been previously described and validated against 24-h recalls of a multi-ethnic Hawaiian/Southern Californian population[184, 185]. See Appendix 2. The FFQ surveyed regular food consumption, and cooking methods of 170 common foods about one years before their diagnosis for cases or their interview for controls. Participants were asked to choose the portion size of their usual serving for each listed food item from ‘Regular’, ‘Small’ or ‘Large’. The frequency of food consumption was assessed using 8 options (never or hardly ever, once a month, 2-3 times a month, once a week, 2-3 times a week, 4-6 times a week, once a day, 2 or more times a day). Subjects were also asked to provide information on their use of multi- or single vitamin and/or mineral supplements, including the usual brand, dosage, and duration of supplement intake.

FFQ administered in NL was developed from the FFQ used in Ontario to adapt to the
unique food consumption pattern if the province. Participants were asked to estimate the frequency and portion size of 169 food items one year prior to their diagnosis or participation in this study. For each food item, subjects were asked to estimate the frequency of food consumption (daily, weekly, monthly and never scales) and their usual portion size (average, smaller or larger) about one year their diagnosis for cases or their interview for controls. The information on vitamins and other dietary supplements was also collected.

3.5.3 Family History Questionnaire (FHQ)

The FHQ helped to collect information of the diagnosed type of cancer or tumour history of participants. The same questions were used to survey the participant’s mother, father, children, brothers and sisters, mother’s brothers and sisters (NL only), father’s brothers and sisters (NL only) and other relatives who had cancer.

3.5.4 Study Outcomes and Exposure Variables

For both cases and controls, CRC was the outcome in this thesis. For the first objective of this thesis, the main study exposure was recreational physical activity. It was measured by self-reported data from the PHQ on current and past activities of participants: 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. The questions regarding physical activity were “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. Walking-yes or no; For how many years? During those years, for how many months per year? During those months, on average, for how many minutes or
hours per week?” The same questions were asked of jogging, running, bicycling, swimming and so on addressing three periods in total (20-30s, 30-50s, and 50s plus). Participants were asked to specify the frequency and duration of activities not included on the questionnaire but participants did consider to be recreational exercise.

The derived time taking frequency and duration into consideration, that the participant spent on each exercise after they reached the age of 20 was multiplied by its specific metabolic equivalents score (METs) to yield a MET-hour score [186, 187]. Average weekly MET hours for walking, non-walking exercise and total recreational physical activity were calculated. After calculation, walking, non-walking exercise and total recreational physical activity were further divided into quintiles according to percentage distribution of controls (<Q20, <Q40, <Q60, <Q80, ≥Q80).

For the second objective of this thesis, the complex inter-relationships among socioeconomic status (SES), lifestyles, diet, and health involve a wide range of exposures. The core variables were divided into several aspects. Putative covariates for the main exposure variables included: 1) demographic factors: age (18-39, 40-49, 50-59, 60-69,70+), sex (male, female), marital status (single or never married, currently married or living as married, separated, divorced or widowed), 2) socio-economic status: educational levels, household income(0-$11,999, $12,000-$29,999, $30,000-$49,999, $50,000 plus), residence (rural, urban); 3) medical history: any screening procedure which included hemoccult test, sigmoidoscopy test and colonoscopy, indicated as dichotomous (yes/no); self-reported health conditions were coded as “yes/no”: polyps, familial adenomatous polyposis, Crohn’s, colitis, diabetes, high triglycerides/cholesterol; use of medications and supplements: non-steroidal anti-inflammatory drugs, bulk forming laxatives, non-bulk forming laxatives; 4) dietary
patterns measured by food groups (units: gram or servings/day); 5) average weekly MET hours of physical activity level at ages of 20-29, 30-49, 50+, and lifetime; 6) alcohol consumption: average weekly drinks at ages of 20-29, 30-49, 50+, and lifetime; 7) smoking: cigarette smoking status (current, former and never) and pack-years; 8) BMI categorized by World Health Organization (WHO) criteria: underweight (<18.5 kg/m²); normal weight (18.5-24.9 kg/m²); overweight (25-29.9 kg/m²); and obese (≥30 kg/m²). Two BMI indices were used for this analysis: first, recent-BMI was calculated from body weight during the reference period (one year prior to diagnosis for cases or one year prior to participation for controls); second, BMI at about the age of 20 was estimated from their self-reported body weight at the age of 20. Other primary exposures of interest included adult weight gain, which was derived by getting the difference between their weight (kg) at 20 years of age and recent weight (kg), and adulthood height (m). Among women only, additional potential confounders included: ages at menarche, first birth, and menopause; parity; hysterectomy; oophorectomy; menopausal status; and reason for menopause. The main study variables were also assessed for confounding influence on each other.

3.6 Data Analysis

To analyze the data collected for the first objective, SAS statistical software (version 9.1 SAS Institute, Cary, NC, USA) was used. M-PLUS 5.0 software (Muthen & Muthen) were used to perform statistical analyses for the second objective of this thesis.

3.6.1 Descriptive Analysis

Uni-variate analysis was done to examine distributions and detect outliers. The exposure variables of cases and controls were compared by t tests for continuous variables, and
chi-square test for categorical variables. All tests of statistical inference employed a
two-sided alpha level of 0.05.

**3.6.2 Multivariable Regressions**

To address the first objective of this thesis, sex specific age-adjusted and multivariate
adjusted odds ratios (OR) and their corresponding 95% confidence intervals (CI) were
calculated using unconditional logistic regression to assess the associations between physical
activity and CRC risk. Tests for linear trend were done by modeling the median value of each
quintile of physical activity measured by metabolic equivalent (MET) hours per week into the
logistic regression model.

**3.6.3 Structural Equation Modelling**

The direct and indirect effects for various risk factors on colorectal cancer were tested
using structural equation modeling (SEM). SEM is a multivariate technique combining
aspects of multiple regressions examining dependent relationships and factor analysis
representing non-directly measurable concept or latent variables measured through multiple
indicators to simultaneously estimate a series of interrelated dependence relationships [188,
189].

SEM analysis is primarily confirmatory in nature and basically consists of two primary
components, the measurement model and the structural equation model [188, 189]. The
measurement model involves using factor analysis to develop an acceptable model, which
reduces observed measured variables to a smaller number of latent variables factors and to
ensure that the indicator variables loaded significantly on underlying latent factors. The
structural equation model defines the relationships among these observed variables, latent factors and covariates.

Traditional techniques, such as regression and path analysis, analyze only measured variables; however, SEM takes into account of measurement error and could deal with latent variables which are not directly measurable. Factors are signified with circles and the observed variables are represented with rectangles. Using measured variables as indicators of latent factors rather than simply taking the sum or average of the measured items as a scale allows for estimation and removal of the measurement error associated with observed variables [188].

Food groups dietary patterns and lifestyles were represented by latent variables. However, due to the complexity of the dietary and life styles factors, several approaches (single latent, multiple latent, and manifest variables) were explored and compared. This was guided by exploratory factor analysis, and our understanding of the associations of interest. Genetic factors should be considered in building models so this study took the family history score of CRC (previously derived) as a continuous variable into consideration. We felt this simplification was necessary in order not to lose sight of the main objective. Other factors, such as age, gender, and comorbidities have also been considered. However, since other variables are not our primary interest, this study only considered some main common candidate risk factors of CRC as potential confounding factors. The conceptual models would also be revised and compared with a number of competing models.

Model fit indices were evaluated based on the following: Comparative Fit Index (CFI), the Tucker Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA),
Weighted Root Mean Square Residual (WRMR), and Standardized Root Mean Square Residual (SRMR).
Chapter 4  Project 1: Walking, Non-walking Exercise and Colorectal Cancer - a large population based case-control study in Canada

4.1 Abstract

Background:

Higher levels of physical activity have been consistently associated with a lower risk of colorectal cancer (CRC) in previous studies. Nevertheless, the specific mode, intensity, frequency, and duration of physical activity required for colorectal cancer prevention are not well known and remain controversial. This study examined the associations among walking, non-walking exercise, total recreational physical activity and colorectal cancer risk.

Methods:

This study used data collected from an existing population based case-control study in Ontario and Newfoundland and Labrador, which collected participant's personal history, lifestyle and dietary information using a Personal History Questionnaire (PHQ), Food Frequency Questionnaire (FFQ) and Family History Questionnaire (FHQ). Multivariate logistic regression analysis was used to estimate odds ratios (OR) and 95% confidence interval (95%CI) after adjusting potential confounding covariates.

Results:

Result from this study showed that the highest quintile of walking was associated with increased colorectal cancer risk for both males and females in both provinces (highest VS lowest: ON: OR=1.51, 95%CI=1.07-2.13; NL: OR=2.01, 95%CI=1.25-3.22; pooled analysis: OR=1.70, 95%CI=1.09-2.66). However, this result could be biased because a higher proportion of cases responded to this item than controls. Non-walking exercise was not significantly associated with reduced risk of colorectal cancer for both sex and provinces. Total recreational physical activity was not substantially associated with CRC risk.
Conclusions:

These findings suggest that increasing amounts of non-walking exercise suggested a non-significantly reduced risk of colorectal cancer while walking does not. Further large population based prospective studies on physical activity (walking, non-walking, and total activities) are needed to evaluate effective frequency, duration and intensity of physical activity in relation to colon and rectal cancer prevention.

4.2 Introduction

Colorectal cancer (CRC) is the third most common cancer in Canada, with an estimated 22,500 new cases and 9,100 deaths in 2010 [11]. Engaging in physical activity has long been considered as an effective strategy for cancer prevention [12]. Comprehensive reviews found that increased physical activity is a substantial protective factor against colon or colorectal cancer [13-16]. A large number of prospective [17-20] and case-control [21, 22] studies have found statistically significant associations between physical activity and colon cancer, especially for men, while a few studies have examined associations in rectum cancer indicated no significant associations [23-25]. Studies have indicated that physical activity has differential effects on sub-site of colorectal cancer [190-194]. Therefore, the beneficial role of physical activity in the prevention of colon and/or rectal cancer is inconsistent and varied between women and men [17, 21, 25, 26, 150, 151]. The measurement of physical activity in these studies varied and was based on limited type of activity. The type, frequency, duration and intensity of activities are important components of public health knowledge as they pertain to reduce risk of colorectal cancer [12, 26]; however, this kind of information is limited.

Walking is one of the most common forms of moderate level physical activity among
middle-aged and older people [195]. Its impact on CRC risk has only been examined by a few studies [196-198]. Guidelines from the WHO Library Cataloguing in Publication Data [199], Centers for Disease Control and Prevention, American College of Sports Medicine [200], as well as the Surgeon General’s Report on Physical Activity and Health[201], all recommended at least 30 minutes of moderate intensity physical activity on five or more days a week and advise some regular vigorous exercise for better health. This differs from earlier guidelines that advised vigorous exercise for at least 20 minutes three or more times per week [202]. Although the guidelines can be easily met by most of the population, the potential benefits of moderate intensity physical activity, particularly the specific role of walking in cancer prevention, are unclear. In addition, the actual role of non-walking exercise against colorectal cancer remains relatively unexplored.

The purpose of this paper was to 1) examine the associations of walking, non-walking exercise, total recreational physical activity and colorectal cancer risk using the data-base of a large population based case-control study in Canada; 2) compare the roles of walking, and non-walking exercise in colorectal cancer risk; 3) examine whether different effects of physical activity on colorectal cancer exists between Ontario (ON) and Newfoundland and Labrador (NL).

4.3 Methods

Study population

This study used the data of Newfoundland and Ontario Colorectal Cancer case-control study. Incident CRC cases were recruited from the provincial cancer registries, resulting in the establishment of Ontario Familial Colorectal Cancer Registry (OFCCR) and Newfoundland Familial Colorectal Cancer Registry (NFCCR). Cases aged 20-74 years and
diagnosed during 1997-2000 (phase I), 2003-2006 (phase II) in ON, and 2003-2006 in NL were identified; and their pathology reports were verified by study staff (pathology confirmed ICD 9th revision codes: 153.0-153.9, 154.1-154.3, and 154.8; or ICD-0 codes: 18.0-18.7, 19.9, 20.9).

Controls were a random sample of residents aged 20-74 years old in ON and NL. In Ontario, controls were recruited through a list of residential phone numbers or population-based assessment rolls provided by Bell Canada and the provincial government, respectively. In NL, controls were identified through random digit dialing.

Data collection

Once verbal consent for participation was attained through telephone contact, a survey package was forwarded to each potential participant. The package contained a pamphlet of general information concerning the study, a consent form, a self-administered Personal History Questionnaire (PHQ), Food Frequency Questionnaire (FFQ), Family History Questionnaire (FHQ), and a self-addressed stamped envelope. If a participant did not return complete questionnaires within 6-8 weeks, and a follow-up telephone call were sent to ensure that participants received and returned the study package. A telephone interview or assistance was offered when illiteracy or physical disability was a concern.

Measures of exposure

The PHQ was designed to investigate 74 items of information on participants, addressing detailed demographic characteristics, medical conditions, physical activity, screening history, use of medication, and the consumption of alcohol and tobacco. Among female participants, additional questions regarding reproductive concerns were surveyed. The FFQ administered
in the ON population was the well-known Hawaii FFQ. The FFQ in NL was adapted to address the unique food consumption pattern of that province. The NL FFQ was a revision of the FFQ used in Ontario. Participants were asked to estimate the frequency and portion size of food items one year prior to their diagnosis or participation in this study.

Recreational physical activity was measured using PHQ by 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 sports during their 20-30’s, 30-50’s, and 50’s and beyond. The questions regarding physical activity were “In your 20’s, did you participate regularly in physical activity for a total of at least 30 minutes a week? Please describe your activities below. Walking-yes or no; For how many years? During those months, on average, for how many minutes or hours per week?” The same questions were asked of jogging, running, bicycling, swimming and so on addressing three periods in total (20-30’s, 30-50’s, and 50’s plus). Participants were asked to specify the frequency and duration of activities which our survey questionnaire did not specify but yet participants considered being recreational exercise.

The derived time, taking frequency and duration into consideration, spent on each exercise after the participant reached the age of 20 was multiplied by its specific metabolic equivalents score (METs) to yield a MET-hour score [186, 187]. Average weekly MET hours for walking, non-walking exercise and total recreational physical activity were calculated. Next, walking, non-walking exercise and total recreational physical activity were further divided into quintiles according to percentage distribution of controls (<Q20, <Q40, <Q60, <Q80, ≥Q80).
For the analysis, participants with implausibly high or low total energy intakes (<2.5% or >2.5%: in NL, 925 and 4700 kcal for men; 1100 and 4900 kcal for women; in ON, 1040 and 5200 kcal for men; 835 and 4100 kcal for women) [183], and the patients who had familial adenomatous polyposis (FAP) and an in-situ tumor were excluded from the analysis. After these exclusions, based on those who completed both the PHQ and FFQ, 3102 subjects (1272 cases and 1830 controls) from ON and 1139 subjects (488 cases and 651 controls) from NL remained for the analysis.

Statistical analysis

Potential confounding covariates were selected based on their observed relationships to colorectal cancer through Chi-square testing ($P<0.10$) and previous studies that suggested plausible associations with physical activity and colorectal cancer. Covariates included in the final multivariate model were age; sex; household income ($<$12,000, 12,000-29,999, 30,000-49,999, $\geq$50,000); education (lower than high school, high school graduate, college, bachelor or higher); marital status (married, single or never married, separated or divorced or widowed); diabetes (yes or no); hypercholesterolemia (yes or no); use of aspirin (yes or no), non-steroidal anti-inflammatory drugs (yes or no), laxatives (yes or no), and alcohol (unit in gram); total intake of iron (unit in milligram), calcium (unit in milligram), vitamin D (unit in microgram), dietary fibre (unit in gram), folate acid (unit in microgram) and saturated fat (unit in gram); total energy intake (kCal); pack years of smoking ($<$1 year, $<$10, $<$20, $<$40, $\geq$40); Body Mass Index (underweight $<$18.5, normal18.5-25, overweight $\geq$25) and BMI change (BMI 2 years before diagnosis minus BMI in their 20’s).

Descriptive statistics were used to compare characteristics of cases and controls. The study used multivariate logistic regression to estimate Odds Ratios (OR) and a 95%
Confidence Interval (95%CI) of the associations between different levels of walking, non-walking, total recreational physical activity and colorectal cancer after adjusting for potential confounders. \( P \) values for linear trend were assessed by modeling the median value of each category (MET hours per week) of walking, non-walking, and total recreational activities. The interactions between quintiles of physical activity and Body Mass Index (underweight\(<18.5\), normal\(18.5\)–\(25\), overweight\(\geq25\)) were evaluated. All tests of statistical significance were two-sided. SAS 9.1 has been used in statistical analysis (version 9.1 SAS Institute, Cary, NC, USA).

### 4.4 Results

**Participant characteristics**

The final analysis included 1272 cases and 1830 controls in Ontario, 488 cases and 651 controls in NL. There was no sex difference between cases and controls in both provinces.

In Ontario, cases were younger than controls and had higher proportions of diabetes; first degree relatives with CRC; laxatives use; non-steroidal anti-inflammatory drugs use; overweight at the age of 20s; polyps; dietary intakes of energy, iron, and total saturated fat; yet lower dietary intakes of calcium and vitamin D; lower percentage of CRC screening; and lower educational level. In NL, cases were older and had higher rates of diabetes; first degree relatives with CRC; former and/or current smoking; laxatives use; overweight; polyps; and dietary intakes of total energy, iron, and total saturated fat; but lower dietary intakes of vitamin D; lower percentage of CRC screening; lower education level and lower household income. See Table 4.6.1 for details.

In Ontario, men who fell into different recreational physical activity levels had significantly distinct dietary intake levels of total energy, saturated fat, calcium, vitamin D,
and folic acid, BMI, the proportion of current and/or past smokers, education level and regular multivitamin use. For Ontario women, the proportion on hormone replacement treatment; the regular use of multivitamin supplement; and the dietary consumption of total energy, calcium, vitamin D, folic acid, fruits and vegetables substantially varied across physical activity levels. In NL, men who were in different categories of physical activity appeared to have different levels of education, income, dietary intake of total energy and saturated fat intake. For NL women, education level; income; and dietary intakes of vitamin D, fruits and vegetables varied with quintiles of physical activity. See Table 4.6.2 and 4.6.3 for details.

For men in Ontario, age-adjusted regression analysis suggested that the highest quintile of walking was related to an increase in risk of colorectal cancer (OR=1.37, 95%CI=1.00-1.89); non-walking exercise was inversely associated with risk of colorectal cancer although the associations were not statistically significant (Odds Ratios, 1.00, 0.79, 0.59, 0.75, 0.95, respectively); and no dose-response relationship was observed (P for trend 0.34); for increasing total physical activity levels, only the second and the third quintiles of exercise were significantly associated with reduction in risk (OR=0.71, 95%CI=0.51-0.98; OR=0.63, 95%CI=0.46-0.88). Multivariable analysis showed that no significant associations were observed between walking, non-walking exercise, total recreational physical activity and CRC risk. The overall directions of associations examined in multivariable analysis were similar with that in age-adjusted regression analysis. See Table 4.6.4 for details.

For women in Ontario, the highest level of walking in multivariable analysis was significantly associated with increased CRC risk (OR=1.75, 95%CI=1.01-3.00) while the second quintile of total recreational physical activity in age-adjusted regression analyses
reduced the CRC risk (OR=0.73, 95%CI=0.53-1.00). All other age-adjusted analyses and multivariable analyses showed non-significant associations of CRC risk as in males. Therefore, a combined analysis of both sexes was done to examine possible overall associations. As was found in the individual analysis of men and women, the highest level of walking in multivariable analysis was significantly associated with increased CRC risk (OR=1.51, 95%CI=1.07-2.13). Non-walking exercise was inversely associated with reduced CRC risk but the associations were non-significant. See Table 4.6.4 for details.

In NL, the overall risk reductions for walking, non-walking exercise and total physical activity were not significant with the exception that the highest level of walking was associated with increased CRC risk for men in age-adjusted regression analysis (OR=2.10, 95%CI=1.31-3.39), multivariable analysis (OR=2.28, 95%CI=1.28-4.05) and the combined sexes group in multivariable analysis (OR=2.01, 95%CI=1.25-3.22). Although non-walking exercise was linked to CRC risk reduction, only the fourth quintile compared to the lowest quintile showed the significant reduced risk for women in age-adjusted regression analysis (OR=0.53, 95%CI=0.29-0.98). See Table 4.6.5 for details.

The results of the ON and NL populations were similar; therefore, a pooled analysis was performed to examine the effects of walking, non-walking exercise, and total recreational physical activity on CRC. Results from this investigation showed that the highest quintile of walking was associated with increased colorectal cancer risk for both males and females in both provinces (highest VS lowest: OR=1.70, 95%CI=1.09-2.66). Non-walking exercise was not significantly associated with reduced risk of colorectal cancer for both sexes and provinces. Middle levels of total recreational physical activity were not substantially associated with CRC risk reduction while the 5th quintile of total recreational physical activity
suggested an increased risk of colorectal cancer (highest VS lowest: OR=1.10, 95%CI=0.86-1.41). See Table 4.6.6 for details.

When considering that exercise may have differential effect on colon and rectum cancers, we additionally performed extra sub-site analysis. In ON, walking was associated with borderline significantly increased rectum risk for men (OR=1.02, 95%CI=1.00-1.04, P for trend 0.04) and the combined sexes group (OR=1.01, 95%CI=1.00-1.03, P for trend 0.05) but not for women. In NL, the highest level of walking was associated with increased rectum cancer for men (OR=3.39, 95%CI=1.64-7.01), women (OR=7.27, 95%CI=1.53-34.45) and both sexes (OR=3.71, 95%CI=1.98-6.96). The details are not shown in tables.

4.5 Discussions

In this large Canadian population based case-control study, we found that non-walking exercise were indicated to be inversely associated with lower risk of colorectal cancer while the highest level of walking and total recreational activity were linked to an increased colorectal cancer risk in both Ontario and Newfoundland and Labrador.

Walking is a common form of moderate exercise [195, 199]; however, only a few studies have been implemented to investigate its role in cancer prevention. The evidence that walking alone can be considered as an effective cancer prevention strategy is inconsistent [12, 25, 196, 203]. One cohort study in Japan indicated that walking daily was inversely associated with colon risk in men but not women [203]. The same study found that walking did not reduce the risk of rectal cancer [203]. However, the statistical power in this study is limited because of its small sample of cases [203]. Another two prospective studies were not able to demonstrate that walking as a sole means of exercise had a significant beneficial role in
colorectal cancer prevention [12, 25]. Studies have also indicated that a vigorous walking pace was more useful in CRC prevention as compared to a longer time spent walking [25, 204].

The phenomenon seen in the results of this study that the highest category of walking was associated with higher CRC risk was unexpected. It may be explained by several estimations but there was no sufficient evidence. From the aspect of data collection, recall and differential bias could exist in this case-control study, which may have resulted in misclassified physical activity levels for participants. Since walking is a common exercise, it was possibly more common for participants to report inaccurate levels. In total, 32.11% cases and 32.38% of controls have missing information or reported an extremely low level (≤0.05 MET hours per week) of exercise. The validity of this study could be compromised due to large amounts of missing information on main exposures. In addition, cases were aware of their disease status; hence, they were more willing to report their past exposures compared to controls. It is also possible that there are some covariates that have a greater impact on CRC risk than physical activity when physical activity reaches certain levels since we only found the highest level of walking was associated with an increased CRC risk. Thun et al [20] found that physical activity is a weaker protective factor in the prevention of colorectal cancer compared to aspirin use and dietary intake of vegetables and grains. Not all of the studies found consistent beneficial effect of leisure time activity [17]. In addition, the NL population has higher genetic predisposition for CRC and more unique lifestyle factors as compared to many other population groups, even within Canada [180, 205]. This may have more relevance than physical activity to CRC prevention. Besides, this study did not collect information on the walking pace, which is a key measurement of intensity for walking. This lack of detailed information may influence the results as well. Occupational physical activity
was not included in the analysis because the data regarding occupational physical activity was not available for this analysis. Hopefully, education levels and incomes could explain a proportion of the variation associated with the occupation.

A large body of literature suggests that intense activity is needed to decline the colorectal cancer risk and approximate 3 to 4 hours per week is required to reduce the risk [12, 18, 151, 192, 199, 206]. Slattery [192] reported that lower risk of colon cancer was found to be associated with long term vigorous but not moderate activity. Another study has indicated that association was strongest for intense activities among men [26]. Chao et al [207] indicated that walking plus performing other activities showed more clear risk reduction than walking alone. Our study observed non-walking exercise (which is composed of vigorous exercise and other types of physical activity except walking) had a much stronger association with CRC risk reduction than walking alone, which is consistent with these studies. Our preliminary analysis found that cases and controls took part in similar amounts of non-walking exercise in this study; therefore, the non-significant associations between non-walking exercise, total recreational physical activity and CRC risk were acceptable in this study.

Many past studies have found that physical activity in general was an independent factor of colorectal cancer prevention [12, 15, 20, 24, 208]. Studies have also suggested that physical activity is beneficial for the prevention of colon cancer but no similar results were found for rectal cancer [24, 196, 208]. Two studies have shown that increased physical activity was linked with a non-significant increase in CRC risk [18, 209]. One meta-analysis indicated that physical activity was not associated with decreased risk of rectal cancer [14]. We only observed that the highest level of walking was associated with rectal cancer in men,
women and both sexes combined groups. We did not find that the interactions of physical inactivity and obesity together affect the risk of CRC. This is consistent with results from another study, which suggested physical activity is independently associated with CRC risk rather than acting through BMI [12].

Several biological mechanisms have been proposed to explain the association between physical activity and colorectal cancer. Physical activity shortens the fecal transit time; therefore, decreases the exposure time of epithelium to carcinogens [210]. Physical inactivity is associated with insulin resistance and a hyper-insulinemic state which leads to colorectal cancer through growth factors [211]. Physical activity may act through the immune system to produce anti-inflammatory cytokines and an increase of cytokine inhibitors [212-215] that inhibit colonic cell proliferation and decrease colonic motility. Vigorous physical activity is needed for stimulation of the vagus nerve responsible for increasing propulsion [216, 217], which supports the observation that intense activities are most protective.

Some colorectal cancer case-control studies examined the most recent physical activity; however, these studies did not investigate a long term physical activity as we did in this study. In this large Canadian population based case-control study of colorectal cancer, we investigated participant’s self-reported exercise from the age of 20 with specific, details on type, frequency and duration of exercise allowing MET hours of exercise per week to be calculated. In addition, we collected information on demographic characteristics, diet, family history medical conditions, and lifestyles through self-administrated questionnaires [180, 205]. The study enabled us to investigate multiple potential confounders and effect modifiers.

As in most of the case-control studies, selection bias should be a concern because
controls might care more about their healthy lifestyles and consequently be much more willing to participate in this kind of study. Another limitation of this study is the ability of the study subjects to accurately recall their past physical activity or even their other lifestyle factors that are used as covariates in our study. Currently, better techniques are not yet available to monitor physical activity in large population groups and physical activity has been proven to be important; therefore should be monitored thus we have little choice but to collect data through self-administered questionnaires. Differential misclassification of physical activity reports between cases and controls may exaggerate the increased risk of exercise in this study. Both the selection and recall bias impact the reliability and validity of findings. Future prospective cohort studies could minimize these bias and provide more reliable data.

Our results show that increasing amounts of non-walking exercise non-significantly reduces the risk of colorectal cancer. Walking alone does not seem to be a strong effective strategy for the prevention of colorectal cancer. The frequency, duration and intensity of exercise appear to be important and should be considered when making public health recommendations. Further population based prospective studies on physical activity are needed to evaluate the effect of frequency, duration and intensity of physical activity in relation to colon and rectal cancer prevention.

4.6 Tables
Table 4.6.1 Selected demographic and lifestyle characteristics of cases and controls of the
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Ontario Case (N=1272)</th>
<th>Ontario Control (N=1830)</th>
<th>Newfoundland and Labrador Case (N=488)</th>
<th>Newfoundland and Labrador Control (N=651)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>1272</td>
<td>1830</td>
<td>488</td>
<td>651</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58.4±10.9*</td>
<td>61.5±9.6</td>
<td>61.9±9.0*</td>
<td>59.8±9.4</td>
</tr>
<tr>
<td>Polyps</td>
<td>626(49.2)*</td>
<td>180(9.8)</td>
<td>235(48.0)*</td>
<td>84(12.9)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs use</td>
<td>433(34.0)*</td>
<td>787(43.0)</td>
<td>164(33.5)</td>
<td>252(38.7)</td>
</tr>
<tr>
<td>Any laxatives use</td>
<td>237(18.6)*</td>
<td>191(10.4)</td>
<td>40(8.2)*</td>
<td>35(5.3)</td>
</tr>
<tr>
<td>Current and/or past smoker</td>
<td>733(57.6)</td>
<td>1078(58.9)</td>
<td>353(72.3)*</td>
<td>400(61.5)</td>
</tr>
<tr>
<td>Overweight</td>
<td>769(62.4)</td>
<td>1032(60.1)</td>
<td>346(71.0)*</td>
<td>441(67.8)</td>
</tr>
<tr>
<td>Overweight in 20 years old</td>
<td>266(20.9)*</td>
<td>290(15.8)</td>
<td>98(20.1)</td>
<td>113(17.4)</td>
</tr>
<tr>
<td>Higher Household income</td>
<td>570(44.8)</td>
<td>868(47.4)</td>
<td>118(24.2)*</td>
<td>241(37.0)</td>
</tr>
<tr>
<td>Higher Education</td>
<td>706(55.5)*</td>
<td>1092(59.7)</td>
<td>181(37.1)*</td>
<td>353(54.2)</td>
</tr>
<tr>
<td>First degree relatives with CRC(%)</td>
<td>341(26.8)*</td>
<td>223(12.2)</td>
<td>163(33.4)*</td>
<td>114(17.5)</td>
</tr>
<tr>
<td>Reported any screening</td>
<td>199(15.6)*</td>
<td>476(26.0)</td>
<td>60(12.3)*</td>
<td>145(22.3)</td>
</tr>
<tr>
<td>Total energy intake (kCal/day)</td>
<td>2266.0±796.1*</td>
<td>2161.5±757.7</td>
<td>2367.0±838.2*</td>
<td>2236.3±744.9</td>
</tr>
<tr>
<td>Fibre intake</td>
<td>25.5±10.7</td>
<td>25.5±11.3</td>
<td>21.2±9.6</td>
<td>21.7±11.3</td>
</tr>
<tr>
<td>Iron intake</td>
<td>30.5±40.8*</td>
<td>25.1±22.8</td>
<td>22.4±90.3*</td>
<td>18.6±33.1</td>
</tr>
<tr>
<td>Total saturated fatty acid</td>
<td>27.5±12.2*</td>
<td>25.7±11.7</td>
<td>28.4±12.8*</td>
<td>26.6±12.1</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>14.8±27.9</td>
<td>13.9±24.1</td>
<td>9.2±22.4</td>
<td>7.8±20.0</td>
</tr>
<tr>
<td>Calcium intake</td>
<td>1163.7±565.0*</td>
<td>1213.1±623.3</td>
<td>976.4±515.7</td>
<td>1040±571.8</td>
</tr>
<tr>
<td>Vitamin D intake</td>
<td>8.1±5.6*</td>
<td>8.7±6.1</td>
<td>8.00±6.4*</td>
<td>9.2±7.5</td>
</tr>
<tr>
<td>Folate acid intake</td>
<td>967.3±542.7</td>
<td>1007.4±596.2</td>
<td>384.3±206.5*</td>
<td>423.2±239.3</td>
</tr>
</tbody>
</table>

* Continuous variables were presented as mean±SD (standard deviation). The differences between cases and controls were based on t-tests.

b Categorical variables were presented as number(%). The differences between cases and controls were based on chi-square tests.

c High level of education included some college, university or post-secondary school; High household income included an average household income>$50,000/year.

Significant difference between cases and controls (p<0.05).
Table 4.6.2 Selected demographic and lifestyle characteristics of cases and controls among men by province and physical activity level \(^a\)\(^b\)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>314</td>
<td>305</td>
<td>309</td>
<td>345</td>
<td>338</td>
<td>139</td>
<td>109</td>
<td>133</td>
<td>140</td>
<td>159</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>61.3</td>
<td>61.0</td>
<td>60.5</td>
<td>61.5</td>
<td>62.0</td>
<td>63.0</td>
<td>61.6</td>
<td>61.4</td>
<td>62.0</td>
<td>61.8</td>
</tr>
<tr>
<td>Mean BMI (kg/m2)</td>
<td>27.5</td>
<td>26.3</td>
<td>27.2</td>
<td>26.9</td>
<td>27.3*</td>
<td>28.4</td>
<td>27.2</td>
<td>28.0</td>
<td>27.4</td>
<td>27.9</td>
</tr>
<tr>
<td>Polyps (%)</td>
<td>30.8</td>
<td>24.2</td>
<td>24.2</td>
<td>26.0</td>
<td>31.3</td>
<td>31.8</td>
<td>27.6</td>
<td>30.3</td>
<td>30.9</td>
<td>32.7</td>
</tr>
<tr>
<td>Regular Multivitamin use (%)</td>
<td>28.0</td>
<td>35.4</td>
<td>38.2</td>
<td>37.5</td>
<td>31.2*</td>
<td>16.8</td>
<td>17.4</td>
<td>14.4</td>
<td>20.0</td>
<td>22.2</td>
</tr>
<tr>
<td>Current and/or ever smokers (%)</td>
<td>68.3</td>
<td>69.0</td>
<td>62.7</td>
<td>63.3</td>
<td>68.6*</td>
<td>82.4</td>
<td>77.1</td>
<td>75</td>
<td>70.5</td>
<td>72.8</td>
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<tr>
<td>Higher education (%)^c</td>
<td>54.1</td>
<td>64.9</td>
<td>65.1</td>
<td>59.7</td>
<td>55.0*</td>
<td>40.3</td>
<td>52.3</td>
<td>57.9</td>
<td>53.6</td>
<td>33.3*</td>
</tr>
<tr>
<td>Higher income (%)^c</td>
<td>36.6</td>
<td>38.4</td>
<td>38.2</td>
<td>37.1</td>
<td>34.9</td>
<td>25.9</td>
<td>39.5</td>
<td>38.4</td>
<td>35.0</td>
<td>26.4*</td>
</tr>
<tr>
<td>First degree relatives with CRC (%)</td>
<td>15.6</td>
<td>18.4</td>
<td>15.2</td>
<td>13.6</td>
<td>20.1</td>
<td>23.7</td>
<td>23.9</td>
<td>26.3</td>
<td>24.3</td>
<td>23.3</td>
</tr>
<tr>
<td>Reported any screening (%)</td>
<td>27.1</td>
<td>26.9</td>
<td>26.2</td>
<td>23.8</td>
<td>24.0</td>
<td>16.9</td>
<td>16.4</td>
<td>19.6</td>
<td>19.4</td>
<td>17.8</td>
</tr>
<tr>
<td>Mean daily intakes</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruit servings per week</td>
<td>9.0</td>
<td>9.3</td>
<td>10.0</td>
<td>9.4</td>
<td>9.8</td>
<td>7.9</td>
<td>9.3</td>
<td>8.5</td>
<td>8.4</td>
<td>8.5</td>
</tr>
<tr>
<td>Vegetables servings per week</td>
<td>10.3</td>
<td>11.0</td>
<td>11.0</td>
<td>11.7</td>
<td>10.9</td>
<td>9.8</td>
<td>9.6</td>
<td>9.5</td>
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<td>10.9</td>
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<td>Red meat servings per week</td>
<td>4.2</td>
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<td>4.4</td>
<td>4.7</td>
<td>4.7</td>
<td>3.8</td>
<td>3.3</td>
<td>3.4</td>
<td>3.6</td>
<td>4.0</td>
</tr>
<tr>
<td>Total energy intake (Kcal/day)</td>
<td>2333.5</td>
<td>2284.7</td>
<td>2460.2</td>
<td>2358.3</td>
<td>2576.2*</td>
<td>2311.4</td>
<td>2311.3</td>
<td>2319.5</td>
<td>2488.4</td>
<td>2577.1*</td>
</tr>
<tr>
<td>Total fibre</td>
<td>24.2</td>
<td>25.1</td>
<td>26.7</td>
<td>26.0</td>
<td>27.5*</td>
<td>20.7</td>
<td>21.7</td>
<td>21.1</td>
<td>21.9</td>
<td>22.3</td>
</tr>
<tr>
<td>Iron</td>
<td>22.8</td>
<td>25.4</td>
<td>26.2</td>
<td>27.7</td>
<td>26.8</td>
<td>18.1</td>
<td>19.7</td>
<td>31.7</td>
<td>17.7</td>
<td>31.4</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>27.9</td>
<td>27.1</td>
<td>29.4</td>
<td>29.0</td>
<td>31.5*</td>
<td>27.5</td>
<td>27.9</td>
<td>27.4</td>
<td>30.1</td>
<td>32.0*</td>
</tr>
<tr>
<td>Alcohol (g)</td>
<td>20.9</td>
<td>17.9</td>
<td>21.7</td>
<td>18.0</td>
<td>21.7</td>
<td>12.4</td>
<td>9.5</td>
<td>16.6</td>
<td>18.2</td>
<td>15.3</td>
</tr>
<tr>
<td>Calcium</td>
<td>1004.9</td>
<td>1046.8</td>
<td>1151.1</td>
<td>1126.8</td>
<td>1170.6*</td>
<td>898.8</td>
<td>973.3</td>
<td>996.2</td>
<td>1032.6</td>
<td>1000.9</td>
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<tr>
<td>Vitamin D</td>
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<td>8.5</td>
<td>8.4</td>
<td>8.7</td>
<td>8.5*</td>
<td>8.3</td>
<td>9.3</td>
<td>9.0</td>
<td>9.1</td>
<td>8.7</td>
</tr>
<tr>
<td>Folate acid</td>
<td>893.9</td>
<td>983.1</td>
<td>1031.0</td>
<td>1046.7</td>
<td>1005.2*</td>
<td>359.8</td>
<td>396.1</td>
<td>385.3</td>
<td>392.0</td>
<td>391.1</td>
</tr>
</tbody>
</table>

^a Continuous variables were presented as means. Category variables were presented in proportions.

^b Categorical variables were presented as number(%). The differences between cases and controls were based on chi-square tests.

^c High level of education included some college, university or post-secondary school; High household income included an average household income>50,000/year.

* Significant difference between cases and controls (p≤0.05).
| Characteristics                                      | Ontario |             |             |              | Newfoundland and Labrador | Q1 | Q2 | Q3 | Q4 | Q5 | Q1 | Q2 | Q3 | Q4 | Q5 |
|------------------------------------------------------|---------|-------------|-------------|--------------|---------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| No of participants                                   | 344     | 306         | 304         | 264          | 273                       | 98 | 116| 92 | 87 | 66 |     |    |    |    |    |    |    |
| Mean age (years)                                     | 59.1    | 58.6        | 58.3        | 59.3         | 60.3                      | 60.8| 60.6| 59.6| 60.9| 61.4|
| Mean BMI (kg/m2)                                     | 26.3    | 26.1        | 25.7        | 25.4         | 25.8                      | 27.4| 26.3| 27.2| 26.7| 27.1|
| Polyps (%)                                           | 23.6    | 19.0        | 28.6        | 27.8         | 21.5*                     | 22.7| 27.0| 20.0| 24.4| 25.0|
| Regular Multivitamin supplement use (%)              | 36.0    | 44.8        | 43.7        | 48.3         | 42.3*                     | 16.7| 33.6| 29.4| 29.4| 22.7|
| Current smokers (%)                                  | 20.0    | 17.8        | 14.5        | 15.3         | 13.7                      | 16.3| 15.7| 14.1| 16.3| 21.2|
| Higher education (%)                                 | 49.7    | 58.8        | 59.2        | 65.5         | 48.7*                     | 32.7| 61.2| 53.3| 51.7| 28.8*|
| Higher income (%)                                    | 33.7    | 37.6        | 37.5        | 37.5         | 28.6                      | 22.5| 37.1| 37.0| 34.5| 13.6*|
| First degree relatives with CRC (%)                 | 19.5    | 18.6        | 19.4        | 21.6         | 20.9                      | 30.6| 25.9| 19.6| 21.8| 22.7|
| Reported any screening (%)                           | 15.7    | 22.6        | 17.1        | 18.6         | 14.3                      | 20.4| 13.8| 22.8| 16.1| 16.7|
| Hormones replace treatment (%)                       | 31.7    | 42.9        | 49.2        | 43.6         | 37.4*                     | 39.2| 34.8| 33.7| 34.9| 22.8|
| Mean daily intakes                                   |         |             |             |              |                           |     |    |    |    |    | 11.0| 12.2| 14.0| 13.7| 13.7*|
| Fruit servings per week                              | 11.0    | 12.2        | 14.0        | 13.7         | 13.7*                     | 10.6| 13.1| 13.4| 14.4| 11.1*|
| Vegetables servings per week                         | 13.8    | 15.8        | 16.8        | 18.0         | 16.5*                     | 11.9| 14.3| 15.4| 15.1| 10.8*|
| Red meat servings per week                           | 4.3     | 4.1         | 3.8         | 3.9          | 3.7                       | 3.4 | 3.4 | 4.0 | 3.0 | 3.4 |
| Total energy intake (Kcal/day)                       | 1941.9  | 1923.4      | 2039.5      | 1960.1       | 2088.5*                   | 2206.5| 2361.7| 2203.9| 2249.5| 2365.7|
| Total fibre (g/day)                                  | 23.4    | 23.3        | 26.1        | 25.7         | 27.1*                     | 21.6| 24.6| 23.1| 24.4| 24.0|
| Iron (mg/day)                                        | 31.0    | 24.4        | 30.4        | 29.7         | 28.8                      | 27.7| 19.0| 33.8| 28.3| 27.1|
| Saturated fat (g/day)                                | 23.2    | 23.5        | 23.9        | 22.7         | 24.7                      | 27.8| 27.9| 26.8| 25.9| 28.3|
| Alcohol (g/day)                                      | 7.7     | 8.1         | 5.8         | 10.7         | 7.5                       | 2.1 | 4.6 | 3.3 | 4.1 | 2.6 |
| Calcium (mg/day)                                     | 1202.0  | 1207.6      | 1382.0      | 1368.1       | 1322.4*                   | 1035.7| 1306.8| 1170.8| 1186.3| 1110.4|
| Vitamin D (mg/day)                                   | 8.1     | 8.2         | 9.4         | 9.1          | 9.1*                      | 7.7 | 11.1| 9.4 | 11.8| 9.1*|
| Folate acid (mg/day)                                  | 896.2   | 940.0       | 1029.3      | 1030.8       | 1073.5*                   | 370.3| 472.5| 438.7| 479.7| 429.6|

*Continuous variables were presented as means. Category variables were presented in proportions.

Categorical variables were presented as number(%). The differences between cases and controls were based on chi-square tests.

High level of education included some college, university or post-secondary school; High household income included an average household income> $50,000/year.

*Significant difference between cases and controls (p<0.05).
Table 4.6.4 Odds ratio and 95% CI for the association between physical activity and colorectal cancer risk stratified by sex in Ontario

<table>
<thead>
<tr>
<th>Quintile (MET hours per week)</th>
<th>Men</th>
<th>Women</th>
<th>Women &amp; men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases^a</td>
<td>Controls</td>
<td>Age adjusted OR</td>
</tr>
<tr>
<td>Walking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>21.7</td>
<td>22.4</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>17.7</td>
<td>17.0</td>
<td>1.17 (0.84-1.64)</td>
</tr>
<tr>
<td>Q3</td>
<td>17.1</td>
<td>19.8</td>
<td>1.03 (0.74-1.44)</td>
</tr>
<tr>
<td>Q4</td>
<td>17.9</td>
<td>19.8</td>
<td>1.09 (0.78-1.53)</td>
</tr>
<tr>
<td>Q5</td>
<td>25.6</td>
<td>21.0</td>
<td>1.37 (1.00-1.89)</td>
</tr>
<tr>
<td>P for trend^e</td>
<td>0.12</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Non-walking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>25.0</td>
<td>18.9</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>18.0</td>
<td>19.3</td>
<td>0.79 (0.57-1.11)</td>
</tr>
<tr>
<td>Q3</td>
<td>15.9</td>
<td>22.2</td>
<td>0.59 (0.42-0.84)</td>
</tr>
<tr>
<td>Q4</td>
<td>19.1</td>
<td>20.8</td>
<td>0.75 (0.54-1.06)</td>
</tr>
<tr>
<td>Q5</td>
<td>22.0</td>
<td>18.8</td>
<td>0.95 (0.67-1.33)</td>
</tr>
<tr>
<td>P for trend^e</td>
<td>0.34</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>Total activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>21.8</td>
<td>18.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>17.4</td>
<td>19.9</td>
<td>0.71 (0.51-0.98)</td>
</tr>
<tr>
<td>Q3</td>
<td>16.6</td>
<td>20.8</td>
<td>0.63 (0.46-0.88)</td>
</tr>
<tr>
<td>Q4</td>
<td>20.0</td>
<td>22.4</td>
<td>0.73 (0.53-1.01)</td>
</tr>
<tr>
<td>Q5</td>
<td>24.2</td>
<td>18.9</td>
<td>1.08 (0.79-1.48)</td>
</tr>
<tr>
<td>P for trend^e</td>
<td>0.045</td>
<td>0.21</td>
<td></td>
</tr>
</tbody>
</table>

^a The number of cases and controls in quintiles were represented as percentage.
^b OR: Odds Ratio; 95% CI: 95% confidence interval.
^c Adjusted for age, walking and non-walking exercise are mutually adjusted.
^d Adjusted for age, diabetes, BMI, first-degree relatives with CRC, polyps, smoking status, regular NSAID use, colorectal cancer screening, inflammatory colitis, daily total energy intake, total fibre, calcium, iron, folate acid, vitamin D, total saturated fatty acid intake, alcohol drinking, education attainment, household income, and hormone replacement treatment in women.
^e Linear trend was tested by modeling physical activity as continuous variables by using the median value of each category.
Table 4.6.5 Odds ratio and 95% CI for the association between physical activity and colorectal cancer risk stratified by sex in NL

<table>
<thead>
<tr>
<th>Quintile (MET hours per week)</th>
<th>Men</th>
<th>Women</th>
<th>Women &amp; men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=296)</td>
<td>Controls (N=384)</td>
<td>Age adjusted OR (95%CI)</td>
</tr>
<tr>
<td>Walking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>20.6</td>
<td>25.1</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>21.3</td>
<td>20.0</td>
<td>1.36 (0.84-2.20)</td>
</tr>
<tr>
<td>Q3</td>
<td>13.2</td>
<td>15.5</td>
<td>1.07 (0.63-1.83)</td>
</tr>
<tr>
<td>Q4</td>
<td>13.5</td>
<td>20.5</td>
<td>0.87 (0.52-1.47)</td>
</tr>
<tr>
<td>Q5</td>
<td>31.4</td>
<td>18.9</td>
<td>2.10 (1.31-3.39)</td>
</tr>
<tr>
<td>Non-walking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>19.2</td>
<td>19.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>17.9</td>
<td>17.7</td>
<td>0.82 (0.48-1.38)</td>
</tr>
<tr>
<td>Q3</td>
<td>20.3</td>
<td>21.6</td>
<td>0.80 (0.48-1.34)</td>
</tr>
<tr>
<td>Q4</td>
<td>18.6</td>
<td>21.1</td>
<td>0.70 (0.41-1.19)</td>
</tr>
<tr>
<td>Q5</td>
<td>24.0</td>
<td>20.6</td>
<td>0.89 (0.53-1.50)</td>
</tr>
<tr>
<td>Total activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
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<td>20.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Q2</td>
<td>14.2</td>
<td>17.5</td>
<td>0.80 (0.48-1.34)</td>
</tr>
<tr>
<td>Q3</td>
<td>18.2</td>
<td>20.6</td>
<td>0.88 (0.54-1.43)</td>
</tr>
<tr>
<td>Q4</td>
<td>18.2</td>
<td>22.4</td>
<td>0.80 (0.49-1.29)</td>
</tr>
<tr>
<td>Q5</td>
<td>28.4</td>
<td>19.5</td>
<td>1.44 (0.91-2.28)</td>
</tr>
</tbody>
</table>

* The number of cases and controls in quintiles were represented as percentage.
** OR: Odds Ratio; 95% CI: 95% confidence interval.
*** Adjusted for age, walking and non-walking exercise are mutually adjusted.
**** Adjusted for age, diabetes, BMI, first-degree relatives with CRC, polyps, smoking status, regular NSAID use, colorectal cancer screening, inflammatory colitis, daily total energy intake, total fibre, calcium, iron, folate acid, vitamin D, total saturated fatty acid intake, alcohol drinking, education attainment, household income, and hormone replacement treatment in women.
***** Linear trend was tested by modeling physical activity as continuous variables by using the median value of each category.
Table 4.6.6 Odds ratio and 95% CI for the association between physical activity and colorectal cancer stratified by sex in Ontario and NL

<table>
<thead>
<tr>
<th>Quintile (MET hours per week)</th>
<th>Cases(^a) (N=933)</th>
<th>Controls (N=1358)</th>
<th>Men Age adjusted OR (95% CI)(^b)</th>
<th>Multivariate OR (95% CI)(^d)</th>
<th>Cases (N=827)</th>
<th>Controls (N=1123)</th>
<th>Women Age adjusted OR (95% CI)(^b)</th>
<th>Multivariate OR (95% CI)(^d)</th>
<th>Women &amp; men Multivariate OR (95% CI)(^d)</th>
</tr>
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<tr>
<td>Walking</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>21.0</td>
<td>22.4</td>
<td>1.00</td>
<td>1.00</td>
<td>15.9</td>
<td>17.2</td>
<td>1.00 (0.84, 1.53)</td>
<td>1.14 (0.82, 1.52)</td>
<td>1.27 (0.91, 1.76)</td>
</tr>
<tr>
<td>Q2</td>
<td>19.2</td>
<td>18.6</td>
<td>1.16 (0.89, 1.52)</td>
<td>1.00 (0.69, 1.45)</td>
<td>23.1</td>
<td>21.7</td>
<td>1.19 (0.79, 1.80)</td>
<td>1.22 (0.80, 1.87)</td>
<td>1.22 (0.79, 1.86)</td>
</tr>
<tr>
<td>Q3</td>
<td>15.0</td>
<td>17.7</td>
<td>1.00 (0.75, 1.33)</td>
<td>1.08 (0.73, 1.61)</td>
<td>20.1</td>
<td>22.7</td>
<td>0.98 (0.72, 1.33)</td>
<td>1.33 (0.88, 2.03)</td>
<td>1.32 (0.87, 2.00)</td>
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<tr>
<td>Q4</td>
<td>15.4</td>
<td>18.8</td>
<td>0.98 (0.73, 1.30)</td>
<td>1.00 (0.67, 1.49)</td>
<td>21.8</td>
<td>21.4</td>
<td>1.12 (0.82, 1.52)</td>
<td>1.22 (0.80, 1.87)</td>
<td>1.22 (0.79, 1.86)</td>
</tr>
<tr>
<td>Q5</td>
<td>29.4</td>
<td>22.5</td>
<td>1.50 (1.16, 1.95)</td>
<td>1.64 (1.16, 2.31)</td>
<td>19.1</td>
<td>17.0</td>
<td>1.27 (0.91, 1.76)</td>
<td>1.69 (1.08, 2.65)</td>
<td>1.70 (1.09, 2.66)</td>
</tr>
<tr>
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<td>&lt;0.01</td>
<td></td>
<td></td>
<td>0.20</td>
<td>0.05</td>
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<td>&lt;0.01</td>
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<td></td>
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<tr>
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<td>23.9</td>
<td>19.6</td>
<td>1.00</td>
<td>1.00</td>
<td>26.6</td>
<td>23.3</td>
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<td>0.93 (0.64, 1.36)</td>
<td>0.93 (0.64, 1.37)</td>
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<tr>
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<td>18.8</td>
<td>0.81 (0.61, 1.07)</td>
<td>0.77 (0.52, 1.13)</td>
<td>20.3</td>
<td>20.8</td>
<td>0.95 (0.72, 1.26)</td>
<td>0.93 (0.64, 1.36)</td>
<td>0.93 (0.64, 1.37)</td>
</tr>
<tr>
<td>Q3</td>
<td>16.0</td>
<td>20.8</td>
<td>0.64 (0.48, 0.85)</td>
<td>0.79 (0.53, 1.16)</td>
<td>16.8</td>
<td>18.3</td>
<td>0.88 (0.65, 1.18)</td>
<td>0.87 (0.58, 1.31)</td>
<td>0.88 (0.58, 1.31)</td>
</tr>
<tr>
<td>Q4</td>
<td>18.5</td>
<td>20.5</td>
<td>0.74 (0.56, 0.98)</td>
<td>0.79 (0.53, 1.16)</td>
<td>17.8</td>
<td>18.7</td>
<td>0.91 (0.67, 1.23)</td>
<td>0.85 (0.57, 1.28)</td>
<td>0.86 (0.57, 1.28)</td>
</tr>
<tr>
<td>Q5</td>
<td>23.7</td>
<td>20.3</td>
<td>0.91 (0.69, 1.20)</td>
<td>0.80 (0.55, 1.17)</td>
<td>18.5</td>
<td>18.9</td>
<td>0.92 (0.68, 1.25)</td>
<td>0.80 (0.54, 1.21)</td>
<td>0.81 (0.54, 1.21)</td>
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<tr>
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<td>0.16</td>
<td></td>
<td></td>
<td>0.71</td>
<td>0.33</td>
<td></td>
<td></td>
<td>0.29</td>
</tr>
<tr>
<td>Total activity</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1</td>
<td>22.1</td>
<td>19.0</td>
<td>1.00</td>
<td>1.00</td>
<td>24.8</td>
<td>22.7</td>
<td>1.00 (0.61, 1.05)</td>
<td>1.07 (0.74, 1.55)</td>
<td>0.94 (0.72, 1.22)</td>
</tr>
<tr>
<td>Q2</td>
<td>15.5</td>
<td>18.5</td>
<td>0.71 (0.54, 0.94)</td>
<td>0.85 (0.58, 1.24)</td>
<td>18.7</td>
<td>21.4</td>
<td>0.80 (0.61, 1.05)</td>
<td>1.07 (0.74, 1.55)</td>
<td>0.94 (0.72, 1.22)</td>
</tr>
<tr>
<td>Q3</td>
<td>16.5</td>
<td>19.8</td>
<td>0.70 (0.53, 0.92)</td>
<td>0.89 (0.61, 1.29)</td>
<td>19.0</td>
<td>19.9</td>
<td>0.86 (0.65, 1.13)</td>
<td>1.00 (0.68, 1.46)</td>
<td>0.92 (0.71, 1.20)</td>
</tr>
<tr>
<td>Q4</td>
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<td>21.9</td>
<td>0.74 (0.57, 0.96)</td>
<td>0.98 (0.68, 1.40)</td>
<td>18.4</td>
<td>17.4</td>
<td>0.97 (0.73, 1.29)</td>
<td>1.06 (0.72, 1.56)</td>
<td>1.00 (0.77, 1.30)</td>
</tr>
<tr>
<td>Q5</td>
<td>27.0</td>
<td>20.8</td>
<td>1.12 (0.87, 1.44)</td>
<td>1.18 (0.84, 1.66)</td>
<td>19.1</td>
<td>18.6</td>
<td>0.96 (0.73, 1.27)</td>
<td>0.99 (0.68, 1.45)</td>
<td>1.10 (0.86, 1.41)</td>
</tr>
<tr>
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<td>0.09</td>
<td></td>
<td></td>
<td>0.61</td>
<td>0.90</td>
<td></td>
<td></td>
<td>0.22</td>
</tr>
</tbody>
</table>

\(^a\) The number of cases and controls in quintiles were represented as percentage.
\(^b\) OR: Odds Ratio; 95% CI: 95% confidence interval.
\(^c\) Adjusted for age, sex, and non-walking exercise are mutually adjusted.
\(^d\) Adjusted for age, sex, BMI, first-degree relatives with CRC, polyps, smoking status, regular NSAID use, colorectal cancer screening, inflammatory colitis, daily total energy intake, total fibre, calcium, iron, folate acid, vitamin D, total saturated fatty acid intake, alcohol drinking, education attainment, household income, and hormone replacement treatment in women.
\(^e\) Linear trend was tested by modeling physical activity as continuous variables by using the median value of each category.
Chapter 5  Project 2: Examining the Direct and Indirect Effects of Socioeconomic Status (SES) on Colorectal Cancer Risk using Structural Equation Modeling

5.1 Abstract

Background:
Existing epidemiologic studies have not investigated how risk factors work together to increase the incidence of colorectal cancer (CRC) so the true effect of each factor could be under- or over estimated. This study explored how socio-economic status (SES) directly influenced the risk of developing CRC and its mediated effect on CRC risk through diet pattern while adjusting for the possible risk factors of alcohol intake, smoking, physical inactivity, and obesity.

Methods:
This study used data collected from an existing population based case-control study of Newfoundland and Labrador, in which data pertaining to personal demographic characteristics, medical history, diet and other lifestyle factors were collected using self-administered questionnaires. Measurement and structural modeling was used to test conceptual models. Exploratory factor analysis was used to identify dietary patterns measured by 39 food groups. Then, the direct and intermediate effects of risk factors were examined using structural equation modeling.

Results:
The results from multivariate regression analysis indicated that age (OR=1.03), SES (OR=0.89), processed meat intake (OR=1.08), no CRC screening (OR=2.67), smoking (OR=1.44, 1.85 (ever, current)), and family history score of CRC (OR=1.06), were significantly associated with the risk of CRC. SES has a direct effect (β=0.05) on the risk of CRC. An indirect effect (β=0.06) of SES on CRC risk also existed by influencing processed
meat intake (β=0.01), vegetables intake (β=0.01), screening frequency (β=0.02), and smoking (β=0.02).

Conclusions:
This study suggested that the NL population has three major dietary patterns: (1) processed meats plus root vegetables; (2) vegetables; and (3) fruits. Structural equation modeling, a relatively new approach to epidemiology studies, provided unique information on the direct effect of socioeconomic status on the development of CRC but also SES’s indirect effect through a set of common CRC risk factors.

5.2 Introduction
Colorectal cancer (CRC) is the third most common type of cancer in Canadian males and females [11]. Inherited familial CRC explains about 10%-15% of all CRC cases [51-53]. The majority of CRC cases result from gene-environment interactions [52, 54, 55]. Lifestyle factors such as dietary intakes play an important role in the development of CRC.

Considering that 75%-85% of CRC are sporadic, identifying different pathways of CRC through examining its risk factors is of public health importance. Important modifiable risk factors for CRC include tobacco use, unhealthy diet, physical inactivity and excessive consumption of alcohol [47, 218].

A large number of existing epidemiological studies have investigated the associations of dietary factors [96, 124, 142, 219], physical inactivity [15, 17, 18, 150, 152, 220], smoking [158, 205, 221], alcohol consumption [161, 222, 223], and socioeconomic status [224] with the occurrence of CRC. One major limitation of traditional epidemiologic research is its focus on one major risk factors of interest while controlling for other covariates. This likely over simplifies the complicated and interdependent relationships among various candidate factors.
of interest [37]. Consequently, most reported studies have been unable to specify how these candidate risk factors work together to increase the occurrence of CRC and the true effect of each factor would be under-estimated [38-40]. Identifying major dietary patterns through exploratory factor analysis, a relatively new approach in epidemiology, has investigated the intercorrelations of multiple food items/nutrients simultaneously, which has overcome the limitation of partially examining dietary risk factors [225]. Therefore, studies such as this one, which are able to delineate and test how candidate risk factors are interrelated and jointly affect the occurrence of CRC, are expected to provide important insights into exploring the etiology of CRC.

Newfoundland and Labrador (NL) has the highest CRC incidence rate in Canada [11]. The province of NL is the eastern most part of North America. Compared with the rest of Canada, NL is geographically isolated and it has a homogeneous population, estimated to be of 98% English or Irish descent [226]. According to the 2006 Statistics Canada report, the population in NL is about 510,000 with over 40% of the residents living in rural communities [227]. Due to its distinct geography and heritage, NL is known for traditional foods, such as pickled meat and game (wild animal) meat [228]. Residents of NL are more likely to smoke cigarettes and less likely to engage in leisure time physical activity than other Canadians [205]; further, people in NL are believed to eat fewer fruits and vegetables and consume more preserved foods [180]. Given the distinct diet, lifestyles, and high CRC incidence rate, an investigation of the NL population should be ideal to explore the interrelationships of risk factors for CRC [180, 227].

Although the inter-dependent relationships among socioeconomic status (SES), lifestyles, diet, and health have been well recognized [41-43], their complex inter-relationships in
relevance to CRC have not been examined. The proposed research hypothesized that lower SES predisposes people to certain risk factors (e.g. fewer vegetables and fruits consumed, higher proportion of smoking, lower percentage participating in CRC screening, etc), which in turn may interact with genetic factors and lead to the occurrence of colorectal cancer. The objectives of this study were to: 1) explore the potential association among CRC risk factors; 2) posit a conceptual model that delineates the interrelationships with respect to how SES, dietary factors, and lifestyles work together to give rise to CRC; and 3) operationalize the proposed conceptual model using the database of Newfoundland and Ontario Colorectal-cancer Study (NOCS). It is important to note that only the NL data was used in this study.

5.3 Study Population and Methods

5.3.1 Study Population

The Newfoundland Cancer Treatment and Research Foundation data were used to identify newly diagnosed cases of colon or rectal cancer and cases were recruited into the Newfoundland Familial Colorectal Cancer Registry (NFCCR). Pathologists in the study confirmed the pathology reports of cases. Inclusion criteria for cases:

1) Incident primary invasive colon or rectal cancer [pathology confirmed International Classification of Diseases 9th revision codes: 153.0-153.9, 154.1-154.3 and 154.8 (ON & NL); or ICD-10 codes: 18.0-18.7, 19.9, 20.9 (NL only)];

2) Diagnosed between January 1999 and December 2003 in NL;

3) Diagnosed at ages between 20 and 74 years old; and

4) Residents of NL at the time of diagnosis.

Controls recruited by the NFCCR were comprised of a random sample of residents aged
20-74 years through random digit dialing [182]. Within a frequency matched case-control study, controls were 5-year age group and sex matched with the colorectal cancer cases. Initially, a set of 192,000 possible residential telephone numbers were generated and randomly arranged. Research assistants with prior experience in telephone surveying made the initial contacts by dialing those numbers in a sequential order until the desired number of controls was reached. A screening interview of potential control subjects was conducted to identify if any household member was eligible based upon their age, sex and willingness to participate in the study.

5.3.2 Data Collection

Once verbal consent for participation was obtained through telephone contact, a survey package was forwarded to each potential participant. The package included an information pamphlet with general information concerning the study, a consent form, a self-administered Personal History Questionnaire (PHQ), Food Frequency Questionnaire (FFQ), Family History Questionnaire (FHQ), as well as a self-addressed stamped envelope. If a participant did not return the completed questionnaires within three weeks, a follow-up telephone call was made to ensure the study package had been received. A telephone interview or assistance was offered when illiteracy or physical disability was a concern.

The PHQ was designed to investigate 74 items of information on participants including detailed information pertaining to demographic characteristics (age, sex and marital status), bowel screening history, medication use (non-steroidal anti-inflammatory drugs), physical activity (walking, jogging, running etc. both currently and during participant’s 20-30’s, 30-50’s, and 50’s+), alcohol consumption , tobacco use (never smoker, former smoker and current smoker), education (less than high school, high school, some college, bachelor or
higher), income (less than $12,000, $12,000-$29,999, $30,000-$49,999, $50,000 and higher), 
residence (rural or urban) and anthropometric measures (height and body mass index).

The FFQ was adapted from a FFQ for the previously validated multi-ethnic 
Hawaiian/Southern Californian to incorporate the unique food consumption pattern of the NL 
population. Participants were asked to estimate the frequency and portion size of 169 food 
items one year prior to their diagnosis for cases or participation in this study for controls. For 
each food item, subjects were asked to estimate the frequency of food consumption (daily, 
weekly, monthly or never) and their usual portion size (average, smaller or larger). 
Information on vitamin and other dietary supplements was also collected. Dietitians on the 
study team helped convert the 169 food items into units of daily grams of food for each 
participant. Foods were also categorized into thirty-nine groups. The food grouping was 
developed based upon the primary role of foods in the diet and their possible relationships 
with cancer etiology [141]. Food groups include milk, yogurt, coffee, tea, sugar, soft drinks, 
egg, cheese, mixed dishes, red meat, game, cured or processed red meat, cured or processed 
total meat, poultry, fish, processed fish, fruit juice, root vegetables, cruciferous vegetables, 
total cereals and grains, whole grains, deserts, sweets, vegetables juice, beer, white wine, red 
wine, liquor, citrus, berries, dried fruit, canned fruit, other fruit, pies, jam and pickled 
vegetables.

The FHQ collected information on the diagnosed type of cancer or tumour as well as the 
cancer history of participants. The same questions were asked of the participant’s mother, 
father, children, brothers and sisters, mother’s brothers and sisters, father’s brothers and 
sisters and other relatives who had also been diagnosed with cancer. Family history score was 
derived from collected information [229].
5.3.3 Statistical Analysis

For the analysis, participants with implausibly high or low total energy intakes (<2.5% or >2.5%: 925 and 4700 kcal for men, 1100 and 4900 kcal for women) [181, 230], and the patients who had familial adenomatous polyposis (FAP) or an in-situ tumor were excluded. After these exclusions, based on those who completed both the PHQ and FFQ, 1139 subjects (488 cases and 651 controls) remained for the analysis.

Descriptive statistics (frequency, means and standardized deviations) were used to describe the characteristics of cases and controls. Before the analysis, potential indicators of possible factors were standardized using the Z scores method [231], which is a common way to summarize and standardize data with large variability.

\[ Z = \frac{X - \mu}{\sigma} \]

When establishing a measurement model, potential risk factors of CRC that cannot be directly observed or measured were presented as a factor with a factor score, which was the sum of standardized scores (Z scores) of each factor’s corresponding indicators that loads on the same factor without considering the weights [231]. SES was measured by education, income and resident region. Although education and income were ordinal variables, Z scores were calculated based on the median value of each category. For the variable of region, Z score was assigned as -0.5 and 0.5 for rural and urban area, respectively.

The dietary pattern was explored by examining the 39 food groups through exploratory factors analysis (EFA), which was used to identify the possible number of factors. The food
groups with factor loadings equal to or greater than 0.25 were considered to comprise its
dietary patterns. According to the results of EFA, literature review, and an understanding of
dietary patterns in NL, three major dietary patterns were found: (1) processed meats plus root
vegetables; (2) vegetables; and (3) fruits). To derive the factor score of processed meats, the
sum of the Z scores of red meat, cured/processed (red) meat, fish, processed fish, and root
vegetables were calculated. To derive the factor score of the vegetables pattern, the Z scores
of cruciferous vegetables, other greens, beans, peas, tomato sauce and other vegetables
excluding root vegetables were added. The factor score of fruits intakes was calculated by
combining the Z score of citrus fruits, berries, dried fruit and other fruits. In order to explore
potentially important risk factors of CRC, the study used binary and multivariable logistic
regression to estimate odds ratios (OR) and 95% confidence intervals (95%CI). This was
used to explore of the potential associations among age; sex; SES; BMI; family history score
of colorectal cancer; history of inflammatory bowel disease; non-steroidal anti-inflammatory
drug use; physical activity; history of CRC screening; smoking; intakes of processed meat
plus root vegetables; vegetables and fruits. SAS 9.1 was used for the analysis of basic
characteristics and regression models (SAS Institute, Cary, NC).

To further explore the possible direct and indirect effects of SES on other potential risk
factors, factor analysis and structural equation modeling were performed using 5.1 M-plus
software (Muthen & Muthen). The goodness of model fit was evaluated by indices: (1) the
Comparative Fit Index (CFI), which is an incremental fit index that assesses model fit
compared to a baseline model. It is resistant of non-normality and a small sample size; and a
value exceeding 0.9 indicates acceptable model fit [232] while some studies have suggested
using 0.95 as a cut-off point[233]; (2) the Tucker Lewis Index (TLI), also known as NNFI,
where a recommended good fit value is more than 0.9 [234] or 0.95 [233]; a small sample
size does not influence this index; (3) the root mean square error of approximation (RMSEA), an indicator of the fit of population data to the model, which aims to remove sampling error from model fit. The acceptable level is less than 0.08 or 0.06 [233]. (4) Weighted root mean square residual (WRMR) for categorical data was estimated and its value was less than 1.0 indicating a good fit. (5) Standardized Root Mean Square Residual (SRMR) is a fit index for continuous data. A value less than .08 is generally considered a good fit [233]. The significance level of each path coefficient in the model was evaluated by the $P$ value of 0.05.

5.4 Results

5.4.1 Descriptive Characteristics

Important demographic characteristics of the 488 cases and 651 controls were presented in Table 5.6.1. A lower proportion of CRC cases participated in CRC screening; were older; a higher proportion of polyps history; and were more likely to be former and/or current smokers; have first-degree relatives with CRC, be overweight, have higher total energy intakes; reside in rural areas, have lower education levels and have lower household incomes.

5.4.2 Exploratory Factors Analysis (EFA)

Preliminary EFA suggested that six factors could represent the dietary pattern. See Table 5.6.2 for details. The model fit indices were: CFI=0.86, TLI=0.80, RMSEA=0.04 and SRMR=0.03. The scree plot is shown in Figure 5.6.1 and factor loadings of EFA are presented in Table 5.6.2. Six potential factors were further reduced to three factors based on the following criteria: (1) deleting factors with cross loadings; (2) deleting factors with less than three indicating variables; (3) considering potential dietary patterns reported in the literature; and (4) understanding of the dietary culture in NL. The final three factors were: (1) processed meat plus root vegetables; (2) vegetables; and (3) fruits. After deleting irrelevant variables based on preliminary EFA, secondary EFA was performed and model fit indices
were: CFI=0.97, TLI=0.93, RMSEA=0.04 and SRMR=0.02. As suggested by model fit indices, factors of processed meat and root vegetables consumption, vegetables intake and fruits intake were adequately measured by the selected variables and well represent the dietary pattern in NL.

5.4.3 Regression Results

Binary regression model of examining SES on CRC risk showed that higher SES reduced the risk of CRC (OR=0.80, 95%CI=0.75-0.86). The results from multivariate regression analysis indicated that age, SES, processed meat intake, non-screening, smoking and family history score of CRC were significantly associated with risk of CRC. See Table 5.6.3.

5.4.4 Structural Equation Modeling

As conceptualized in our theoretical model, the direct and mediated effects of potential risk factors of CRC were tested in SEM (see Figure 5.6.2). Older age (β=-0.01), no CRC screening (β=-0.33), ever or current smokers (β=-0.17), higher family history score of CRC (β=-0.03), processed meat intake (β=-0.04) and non-NSAID use (β=-0.19) increased the risk of CRC. Higher socioeconomic status (β=0.05) and vegetables intake (β=0.03) were linked to reduced risk of CRC.

Being female (β=-0.74) and have a higher SES (β=-0.38) decreased the likelihood of processed meat intake. Older age (β=0.05), being female (β=1.31) and higher SES (β=0.34) were associated with an increased consumption of vegetables. Subjects with a higher SES have a higher chance of participating in CRC screening (β=-0.07) and were less likely to have smoked or to be a current smoker (β=-0.11). SES appeared to have a direct effect on the risk of CRC (β=0.05) and an indirect effect (β=0.06) which existed through a high processed meat intake (β=0.01), lower prudent vegetable intake (β=0.01), fewer CRC screening (β=0.02) and
smoking ($\beta=0.02$). Fruit intake appeared to be a protective factor in preventing CRC but it was not included in the final SEM model because of the model fit issue. Model fit indices of path analysis were: CFI=0.59, TLI=0.37, RMSEA=0.08 and WRMR=1.94.

5.5 Discussion

Using the standardized score approach, three dietary patterns have been identified: (1) processed meat plus root vegetables; (2) vegetables; and (3) fruits. These dietary patterns were consistent with previous established dietary patterns in the North American and European population [144, 225]. During the process of identifying dietary patterns, total energy intake adjustment was not completed because other studies indicated the robustness of total energy adjustment when using the dietary patterns approach [225]. When assigning food groups through aggregating hundreds of food items in the FFQ and identifying potential dietary patterns, many subjective decisions were made according to literature reports and our understanding of the culture in NL. Labels of dietary patterns were assigned arbitrarily based on the consideration of data interpretation and understanding of the food culture in NL. However, the limitation of subjective decision was unavoidable because no better techniques are available. Different studies have labeled dietary patterns differently, such as using “Fruits and vegetables” [235] or “Prudent” [236] or “salad” [225] for vegetables and fruit intake while using “high meat consumption” [225] or “westernized” [236] for high consumption of (processed) meat. Some studies suggested possible “sweets” [235] and “alcohol” [235, 237] patterns as having influence on risk of CRC, but neither pattern was obvious in this study.

Based on the results of this population based case-control study, this research supports the hypothesis that potential risk factors work together to increase the occurrence of CRC. The common risk factors studies were dietary factors [96, 124, 142, 219], physical inactivity [15, 17, 18, 150, 152, 220], smoking [205, 221], alcohol consumption [161, 222, 223], and
socioeconomic status [224]. These were examined in structural equation modeling to detail how SES influences these other candidate risk factors and subsequently the development of CRC. Higher SES directly reduced the risk of developing CRC and its mediated effects on CRC risk through diet patterns, smoking status, and CRC screening were suggested. The utilization of structural equation modeling in this study specified the direct and indirect effect of candidate risk factors, which helped to uncover the “web” like associations by measuring a set of variables simultaneously [238]. Due to the complexity of causal model in cancer, this study mainly focused on investigating the direct effect of SES on the development of CRC and its indirect effect through some common risk factors. It is possible that a more comprehensive model would explain data better than our proposed model. Model fit indices of structural equation modeling in this study were lower than what was suggested in the psychological area of the literature. This could be explained by the fact that psychometric measures are usually highly correlated which can be called an underlying “construct” or “factor” or “factor structure” or “trait” [239]; while items measured in epidemiological investigations do not necessarily reflect such a potential structure [225].

Previous studies have indicated that factor analysis of dietary patterns has provided a better understanding of the relationship between diet and cancer than the analysis of single nutrients or foods [144, 148, 225]. To our knowledge, this is the first study utilizing structural equation modeling to explore the epidemiologic etiology of cancer. This could provide more insight into the entangled interrelationships among a series of risk factors. This study only presented one ‘corner’ of the much larger “web” of associations in cancer etiology. The results in this study presented unique information not only pertaining to the direct of effect of SES on the development of CRC but also its indirect effects through a set of common CRC risk factors. Future research in this area should focus on investigating the interrelations of
obesity, physical inactivity, history of cancer related disease, medication use and other
candidate risk factors of developing cancer.
### 5.6 Figure and Tables

**Table 5.6.1 Selected demographic and lifestyle characteristics of cases and controls of the Colorectal cancer case-control study in Newfoundland**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Newfoundland and Labrador</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case (N=488)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>61.9±9.0*</td>
</tr>
<tr>
<td>Male (%)</td>
<td>296 (60.6%)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Single or never married</td>
<td>27 (5.5%)</td>
</tr>
<tr>
<td>Currently married or living as married</td>
<td>385 (78.9%)</td>
</tr>
<tr>
<td>Separated, divorced or widowed</td>
<td>76 (15.6%)</td>
</tr>
<tr>
<td>Missing</td>
<td></td>
</tr>
<tr>
<td>Polyps b</td>
<td>235 (48.0)*</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs use b</td>
<td>164 (33.5)</td>
</tr>
<tr>
<td>Current and/or past smoker b</td>
<td>353 (72.3)*</td>
</tr>
<tr>
<td>Overweight</td>
<td>346 (71.0)*</td>
</tr>
<tr>
<td>Overweight at 20 years of age b</td>
<td>98 (20.1)</td>
</tr>
<tr>
<td>Higher Household income c</td>
<td>118 (24.2)*</td>
</tr>
<tr>
<td>Higher Education c</td>
<td>181 (37.1)*</td>
</tr>
<tr>
<td>Region (rural)</td>
<td>278 (57.2%)*</td>
</tr>
<tr>
<td>First degree relatives with CRC (%) b</td>
<td>163 (33.4)*</td>
</tr>
<tr>
<td>Reported any CRC screening b</td>
<td>60 (12.3)*</td>
</tr>
<tr>
<td>Alcohol consumption a</td>
<td>9.2±22.4</td>
</tr>
</tbody>
</table>

---

*Continuous variables were presented as mean±SD (standard deviation). The differences between cases and controls were based on t-tests.

* Categorical variables were presented as number(%). The differences between cases and controls were based on chi-square tests.

* High level of education included some college, university or post-secondary school; High household income included an average household income>$50,000/year.

* Significant difference between cases and controls (p≤0.05).
Figure 5.6.1 Eigenvalues for exploratory factor analysis among 39 food groups
Table 5.6.2 Factor loadings of dietary pattern in exploratory factor analysis of the NOCS (Newfoundland)

<table>
<thead>
<tr>
<th></th>
<th>Mixed</th>
<th>Processed meat</th>
<th>Meat</th>
<th>Prudent vegetables</th>
<th>Fruit</th>
<th>High sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>0.08</td>
<td>-0.02</td>
<td>-0.03</td>
<td>0.18</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Yogurt</td>
<td>0.03</td>
<td>0.00</td>
<td>-0.01</td>
<td>0.19</td>
<td>0.13</td>
<td>-0.02</td>
</tr>
<tr>
<td>Coffee</td>
<td>-0.47</td>
<td>-0.04</td>
<td>0.20</td>
<td>0.04</td>
<td>-0.01</td>
<td>0.05</td>
</tr>
<tr>
<td>Tea</td>
<td>0.60</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td>-0.04</td>
<td>-0.01</td>
</tr>
<tr>
<td>Sugar</td>
<td>0.14</td>
<td>-0.04</td>
<td>0.14</td>
<td>-0.12</td>
<td>-0.09</td>
<td>0.05</td>
</tr>
<tr>
<td>Soft drinks</td>
<td>-0.15</td>
<td>0.04</td>
<td>0.14</td>
<td>-0.08</td>
<td>-0.07</td>
<td>0.04</td>
</tr>
<tr>
<td>Egg</td>
<td>0.06</td>
<td>0.03</td>
<td>0.21</td>
<td>0.01</td>
<td>-0.04</td>
<td>0.02</td>
</tr>
<tr>
<td>Cheese</td>
<td>-0.08</td>
<td>0.00</td>
<td>0.16</td>
<td>0.26</td>
<td>-0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Mixed dishes</td>
<td>0.01</td>
<td>-0.04</td>
<td>0.37</td>
<td>0.21</td>
<td>-0.01</td>
<td>0.08</td>
</tr>
<tr>
<td>Red meat</td>
<td>-0.07</td>
<td>0.04</td>
<td>0.65</td>
<td>0.11</td>
<td>-0.07</td>
<td>0.04</td>
</tr>
<tr>
<td>Game</td>
<td>-0.08</td>
<td>0.04</td>
<td>0.16</td>
<td>-0.04</td>
<td>0.12</td>
<td>-0.03</td>
</tr>
<tr>
<td>Cured/Processed meat</td>
<td>0.06</td>
<td>0.34</td>
<td>0.63</td>
<td>-0.07</td>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Cured/Processed meat</td>
<td>0.02</td>
<td>0.98</td>
<td>0.21</td>
<td>-0.08</td>
<td>-0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>Poultry</td>
<td>0.02</td>
<td>0.16</td>
<td>-0.07</td>
<td>0.20</td>
<td>0.01</td>
<td>-0.03</td>
</tr>
<tr>
<td>FISH</td>
<td>0.00</td>
<td>0.75</td>
<td>-0.29</td>
<td>0.16</td>
<td>0.02</td>
<td>0.00</td>
</tr>
<tr>
<td>Processed fish</td>
<td>-0.01</td>
<td>0.58</td>
<td>-0.13</td>
<td>0.13</td>
<td>0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>Fruit Juice</td>
<td>0.16</td>
<td>-0.05</td>
<td>0.08</td>
<td>0.18</td>
<td>0.05</td>
<td>0.08</td>
</tr>
<tr>
<td>Other fruit</td>
<td>-0.02</td>
<td>-0.01</td>
<td>0.02</td>
<td>-0.02</td>
<td>0.84</td>
<td>-0.01</td>
</tr>
<tr>
<td>Root Vegetables</td>
<td>0.10</td>
<td>0.03</td>
<td>0.27</td>
<td>0.13</td>
<td>-0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>Cruciferous Vegetables</td>
<td>0.01</td>
<td>0.02</td>
<td>0.00</td>
<td>0.55</td>
<td>0.08</td>
<td>-0.02</td>
</tr>
<tr>
<td>Other Greens</td>
<td>-0.10</td>
<td>0.02</td>
<td>-0.10</td>
<td>0.63</td>
<td>0.07</td>
<td>-0.04</td>
</tr>
<tr>
<td>Beans, Peas</td>
<td>0.13</td>
<td>0.00</td>
<td>0.13</td>
<td>0.42</td>
<td>-0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>Tomato Sauce</td>
<td>0.01</td>
<td>-0.01</td>
<td>0.09</td>
<td>0.58</td>
<td>0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>Other Vegetables</td>
<td>0.03</td>
<td>0.00</td>
<td>0.13</td>
<td>0.60</td>
<td>-0.01</td>
<td>-0.04</td>
</tr>
<tr>
<td>Total cereals and grains</td>
<td>0.23</td>
<td>-0.05</td>
<td>0.18</td>
<td>0.22</td>
<td>0.15</td>
<td>0.06</td>
</tr>
<tr>
<td>Whole grains</td>
<td>0.12</td>
<td>0.00</td>
<td>-0.09</td>
<td>0.29</td>
<td>0.03</td>
<td>-0.05</td>
</tr>
<tr>
<td>Desserts and sweets</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.01</td>
<td>0.00</td>
<td>0.00</td>
<td>1.13</td>
</tr>
<tr>
<td>Vegetable juice</td>
<td>0.01</td>
<td>-0.03</td>
<td>0.06</td>
<td>0.24</td>
<td>-0.04</td>
<td>-0.02</td>
</tr>
<tr>
<td>Beer</td>
<td>-0.18</td>
<td>0.06</td>
<td>0.12</td>
<td>-0.03</td>
<td>-0.07</td>
<td>-0.03</td>
</tr>
<tr>
<td>White Wine</td>
<td>-0.18</td>
<td>-0.03</td>
<td>0.09</td>
<td>0.16</td>
<td>-0.09</td>
<td>-0.02</td>
</tr>
<tr>
<td>Red wine</td>
<td>-0.13</td>
<td>0.03</td>
<td>-0.01</td>
<td>0.06</td>
<td>-0.04</td>
<td>-0.01</td>
</tr>
<tr>
<td>Liquor</td>
<td>-0.07</td>
<td>0.04</td>
<td>0.05</td>
<td>0.00</td>
<td>-0.09</td>
<td>-0.03</td>
</tr>
<tr>
<td>Citrus</td>
<td>0.08</td>
<td>0.01</td>
<td>0.00</td>
<td>0.11</td>
<td>0.29</td>
<td>0.00</td>
</tr>
<tr>
<td>Berries</td>
<td>-0.02</td>
<td>0.04</td>
<td>-0.04</td>
<td>0.05</td>
<td>0.60</td>
<td>0.03</td>
</tr>
<tr>
<td>Dried Fruit</td>
<td>0.06</td>
<td>-0.05</td>
<td>0.02</td>
<td>0.02</td>
<td>0.50</td>
<td>0.01</td>
</tr>
<tr>
<td>Canned Fruit</td>
<td>0.19</td>
<td>-0.04</td>
<td>0.08</td>
<td>0.10</td>
<td>0.06</td>
<td>0.10</td>
</tr>
<tr>
<td>Pies, Tarts</td>
<td>-0.01</td>
<td>0.02</td>
<td>0.00</td>
<td>-0.02</td>
<td>0.01</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>0.24</td>
<td>-0.01</td>
<td>0.01</td>
<td>-0.02</td>
<td>0.06</td>
<td>0.11</td>
</tr>
<tr>
<td>----------------</td>
<td>------</td>
<td>-------</td>
<td>------</td>
<td>-------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Jam, Jelly</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pickled Vegetables</td>
<td>0.14</td>
<td>0.02</td>
<td>0.08</td>
<td>0.19</td>
<td>0.04</td>
<td>0.06</td>
</tr>
</tbody>
</table>
Table 5.6.3 Odds ratios and 95% CI in multivariate logistical regression of the NOCS (Newfoundland)

<table>
<thead>
<tr>
<th>Covariates</th>
<th>OR&lt;sup&gt;a&lt;/sup&gt;</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Socioeconomic status</td>
<td>0.89</td>
<td>(0.82, 0.96)</td>
</tr>
<tr>
<td>Processed meat</td>
<td>1.08</td>
<td>(1.04, 1.12)</td>
</tr>
<tr>
<td>Prudent vegetables</td>
<td>0.93</td>
<td>(0.88, 0.97)</td>
</tr>
<tr>
<td>Fruit</td>
<td>1.00</td>
<td>(0.95, 1.05)</td>
</tr>
<tr>
<td>Sex (female VS male)</td>
<td>1.25</td>
<td>(0.93, 1.67)</td>
</tr>
<tr>
<td>Age</td>
<td>1.03</td>
<td>(1.02, 1.05)</td>
</tr>
<tr>
<td>Screen (no VS yes)</td>
<td>2.67</td>
<td>(1.83, 3.91)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>0.93</td>
<td>(0.38, 2.26)</td>
</tr>
<tr>
<td>NSAID</td>
<td>1.38</td>
<td>(1.04, 1.83)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>1.00</td>
<td>(1.00, 1.00)</td>
</tr>
<tr>
<td>Smoking (former VS never)</td>
<td>1.44</td>
<td>(1.05, 1.97)</td>
</tr>
<tr>
<td>Smoking (former VS never)</td>
<td>1.85</td>
<td>(1.23, 2.79)</td>
</tr>
<tr>
<td>BMI</td>
<td>1.02</td>
<td>(0.99, 1.05)</td>
</tr>
<tr>
<td>Family history score of CRC</td>
<td>1.06</td>
<td>(1.04, 1.08)</td>
</tr>
</tbody>
</table>

<sup>a</sup>: adjusted for Socioeconomic status, Processed meat, Prudent vegetables, Fruit, Sex, Age, Screen, Inflammatory bowel disease, NSAID, Physical activity, Smoking, BMI, Family history score of CRC
Figure 5.6.2 Conceptualized structural equation model of the etiology of colorectal cancer
*: solid lines represented significant path coefficients ($P \leq 0.05$) while dotted lines indicated insignificant path coefficients ($P \geq 0.05$).
Chapter 6 Summary

The two projects included in this thesis mainly explored how physical activity, socioeconomic status and some common candidate risk factors were linked to the development of colorectal cancer. Engaging in physical activity has long been considered as an effective strategy for cancer prevention [12]. Walking is one of the most common forms of moderate level physical activity among middle-aged and older people [195]. Its impact on CRC risk has only been examined by a few studies [196-198]. The potential benefits of moderate intensity physical activity, particularly the specific role of walking in cancer prevention, are unclear. Results from this study showed that the highest quintile of walking was associated with increased colorectal cancer risk for both males and females in both provinces (highest VS lowest: ON: OR=1.51, 95%CI=1.07-2.13; NL: OR=2.01, 95%CI=1.25-3.22; pooled analysis: OR=1.70, 95%CI=1.09-2.66). However, this result could be biased because a higher proportion of cases respond to the walking item in PHQ than controls. In addition, walking is only a part of total recreational physical activity. Therefore, walking did not appear to be an effective strategy for colorectal cancer prevention in this study.

Non-walking exercise was not significantly associated with reduced risk of colorectal cancer for both sexes and provinces. These findings suggested that increasing amounts of non-walking exercise could reduce the risk of colorectal cancer. Occupational physical activity was not included in the analysis because the data regarding occupational physical activity was not available for this analysis. However, education levels and incomes could explain a proportion of the variation associated with occupation. Future prospective studies in large populations on physical activity are needed to evaluate effective frequency, duration and
intensity of physical activity in relation to colon and rectal cancer prevention.

Dietary factors [96, 124, 142, 219], physical inactivity [15, 17, 18, 150, 152, 220], smoking [158], alcohol consumption [161, 222, 223], smoking [205, 221] and socioeconomic status [224] have been linked to the development of CRC. Existing epidemiologic studies have not studied how risk factors work together to increase the incidence of CRC so the true effect of each factor could be under- or over-estimated. The second component of this thesis was to explore how SES directly influences the risk of developing CRC and its mediated effect on CRC risk through diet while adjusting for possible risk factors of alcohol intake, smoking, physical inactivity, and obesity.

Identifying major dietary patterns through exploratory factor analysis, a relatively new approach in epidemiology, has allowed us to investigate the interrelations of multiple food items or nutrients simultaneously, which has overcome the limitation of partially examining dietary risk factors [225]. In this study, exploratory factor analysis was used to identify dietary patterns measured by the 39 food groups. Then, the direct and intermediate effects of risk factors were examined using structural equation modeling. The results from multivariate regression analysis indicated that age (OR=1.03), SES (OR=0.89), processed meat intake (OR=1.08), no CRC screening (OR=2.67), smoking (OR=1.44, 1.85 (ever, current)), and family history score of CRC (OR=1.06), were significantly associated with the risk of CRC. In addition to the direct effect of SES ($\beta=0.05$) on the risk of CRC, the indirect effect ($\beta=0.06$) of SES on the risk of CRC also appeared to exist through processed meat intake ($\beta=0.01$), lower vegetables intake ($\beta=0.01$), less likely to have CRC screening ($\beta=0.02$), and smoking ($\beta=0.02$). This study suggested that the NL population has three major dietary patterns: (1) processed meat plus root vegetables; (2) vegetables; and (3) fruits. In addition, structural
equation modeling used in this study, a relatively new approach in epidemiological studies, provided unique information of the direct effect of socioeconomic status on the development of CRC and its indirect effects through a set of candidate CRC risk factors.

This study only presented one 'corner' of the much larger "web" of associations in cancer etiology. It is possible that a more comprehensive model could explain data better than our suggested model. Future research in this area should focus on investigating the interrelations of obesity, physical inactivity, history of cancer related diseases, medication use and other candidate risk factors of developing cancer.
References


176. Martinez, M.E., et al., Pronounced reduction in adenoma recurrence associated with aspirin use and a


183. S.U.N. Z., Association of dietary intakes with risk of colorectal cancer: results from a population-based case-control study in Newfoundland and Labrador, in Division of Community Health and Humanities2010, Memorial University of Newfoundland: St John's.


229. Yang, Q., et al., *Family history score as a predictor of breast cancer mortality: prospective data from*


Appendix 1. 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? _____/_____/_____
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

3. What is your age?
   day _____
   month _____
   year _____
   O don’t know day
   O don’t know month
   O don’t know year

4. 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
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

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

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
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?

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

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 # 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
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: ____________________________
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

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: ____________________________
   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

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

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 _____
   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?
10. Has a doctor ever told you that you had familial adenomatous 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.

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 11</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 11</td>
</tr>
</tbody>
</table>

10a. When did your doctor first tell you that you had FAP?

- age at first diagnosis __ __
- 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.

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 14</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 14</td>
</tr>
</tbody>
</table>

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

- age at first diagnosis __ __
- 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.

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 15</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 15</td>
</tr>
</tbody>
</table>

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

- age at first diagnosis __ __
- year of diagnosis __ __ __ __
- O don’t know

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

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 16</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 16</td>
</tr>
</tbody>
</table>

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

- age at last operation __ __
- year of last operation __ __ __ __
- O don’t know

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

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 17</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 17</td>
</tr>
</tbody>
</table>

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

- age at operation __ __
- year of operation __ __ __ __
- O don’t know

16. Have you had your gallbladder removed?

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 18</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 18</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 18</td>
</tr>
</tbody>
</table>

16a. When did you have your gallbladder removed?

- age at operation __ __
- 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.

<table>
<thead>
<tr>
<th>O yes</th>
<th>Please go to № 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>Please go to № 19</td>
</tr>
<tr>
<td>O don’t know</td>
<td>Please go to № 19</td>
</tr>
</tbody>
</table>
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

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, pills 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 category.

<table>
<thead>
<tr>
<th>times per day or</th>
<th>Pills</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>times per week or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>times per month or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>times per year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>don’t know</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>O yes</th>
<th>O</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>O don’t know</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>number of months or</th>
<th>Pills</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>don’t know</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>times per day or</th>
<th>Pills</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>times per week or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>times per month or</td>
<td></td>
<td></td>
</tr>
<tr>
<td>times per year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>don’t know</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

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?

<table>
<thead>
<tr>
<th>number of months or</th>
<th>Pills</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>don’t know</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>
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?

[Choose from: 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?

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.

[Choose from: ___ 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?

[Choose from: ___ number of months or ___ number of years or O don’t know]

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?

[Choose from: ___ cancer]

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

[Choose from: age at diagnosis ___ ___ or year of diagnosis ___ ___ ___]

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

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?

[Choose from: ___ cancer]

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

[Choose from: age at diagnosis ___ ___ or year of diagnosis ___ ___ ___]

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

O yes
O no
O don’t know

Medications

Have you ever taken any of the following medications regular (at least twice a week
22a. What type of cancer was it?

22b. When did your doctor first tell you that you had this type of cancer?
   - age at diagnosis
   - year of diagnosis
   - don’t know

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

23b. When did your doctor first tell you that you had this type of cancer?
   - age at diagnosis
   - 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 Tylenol, Anacin-3, Panadol)

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

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

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, FibreCon, Serutan, psyllium)

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

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

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.

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.
<table>
<thead>
<tr>
<th>Time per day or</th>
<th>Time per week</th>
<th>O don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>27b. About one year before your recent cancer diagnosis, were you taking it regularly?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O yes</td>
<td>O no</td>
<td>O don’t know</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Time per day or</th>
<th>Time per week</th>
<th>O don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>28b. About one year before your recent cancer diagnosis, were you taking it regularly?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O yes</td>
<td>O no</td>
<td>O don’t know</td>
</tr>
</tbody>
</table>

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.

| Time per day or | Time 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.

| Time per day or | Time per week | O don’t know |

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

| O yes |

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

| O yes |
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

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

32. Calcium-based antacids (such as Tums, Rolaid, Extra-strength Rolaid, 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

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

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

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

O yes
O no
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

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
### 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
- 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

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

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, progestatins 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

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

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

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?

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

- Other reason
  - Please specify: _______________
  - Age when occurred ______ or year when occurred ______
  - O don’t know
  - O not applicable

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

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 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

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-only medication for hormone replacement therapy? 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

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

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
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

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

**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, barbecuing 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?

<table>
<thead>
<tr>
<th>Outside Appearance</th>
<th>Inside Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>O lightly browned</td>
<td>O red (rare)</td>
</tr>
<tr>
<td>O medium browned</td>
<td>O pink (medium)</td>
</tr>
<tr>
<td>O heavily browned or blackened</td>
<td>O brown (well-done)</td>
</tr>
<tr>
<td>O don't know</td>
<td>O don't know</td>
</tr>
</tbody>
</table>

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, barbecuing 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.

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

<table>
<thead>
<tr>
<th>Activity</th>
<th>For how many years?</th>
<th>During those months per year?</th>
<th>During those months, on average, for how many minutes or hours per week?</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

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.

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

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
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 or 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.

<table>
<thead>
<tr>
<th>Activity</th>
<th>For how many years?</th>
<th>During those years, for many months per year?</th>
<th>During those months, on average, for how many minutes or hours per week?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td>O yes →</td>
<td>_____ years</td>
<td>_____ minutes per week / _____ hours per week</td>
</tr>
<tr>
<td></td>
<td>O no →</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jogging (running slower than a mile in)</td>
<td>O yes →</td>
<td>_____ years</td>
<td>_____ minutes per week / _____ hours per week</td>
</tr>
<tr>
<td></td>
<td>O no →</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
10 minutes)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes →</th>
<th>No →</th>
<th>Years</th>
<th>Months</th>
<th>Minutes per week</th>
<th>Hours per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running (running faster than a mile in 10 minutes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bicycling (including using an exercise bicycle)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swimming laps</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tennis, squash racquetball</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calisthenics, aerobics, vigorous dance (including ballet), using a rowing machine, lifting weights</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Football, soccer, rugby, basketball</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heavy household work (examples: using a non-power mower, shoveling, moving heavy loads, scrubbing floors)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Activity Please specify</th>
<th>For how many years?</th>
<th>During those months, for many months per year?</th>
<th>During those months, on average, for how many minutes or hours per week?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>→</td>
<td></td>
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<td></td>
<td>→</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>→</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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 → ___ years consumed ___ number of 12 ounce cans or bottles
O no
O don’t know

Wine
O yes → ___ years consumed ___ number of 4 ounce glasses of wine
O no
O don’t know

Sake, sherry, port
O yes → ___ years consumed ___ number of 1 ounce servings
O no
O don’t know

Spirits, liquor
O yes → ___ years consumed ___ number of 1 ounce

105
mixed drinks, brandy, liqueurs

O no
O don’t know

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 when 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.

<table>
<thead>
<tr>
<th>For how many years?</th>
<th>During those years, how much did you typically consume?</th>
</tr>
</thead>
</table>
| **Beer, hard cider** (at least 3% alcohol) | O yes →  ____ years consumed  ____ number of 12 ounce cans or bottles
O no
O don’t know |
| **Wine** | O yes →  ____ years consumed  ____ number of 4 ounce glasses of wine
O no
O don’t know |
| **Sake, sherry, port** | O yes →  ____ years consumed  ____ number of 1 ounce servings
O no
O don’t know |
| **Spirits, liquor mixed drinks, brandy, liqueurs** | O yes →  ____ years consumed  ____ number of 1 ounce shots liquor or spirits
O no
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

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

---

64. Have you ever smoked at least one 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 \( \rightarrow \) Please go to #66
O don’t know \( \rightarrow \) 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 \( \rightarrow \) Please go to #65f
O don’t know \( \rightarrow \) Please go to #65f

65e. When did you stop smoking at least one pipe a month (we mean stop 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, your 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.

<table>
<thead>
<tr>
<th>Country of birth</th>
<th>Is this person of Jewish descent?</th>
<th>Ashkenazi (East European)</th>
<th>Sephardic</th>
<th>Other</th>
<th>Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>You</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your mother</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your father</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your mother’s mother</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your mother’s father</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your father’s mother</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Your father’s father</td>
<td>O yes</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>O no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O don’t know</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

72. How many years have you lived in Canada?
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.

<table>
<thead>
<tr>
<th></th>
<th>You</th>
<th>Your mother</th>
<th>Your father</th>
<th>Your Mother’s mother</th>
<th>Your Mother’s father</th>
<th>Your Father’s mother</th>
<th>Your Father’s father</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black, From Africa</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Black, from Caribbean</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>(Trinidad, Jamaica, Haiti)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Black from North America</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Black, other</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>White</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>First Nations</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>(Indian, Inuit)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>North African</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>(Egyptian)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Middle East</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>(Iranian)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Filipino</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<tr>
<td>Japanese</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Korean</td>
<td>O</td>
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<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Chinese</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Other South</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>East Asian</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>(Vietnamese)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>South Asian</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>(East Indian, Pakistani)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
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<tr>
<td>Other:</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Please specify</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Don’t know</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>O $0,000 - $49,999</th>
<th>O $50,000 - $79,999</th>
</tr>
</thead>
<tbody>
<tr>
<td>O no income</td>
<td>$40,000</td>
<td>$50,000</td>
</tr>
<tr>
<td>O less than $6,000</td>
<td>$40,000</td>
<td>$49,999</td>
</tr>
<tr>
<td>O $6,000 - $11,999</td>
<td>$50,000</td>
<td>$59,999</td>
</tr>
<tr>
<td>O $12,000 - $19,999</td>
<td>$60,000</td>
<td>$69,999</td>
</tr>
<tr>
<td>O $70,000 - $79,999</td>
<td>$70,000</td>
<td>$79,999</td>
</tr>
</tbody>
</table>

111
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 2. Food Frequency Questionnaire

Canadian Study of Diet and Health

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.*

© M. Jain and J. McLaughlin, 2002
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 (c), 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 POTATeS 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**

<table>
<thead>
<tr>
<th>FOOD</th>
<th>Average Portion Size</th>
<th>Your Portion Size, if NOT Average</th>
<th>HOW OFTEN? (Complete one column only)</th>
<th>If Ate Food in Season Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Smaller</td>
<td>Larger</td>
<td>per DAY</td>
</tr>
<tr>
<td>CREAM CHEESE</td>
<td>2 tbsp/30 ml/1 oz</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>CANTALOUPE</td>
<td>1/2 of 1 slice</td>
<td>O</td>
<td>O</td>
<td>1</td>
</tr>
<tr>
<td>SWEET POTATeS</td>
<td>1 medium 1/2 cup</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
</tbody>
</table>

---

114
<table>
<thead>
<tr>
<th>FOOD</th>
<th>Average Portion Size</th>
<th>Your Portion Size, if NOT Average</th>
<th>HOW OFTEN? (Complete one column only)</th>
<th>If Ate Food In Season Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Smaller</td>
<td>Larger</td>
<td>per DAY (enter a number)</td>
</tr>
<tr>
<td>Dairy Products</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>EGG (boiled, poached)</td>
<td>1 egg</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>EGG (fried, scrambled, omelette)</td>
<td>1 egg</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>26</td>
<td>CREAM CHEESE, Regular fat</td>
<td>2 tbsp/30 ml/1 oz</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>27</td>
<td>CHEESE, Regular fat (such as cheddar, brie, provolone)</td>
<td>1 slice/50 g/1 oz</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>28</td>
<td>CHEESE, Light (6-15% fat, such as cream cheese, cheddar)</td>
<td>1 slice/30 g/1 oz</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>29</td>
<td>CHEESE, Ultra Light (5% fat or less, such as cheddar)</td>
<td>1 slice/30 g/1 oz</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>COTTAGE or RICOTTA CHEESE</td>
<td>125 ml/1/2 cup</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>31</td>
<td>CREAM (coffee, whipping, sour or regular)</td>
<td>1 tbsp/15 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>32</td>
<td>CREAM (half and half, light sour cream)</td>
<td>1 tbsp/15 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>33</td>
<td>COFFEE WHITENER (non-dairy)</td>
<td>1 tbsp/15 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>34</td>
<td>YOGURT, Regular (plain, 2.4% fat or more)</td>
<td>1/4 cup/175 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>35</td>
<td>YOGURT, Light (plain, less than 2.4% fat)</td>
<td>1/4 cup/175 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>36</td>
<td>YOGURT, Regular (fruit flavoured or frozen, 2.4% fat or more)</td>
<td>1/4 cup/175 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>37</td>
<td>YOGURT, Light (fruit flavoured or frozen, less than 2.4% fat)</td>
<td>1/4 cup/175 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Mixed Dishes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>SOUPS (creamised)</td>
<td>1 cup/250 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>39</td>
<td>SOUPS (non-creamised)</td>
<td>1 cup/250 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>40</td>
<td>PEA SOUP</td>
<td>1 cup/250 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>41</td>
<td>PASTA with meat sauce (spaghetti, lasagna)</td>
<td>1 cup/250 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>42</td>
<td>PASTA with tomato sauce (spaghetti)</td>
<td>1 cup/250 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>43</td>
<td>MIXED DISHES with cheese or cheese sauce, lasagna and cheese</td>
<td>1 cup/250 ml</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>44</td>
<td>PIZZA with meat</td>
<td>1 Medium slice</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>45</td>
<td>PIZZA with vegetable only</td>
<td>1 Medium slice</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Section A</td>
<td>Section B YEAR BEFORE DIAGNOSIS</td>
<td>Section C If Ate Food In Season Only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------------------</td>
<td>-------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FOOD</td>
<td>Average Portion Size</td>
<td>Your Portion Size, if NOT Average</td>
<td>HOW OFTEN? (Complete one column only)</td>
<td>enter Months per Year</td>
</tr>
<tr>
<td></td>
<td>Smaller</td>
<td>Larger</td>
<td>per DAY</td>
<td>per WEEK</td>
</tr>
<tr>
<td>46 MEAT STEW with carrots, other vegetables</td>
<td>1 cup/250 ml/ puch A, medium</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>47 CHILI with meat or Corn Cheese</td>
<td>1 cup/250 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td><strong>Vegetables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48 POTATOES (mashed, boiled, baked etc)</td>
<td>1 medium ¾ cup/ 125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>49 FRENCH FRIES or FRIED POTATOES</td>
<td>1 cup/250 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>50 CARROTS (raw or cooked)</td>
<td>1 medium ½ cup/ 125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>51 BROCCOLI</td>
<td>1 cup/250 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>52 CABBAGE, COLESLAW</td>
<td>½ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>53 CAULIFLOWER</td>
<td>½ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>54 CORN</td>
<td>1 ear/1 ½ cup</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>55 PEAS or LIMA BEANS</td>
<td>¾ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>56 GREEN or YELLOW BEANS</td>
<td>½ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>57 BEANS or LENTILS (baked or boiled beans, kidney beans, chickpeas)</td>
<td>½ cup/125 ml cooked</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>58 SPINACH and other green leafy vegetables (greens, collards, kale, mustard greens etc)</td>
<td>½ cup/125 ml cooked or 1 cup raw</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>59 GREEN SALAD (with lettuce)</td>
<td>1 cup/250 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>60 CUCUMBER</td>
<td>½ cup/125 ml shaved</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>61 TOMATOES (fresh)</td>
<td>1 medium</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>62 TOMATOES (canned, pureed or sauced)</td>
<td>¼ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>63 ONIONS (raw or cooked)</td>
<td>½ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>64 BEETS (boiled or pickled)</td>
<td>¼ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>65 TURNIPS or RUTABAGAS</td>
<td>1 medium</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>66 OTHER ROOT VEGETABLES (sweet potatoes, yams, rutab, etc)</td>
<td>½ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>67 YELLOW SQUASH (runner type)</td>
<td>½ cup/125 ml</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
</tbody>
</table>
### Section A

<table>
<thead>
<tr>
<th>FOOD</th>
<th>Average Portion Size</th>
<th>Your Portion Size, if NOT Average</th>
<th>Section B</th>
<th>HOW OFTEN? (Complete one column only)</th>
<th>Section C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>YEAR BEFORE DIAGNOSIS</td>
<td>PER DAY (enter a number)</td>
<td>PER WEEK (enter a number)</td>
</tr>
</tbody>
</table>

### Section B

<table>
<thead>
<tr>
<th>FOOD</th>
<th>Average Portion Size</th>
<th>Your Portion Size, if NOT Average</th>
<th>HOW OFTEN? (Complete one column only)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>PER DAY (enter a number)</td>
</tr>
</tbody>
</table>

### Section C

- **If Ate Food In Season Only** enter Months per Year.
<table>
<thead>
<tr>
<th>FOOD</th>
<th>Your Portion Size, if NOT Average</th>
<th>HOW OFTEN? (Complete one column only)</th>
<th>If Ate Food In Season Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Smaller</td>
<td>Larger</td>
<td>per DAY</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>enter a number</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LIVER</td>
<td>95 g/3 oz</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>FRIED CHICKEN</td>
<td>photo C, medium</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>CHICKEN / TURKEY (roasted or barbecued)</td>
<td>photo C, medium</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>CHICKEN / TURKEY, SKIN REMOVED</td>
<td>photo C, medium</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>SALTED/ DRIED MEAT</td>
<td>photo C, small</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>PICKLED MEAT (brined)</td>
<td>photo C, small</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>SHELLFISH (shrimp, lobster, crab)</td>
<td>85 g/3 oz</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>FRIED FISH</td>
<td>175 g/6 oz</td>
<td>photo B, medium</td>
<td>O</td>
</tr>
<tr>
<td>FISH (baked or broiled)</td>
<td>175 g/6 oz</td>
<td>photo B, medium</td>
<td>O</td>
</tr>
<tr>
<td>CANNED FISH (tuna, salmon)</td>
<td>¼ can/ 48 ml/ 1.7 oz</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>SMOKED FISH or LOX</td>
<td>85 g/3 oz</td>
<td>photo C, small</td>
<td>O</td>
</tr>
<tr>
<td>SALTED/ DRIED FISH</td>
<td>85 g/3 oz</td>
<td>photo C, small</td>
<td>O</td>
</tr>
<tr>
<td>PICKLED FISH</td>
<td>85 g/3 oz</td>
<td>photo C, small</td>
<td>O</td>
</tr>
<tr>
<td>SEA-BIRDS, SEAL</td>
<td>85 g/3 oz</td>
<td>photo C, small</td>
<td>O</td>
</tr>
<tr>
<td>CARIBOU, MOOSE</td>
<td>85 g/3 oz</td>
<td>photo C, small</td>
<td>O</td>
</tr>
<tr>
<td>PARTRIDGE, OTHER WILD BIRDS</td>
<td>85 g/3 oz</td>
<td>photo C, small</td>
<td>O</td>
</tr>
</tbody>
</table>

Cereals and Grains

<table>
<thead>
<tr>
<th>FOOD</th>
<th>Your Portion Size, if NOT Average</th>
<th>HOW OFTEN? (Complete one column only)</th>
<th>If Ate Food In Season Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>per DAY</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>enter a number</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>1/2 cup/ 125 ml</td>
<td></td>
<td></td>
<td>O</td>
</tr>
</tbody>
</table>

118
<table>
<thead>
<tr>
<th>Section A</th>
<th>Section B</th>
<th>Section C</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOOD</td>
<td>Average Portion Size</td>
<td>Your Portion Size, if NOT Average</td>
</tr>
<tr>
<td></td>
<td></td>
<td>per DAY</td>
</tr>
<tr>
<td>113 100% WHOLE GRAIN or DARK BREAD</td>
<td>1 slice</td>
<td>0</td>
</tr>
<tr>
<td>114 80% WHOLE GRAIN, LIGHT RYE</td>
<td>1 slice</td>
<td>0</td>
</tr>
<tr>
<td>115 WHITE BREAD</td>
<td>1 slice</td>
<td>0</td>
</tr>
<tr>
<td>116 WHITE BREAD ROLLS (including hot dog buns etc)</td>
<td>1 roll</td>
<td>0</td>
</tr>
<tr>
<td>117 WHOLE WHEAT ROLLS</td>
<td>1 roll</td>
<td>0</td>
</tr>
<tr>
<td>118 CRACKERS (snack or toddler type)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>119 BRAN/OAT MUFFIN</td>
<td>1 medium</td>
<td>0</td>
</tr>
<tr>
<td>120 OTHER MUFFIN (plain cake, with berries)</td>
<td>1 medium, 1 extra large</td>
<td>0</td>
</tr>
<tr>
<td>121 PANCAKES, WAFFLES</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>122 MACARONI, SPAGHETTI, NOODLES (plan)</td>
<td>1 cup cooked 250 ml</td>
<td>0</td>
</tr>
<tr>
<td>123 RICE</td>
<td>½ cup cooked 125 ml</td>
<td>0</td>
</tr>
<tr>
<td>124 CRISP SNACKS (potato chips, popcorn, pretzels etc)</td>
<td>small bag or 1 cup</td>
<td>0</td>
</tr>
<tr>
<td><strong>Fruits</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>125 APPLE, PEAR</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>126 CITRUS FRUITS (orange, grapefruit)</td>
<td>1 orange, ½ grapefruit</td>
<td>0</td>
</tr>
<tr>
<td>127 BERRIES (strawberries, blueberries, blackberries)</td>
<td>½ cup 125 ml</td>
<td>0</td>
</tr>
<tr>
<td>128 GRAPE</td>
<td>½ cup 125 ml</td>
<td>0</td>
</tr>
<tr>
<td>129 BANANA</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>130 PEACH, PLUM, NECTARINE, APRICOT, CANTALOupe</td>
<td>1/8 or 1 slice</td>
<td>0</td>
</tr>
<tr>
<td>131 WATERMELON</td>
<td>1 wedge, 1/4 large</td>
<td>0</td>
</tr>
<tr>
<td>132 HONEYDEW MELON</td>
<td>1/8 or 1 slice</td>
<td>0</td>
</tr>
<tr>
<td>133 MANGO</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>134 PAPAYA</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>135 APPLESAUCE</td>
<td>½ cup 125 ml</td>
<td>0</td>
</tr>
<tr>
<td>Section A</td>
<td>Section B</td>
<td>Section C</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>FOOD</strong></td>
<td><strong>AVERAGE PORTION SIZE</strong></td>
<td><strong>YEAR BEFORE DIAGNOSIS</strong></td>
</tr>
<tr>
<td></td>
<td>Smaller</td>
<td>Larger</td>
</tr>
<tr>
<td></td>
<td>per DAY</td>
<td>per WEEK</td>
</tr>
<tr>
<td></td>
<td>enter a number</td>
<td>enter a number</td>
</tr>
<tr>
<td><strong>DRIED FRUITS</strong> (raisins, dates, prunes)</td>
<td>2 lbs/2 dates</td>
<td>O</td>
</tr>
<tr>
<td><strong>CANNED FRUIT</strong> all kinds</td>
<td>¼ cup/125 ml</td>
<td>O</td>
</tr>
<tr>
<td><strong>ALL OTHER FRUIT</strong> (fresh, canned, pomegranate, etc.)</td>
<td>1</td>
<td>O</td>
</tr>
<tr>
<td><strong>DESSERTS AND SWEETS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CAKES</strong></td>
<td>1 slice, 2” x 4” x 1”</td>
<td></td>
</tr>
<tr>
<td><strong>PIES and TARTS</strong></td>
<td>1 slice</td>
<td></td>
</tr>
<tr>
<td><strong>DONUTS and SWEET ROLLS</strong></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>COOKIES</strong></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>ICE CREAM</strong></td>
<td>½ cup/125 ml</td>
<td>O</td>
</tr>
<tr>
<td><strong>LIGHT or DIET ICE CREAM</strong></td>
<td>½ cup/125 ml</td>
<td>O</td>
</tr>
<tr>
<td><strong>PUDDING</strong></td>
<td>½ cup/125 ml</td>
<td>O</td>
</tr>
<tr>
<td><strong>DIET or LIGHT PUDDING</strong></td>
<td>½ cup/125 ml</td>
<td>O</td>
</tr>
<tr>
<td><strong>JELLO</strong></td>
<td>½ cup/125 ml</td>
<td>O</td>
</tr>
<tr>
<td><strong>POPSICLES, FREEZIES</strong></td>
<td>1</td>
<td>O</td>
</tr>
<tr>
<td><strong>CHOCOLATE BAR and CHOCOLATE CANDY</strong></td>
<td>1 bar/50g or 5 candy size</td>
<td>O</td>
</tr>
<tr>
<td><strong>CANDY</strong> (without chocolate)</td>
<td>1 caramel</td>
<td>O</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOFU, TEMPEH</strong></td>
<td>½ cup, 2” x 2” x 1” piece</td>
<td>O</td>
</tr>
<tr>
<td><strong>KETCHUP</strong></td>
<td>1 lbs</td>
<td>O</td>
</tr>
<tr>
<td><strong>MAYONNAISE/MIRACLE WHIP, Regular fat</strong> on bread, salad, meat, etc.</td>
<td>1 lbs</td>
<td>O</td>
</tr>
<tr>
<td><strong>MAYONNAISE/MIRACLE WHIP, Light</strong> on bread, salad, meat, etc</td>
<td>1 lbs</td>
<td>O</td>
</tr>
<tr>
<td><strong>SALAD DRESSING, Regular fat (French, Italian, etc.)</strong></td>
<td>1 lbs</td>
<td>O</td>
</tr>
<tr>
<td><strong>OIL (in cooking)</strong></td>
<td>1 tsp</td>
<td>O</td>
</tr>
<tr>
<td>Section A</td>
<td>Section B</td>
<td>Section C</td>
</tr>
<tr>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>FOOD</td>
<td>YEAR BEFORE DIAGNOSIS</td>
<td>If Ate Food In Season Only</td>
</tr>
<tr>
<td></td>
<td>Average Portion Size</td>
<td>HOW OFTEN? (Complete one column only)</td>
</tr>
<tr>
<td></td>
<td>Smaller Larger</td>
<td>per DAY (check)</td>
</tr>
<tr>
<td>156 BUTTER</td>
<td>1 pat, 1 tsp</td>
<td>O</td>
</tr>
<tr>
<td>150 MARGARINE</td>
<td>1 pat, 1 tsp</td>
<td>O</td>
</tr>
<tr>
<td>100 PEANUT BUTTER</td>
<td>1 tbs</td>
<td>O</td>
</tr>
<tr>
<td>101 PEANUTS</td>
<td>30g, 1 oz</td>
<td>O</td>
</tr>
<tr>
<td>104 GRAVY</td>
<td>4 tbs</td>
<td>O</td>
</tr>
<tr>
<td>165 CHOCOLATE</td>
<td>1 tbs</td>
<td>O</td>
</tr>
<tr>
<td>166 CHOCOLATE SPREADS</td>
<td>1 tbs</td>
<td>O</td>
</tr>
<tr>
<td>107 SAUCES</td>
<td>30 ml, 1 tsp</td>
<td>O</td>
</tr>
<tr>
<td>108 WHEAT BRAN</td>
<td>1 tbs</td>
<td>O</td>
</tr>
<tr>
<td>109 WHEAT GERM</td>
<td>1 tbs</td>
<td>O</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. About 1 year before diagnosis, how much of the visible fat on your meat did you eat?</td>
<td>☐️ Most of it. ☐️ Some of it. ☐️ As little as possible. ☐️ Do not eat meat</td>
</tr>
<tr>
<td>2. About 1 year before diagnosis, how often did you eat the skin on chicken?</td>
<td>☐️ Most of it. ☐️ Some of it. ☐️ As little as possible. ☐️ Do not eat chicken</td>
</tr>
<tr>
<td>6. About 1 year before diagnosis, what type of oil did you use in other preparations (for example, in salad dressings)?</td>
<td>☐️ Regular. ☐️ Light. ☐️ Both. ☐️ None.</td>
</tr>
<tr>
<td>8. About 1 year before diagnosis, were you a (please check one box only):</td>
<td>☐️ Non-vegetarian (eats all meat, chicken, fish). ☐️ Partly non-vegetarian (eats chicken, fish, no meat). ☐️ Vegan (eats no dairy, no eggs, no meat). ☐️ Lacto-vegetarian (eats dairy, no eggs, no meat). ☐️ Lacto-ovo vegetarian (eats dairy &amp; eggs, no meat).</td>
</tr>
<tr>
<td>9. About 1 year before diagnosis, were you on a special diet?</td>
<td>☐️ No. ☐️ Yes.</td>
</tr>
</tbody>
</table>

If yes, what type of diet?  

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.

<table>
<thead>
<tr>
<th>Vitamin and Amount - if used</th>
<th>How many pills did you take per week?</th>
<th>How long had you taken them?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C</td>
<td>0 5 per week</td>
<td>24 months</td>
</tr>
<tr>
<td>Multivitamins that include minerals</td>
<td>0 No 0 Yes if yes, usual brand</td>
<td></td>
</tr>
<tr>
<td>Multivitamins, no minerals</td>
<td>0 No 0 Yes if yes, usual brand</td>
<td></td>
</tr>
<tr>
<td>B Complex vitamins</td>
<td>0 No 0 Yes if yes, usual brand</td>
<td></td>
</tr>
</tbody>
</table>

In the following items, DO NOT INCLUDE use of the above MULTIVITAMINS

<table>
<thead>
<tr>
<th>Vitamin A</th>
<th>0 None 0 Below 1000 0 1000-1500 0 above 15000 IU</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C</td>
<td>0 None 0 Below 500 0 500-1000 0 above 1000 mg</td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>0 None 0 Below 400 0 400-500 0 above 800 IU</td>
<td></td>
</tr>
<tr>
<td>Beta-carotene</td>
<td>0 None 0 Below 10000 0 10000-15000 0 above 15000 IU</td>
<td></td>
</tr>
<tr>
<td>Folic acid</td>
<td>0 None 0 Below 1.0 0 1.0 mg 0 above 1.0 mg</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>0 None 0 Below 250 0 250-500 0 above 500 mg</td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td>0 None 0 Below 100 0 100-200 0 above 200 mg</td>
<td></td>
</tr>
<tr>
<td>Other dietary supplements (e.g., yeast, cod liver oil, etc)</td>
<td>0 No 0 Yes, specify type:</td>
<td></td>
</tr>
</tbody>
</table>

* 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): ________________