



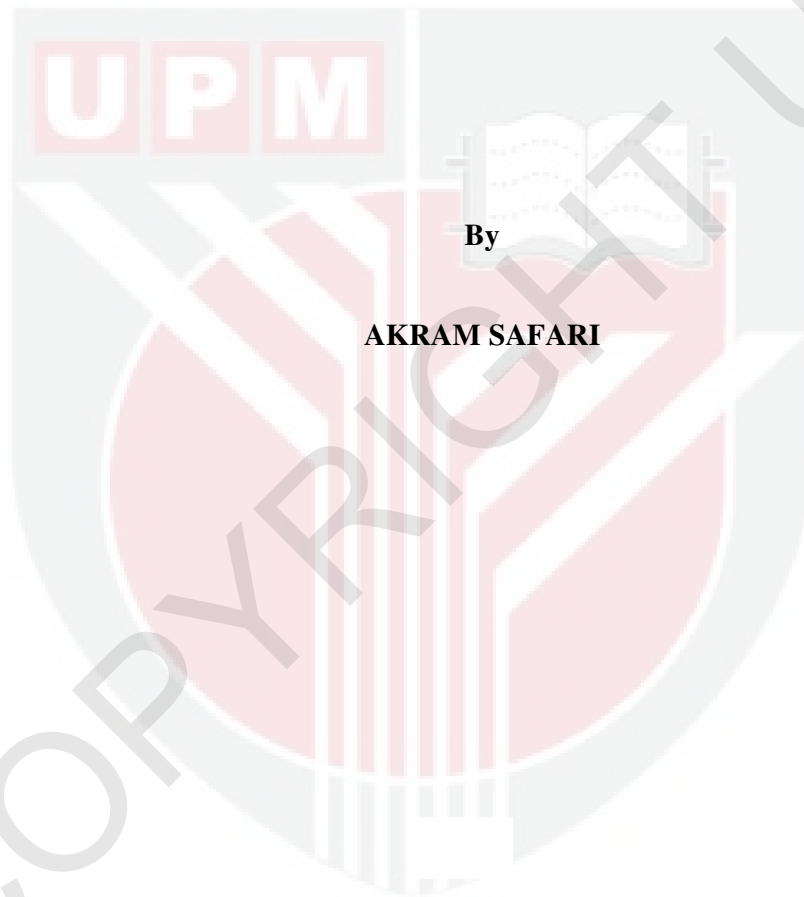
UNIVERSITI PUTRA MALAYSIA

***DIETARY PATTERNS AND OTHER FACTORS IN RELATION TO
COLORECTAL CANCER RISK IN TEHRAN PROVINCE, IRAN***

AKRAM SAFARI

FPSK(M) 2012 48

**DIETARY PATTERNS AND OTHER FACTORS IN RELATION TO
COLORECTAL CANCER RISK IN TEHRAN PROVINCE, IRAN**



By

AKRAM SAFARI

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia,
In Fulfillment of the Requirement for the degree of Master of Science**

October 2012

DEDICATION

This thesis is dedicated to my husband and son who supported me throughout this study. Their understanding, patience and love made completion of this work possible. Additionally, I dedicate this thesis to the memory of my parents who taught me seeking knowledge is a lifelong duty.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in
Fulfillment of the requirement for the degree of Master of Health Science

**DIETARY PATTERNS AND OTHER FACTORS IN RELATION TO
COLORECTAL CANCER RISK IN TEHRAN PROVINCE, IRAN**

By

AKRAM SAFARI

October 2012

Chairman: Dr. Zalilah Mohad Sharif, PhD

Faculty: Medicine and Health Sciences

The mortality and morbidity of cancer are becoming major public health problems in many developed and developing countries. In Iran, colorectal cancer (CRC) is the third most common type of cancer in men and the fourth among women. Colorectal cancer is a multi-factorial disease and diet has a significant role in its etiology and progress. Examination of dietary patterns has been recommended as a promising method in nutrition epidemiology for understanding dietary risk of chronic diseases. The aim of this case-control study was to identify dominant dietary patterns and determine the relationship between dietary patterns and risk of colorectal cancer in Tehran, Iran.

A total of 71 patients with CRC (case group) and 142 patients without CRC (control group) between age 40-75 years old were recruited from four hospitals in Tehran city. Cases and controls were measured for body mass index and interviewed for information on social- demographic status, lifestyle behaviors, family history of cancer and dietary intake. Food intakes during the year before being diagnosed with

CRC in the case group and during the year before the interview for the control group were assessed. Principal component analysis (PCA) method was applied to determine dietary patterns based on the correlation coefficients among the identified 23 food groups.

Both family history of CRC in first ($\chi^2=8.535$, $P= 0.004$) and second degree relative ($\chi^2=8.937$, $P= 0.003$) and intake of mineral supplement ($\chi^2=5.729$, $P= 0.017$), aspirin ($\chi^2=6.265$, $P= 0.012$) and acetaminophen ($\chi^2=7.907$, $P= 0.049$) were found to be significantly different between case and control groups. In this study two dietary patterns were identified – Healthy dietary pattern (high intake of fruits, vegetables, liquid oil, olive, carrot, fish, yoghurt drink, whole grains, low-fat dairy products and nuts) and Western dietary pattern (high intake of sweets, desserts, processed and red meat, animal butter, refined cereals, tea, pickles, carbonated beverage, and sugars). The Healthy dietary pattern was related to respondents who were non-married, had diploma or higher degree, self-employed and with higher income, used acetaminophen and vitamins and consumed raw/ fresh vegetable. The Western dietary pattern was related to being married, current smoker, not using vitamins and aspirin and had high energy intake. After adjusting for confounding factors, the Healthy dietary pattern was associated with a decrease risk of CRC (OR= 0.227; 95% CI=0.108-0.478) while an increased risk of CRC was observed with the Western dietary pattern (OR=2.616; 95% CI= 1.361- 5.030).

In conclusion, this study confirms the beneficial effect of a healthy dietary pattern against the risk of colorectal cancer and the increased risk of colorectal cancer with a Western dietary pattern. Although the exact mechanism for dietary patterns to confer effects on risk of colorectal cancer remains unknown, results from this study support

the importance of using dietary pattern method to investigate the compound relationship between diet and colorectal cancer. This diet-disease relationship can be used for developing interventions that aim to promote healthy eating for the prevention of chronic diseases, particularly colorectal cancer in the Iranian population.



Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

**PATTEN DIETARI DAN PUNCA LAIN YANG BERHUBUNG KAIT
DENGAN RISIKO KANSER KOLOREKTUM DI WILAYAH
TEHRAN, IRAN**

Oleh

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Mortaliti dan morbiditi kanser merupakan masalah kesihatan di kebanyakan negara maju dan juga negara membangun. Di Iran, kanser kolorektal (CRC) adalah kanser yang ketiga paling biasa dalam kalangan lelaki dan keempat dalam kalangan wanita. Kanser kolorektal merupakan penyakit yang berkait dengan pelbagai faktor dan diet mempunyai peranan yang penting dari segi etiologi dan progres. Pemeriksaan corak pengambilan makanan telah dicadangkan sebagai satu kaedah dalam pemakanan epidemiologi yang dapat memberikan maklumat berkaitan risiko diet terhadap penyakit kronik. Tujuan kajian kawalan kes ini adalah untuk mengenalpasti corak pengambilan makanan yang dominan dan menentukan hubungkait di antara corak pengambilan makanan ini dengan risiko kanser kolorektal di Tehran, Iran.

Seramai 71 pesakit dengan CRC (kumpulan kes) dan 142 tidak menghidap CRC (kumpulan kawalan) berusia di antara 40-75 tahun telah direkrut dari empat buah hospital di Tehran. Kumpulan kes dan kumpulan kawalan telah diukur indeks jisim tubuh (IJT) dan ditemubual untuk maklumat tentang status sosio-demografi, gaya

hidup, sejarah kanser keluarga dan pengambilan makanan .Pengambilan makanan semasa tahun sebelum didiagnos dengan CRC untuk kumpulan kes dan semasa tahun sebelum temu bual untuk kumpulan kawalan telah diperolehi. Kaedah *Principle Component Analysis* (PCA) telah digunakan untuk mengenal pasti corak pengambilan makanan berdasarkan korelasi koefisien dalam kalangan 23 kumpulan makanan yang dikenalpasti.

Terdapat perbezaan yang signifikan di antara kumpulan kes dan kawalan bagi sejarah keluarga CRC pada peringkat pertama ($\chi^2=8.535$, $P= 0.004$) dan peringkat kedua ($\chi^2=8.937$, $P= 0.003$) serta pengambilan suplemen mineral ($\chi^2=5.729$, $P= 0.017$), aspirin ($\chi^2= 6.265$, $P= 0.012$) dan acetaminophen ($\chi^2=7.907$, $P= 0.049$). Dalam kajian ini, corak pengambilan makanan yang dikenalpasti adalah corak pengambilan makanan sihat (*Healthy Dietary Pattern – HDP*) (pengambilan yang tinggi untuk buah-buahan, sayur-sayuran, minyak cecair, buah zaitun, lobak merah, ikan, minuman yogurt, bijirin penuh, produk tenusu rendah lemak dan kekacang) dan corak pengambilan makanan Barat (*Western Dietary Pattern*) (pengambilan tinggi untuk manisan, pencuci mulut, daging merah dan produk daging proses, mentega dari sumber haiwan, bijirin proses, teh , jeruk, minuman berkarbonat dan gula). HDP adalah berkait secara signifikan dengan responden yang belum berkahwin, berkelulusan diploma ataupun ijazah, bekerja sendiri, mempunyai pendapatan yang tinggi, menggunakan acetaminophen dan suplemen vitamin dan mengambil sayur-sayuran yang segar/mentah. WDP pula berhubungkait secara signifikan dengan responden yang telah berkahwin, menghisap rokok, tidak menggunakan suplemen vitamin dan aspirin dan mempunyai pengambilan tenaga yang tinggi. Selepas pelarasan untuk faktor-faktor risiko yang lain, HDP dikaitkan dengan risiko CRC

yang rendah (OR= 0.227; 95% CI = 0.108-0.478) manakala peningkatan risiko CRC dilihat dengan corak WDP (OR=2.616; 95% CI = 1.361- 5.030).

Sebagai kesimpulan, kajian ini mengesahkan kebaikan corak pengambilan makanan sihat (HDP) untuk mengurangkan risiko kanser kolorektal dan peningkatann risiko kanser kolorektal dengan corak pengambilan makanan barat (WDP). Walaupun mekanisma sebenar untuk corak pengambilan makanan memberi kesan kepada kanser kolorektal masih belum dikenal pasti, hasil kajian ini menyokong kepentingan penggunaan kaedah corak pengambilan makanan untuk menyiasatkan perkaitan di antara kanser kolorektal dengan diet. Hubungan antara penyakit dan diet ini boleh digunakan untuk membentuk intervensi yang bertujuan mempromosikan tabiat makan yang sihat bagi mencegah penyakit kronik, terutamanya kolorektal kanser dalam populasi Iran.

ACKNOWLEDGEMENTS

Praise to God, the most merciful for blessing me with the strength to complete this undertaking. I wish to convey my sincere appreciation to all kind hearted people mentioned or otherwise in this limited space for their contribution and support throughout my study.

I would like to express my sincere gratitude and thanks to my supervisor Associate Professor Dr. Zalilah Mohd Shariff for her guidance and concern in the preparation of this thesis. She has put in great effort in supervising my research work, offering her valuable expertise and advising me at all times. I thank her for all the encouragement given to me at difficult moments. I would especially like to thank my co-supervisors, Prof. Dr. Mirnalini Kandiah and Associate Professor Dr. Bahram Rashidkhani for their careful reviewing of manuscript, encouragement and many helpful comments during my graduate study.

I appreciate the surgeons and staff of the Surgical Department of Cancer Institute of Imam Khomeini Hospital Complex, Surgical unit Hospital of Shariati, Imam Hussein and Ayatollah Taleghani for their co-operation and commitment in making this researches a success. My appreciation is also extended to all patients who have helped me to in gathering data and completing the questionnaires. Without their participation, this study would not have been possible. I am grateful to the department members of Nutrition and Dietetics of the Faculty Medicine and Health Sciences Universiti Putra Malaysia (UPM) for their views and critics. Appreciation also goes to the colleagues of the Faculty of Nutrition Science and Food Industries, University of Shahid Beheshti Medical Sciences, University of Tehran Medical

Sciences and University of Ghazvin Medical Sciences for the opportunity of my study.

Finally and most crucially, I would like to thank my family for their love, patience and prayers. Not forgetting my friends, who have been great supports. As there are too many of them, it is impossible to name everyone. Nevertheless all of them will always be remembered.

Thank you!



I certify that a Thesis Examination Committee has met on 19 October 2012 to conduct the final examination of Akram Safari on her thesis entitled "Dietary Patterns And Other Factors In Relation To Colorectal Cancer In Tehran Province" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U. (A) 106] 15 March 1998. The Committee recommends that the student be awarded the degree of Master of Science.

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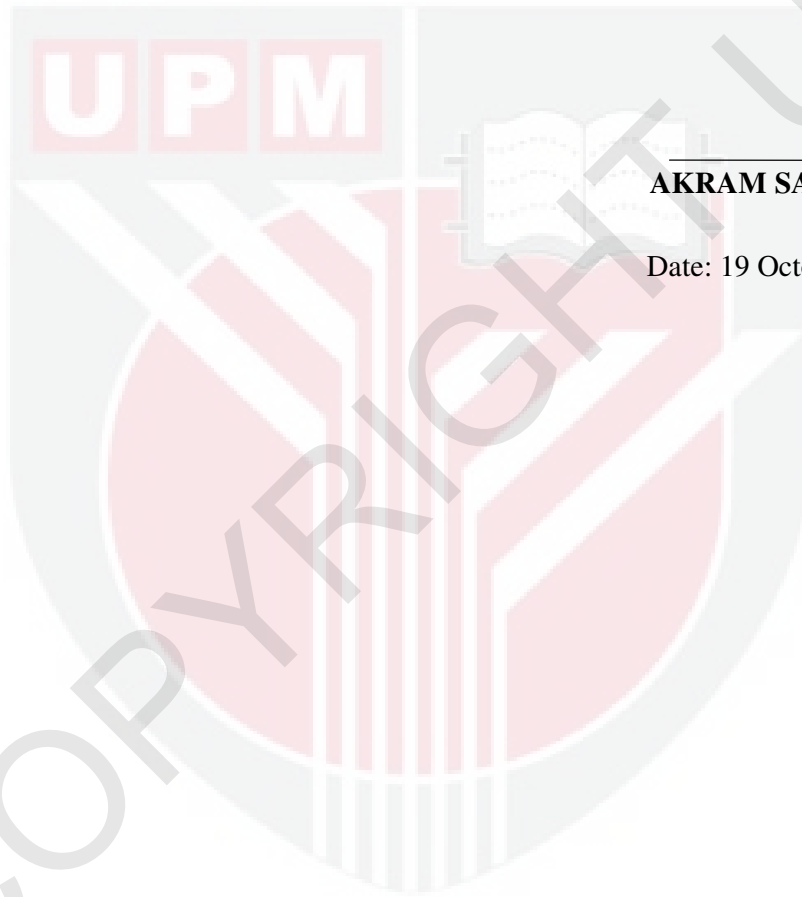
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DECLARATION

I declare that the thesis is original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institutions.



AKRAM SAFARI

Date: 19 October 2012

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LIST OF ABBREVIATIONS

ACS	American Cancer Society
AICR	American Institute for Cancer Research
ASR	Age Standardized Incidence Rate
BMI	Body Mass Index
CI	Confidence Interval
CRA	Colorectal Adenomas
CRC	Colorectal Cancer
CRN	Colorectal Neoplasm
COX-2	Cyclooxygenase-2
FAO	Food and Agriculture Organization
FAP	Familial Adenoma Polyposis
FOBT	Fecal occult blood test
FFQ	Food frequency questionnaire
EI	Energy intake
ENT	Ear Nose Throat
GI	Gastrointestinal
GF1	Growth Factor1
HAAs	Heterocyclic Aromatic Amines
HDP	Healthy Dietary Pattern
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
IBD	Inflammatory Bowel disease
ICD-O	International Classification of Disease-oncology
IGFs	Insulin like growth factors
Kcal	kilocalories
METs	Metabolic Equivalent
MOR	Morbidity odds ratios
NFCR	National Foundation for Cancer Research
NIH	National Institutes of Health
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
NOCs	N-Nitroso Compounds
NHS	National Health Surveys
OR	Odds Ratio
PA	Physical activity
PCA	Principal Component Analysis
PAHs	Polycyclic Aromatic Hydrocarbons
PUFAs	polyunsaturated fatty acids
RR	Relative Risk
SD	Standard Deviation
SFAs	Saturated Fatty Acids
TSNAs	Tobacco Specific Nitrosamines
WDP	Western Dietary Pattern

CHAPTER 1

INTRODUCTION

1.1 Introduction

Cancer is the abnormal growth and division of cells, which can then invade and destroy nearby tissues and other parts of the body through the lymphatic and blood systems (American Cancer Society, 2010). It is usually considered as a single disease but actually comprises more than 100 disorders that are caused by nearly 300 different growths (U.S. National Cancer Institute, National Institute of Health, 2006).

The global burden of cancer has more than doubled during the past three decades (World Cancer Report, 2008). The prevalence of cancer worldwide was approximately 10 million in 2000 and is estimated to reach 27 million in 2030. Furthermore, the total number of deaths from cancer is projected to rise from 6.2 million people in 2000 to 17 million in 2030 (Boyle *et al.*, 2008; Thun *et al.*, 2010). The mortality and morbidity of cancer are becoming a major public health problem in many countries. The World Health Organization (WHO) reported that a higher proportion of cancer occurred in developing and newly developed countries with more than 50% of all cancer cases and 70% of deaths by 2008 (WHO, 2011).

In Iran, there was an increase in newly diagnosed cancer from 17,765 in 2000 to 47,217 in 2005 (Iran National Cancer Registry, 2001; 2006). The prevalence of cancer is high in Iran and mortality due to cancer is growing steadily. Cancer has recently become the third most common cause of death in Iran after car accidents and heart disease (Mousavi *et al.*, 2008; Kolahehdoozan *et al.*, 2010). An earlier study

indicated that the highest incidence rate of cancer was in Tehran city (capital of Iran), which had nearly half of all cancer patients in Iran (Sadjadi *et al.*, 2005).

One of the main types of cancer is colorectal cancer (CRC). In 2008, CRC was estimated to be the third and second most commonly diagnosed cancer in the world with 10.0% and 9.4 % of total cancer cases among males and females respectively (Center *et al.*, 2009 ; Ferlay *et al.*, 2010). In Iran, CRC is becoming the third most common type of cancer in men with an Age Standardized Incidence Rate (ASR) of 8.19 - 8.3 per 100,000 people and the fourth among women with an ASR of 6.5-7.56 per 100,000 (Moghibi *et al.*, 2008 ; Kolahdoozan *et al.*, 2010). Colorectal cancer seems to affect people in the second part of their lifespan and the incidence is related with increasing age (World Cancer Research Fund and American Institute for Cancer Research, 2010; American Cancer Society, 2005). Approximately up to 20% of the recognized risk factors for colon cancer cases are somehow genetically linked (Haggard *et al.*, 2009; Peppone *et al.*, 2009).

There is a general agreement that some features of the western diet can cause colorectal cancer disease. The risk of disease can increase if diets are high in calories, fat, red and processed meat, desserts, high fat dairy products, refined cereals along with inadequate in fruits, vegetables, and whole grains (WHO, 2003). It has also been hypothesized that colorectal cancer is caused by several lifestyle behaviours that include cigarette smoking, physical inactivity, alcohol consumption, obesity (American Cancer Society, 2008) and cooking methods (Mirvish *et al.*, 2002; Raju *et al.*, 2006). In addition, epidemiologic and laboratory studies indicate that the use of aspirin or other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) (Harris *et al.*, 2008 ; Zhang *et al.*, 2008) and also vitamin and mineral supplements such as

calcium, folate, and vitamin A, C and D can have a chemo-preventive effect against large intestine cancer (GrauMv *et al.*, 2003 ; Greenwald *et al.*, 2007).

1.2 Statement of Problem

In Iran, the National Health Survey (NHS) indicated that the causes of mortality since 1992 have changed from infectious diseases to non-infectious diseases and the number of mortality attributable to cancer, heart diseases, accidents and diabetes has grown very rapidly in recent decades (Ghassemi *et al.*, 2002). Moreover, statistics show that deaths due to colorectal cancer have been rising steadily. In 1995, the mortality rate from CRC was 4.25 per 100,000 population. In 2003, this figure rose dramatically to 32.2 per 100,000 population (Mousavi *et al.*, 2008; Pourhoseingholi *et al.*, 2010). A noticeable increase in the incidence of CRC disease was reported in Tehran city (capital of Iran) with 82% Morbidity odds ratios (MOR) during the last three decades (Yazdizadeh *et al.*, 2005 ; Malekzadeh *et al.*, 2009). A shift in the patterns of mortality and high population growth, the increasing trend of urbanization and lack of economic development have been major contributing factors to changes in food consumption and lifestyle patterns of Iranians since 1980 and the consequent dramatic rise in chronic diseases (Ghassemi *et al.*, 2002).

A comparison between the first nationwide household food consumption survey (1991-1995) and the second survey (1995-1998) which were obtained from 24 provinces of Iran showed that the total energy intake (EI) increased from 2600 to 2700 kcal/day with the mean intake already exceeded requirements. There was an increase in the consumption of cereals, fruits, vegetable, meat, and eggs but the consumption of sugar and dairy products remained steady. The results also indicated

that, the average daily intake of total fat increased twofold from 17.5% to 39% which was higher than the recommended range for macronutrients (RDAs). The intake of saturated fatty acids (SFA) as percentage of total EI was high (10%-15%) in the majority of provinces (n=19) with Tehran having the highest level (>15%) (Kimiagar *et al.*, 1998; Ghassemi *et al.*, 2002).

The National Health Surveys in 1999 reported that the prevalence of both overweight and obesity in adults between the ages of 40-69 years for women and men in the urban areas of Iran were 28% and 11% respectively. A recent study of Tehranian adults revealed that there was a sharp trend in the prevalence of obesity from 1999 to 2008 in both sexes with 21% and 38.6% of men and women were obese, respectively (Azizi *et al.*, 2008). The increasing prevalence of overweight and obesity is also related to the increasing prevalence of physical inactivity (WHO, 2006). The Third National Surveillance of Risk Factors of Non-Communicable Disease (SURFNCD, 2007) reported physical activity of 4,120 Iranian adults aged 15-64 years. About 40% of Iranians had moderate activity while 15% were sedentary. Inactive lifestyle was more common in females and in older adults (Ghassemi *et al.*, 2002; Esteghamati *et al.*, 2011).

Numerous studies have investigated the relationship between diet and incidence of CRC but mainly focused on the intake of single nutrients or a few foods, particularly high intake of fat, red meat, and low intake of fruits/vegetables (Terry *et al.*, 2001; Jarvinen *et al.*, 2001; Larsson *et al.*, 2005). Although, these analyses are quite valuable, they give little information on the total diet, which includes a diversity of foods with complex combinations of nutrients (Hu, 2002; Yang *et al.*, 2005; Moeller *et al.*, 2007). Therefore, dietary pattern is considered a suitable technique as it

reflects the overall diet or total eating patterns of people. However, the relationship between dietary patterns and the risk of colorectal cancer is not well understood. As there is no study on the relationship between dietary pattern and the risk of colorectal cancer in Iran, this case- control study aimed to address the following research questions:

1. What are the dietary patterns of the case (with colorectal cancer) and control (without colorectal cancer) groups?
2. Does the case group differ from the control group with respect to:
 - a) Dietary patterns?
 - b) Socio-demographic factors (education, marital status, occupation, and monthly household income)?
 - c) Family history of colorectal cancer
 - d) Lifestyle factors (cigarette smoking, physical activity, cooking methods and medication use)?
 - e) Body mass index (BMI)?
3. Is there any relationship between socio-demographic status, family history of CRC, BMI and lifestyle patterns with identified dietary patterns?
4. Is there any relationship between identified dietary patterns, socio-demographic status, family history of CRC, BMI and lifestyle patterns with case and control group?

1.3 Objectives of Study

1.3.1 General Objective

To determine dietary patterns and its relationship with colorectal cancer

1.3.2 Specific Objectives

1. To determine dietary patterns of case and control groups
2. To examine the differences between case and control groups in relation to
 - a. Dietary patterns
 - b. Socio-demographic factors
 - c. Family history of colorectal cancer
 - d. Lifestyle factors
 - e. Body mass index (BMI)
3. To determine the relationship between
 - a. Socio-demographic factors
 - b. Family history of colorectal cancer
 - c. Lifestyle factors
 - d. Body mass index
 - e. Dietary pattern
and risk of CRC.
4. To determine the relationship between
 - a. Socio-demographic factors

b. Family history of colorectal cancer

c. Lifestyle factors

d. Body mass index

and dietary pattern

5. To determine the independent effect of dietary patterns on the risk of colorectal cancer.

1.4 Hypothesis

1. There is a significant difference between case and control groups related to

a. Socio-demographic status

b. Family history of colorectal cancer

c. Lifestyle factors

d. Body mass index (BMI)

e. Dietary patterns

2. There is a significant relationship between

a. Socio-demographic factors

b. Family history of CRC

c. Lifestyle factors

d. Body mass index

e. Dietary patterns

and risk of colorectal cancer.

3. There is a significant independent effect of dietary patterns on risk of colorectal cancer.

1.5 Research Conceptual Framework

As shown in Figure 1.1, this study examined the risk factors of colorectal cancer, which are namely, socio-demographic, lifestyle, family history of CRC, anthropometric and dietary factors (Heavey *et al*, 2004, Raju *et al.*, 2006; Tamakoshi *et al.*, 2004; Howard *et al.*, 2008; Popkin, *et al.*, 2001; Giovannucci *et al.*, 2002). Socio-demographic factors comprised age, education, marital status, household monthly income and family history of CRC. Lifestyle factors included smoking status, physical activity pattern, cooking methods and medication use. Body mass index was also determined. Dietary patterns were determined using a 125 food items frequency questionnaire. The associations between independent risk factors and CRC were identified. Finally the association between the identified dietary patterns and the risk of CRC was assessed independently of the potential confounders.

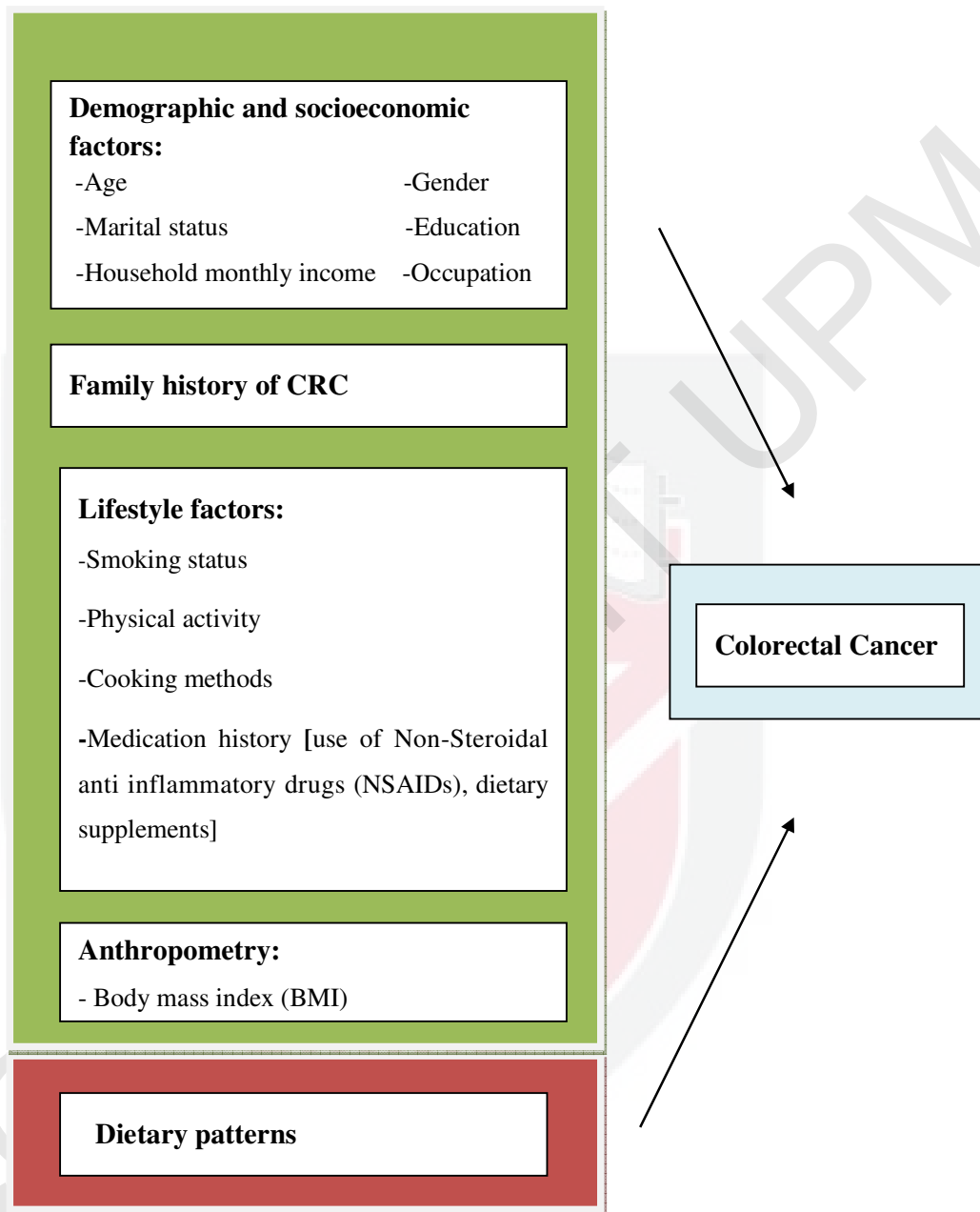


Figure 1.1: Research conceptual framework

1.6 Significance of the Study

In recent years, examination of patterns of dietary intake rather than focusing on the individual nutrients is recommended as a complementary and suitable approach for clarifying relationships between diet and health. These patterns are derived using factor analysis of commonly consumed food items and are based on the correlation between food and nutrient intake. They represent an extensive picture of nutrient and food compositions of diets. The study of dietary patterns definitely has significant implications for public health because these patterns may be easier for people to understand (e.g. healthy and less healthy dietary patterns) and can be used in the prevention of diseases.

The prevalence of CRC is gradually increasing in Iran. Therefore, identification of existing dietary patterns and lifestyle factors such as physical inactivity, obesity, cigarette smoking and alcohol consumption that are associated with CRC risk can be a basis for recommendations to the Ministry of Health on dietary and lifestyle modification strategy for prevention of colorectal cancer. In addition, these information can be used as baseline data by researchers and health professionals for planning intervention programs for patients with colorectal cancer.

Most of the existing data on cancer and its risk factors are collected from developed countries with almost two-thirds of these surveys conducted in either North America or Europe. There are only few published data on factors associated with colorectal cancer in developing and newly developed countries. More studies are

needed to understand risk factors of cancer in these countries as they may differ from those in developed countries due to different genetic predispositions and lifestyle behaviours. The findings of this study could add new knowledge to the existing literature on risk factors of CRC in developing countries.

1.7 Glossary of terms

Glossary of terms for some variables used in this study is as bellow:

1. **Colorectal cancer:** uncontrolled neoplastic cells that develop and grow within the walls of the colon and rectum tissue.
2. **Family history of cancer:** a family history of certain malignancies can place persons at increased risk of developing cancer.
3. **Dietary supplement:** any dietary ingredient that contains minerals, vitamins, herbs or plant products, enzymes and amino acids or a dietary substance used to supplement the diet by increasing total dietary intake.
4. **Non-Steroidal anti-inflammatory drugs:** medicines with anti-fever (or antipyretic) and pain-reducing (or analgesic) effects.
5. **Physical activity:** any bodily movement produced by skeletal muscle that results in a substantial increase over the resting energy expenditure.
6. **Cooking methods:** a method to prepare food by heat and undoubtedly has a functional impact on humans.

7. **Body mass index:** a mathematical formula that correlates with body fat and is expressed as weight in kilograms divided by height in meters squared.

8. **Factor analysis:** It is a method to reduce a large number of variables into smaller independent factors, for use future studies.

9. **Dietary pattern:** classification of food items into 'Healthy' and 'Western' patterns using factor analysis in relation to risk of colorectal cancer.

10. **Food frequency questionnaire (FFQ):** a semi-quantitative questionnaire that consisted of 125 food items commonly consumed by Iranians. Frequency and amount of food consumed were examined as intake prior to development of CRC (cases) or hospital admission (controls).

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