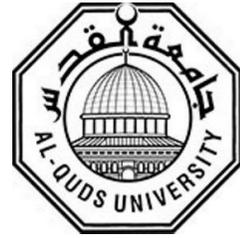


Deanship of Graduate Studies

Al-Quds University



**Determinants of Colorectal Cancer among Patients Attending
Biet Jala Governmental Hospital: A Case-control Study**

Issa Khaled Ghrouz

M.Sc. Thesis

Jerusalem – Palestine

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**Determinants of Colorectal Cancer among Patients Attending Biet Jala
Governmental Hospital: A Case-control Study**

**Prepared by:
Issa Khaled Ghrouz**

B.Sc in Medical Laboratory Sciences /Al Quds University/ Palestine

Supervisor: Dr. Nuha El Sharif

**A thesis submitted in partial fulfillment of requirement for the degree of
Master of Public Health/School of Public Health/ Al-Quds University**

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Thesis approval

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Hospital: A Case-control Study**

Prepared by: Issa Khaled Ghrouz

Registration No.: 21411146

Supervisor: Dr. Nuha El Sharif

Master thesis submitted and accepted, Date: 28-5-2019.

The names and signatures of the examining committee members are as follows:

- | | | | |
|-----------------------------|---------------------------|------------------|--|
| 1. Head of committee | Dr. Nuha El Sharif | Signature |  |
| 2. Internal examiner | Dr. Khaldoun Bader | Signature |  |
| 3. External examiner | Dr. Azzam Salah | Signature |  |

Jerusalem – Palestine

Dedication

I dedicate this work to my dear parents.

To my Grandparents

To my uncle Dr Ibrahim

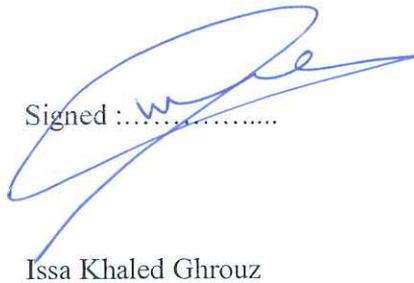
To my beloved wife Aseel

To my brothers and sisters

DECLARATION

I certify that this thesis submitted for the degree of Master is the result of my own research, except where otherwise acknowledged and that this thesis (or any part of the same) has not been submitted for a higher degree to any other university or institution.

Signed :

A handwritten signature in blue ink, appearing to be 'Issa Khaled Ghrouz', written over a dotted line.

Issa Khaled Ghrouz

Date:28/5/2019

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الحمد لله رب العالمين الذي وفقني وأعانني على إتمام هذا العمل

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Executive summary

Background: In Palestine, colorectal cancer is the second most occurring cancer in following Lung cancer. It accounts for 9.9% of all cancer cases. This percentage is considered high when compared to the surrounding countries.

Study problem and justification: There is no screening program for colorectal cancer in Palestine. Also, no study investigated the risk and the protective factors of colorectal cancer. Therefore, we are planning this study to be a baseline study for decision makers to help in planning for a national strategy that can help in preventing this cancer and/or its complications.

Aim & objectives: This study aims to identify the determinants of colorectal cancer among patients attending the oncology department at Biet Jala Governmental Hospital. Its objectives are to determine the associations between the various lifestyle aspects, socio-demographic characteristics, family history of malignancy factors, patients' health status, personal or family colon polyps, radiation therapy, and consanguinity with the risk of developing colorectal cancer.

Study methodology: The study is a matched case control study. Study cases and control were matched by age and gender. The study consisted of 210 participants (105 cases and 105 controls). Males composed 54% of the study population. Cases were Colorectal cancer patients attending the daycare and the oncology department at Beit Jala governmental hospital. Control were any other patients attending other hospital departments. All controls were tested for fecal occult blood test and all were negative. An interview-based questionnaire structured on the risk factors of colorectal cancer was used for data collection.

Statistical Analysis: SPSS version 23 was used for data entry and analysis. Continuous variables were compared between the cases and controls by t test. Chi-square test was used for comparison of categorical variables between the two groups (cases and controls). Conditional logistic regression models were used in the multivariate analysis to generate the odds ratio.

Ethical Considerations: this study was submitted to Al Quds University-SPH graduate studies committee. Approval was obtained from the MOH to start the study at the hospital. A consent form was signed by cases and controls who agreed to participate in the study.

Results: Analysis of the study cases data showed that the mean age of the participants was 61 ± 12 (mean \pm SD) years, and the mean age of the cases at diagnosis was 59.5 years old. Of the cases 54% were males, 88.6% were married, 86.3% of were employed, 77.1% lived in the southern region of the West Bank, 63% of the cases lived in cities, and 92.4% of them were colon cancer patients only.

On the other hand, analysis of control group data showed that the mean age of the participants was same as the cases due to the age and gender matching. Of them 90.5% were married, 82.4 % were employed, 97.1% of them live in the southern region of the west bank, and 31.4% of them lived in cities while 62.9% of them lived in villages.

The multivariate analysis showed that living in villages lowers the risk of colorectal cancer by 34%, while living in the southern region of the West Bank increases the risk of colorectal cancer by 12 folds (AOR= 12.439 CI= 2.724 – 56.809). Also, parental consanguinity almost triples the risk of colorectal (AOR=2.887 CI= 1.171- 7.118). Smoking increases the risk of colorectal cancer by 5.5 folds (AOR= 5.503 CI= 1.866- 16.227). Consuming fruits more than two meals a week reduces the risk of colorectal cancer by about 8 folds (AOR= 0.082 CI=0.032-0.206), while consuming grilled red meat increase the colorectal cancer risk (AOR= 2.847 CI= 1.289-6.287). Taking aspirin was associated with a reduced colorectal cancer risk with (AOR 0.248 CI= 0.099-0.621).

Conclusion: This is one of the very few studies in Palestine that address the case of Colorectal cancer. Most studies were conducted on datasets that were collected from patient’s medical records. Our study used the classical matched case-control, which made it distinctive in its results. Our results confirmed the associations between red meat intake and smoking with colorectal cancer, but also, it showed that parental consanguinity, which is very common in the Arab societies, to be a risk factors for having this cancer. Also, aspirin intake and the consumption of fruits were shown as “protective” factors from colorectal cancer. Further longitudinal studies are needed on those at risk to develop colorectal cancer in order to be able to prevent such a fetal disease.

محددات الإصابة بسرطان القولون والمستقيم لدى المرضى المسجلين في مستشفى بيت جالا الحكومي: دراسة الحالات والضوابط

إعداد: عيسى خالد غروز

إشراف: د. نهى الشريف

الملخص

خلفية الدراسة: إن سرطان القولون والمستقيم يعد ثاني أكثر السرطانات انتشارا في فلسطين بعد سرطان الرئتين حيث يحتل ما نسبته 9.9% من جميع السرطانات. وهذه النسبة تعتبر عالية مقارنة بالدول المحيطة.

هدف الدراسة الرئيسي: تهدف هذه الدراسة لمعرفة محددات مرض سرطان القولون والمستقيم في مرضى السرطان الذين يتلقون العلاج في مستشفى بيت جالا الحكومي. كما تهدف هذه الدراسة لمعرفة العلاقة بين نمط الحياة، العوامل الاجتماعية والسكانية وتاريخ العائلة المرضي والحالة الصحية وزواج الأقارب وخطر الإصابة بمرض سرطان القولون والمستقيم.

منهجية الدراسة: نمط هذه الدراسة هي دراسة للحالات والضوابط حيث تم مطابقة الحالات والضوابط بالعمر والجنس. تكونت هذه الدراسة من 210 مشترك (105 ضابط و105 حالة). الحالات جميعها كانت مرضى مصابين ومشخصين مسبقا بمرض سرطان القولون والمستقيم وكانوا إما مرضى مقيمين في قسم الأورام أو مرضى يتلقون العلاج في العناية النهارية. الضوابط كانوا أي مرضى آخرين غير مرضى السرطانات سواء كانوا مرضى مقيمين في قسم من أقسام المستشفى غير الأورام أو كانوا مرضى العيادات الخارجية. تم عمل فحص الدم المخفي في البراز لجميع الضوابط وكانت نتائجهم جميعا سلبية. ثم قام المشاركون في الدراسة بالإجابة على اسئلة الاستبيان المعد للدراسة عن طريق مقابلتهم جميعا

التحليل الإحصائي: تم إدخال جميع البيانات وتحليلها باستخدام برنامج SPSS-IBM في المرحلة الأولى، تم حساب التكرارات لجميع المتغيرات، وقد عرضت البيانات في جداول وأشكال بيانية، أما في المرحلة الثانية تم فحص العلاقة بين سرطان القولون والمستقيم و عوامل الخطر عند مستوى الدلالة الإحصائية ($p < 0.05$)، كما تم حساب فحص العامل المستقل (t-test) لرصد الاختلاف بين العوامل الخطية بين حالات الدراسة والمجموعة الضابطة، كذلك تم حساب نموذج الانحدار اللوجستي المتعدد لجميع المتغيرات عند الدلالة الإحصائية ($p < 0.05$) في تحليل وحيد المتغير للحصول على نسبة الترجيح ودرجة الثقة 95%.

الاعتبارات الأخلاقية: قدمت هذه الدراسة للجنة البحث العلمي والدراسات العليا في جامعة القدس. تم اخذ الموافقة للبدء في الدراسة والعمل في المستشفى من وزارة الصحة الفلسطينية. قام جميع المشاركون في الدراسة بالموافقة على المشاركة عن طريق التوقيع على نموذج موافقة.

النتائج: تحليل معلومات الدراسة أظهر أن معدل أعمار الحالات المشاركة في الدراسة هو 61 عاما. حيث احتل الذكور ما نسبته 54% منهم وكان 88.6% منهم متزوجا و 86.3% منهم كان يعمل و 77.1% منهم يعيش في الجزء الجنوبي للضفة الغربية و 63% كان يعيش في المدن و 92.4% كانوا مرضى سرطان قولون.

بالجهة المقابلة كان معدل أعمار ونسبة الذكور والإناث في الضوابط مطابق للحالات بسبب المطابقة المتبعة في الدراسة. لكن 90.5% منهم كانوا متزوجين و 82.4% منهم كانوا يعملون و 97.1% يعيش في المنطقة الجنوبية من الضفة الغربية حيث كان 31.4% منهم يعيش في المدن و 62.9% منهم يعيش في قرى و 31.4% منهم يعيش في المدن.

وقد أظهرت نتائج تحليل نموذج الانحدار اللوجستي المتعدد أن سكان القرى أقل عرضة لخطر الإصابة بالمرض. وأظهرت أن السكن في المنطقة الجنوبية من الضفة الغربية يزيد خطر الإصابة بالمرض ب 12 ضعف عن يسكنون بمناطق أخرى. أيضا زواج الأقارب يزيد من خطر الإصابة بالمرض والتدخين يزيد من خطر الإصابة بالمرض بنسبة 550% مقارنة بالذين لا يدخنون. بالنسبة للعوامل الغذائية، أظهرت الدراسة أن الفواكه تقلل من خطر الإصابة بالمرض ولكن اللحم الأحمر المشوي يزيد من خطر الإصابة بالمرض. تناول الأسبيرين أيضا يقلل من خطر الإصابة بالمرض.

الخلاصة: هذه واحدة من الدراسات القليلة في فلسطين التي تطرقت لموضوع مرض سرطان القولون والمستقيم. هذه الدراسة هي دراسة للحالات والضوابط وهذا ما يجعلها مميزة بنتائجها.

الدراسة أكدت أن التدخين، أكل اللحم الأحمر، السكن في الجنوب، زواج الأقارب كلها تزيد من خطر الإصابة بالمرض. وأظهرت أيضا ان تناول الأسبيرين والسكن في القرى وتناول الفاكهة كلها تقلل من خطر الإصابة بالمرض.

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List of abbreviations

BJGH	Biet Jala Governmental Hospital
CI	Confidence Interval
MOH	Ministry of Health
AOR	Adjusted Odds Ratio
CRC	Colorectal Cancer
FOBT	Fecal Occult Blood Test
SPSS	Statistic Package for Social Sciences
ENT	Ear, Nose, Throat
BMI	Body Mass Index
NSAIDs	Non-Steroidal Anti-inflammatory Drugs
MET	Metabolic Equivalent of Task

Chapter One: Introduction

1.1 Background

Colorectal cancer (CRC), is any development of cancer from the colon or rectum (NCI, 2018). It is also known as bowel cancer. CRC may be diagnosed by taking a biopsy from the colon during a colonoscopy or sigmoidoscopy(NCI, 2018). Colorectal cancer treatment may include surgery, radiation therapy, chemotherapy and targeted therapy(NCI, 2018). However, Screening for the disease is still an important procedure for early detection and improvement of the prognosis. The main screening method used for CRC is the fecal occult blood test (FOBT).

Colorectal Cancer is one of the major causes of morbidity and mortality worldwide. It is the third most common cancer in the world after lung and breast cancers, and the fourth in mortality (Wolf et al., 2018). It accounts for 9.7% of all cancer incidence in the world. It is estimated that 1.4 million new cases of colorectal cancer were diagnosed and 693,900 deaths worldwide in 2012. Colorectal Cancer is the third most common cancer in men after lung and prostate cancers, and the second in women after breast cancer(WHO, 2012).

Colorectal cancer is more common in the developed countries (Bener et al, 2011), where it accounts for over 63% of all colorectal cancer cases in the world, and its incidence rate is up to 10 times more in developed countries compared to the other countries(Hagggar & Boushey, 2009). The highest incidence rates are found in Australia, New Zealand, Canada, the United States, and parts of Europe, where as the lowest rates are found in Africa, South-Central Asia and South America(Hagggar & Boushey, 2009).

The incidence of colorectal cancer in the Arab world is low, despite its rank is second to breast cancer in some countries (Bener et al, 2009). In Palestine colorectal cancer ranks second to breast cancer as it composes 9.9% of all cancer cases (PHIC, 2016). This percentage is considered high in comparison to the Arab world and surrounding countries. For example, in Egypt it composes 4.4% and Jordan 9 % colorectal cancer cases of all cancers (Freedman et al, 2006).

Many factors have been found to be associated with or protective against colorectal cancer. About 70% of the colorectal cancer risk can be attributed to environmental factors (Saikali et al, 2004).

Risk factors for colorectal cancer include diets that contains low fiber intake and high in fat, type 2 diabetes mellitus, high body mass index (BMI), physical inactivity, alcohol consumption and smoking (Frezza et al, 2006; Ulrich-Pur et al., 2001).

On the other hand, some factors are protective against colorectal cancer that include: physical activity, younger age, higher education level, hormone replacement therapy, intake of calcium, vitamin D, folate, some antioxidant vitamins and minerals, nonsteroidal anti-inflammatory drugs NSAIDs and a diverse diet including yogurt and resistant starches (Slattery ML et al. 1997). Working to promote the protective factors such as quit smoking, eating a healthy diet and exercising may also help in preventing CRC. The low incidence of colorectal cancer in the Arab countries could be due to the dietary factors, with high intake of fruit and vegetables (Al-Shamsi et al., 2003). However, in Palestine no study investigated the risk factors for CRC.

1.2 Study Justification

Colon cancer is ranked second to breast cancer as the most common cancer among all cancers in Palestinian community with 9.9% of all reported cancer cases (PHIC, 2016). It is noticed that this prevalence percentage is higher than the surrounding countries. For example, CRC counts for 4.4% of all cancer cases in Egypt and 9% in Jordan (Freedman et al, 2006). CRC mortality in Palestine is the second among all cancer mortalities with 13% of all cancer deaths (PHIC, 2016). In the past 14 years, it was noticed that CRC incidence fluctuated but in the overall increased dramatically from 5.7% in 2000 to 10.8% in 2013, and 9.9% in 2014 (PHIC, 2016). (See figure 1)

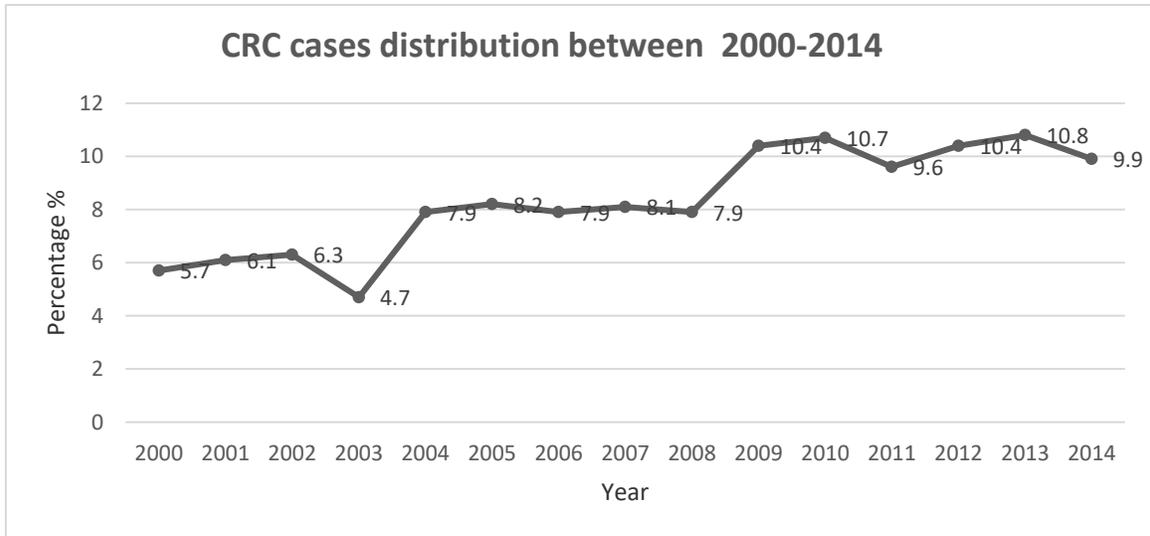


Figure 1: Percentage of reported CRC cases from all reported cancer cases in West Bank between years 2000-2014 (PHIC, 2016)

To date, no study was conducted in Palestine that addresses the factors that contribute for this increase in the incidences over the past 10 years or investigated the risk factors for developing CRC.

Services presented to CRC patients such as treatment and follow up are mainly offered in the cancer care centers distributed along the West Bank. BJGH in the central and the southern districts, and Al Watani governmental hospital in the northern districts are the two Ministry of health governed cancer care centers. On the other hand, Augusta Victoria Hospital in Jerusalem is a private referral hospital where certain services are presented to CRC patients. Treatment services including surgery, chemotherapy, and hormone therapy are delivered in the MOH governed cancer care centers. Since the radiation therapy is not available in the MOH governed cancer care centers, CRC patients who need such a treatment are referred to Augusta Victoria Hospital. CRC patients follow up are presented in the oncology clinics of the MOH governed cancer care centers. In some limited cases, the patient may be referred to neighboring countries to get the needed services.

However, there is no active screening or preventive program dealing with CRC in the Palestinian community. Hence, any research that focuses on the issue of CRC determinants would be of great value to help start establishing national programs dealing with the risk and protective factors of CRC. This study is a baseline study for decision makers to help in planning for a national strategy that can help in preventing this cancer and/or its complications.

1.3 Problem Statement

To our knowledge, no study has been carried out in Palestine to investigate the determinants and the risk factors of colorectal cancer. As a result, there is no clear picture about the epidemiology of CRC in the Palestinian Community and the reasons for its increase in comparison to the Arab world.

Therefore, it is very important to specify the factors that play a role as risk/protective factors among the Palestinian Community. This data is not available in Palestine, which makes it a need. Results of this research will be a baseline for any future plans in the area of prevention, whether primary or secondary prevention, of CRC.

1.4 Study Aim

To identify the determinants of colorectal cancer among patients attending the oncology department at Biet Jala governmental hospital.

1.5 Study Objectives

- a. To determine the relationship between lifestyle factors such as diet, physical activity, obesity, alcohol consumption and smoking with colorectal cancer.
- b. To examine the association between various socio-demographic factors and occupational factors with colorectal cancer.
- c. To determine the association between patient's health status such as diabetes and colorectal cancer.
- d. To investigate the association between family history of cancer and the occurrence of colorectal cancer.
- e. To investigate the association between personal or family colon polyps with the occurrence of colorectal cancer.
- f. To investigate the association between consanguinity marriage and the risk of colorectal cancer.

1.6 Expected Outcome

The study of the determinants and risk factors of CRC would increase the knowledge about these determinants and reveals the specific risk and protective factors in the Palestinian community, as well as addresses the risky groups. Thereafter, programs can be planned or implemented focusing directly on these risky groups and working on the specific risk and protective factors in the large community.

Chapter Two: Literature Review

2.1 Introduction

Literature showed that many factors are associated with colorectal cancer. Those factors are divided into: Socio-demographic factors such as age and gender. Lifestyle factors such as smoking, alcohol consumption, diet, and physical activity, patient's health status such as diabetes and hypertension., family history of colorectal cancer, personal and family history of colon polyps, and the relationship between consanguinity marriage and colorectal cancer. In this chapter, we are presenting the literature review concerning those factors.

2.2 Socio-demographic risk factors

Several epidemiological studies showed that age and sex as risk factors for increased risk of Colorectal cancer.

2.2.1 Age

Table 2.1 shows the studies that investigated the association between Age and CRC.

A population-based study was carried out in Denmark to compare the relative risk of colorectal cancer among patients older than 75 years with that of younger patients during the period 1977 to 1999 found out that CRC is highly affected by age and there is a simultaneous increase in the rate of radical resection among elderly patients, reflecting more effective treatment, may underlie this finding (Iversen et al 2005).

Another study was conducted in USA in 2014 to examine age-based colorectal cancer outcomes in an equal-access health care system (Steele et al 2014). The study examined 7984 patients with equal health care access and resulted in young age at presentation (<50 years) was associated with advanced stage and higher recurrence of colorectal cancer, but similar survival in comparison with older patients. Although increased adjuvant therapy use in younger patients may partially account for stage-specific increases in survival, the relative decreased chemotherapy use overall requires further evaluation (Steele et al 2014).

The World Cancer Research Fund and American Institute for Cancer Research Food, Nutrition, Physical Activity, and the Prevention of Cancer published in 2005 that the diagnosis of CRC increases after the age of 40, and highly rising after the age of 50 (WCRF, 2007). More than 90% of colorectal cancer cases occur in people aged 50 or older (WCRF, 2007).

A prospective cohort study was conducted on 2942 patients in Japan between 1995 and 1998 showed that the frequency of colon cancer increases with age (Okamoto et al., 2002).

Another prospective cohort study in the US was conducted to assess the relationship between body Mass Index, Physical Activity, and Colorectal Cancer Risk Associated with β -Catenin (CTNNB1) Status (Morikawa et al., 2013). The study's population was 109,046 women and 47,684 men. The study found that there is an evidence indicating that the risk of colorectal pathogenesis and carcinogenesis increases exponentially around age 50 (Morikawa et al., 2013).

2.2.2 Sex

Literature and studies showed that sex plays a role in the risk of CRC. Most studies showed that men are at more risk than women. Table 2.2 shows the literature that studied the association between sex and CRC risk.

A case control study in Bavaria to assess the Risk of advanced colorectal neoplasia according to age and gender found that the risk is higher in men than women. It was with an odds ratio of 1.95; 95% confidence interval, CI, 1.91 to 2.00).(Kolligs et al., 2011).

A retrospective cohort study was conducted at the US in 1993 to determine the Colonic neoplasia in asymptomatic persons with negative fecal occult blood test (Rex et al., 1993). The study used 310 men and 186 women and it concluded that the prevalence of colonic neoplasia in asymptomatic persons with negative fecal occult blood tests is substantial, particularly in elderly males (Rex et al., 1993)

In Spain a prospective cohort study that aimed to build a predictive model based on a few simple variables that could be used as a guide for identifying average risk adults more suitable for examination with colonoscopy as a primary screening test.

The study's population was 1649 men and 561 women. The study found that gender affects the risk of CRC and used gender as a major variable alongside BMI and age to build its predictive model (Betes et al., 2003).

A cross sectional study in Poland in 2006 that aimed to derive and validate a model for the detection of advanced neoplasia in the large bowel during screening colonoscopy and to determine the number of persons who would have to undergo colorectal-cancer screening in order to detect one advanced neoplasia in various age groups and to compare these numbers in men and women. Results showed that male sex was independently associated with advanced neoplasia (adjusted odds ratio, 1.73; 95% confidence interval, 1.52 to 1.98; $P < 0.001$) (Regula et al., 2006).

2.3 Lifestyle Factors

Lifestyle factors are of a great concern in our study, since some of them are considered risk factors, while the others are considered protective factors. In our study we are going to address the major lifestyle factors of smoking, alcohol consumption, physical activity and Diet.

2.3.1 Smoking

Smoking was shown to be a risk for CRC. Table 2.3 shows the literature that studied the association between smoking and CRC risk.

In two prospective cohort studies one was conducted in USA (Hannan, Jacobs, & Thun, 2009) and the other was conducted in Norway (Parajuli et al., 2014). Both aimed to determine the relationship between CRC and smoking. Both studies found out that smoking increases the risk of CRC.

A case control study was conducted in Newfoundland and Labrador that its objective was to examine if CRC is associated with smoking in NL population. The study used 702 cases and 717 control and resulted that cigarette smoking increased the risk of CRC in the NL population. Current and former smokers OR 1.36 CI= 1.04 - 1.77 and 1.96 CI= 1.40 - 2.76 (Zhao et al., 2010).

Another case control study in Germany that aimed to assess the risk of CRC associated with lifetime cigarette smoking and the effect of smoking cessation, taking into account relevant potential confounders and also to investigate possible effect modification. The study found smoking for a long duration at a high cumulative dose increases the risk for colorectal cancer > 40 pack-years of smoking (OR: 1.92, 95% CI: 1.13–3.28) (Verla-Tebit, Lilla, Hoffmeister, Brenner, & Chang-Claude, 2006).

2.3.2 Alcohol consumption

Many studies resulted that alcohol consumption is a risk factor for colorectal cancer. Table 2.4 shows the literature that studied the association between alcohol consumption and CRC risk.

A case control study in China that evaluated the association between CRC and alcohol consumption resulted in that Alcohol consumption was associated with increased colorectal cancer risk, but OR was significant only among heavy drinkers (OR=2.18, for ≥ 21 drinks/week) (Wang, Yang, Shen, Ge, & Lin, 2017).

A prospective follow up study that investigated whether the association between alcohol consumption and colon cancer risk differed by family history of colorectal cancer in USA. The study followed 87,861 women for 26 years and 47,290 men for 20 years and it concluded that reducing alcohol consumption may decrease the incidence of colon cancer, especially among those with a family history of colorectal cancer. The study concluded that reducing alcohol consumption may decrease the incidence of colon cancer, especially among those with a family history of colorectal cancer (Cho, Lee, Rimm, Fuchs, & Giovannucci, 2012).

A population based case control study in Denmark that aimed to investigate the relationship between amount and type of alcohol and the risk of colon and rectal cancer found that alcohol intake is associated with a significantly increased risk of CRC (Pedersen, Johansen, & Grønbaek, 2003).

2.3.3 Physical Activity

Studies suggest that physical activity plays a protective role against the risk of CRC. Table 2.5 shows the literature that studied the association between physical activity and CRC risk.

A population-based cohort study in Norway that consisted of 53,242 males and 28,274 females that aimed to examine the association between self-reported occupational and recreational physical activity and the subsequent risk of colorectal cancer. The study found that there is a protective effect of physical activity on colon cancer risk with regard to energy balance, dietary factors, age, social class, body mass index and gastrointestinal transit time (Thune & Lund, 1996).

A population-based study of 952 cases of CRC and 1,205 of controls was conducted in Utah and northern California between 1997 and 2002. The study authors evaluated the association between physical activity and rectal cancer and the study concluded that physical activity was associated with reduced risk of CRC (Slattery et al., 2003)

A case control study in Iran that also resulted in that the risk of CRC will decrease in individuals with higher leisure physical activities (OR = 0.82, CI 95%: 0.73–0.98) (Golshiri, Rasooli, Emami, & Najimi, 2016).

A cohort prospective study in the USA that aimed to assess the relationship between the risk of CRC, its mortality and incidence, and physical activity concluded that regular long term physical activity was associated with a lower risk of colon cancer mortality (Wolin et al., 2010).

2.3.4 Diet

Many dietary factors were found to be a risk factor for colorectal cancer. For example, many studies suggested that high intake of red and processed meat is associated with significant increased risk of colorectal cancer. Table 2.6 shows the literature that studied the association between diet and CRC risk.

Three cohort prospective studies in Japan, USA, and Europe (Ribeka et al,2011, Chao et al, 2005, Norat et al 2005), as well two case control studies in KSA (Nashar et al, 2008) and Canada (Chen et al, 2015) all suggested that red and processed meat are risk factors for CRC. Other dietary factors were found to be protective against CRC. In a prospective cohort study in Sweden (Terry et al 2001) it was found that fruits and vegetables are protective against CRC.

In another prospective cohort study conducted in 10 European countries (Murphy et al 2012) they found out that fibers are protective against CRC. Nashar et al case control study in KSA showed similar results in the protection against CRC with the intake of fruits, vegetables, and fibers and Chen et al case control study in Canada also showed that plant-based diet is protective against CRC. (See table 1 for more details)

2.4 Family History

Studies found that a family history of colorectal cancer increases colorectal cancer risk. Table 2.7 shows the literature that studied the association between family history and CRC risk.

A prospective cohort study in the US conducted between 1986 and 2004 consisted of 51,529 male US health professionals that aimed to assess the association between family history and CRC risk found that the number of adenomas was positively associated with a family history of colorectal cancer (Wark, Wu, van 't Veer, Fuchs, & Giovannucci, 2009).

Another cohort prospective study was conducted in USA in 2009 that followed 75,999 participants to evaluate the relationship between Family history of prostate and colorectal cancer and risk of colorectal cancer in the Women's health initiative. The study concluded that the risk of colorectal cancer is increased similarly among women with colorectal cancer only and among those with both colorectal and prostate cancer diagnosed among first-degree family members (Beebe-Dimmer et al., 2017).

A case control study in Iran that aimed to define the colorectal cancer risk associated with a family history of cancer. The study found that a family history of cancer increases the risk of CRC by two folds (Moghimi-Dehkordi et al., 2010).

Another case control by (Kotake, Koyama, Nasu, Fukutomi, & Yamaguchi, 1995) was conducted in Japan in 1994. The objective of the study was to investigate the relation of a family history of cancer and environmental factors to colorectal cancer. The study findings suggest that a family history of colorectal cancer is an important risk factor for this disease (Colon: OR= 2.0, 95% (CI) 1.03-3.87)), (rectal : (OR = 2.1 CI 0.94-4.48))(Kotake et al., 1995).

In Italy another case control study was conducted. The study aimed to investigate the family history of cancer and the risk of CRC. This study confirms that a family history of CRC in first-degree relatives increases the risk of both colon and rectal cancer, the association being stronger at younger ages and for right colon (Negri et al., 1998).

2.5 Personal History of Polyps

According to Mayo Clinic, polyps are a small clump of cells that forms on the lining of the colon. Most colon polyps are harmless. But over time, some colon polyps can develop into colon cancer (Mayo Clinic, 2018).

Coleman et al conducted a prospective cohort study on 6,972 adenoma patients to quantify CRC risk following polypectomy in a large prospective population-based cohort study. The study findings suggest that CRC risk was elevated in individuals following polypectomy for adenoma (Coleman et al., 2015).

2.6 Consanguinity

There is no evidence that consanguinity is a risk for CRC. Many epidemiological studies indicated that consanguinity has very low or no effect on the risk of developing cancers such as the study of Bener in 2006. Very little studies discussed consanguinity and CRC.

A case control study in Qatar aimed to examine whether parental consanguinity affects the risk of cancer in a local Arab highly inbred population. The study included 370 cases and 635 controls.

The results were that consanguinity has no effect on the overall cancers incidence. It also found that there was an increased risk found for leukemia and lymphoma, colorectal and prostate cancer groups, but a reduced risk in breast, skin, thyroid and female genital cancer groups (Bener et al., 2006.).

2.7 Medications and supplements

Many medications and supplements decrease the risk of CRC and act as a preventive against the disease while some other may increase the risk. Table 2.8 shows the literature that studied the association between medications and supplements and CRC risk.

A nested case control study in the UK that aimed to investigate the risk of CRC among new-users of low-dose aspirin (75–300 mg), including risk by stage at diagnosis. The study used two cohort each contain 170,336 participants. The study indicated that the patients who are starting a low dose of aspirin therapy have a reduced risk of Stages B–D CRC (García Rodríguez, Soriano-Gabarró, Bromley, Lanás, & Cea Soriano, 2017).

A meta-analysis study of prospective cohort studies that addressed the relationship between dietary supplement use and the risk of colorectal cancer. The study concluded that the studies suggest that there is a beneficial role for multivitamins and calcium supplements on colorectal cancer risk, while the association with other supplements and colorectal cancer risk is inconsistent (Heine-Bröring et al., 2015).

A case control study of 289 cases and 314 controls in USA between 1994 and 1996 indicated that there is an inverse association of serum 25-(OH)D with colorectal adenoma is suggested to be stronger in subjects with calcium intake above the (Peters et al., 2001).

A randomized trail study for 39,876 female US health professionals to evaluated associations between intakes of folate and vitamin B₆ and colorectal cancer risk in women enrolled in a randomized trial of aspirin and vitamin E. The findings suggest that there is an inverse association between folate intake and the risk of colorectal cancer (Zhang et al., 2006).

Another randomized trial study to examine the association between NSAID use and CRC mortality among 160,143 post-menopausal women enrolled in the Women's Health Initiative. The study results suggest that NSAID use is associated with lower CRC mortality and risk among post-menopausal women who use these medications more consistently over time (Coghill et al., 2012).

A randomized trial study to assess the effect of folic acid supplementation on recurrent colorectal adenoma. The study randomly assigned participants to receive folic acid (1 mg/d) ($n = 338$) or placebo ($n = 334$) for 3–6.5 y. The study findings do not support an overall protective effect of folic acid supplementation on adenoma recurrence (Wu et al., 2009).

2.8 Health Status

The health status of the people plays a key role in their risk of having CRC. Diabetes, BMI and dyslipidemia all affect the risk of CRC. Table 2.9 shows the literature that studied the association between health status and CRC risk.

A prospective cohort study in USA on 599 diabetic and 17,681 nondiabetic adults to quantify the association of treated diabetes with cancer incidence and cancer mortality. The study concluded that diabetes appears to exert a greater influence downstream on the risk of mortality in people with cancer than on upstream risk of incident cancer (Yeh et al., 2012).

Another prospective cohort study to assess the influence of pre-existing diabetes on prognosis of patients with colorectal cancer on 1,213 patients aged 67 or older with colorectal cancer. The study results suggest that pre-existing diabetes increased risk of total mortality among patients with colorectal cancer, especially among cancer patients who had diabetes with complications (Luo, Lin, He, & Hendryx, 2014).

In Japan another prospective cohort study was conducted to estimate whether diabetes mellitus (DM) may be associated with an increased risk of colorectal cancer (CRC) mortality. The study used 40,510 men and 55,571 women and concluded that the risk of

CRC mortality is significantly increased in both sexes and women with diabetes (Tan et al., 2016).

A prospective cohort study to assess if BMI is a risk for CRC or not. The study was on 46,551 participants 50-80 years old and colon cancer mortality was assessed after 30 years of follow-up. The study confirms that there is a relationship between BMI and long-term colorectal cancer mortality. Modulation of BMI may reduce risk of CRC mortality (Shaukat, Dostal, Menk, & Church, 2017).

A retrospective cohort study on 1.79 million Israeli men and women to examine the association between the body mass index (BMI) in late adolescence and the risk of colon and rectal cancer. The study found that being overweight or obese in adolescence was associated with an increased risk of subsequent colon cancers in men and women, whereas obesity was associated with rectal cancer (Levi et al., 2017).

A nest case cohort study on 34,148 subjects in Italy to examine the relationship between CRC risk and dyslipidemia. The study findings suggest that high levels of total and LDL cholesterol increase colorectal cancer risk, particularly in men and postmenopausal women (Agnoli et al., 2014).

Table 2.1: Studies on association between Age and CRC risk

Authors	Location and date	Study design	Sample Size	Conclusion
Iversen et al 2005	Denmark 1977-1999	Population based Study	All patients over 75 years old from 1977 to 1999	A simultaneous increase in the rate of radical resection among elderly patients, reflecting more effective treatment, may underlie this finding.
Steele et al 2014	USA 1993- 2008	retrospective large multi-institutional database analysis.	7948 patients	In an equal-access system, young age at presentation (<50 years) was associated with advanced stage and higher recurrence of colorectal cancer, but similar survival in comparison with older patients.
Okamoto et al 2002	Japan 1995-1998	Prospective cohort study	2942 consecutive patients (1907 men, 1035 women; mean age 61 years, range 11 to 95 years)	The frequency of right-sided colon cancer increases with patient age.
Morikawa et al 2013	USA, Boston 2012	Prospective cohort study	109,046 women and 47,684 men	evidence indicating that the risk of colorectal pathogenesis and carcinogenesis increases exponentially around age 50

Table 2.2: Studies on association between Gender and CRC Risk

Authors	Location and date	Study design	Sample Size	Conclusion
(Kolligs et al., 2011)	Bavaria 2006-2008	Case control	625,918 outpatient	Men are at higher risk of having advanced neoplasia diagnosed upon colonoscopy than women.
(Rex et al., 1993)	USA 1993	Retrospective study	310 males and 186 females	The prevalence of colonic neoplasia in asymptomatic persons with negative fecal occult blood tests is substantial, particularly in elderly males.
(Betes et al., 2003)	Spain 2003	Prospective Study	1649 males and 261 females	Gender increases the risk of CRC. Males are more at risk. Age, gender, and BMI can be used to build a simple score to select those average risk adults who might be candidates for primary screening colonoscopy.
(Regula et al., 2006)	Poland 2006	Cross sectional study	18012 males and 32136 females	The study detected advanced neoplasia at a significantly higher rate in men than in women, which may warrant refinement of the screening recommendations for colorectal cancer.

Table 2.3: Studies on association between Smoking and CRC Risk

Authors	Location and date	Study design	Sample Size	Conclusion
(Wang et al., 2017)	China 2008-2013	Case control	310 cases 620 controls	The study confirmed that heavy alcohol consumption was associated with an increasing risk of colorectal cancer
(Cho et al., 2012)	USA 1980-1986	Prospective cohort	87,861 women and 47,290 men	Reducing alcohol consumption may decrease the incidence of colon cancer
(Pedersen et al., 2003)	Denmark 2002	Prospective cohort	15 491 men and 13 641 women,	Alcohol intake is associated with a significantly increased risk of CRC

Table 2.4: Studies on the association between Alcohol consumption and CRC Risk

Authors	Location and date	Study design	Sample Size	Conclusion
(Wang et al., 2017)	China 2008-2013	Case control	310 cases 620 controls	The study confirmed that heavy alcohol consumption was associated with an increasing risk of colorectal cancer
(Cho et al., 2012)	USA 1980-1986	Prospective cohort	87,861 women and 47,290 men	Reducing alcohol consumption may decrease the incidence of colon cancer
(Pedersen et al., 2003)	Denmark 2002	Prospective cohort	15 491 men and 13 641 women,	Alcohol intake is associated with a significantly increased risk of CRC

Table 2.5: Studies on association between Physical Activity and CRC risk.

Authors	Location and date	Study Design	Sample size	Conclusion
(Thune & Lund, 1996)	Norway 1972-1978	Cohort prospective	53,242 males and 28,274 females	protective effect of physical activity on colon cancer
(Slattery et al., 2003)	Utah and northern California 1997-2002	Case control	952 cases and 1205 controls	physical activity was associated with reduced risk of rectal cancer in these data. The reduced risk was similar to that previously observed for colon cancer.
(Golshiri et al., 2016)	Iran 2006-2008	Case Control	100 cases and 400 controls	that the risk of CRC will decrease in individuals with higher leisure physical activities
(Wolin et al., 2010)	USA 1982- 1997 and 1998-2005	Cohort Prospective	Ten-year physical activity analysis included 1,863 incident and 826 fatal cases, whereas the longer-term exposure analysis included 1,386 incident and 602 fatal colon cancer cases.	Regular long-term physical activity was associated with a lower risk of colon cancer mortality.

Table 2.6: Literature on Association between Diet and CRC risk.

Authors	Study Design	Location and date	Analysis Methods	objectives	Sample size	Protective factors	Risk factors	Conclusion
Ribeka et al 2011	Prospective cohort	Japan 1995-1998	Cox proportional hazards model	To examine associations between the consumption of red and processed meat and the risk of subsite-specific colorectal cancer by gender in a large Japanese cohort.	80,658 men and women aged 45-74 years	non	Red meat Women : HR= 1.48 (1.01, 2.17; trend p=0.03) Men : HR=1.44 (1.06, 1.98; trend p=0.07	red meat intake may modestly increase the risk of colon cancer in middle-aged Japanese, although the highest quintile of red meat consumption could be considered moderate by Western standards.
Chao et al 2005	Prospective cohort	US 1982-1992/1993	Cox proportional hazards model	To examine the relationship between recent and long-term meat consumption and the risk of incident colon and rectal cancer	148 610 adults aged 50 to 74 years	non	processed meat (RR, 1.50; 95% [CI], 1.04-2.17), Red Meat : RR, 1.71; 95% CI, 1.15-2.52; P = .007 for trend	prolonged high consumption of red and processed meat may increase the risk of cancer in the distal portion of the large intestine
Norat et al 2005	Prospective cohort	Europe (10 countries) 1992-1998	Cox proportional hazards model	To examine whether associations exist between intakes of red and processed meat, of poultry, and of fish and colorectal cancer risk	478 040 men and women from	fish (>80 g/day versus <10 g/day, HR = 0.69, 95 % CI = 0.54 to 0.88; P _{trend} <.001)	red and processed meat (highest [>160 g/day] versus lowest [<20 g/day] intake, HR = 1.35, 95% CI = 0.96 to 1.88; P _{trend} =.03)	Our data confirm that colorectal cancer risk is positively associated with high consumption of red and processed meat and support an inverse association with fish intake.

Table 2.6.....Continued

Authors	Study Design	Location and date	Analysis Methods	objectives	Sample size	Protective factors	Risk factors	Conclusion
Nashar et al 2008	Case Control	KSA	odds ratio (OR)	to assess various dietary factors and the nutritional status of hospitalized patients with colorectal cancer.	50:50	Beef (OR=0.18, p<0.02) Bran (OR=0.04, p<0.01) breakfast cereals (OR=0.11, p<0.01), broccoli (OR=0.12, p<0.02), cabbage (OR=0.21, p<0.04), banana (OR=0.2, p<0.01), and grapes (OR=0.23, p<0.01)	lamb (OR=13.5, p<0.01) chicken with the skin and fried eggs (OR=4, p<0.01) and (OR=4.93, p<0.01) milk (OR=9.88, p< 0.04) and (OR=10.5, p<0.03)	The higher consumption of meat and fat from animal sources could increase the risk of colorectal cancer. The high consumption of whole wheat bread, fruits and vegetables with high fiber content could play a protective role against the risk of colorectal cancer in the Saudi society.
Terry et al 2001	Prospective cohort	Sweden 1998	Cox proportional hazards model	To investigate the protective effect of fruit, vegetable, and dietary fiber consumption on colorectal cancer risk.	61 463 women	High consumption of fruits and vegetables	non	Individuals who consume very low amounts of fruit and vegetables have the greatest risk of colorectal cancer.

Table 2.6.....Continued

Authors	Study Design	Location and date	Analysis Methods	objectives	Sample size	Protective factors	Risk factors	Conclusion
Murphy et al 2012	Prospective cohort	Europe 10 countries	Cox proportional hazards model	To estimate the association by cancer sub-site and fiber food source; and to scrutinize the fiber-colorectal cancer relationship further by examining possible interactions by age, sex, and other lifestyle, anthropometric, and dietary variables.	521,448 participants	fiber 0.87, 95% CI: 0.79–0.96	non	Our results strengthen the evidence for the role of high dietary fibre intake in colorectal cancer prevention.
Chen et al.2015	Case Control	Canada 2015	Conditional and unconditional logistic models	to assess if dietary patterns are associated with the risk of CRC in the population of Newfoundland and Labrador (NL)	506 CRC patients (306 men and 200 women) and 673 controls (400 men and 273 women)	plant-based diet OR of 0.55 (95% CI: 0.35-0.87)	Meat-diet (ORs) of 1.84 (95% CI: 1.19-2.86) Sugary-diet OR 2.26 (95% CI: 1.39-3.66)	Meat-diet/Sugary-diet patterns increased and Plant-based diet pattern decreased the risk of CRC

Table 2.7: Literature on Association between Family history and CRC risk

Authors	Location and date	Study Design	Sample size	Conclusion
(Wark et al., 2009)	USA 1984-2004	Prospective cohort	51,529 males	Adenomas was also positively associated with a family history of colorectal cancer.
(Beebe-Dimmer et al., 2017)	USA 2009	Prospective cohort	75,999 participants	Findings suggest risk of colorectal cancer is increased similarly among women with colorectal cancer only and among those with both colorectal and prostate cancer diagnosed among first-degree family members.
(Moghimi-Dehkordi et al., 2010)	Iran 2010	Case control	393 patients (231 males and 162 females) and 393 controls	A family history of cancer increases the risk of CRC by two folds
(Kotake et al., 1995)	Japan 1992-1994	Case Control	363 case and 363 controls	Our findings suggest that a family history of colorectal cancer is an important risk factor for this disease
(Negri et al., 1998)	Italy 1998	Case Control	1225 incident cases of colon cancer, 728 cases of rectal cancer and 4154 controls	This study confirms that a family history of CRC in first-degree relatives increases the risk of both colon and rectal cancer, the association being stronger at younger ages and for right colon.

Table 2.8: Literature on association between Medications and supplements and CRC risk

Authors	Location and date	Study Design	Sample size	Conclusion
(García Rodríguez et al., 2017)	UK 2000 - 2009	Nested Case Control	Two cohorts each 170,336	Patients starting low-dose aspirin therapy have a reduced risk of Stages B–D CRC, suggesting a role for low-dose aspirin in the progression of established CRC
(Peters et al., 2001)	USA 1994-1996	Case Control	289 cases and 314 controls	There is an inverse association of serum 25-(OH)D with colorectal adenoma is suggested to be stronger in subjects with calcium intake above the median (<i>P</i> for multiplicative interaction 0.13).
(Zhang et al., 2006)	USA 1992	Randomized Trial	39,876 female US health professionals	Findings suggest an inverse association between folate intake and the risk of colorectal cancer,
(Coghill et al., 2012)	USA 1993-1998	Randomized Trial	161,808 post-menopausal women	The results support prolonged NSAID use in post-menopausal women for the prevention of poor CRC outcomes.
(Wu et al., 2009)	USA 1996 - 2004	Randomized Trial	338 subjects and 334 placebos	The study results do not support an overall protective effect of folic acid supplementation on adenoma recurrence.

Table 2.9: Literature on association between health status and CRC risk

Authors	Location and date	Study Design	Sample size	Conclusion
(Yeh et al., 2012)	USA 1989-2006	Prospective cohort	599 diabetic and 17,681 nondiabetic adults	Diabetes appears to exert a greater influence downstream on the risk of mortality in people with cancer than on upstream risk of incident cancer.
(Luo et al., 2014)	USA 2009-2012	Prospective cohort	61,213 patients	Pre-existing diabetes increased risk of total mortality among patients with colorectal cancer, especially among cancer patients who had diabetes with complications.
(Tan et al., 2016)	Japan 2009	Prospective cohort	40,510 men and 55,571 women	The risk of CRC mortality is significantly increased in both sexes and women with diabetes.
(Shaukat et al., 2017)	USA 2007	Prospective cohort	46,551 participants	Modulation of BMI may reduce risk of CRC mortality.
(Levi et al., 2017)	Israel 2012	Retrospective cohort	1,087,358 Jewish men and 707,212 Jewish women	Being overweight or obese in adolescence was associated with an increased risk of subsequent colon cancers in men and women, whereas obesity was associated with rectal cancer.
(Agnoli et al., 2014)	Italy 2014	Nested case cohort study	34,148 subjects	The findings suggest that high levels of total and LDL cholesterol increase colorectal cancer risk, particularly in men and postmenopausal women.

Chapter Three: Conceptual Framework

3.1 Introduction

This chapter links the factors that are associated with the incidence of colorectal cancer (i.e. the conceptual framework components). These factors are divided into two main groups: Non-modifiable risk factors such as age, gender family history and hereditary factors, and modifiable factors i.e. environmental and lifestyle factors that may play an important role in the incidence and development of colorectal cancer(Hagggar & Boushey, 2009).

In literature personal history of adenomatous polyps, personal history of inflammatory bowel disease, family history, and inherited genetic factors were shown as non-modifiable risk factors that are associated with the occurrence of CRC (Aicr& WCRF, 2007; American Cancer Society, 2018; Hagggar & Boushey, 2009; Janout & Kollárová, 2001; Mayoclinic, 2018; National Institutes of Health, 2006). On the other hand, diet, physical activity, obesity, cigarette smoking and alcohol consumption were shown as factors associated with CRC but are considered modifiable factors for CRC(Aicr& WCRF, 2007; American Cancer Society, 2018; Hagggar & Boushey, 2009; Janout & Kollárová, 2001; Mayoclinic, 2018; National Institutes of Health, 2006).

3.2 Colorectal cancer definition

Colorectal cancer is a development of tumor from the colon or rectum. It may be benign, or malignant(American Cancer Society, 2018). It is also called bowel cancer. Most colorectal cancer cases are because of old age and lifestyle factors, and some of the cases are due to some genetic disorders (Aicr & WCRF, 2007).

3.3 Colorectal cancer diagnosis

Colorectal cancer may be diagnosed using tests and procedures in which the doctors need to examine the malignant cells. Diagnosis aims to take samples from areas of the colon that are suspicious for tumor development. Samples are taken during colonoscopy or sigmoidoscopy, and that depends on the location of the tumor. Then the sample are confirmed by microscopic examination of the taken sample (Cunningham et al., 2010).

The most common screening and diagnosis procedures and tests are: Fecal occult blood, colonoscopy, sigmoidoscopy, CT scan, and blood tests.

3.4 Theoretical and Conceptual framework

According to literature review and after reviewing all models suggested for risk factors for colon and rectum cancers, the theoretical models in the world summary i.e. American Cancer Society, Mayo Clinic indicates the following:

The risk factors are summarized as follows:

- Socio-demographic factors (e.g. age, sex, and race\ethnicity).
- Life style factors (e.g. diet type, smoking, physical activity and alcohol consumption).
- Family history (e.g. having a close relative with colorectal cancer).
- Medical conditions (e.g. diabetes mellitus)
- Medication (e.g. aspirin).
- A personal history of inflammatory bowel disease
- A personal history of colorectal polyps or colorectal cancer
- Inherited syndromes (e.g. familial adenomatous polyposis (FAP) and Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC))

Conceptual framework for this study:

- Socio-demographic factors (e.g. age, sex, and race\ethnicity).
- Life style factors (e.g. diet type, smoking, physical activity and alcohol consumption).
- Family history (e.g. having a close relative with colorectal cancer).
- Medical conditions (e.g. diabetes mellitus)
- Medication (e.g. aspirin, ibrufen, and supplements).
- A personal history of inflammatory bowel disease
- A personal history of colorectal polyps or colorectal cancer
- Consanguinity marriage that is popular in the Palestinian community.

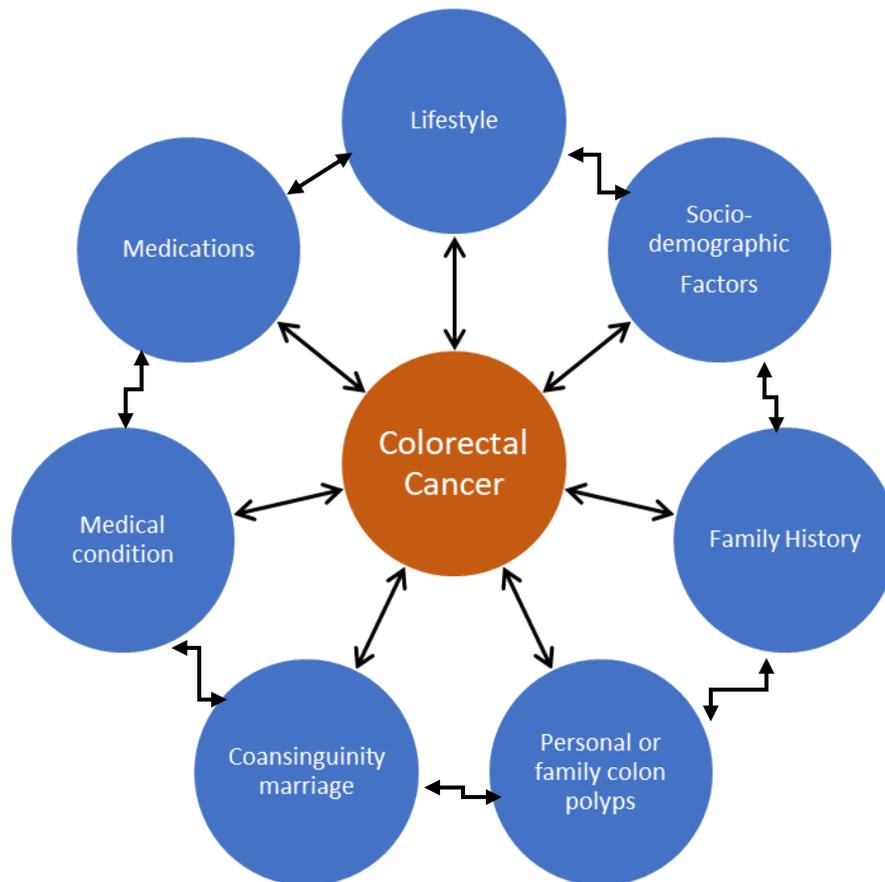


Figure 2: Study Conceptual Framework

3.5 Colorectal Cancer and socio-demographic risk factors

3.5.1 Age

Colorectal cancer diagnosis increases with age. It increases progressively from age 40, rising highly after the age 50 (Rise et al, 2008). 90% and more of colorectal cancer cases occur in people of age 50 and older (Rise et al, 2008). Colorectal cancer incidence rate in people aged 60 to 79 years is more than 50 times higher than people younger than 40 years (ACS, 2009). However, colorectal cancer is increasing among younger people (O'Connell et al, 2003).

3.5.2 Sex

Risk of colorectal cancer (CRC) is considerably higher in men compared to women (Majek et al, 2013).

3.6 Colorectal cancer and lifestyle factors

3.6.1 Smoking

Smoking is harmful to the colon and rectum. It is estimated that about 12% of colorectal cancer deaths are attributed to smoking (Zisman et al, 2006). Evidence shows that the carcinogens that are found in the tobacco increases cancer growth in the colon and rectum, and thus increases the risk of colorectal cancer diagnosis (Janout et al, 2001). Cigarette smoking is crucial for the formation and growth rate of adenomatous polyps, the colorectal cancer precursor lesions. Larger colon polyps were found in the colon and rectum of long-term smokers (Botteri et al, 2008).

3.6.2 Alcohol consumption

Alcohol consumption is associated with increased risk of developing colorectal cancer. Alcohol consumption plays a key factor in the diagnosis of colorectal cancer at a younger age (Zisman et al, 2006). Also alcohol consumption increases the proportion of tumors in the colon (Bazensky et al, 2007). The mechanism is believed to be that the reactive metabolites of alcohol such as acetaldehyde are carcinogenic (Pöschl et al, 2004).

Alcohol may also serve as a solvent, that enhances the penetration of other carcinogenic molecules into mucosal cells (Pöschl et al, 2004). It is also believed that alcohol high consumers may have diets that are low in the essential nutrients, that leads to make the tissues more susceptible to carcinogenesis (Pöschl et al, 2004).

3.6.3 Physical Activity

Physical inactivity and overweight, are reported to be responsible for about about fourth to third of colorectal cancer cases (Boyle et al 2000). It has been proven that higher levels of physical activity are associated with a lower risk of developing colorectal cancer. The relationship is believed to be a dose–response relationship, with the increase of frequency and intensity of physical activity it will inversely lower the risk of developing colorectal cancer (Boyle et al 2000, Lee KJ et al, 2007). Maintaining regular levels physical activity in addition to a healthy diet will decrease the risk of colorectal cancer. The mechanism of the relationship between physical activity and colorectal cancer risk that the physical activity raises the metabolic rate and increases oxygen uptake (Lee KJ et al, 2007). It also increases the body's metabolic efficiency and capacity, and reduces blood pressure and insulin resistance. In addition to all of that, physical activity increases gut motility thus reducing colorectal cancer risk (Lee KJ et al, 2007).

3.6.4 Diet

There's a strong association between diet and the risk of colorectal cancer. It is believed that changes in food habits may reduce up to 70% of colorectal cancer burden (Willett, 2005). High fat diets, especially from animal origin, are considered to be a major risk factor for colorectal cancer (Boyle et al, 2000). High meat consumption has also been associated with increased risk of developing colorectal cancer (Larsson et al, 2006). The mechanisms for this association between red meat consumption and colorectal cancer is believed to be due to that red meat include the presence of heme iron (Kabat et al, 2007). Also cooking meats at high temperatures, results in the production and release of free radicals such as heterocyclic amines and polycyclic aromatic hydrocarbons, that are believed to be carcinogenic (Santarelli et al, 2008). Some studies suggest that people who consume low in fruits and vegetables diets, are at higher risk of colorectal cancer (Boyle et al, 2000).

3.7 Family History of colorectal cancer or colon polyps

About 20% of people who develop colorectal cancer have other family members who have been diagnosed or affected by colorectal cancer (Skibber et al, 2001). People who have one or more first-degree relatives with history of colorectal cancer or adenomatous polyps are at increased risk. The risk of having colorectal cancer is higher among people with a stronger family history, i.e. history of colorectal cancer or adenomatous polyps in any first-degree relative; or history of colorectal cancer or adenomatous polyps in two or more first-degree relatives at any age (Boardman et al, 2007).

3.8 Personal history of personal bowel disease

Inflammatory bowel disease (IBD) is a term used to describe inflammation that occur in the colon and the small intestine. Two diseases, ulcerative colitis and Crohn disease are the major IBD diseases (Baumgart, 2007). Ulcerative colitis is a long-term condition that results in inflammation and ulcers of the colon and rectum (NIDDK, 2014). Crohn disease causes inflammation that may affect any part of the gastrointestinal tract from mouth to anus (NDDIC, 2013). The overall risk of developing colorectal cancer is increased in people who suffer from these conditions. It has been estimated that the relative risk of colorectal cancer in patients with inflammatory bowel disease is between 4- to 20-fold (Janout et al, 2001).

3.9 Personal history of colon polyps

A colorectal polyp is clump of cells that grow on the lining of the colon. Colorectal polyps are harmless but if untreated and overtime can develop into colorectal cancer (Santero et al, 2005). Almost 95% of colorectal cancer cases develop from colon polyps (adenomas) (de Jong et al, 2005). People with history of polyps (adenomas) are at increased risk of developing colorectal cancer, other than people who never had history of adenomas (de Jong et al, 2005).

3.10 Consanguinity

Consanguinity is a marriage between relatives and has various degrees (Stern, 1973). There is a historically high prevalence of consanguineous marriages in many communities throughout the world, especially in countries of the Middle East, Northern Africa and South Asia (Al Awaadi et al, 1985). In Palestine it has been reported that 40% of all marriages are consanguineous and about 20% are between first degree relatives (Freundlich et al, 1984, Zlotogora et al, 2000). Evidences has proven that in a population with a high rate of consanguinity, there is a significant increase in the prevalence of common adult diseases like cancer, mental disorders, heart diseases, gastro-intestinal disorders, hypertension and hearing deficit (Bener et al, 2007).

3.11 Summary

In summary, the literature showed that several risk factors associated with colorectal cancer, which are divided into: socio-demographic factors (e.g. age and sex), lifestyle factors (e.g. diet and smoking), family history (have a close relative diagnosed with colorectal cancer), Personal history of bowel disease (e.g. Crohn's disease), Personal history of polyps, Consanguinity (Relatives marriage). These factors were used to build this study conceptual framework. This chapter is the base for analysis in the coming results chapter and the study results discussion and conclusion.

Chapter Four: Study Methodology

In this chapter, the research methodology is presented. The study area, study population, study design, tools, the sampling method, statistical analysis, ethical considerations, and variables operational definitions are presented.

4.1 Study setting and population characteristics

Our study was conducted in Beit Jala Governmental hospital (BJGH). BJGH is a central hospital in the southern part of the West Bank. It has many vital medical specialties such as orthopedic, cardiovascular, ENT, surgery and oncology departments. Each medical specialty has an in-patient ward and out-patient clinic. All patients' records are kept in a paper filled archives presented within the hospital.

Its oncology department provides primary, secondary, and tertiary health care for cancer patients in the south of the West Bank. Diagnostic and therapeutic procedures are also presented at BJGH. These procedures include medical imaging and laboratory testing for diagnosis and follow-up, surgery and chemotherapy for curative and palliative entities. Patients could be admitted to the oncology ward to be under observation. Also, cancer patients are followed up in the outpatient clinics by medical oncologists (Halahleh & Gale, 2018).

The registered population at the cancer registry of the hospital are mainly coming from the middle governorates (Ramallah, Jerusalem, and Jericho) and southern governorates (Bethlehem and Hebron) regions of the West Bank. The registered patients from Jerusalem only covers those with a Palestinian Nationality not holder of Israeli ID. (see Map 1)

Bethlehem governorate is located 10km south to Jerusalem and it has a total area of around 660 km² (OCHA, 2015).

Bethlehem governorate has a population of about 220,000 people, including over 20,000 of them are living in three refugee camps (Dheisheh, Aida and Beit Jibrin). The most important cities and towns of the governorate are Bethlehem, Beit Jala, and Beit Sahour cities, as well Al Doha, Al Khader, Battir and Artas towns (PCBS, 2017).

Hebron governorate is located in the southern West Bank. It is the largest governorate in Palestine in terms of area and population. The governorate's land area is 1,060 square kilometers and it has a population of 600,364. The Hebron Governorate has a total of seven cities and eighteen towns(PCBS, 2017).

Ramallah governorate covers a large part of the central West Bank. It is located on the north of Jerusalem Governorate. It covers an area of 844 square kilometer and according to the Palestinian Central Bureau of Statistics (PCBS), the governorate has a population of 279,730 (PCBS, 2017).

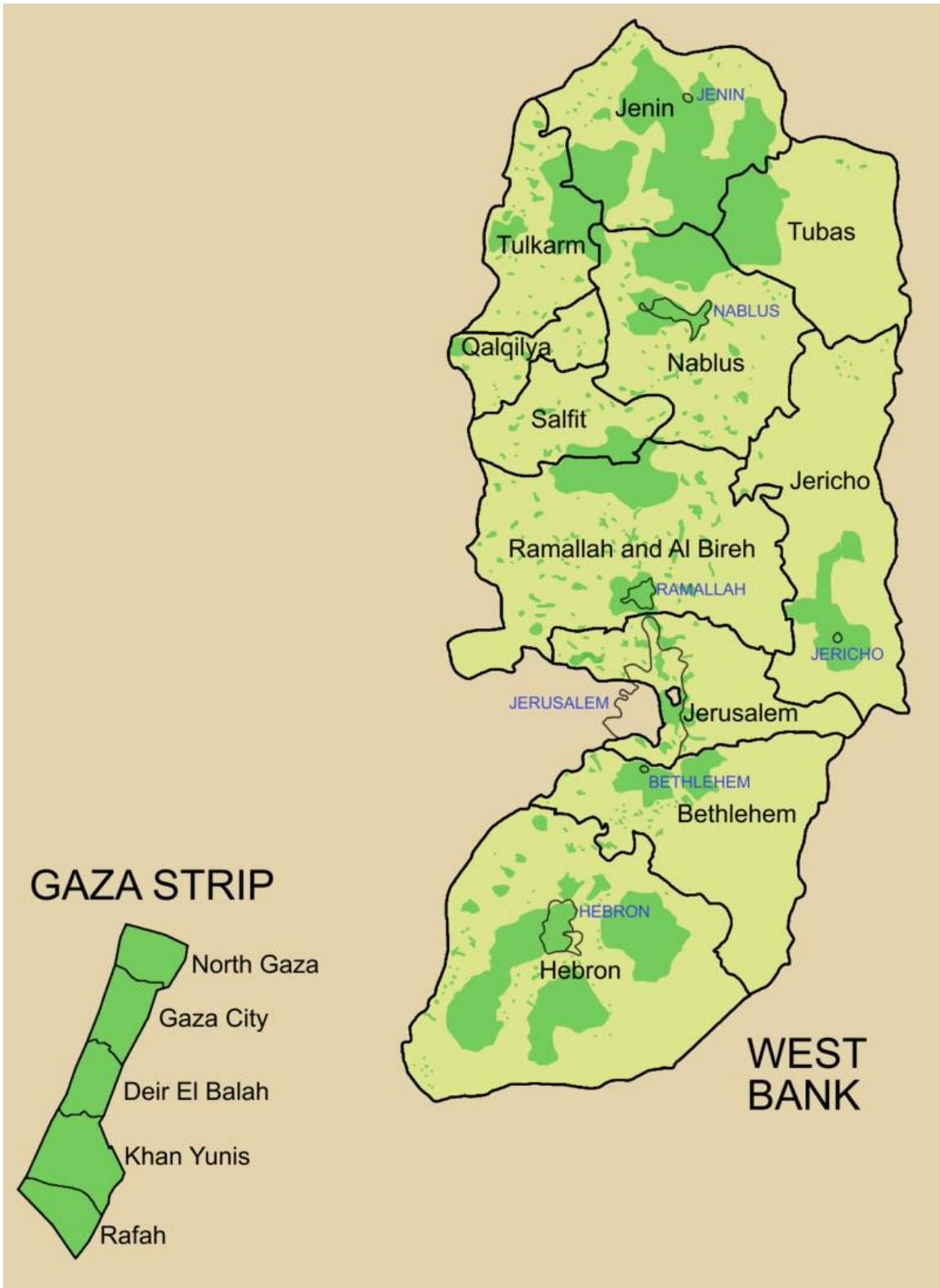
The governorate has 78 localities which 13 of them have the status of municipality. It also has three refugee camps. in its jurisdiction. 13 localities have the status of municipality(PCBS, 2017).

Jericho governorate is located in the eastern areas of the West Bank bordering Jordan. The governorate spans west to the mountains east of Ramallah and the eastern slopes of Jerusalem, including the northern reaches of the Judaeen Desert. The population of the Jericho Governorate was estimated 31,501, including approximately 6,000 living in the governorate's refugee camps Aqbat Jaber and Ein Al Sultan (PCBS, 2017).

The governorate have one city which is the Jericho city, two municipalities, four villages and three refugee camps (PCBS, 2017).

Jerusalem governorate is located in the central of the West Bank. The Governorate has two sub-districts: *Jerusalem J1*, which includes the localities within the territory controlled by the Israeli Jerusalem municipality (East Jerusalem), and *Jerusalem J2*, which includes the remaining parts of the Jerusalem Governorate. The district capital of the Governorate is East Jerusalem (al-Quds)(PCBS, 2017).

The total land area of the governorate is 344 km². According to the PCBS, the governorate had a population of 429,500. Palestinian ID holders account for 10.5% (42,950) of Palestinians living in Jerusalem governorate(PCBS, 2017).



Map 1: Palestine governorates(Wikipedia, 2019)

4.2 Study design

The study design is a group matched case-control study. Cases and controls were matched by age and gender.

4.3 Study sample selection

Study cases: The study cases were every colorectal cancer patient that was previously diagnosed and confirmed to have colorectal cancer as a primary cancer, and are attending to daycare clinics in BJGH for chemotherapy or consultations or were admitted in the oncology department.

Cases were defined by:

1. It should be primary CRC and confirmed by histopathology according to the records.
2. Only alive patients were interviewed therefore it is a survived based study.
3. Cases have a registry cancer file at the hospital.
4. Patients having other cancers which we couldn't confirm if it was primary or secondary cancer.

Study control group: The controls were patients attending other hospital clinics in BJGH e.g. ENT clinic and internal medicine clinic or admitted in any other hospital department other than oncology. Those controls were invited to participate in the study. After consenting to participate an occult blood test was performed for these potential controls to exclude CRC. Controls were selected by a specific age group designed to match the cases and also matched the cases by gender.

The selected controls were excluded if

1. Result of fecal occult was positive.
2. Those who refused to do the fecal occult test (FOBT).
3. Any patient that refuses to participate in the study.
4. Patients who had previously diagnosed with any cancer type.
5. Controls that completed the questionnaire who were found to have previous polyps or any bowel diseases were excluded in the analysis (n=3)

In our study 7 controls were excluded because they were FOBT positive and were referred for further investigation at the hospital outpatient clinic. Also, two other controls were excluded because they refused to perform the FOBT test.

4.4 Sample size determination

Sample size was calculated by the online software tool called “Epitool” (AUVEST, n.d.); for a case control study sample size determination. The following calculation parameters were used: an 80% power, and estimated odds ratio of 3.0 for the association between red meat consumption and CRC with 95% confidence as mentioned in the literature for similar studies carried out in Middle East (Nashar& Almurshed, 2008). Therefore, our target sample was about 174 (87 cases and 87 controls). However, we selected 105 cases and 105 control group (table 3.1).

Table 3.1: Sample size calculation Results

	P = 0.005	P = 0.01	P = 0.02	P = 0.03	P = 0.04	P = 0.05 *	P = 0.1
OR = 2	4749	2395	1218	826	630	513	280
OR = 3	1586	801	409	279	213	174	97
OR = 4	882	446	228	156	120	98	56
OR = 5	596	302	155	106	82	67	38
OR = 10	217	110	57	39	30	25	15

*the least needed sample size for our study

4.5 Data collection

Data collection took place in the period between May 2016 until June 2017. A field researcher was especially trained for the data collection. Our field researcher was trainee nurse at the hospital. She was well trained to use the questionnaire, how to find the patients, and how to use the patient’s medical records. In that period all CRC patients visiting the daycare clinic were eligible to be included in the study. The data collection for the daycare was performed on Mondays and Wednesdays as the daycare for the cancer patients at the hospital work on those days. On those days the field researcher was present to do the survey.

Patients at the daycare were approached and were asked to join the study after explaining the study aim and objectives for them. None of those approached patients refused to participate in the study.

For the admitted patients, the field researcher visited the oncology department and approached the admitted patients. None refused to join the study.

Afterwards, whenever a new case was found in the daycare or admitted to the oncology department from the daycare, their medical records were retrieved from the registration. After the medical records were retrieved for each case, they were selected. At that time, the selected cases approval to participate was taken by signing an informed consent (Informed consents and approval letters are found in Appendix). Then they were interviewed by the field researcher. The admitted cases were interviewed at the oncology department. The daycare patients who came for follow up or chemotherapy were interviewed at the daycare. Each interview took from 20 to 30 minutes.

For each selected case from the oncology department, a control of the same age group and gender was selected from other departments (Internal, surgery, and outpatient clinics). For cases that were selected from the daycare, a matched control who attended the outpatient clinics for regular consultations other than cancer was selected. Controls who met the study's inclusion criteria were selected and approached by the field worker. Each fit control who agreed to participate in the study signed the informed consent. Then his medical record was retrieved and checked not be a cancer patient. After that he was interviewed by the field researcher after explaining the study's aim and objectives. Two control refused to perform the FOBT test.

4.6 Study tools

4.6.1 Medical Record

Medical records were used for both cases and controls. The records were used to confirm the age of the participant, to take the address, the medical record no. was saved, and were used to take the body measurements (Height and weight). For the cases the record was also used to take the age at the diagnosis for each case.

4.6.2 Study Questionnaire

Most of the questionnaire questions were adopted from similar studies questionnaires that were previously prepared and validated, mainly they were adopted from the Risk Factor Questionnaire for Colorectal Cancer Family registry (CFR, 2016).

The Questionnaire was modified based on the aims and objectives of the study and its conceptual framework. It consisted of the following parts:

Section A: Socio-demographic data. Questions A1 to A12.

Section B: Medical History. Questions B1 to B20h.

Section C: Tobacco use and Alcohol. Questions C1 to D16.

Section D: Diet. Questions E1 to E4b.

Section E: Physical Activity. Questions P1 to P16(a-b).

Section F: Physical Measurements. Questions G1 to G4.

Questionnaire Validation

The study questionnaire was reviewed by the study supervisor and then was sent for validation by 3 specialists in this field; two oncologists working at the MOH and a colonoscopy specialist physician. No major changes were made based on the reviewers comments, except for wordings in some sections to make it easier for the field researcher to understand and explain to the patients. Questionnaire was adjusted afterwards based on the given comments. Then the questionnaire was transformed into an application that is especially deigned to work on a tablet to make it easier to enter the data and save it. The application was designed by the researcher himself.

Questionnaires piloting

Questionnaire piloting was conducted at the BJGH. Twenty colorectal cancer patients were interviewed. The Statistical Package for Social Sciences (SPSS version 23.0) was used for data entry and analysis. As a result of the piloting data analysis, the questionnaire reliability measurement showed a Cronbach alpha of 0.81 for the separate questions sections mentioned above

4.6.3 Fecal occult blood test (FOBT)

The lab screening test used in the study was the FOBT. It is a one-step rapid test device which is a chromatographic immunoassay for qualitative detection of human occult blood in feces (Simon 1985). We have chosen the immunoassay method over the traditional guaiac based methods, because it was proven by the literature that the immunoassay method is more sensitive and specific than the other methods (Simon 1985). In addition to that, other methods have diet restrictions prior to testing (Simon 1985).

Stool samples were collected from the controls at the hospital. Special containers were used for the samples that can keep the sample from deterioration and to preserve them until they are tested. Then the samples were transferred to Beit Fajjar Medical Laboratory. This laboratory is a MOH licensed laboratory and is a certified member of the EQAS program (Al Quds university External assurance). The samples were tested there.

4.7 Data Analysis

The data was collected using an electronic questionnaire, then manually coded, cleaned and analyzed using the Statistical Package for Social Sciences (SPSS version 23.0). Descriptive statistics were represented to show frequencies and, percentages for categorical variables, means, and standard deviation for continuous variables. Chi-square test and T-test were used as needed to calculate the difference between cases and controls regarding all variables in the study. A P-value <0.05 was considered statistically significant. Variables that showed a significant difference between cases and controls were included in our multivariate model for risk estimation. Conditional forward logistic regression was used to get odds ratios. Our principal measure of association was the Adjusted Odds Ratios (AORs) with 95% confidence intervals (95% CI).

4.8 Ethical consideration

In order to launch this study, this study's proposal was submitted to Al Quds University-School of public health research committee for discussion and approval. The permission to conduct the study was obtained from the MOH. All the participants were informed about the study aim and objectives and signed a consent form before participating.

Chapter Five: The Results

5.1 Introduction

In this chapter, study results will be presented. Study population characteristics will be shown in a descriptive analysis. Univariate and multivariate analysis will also be presented in this chapter.

5.2 Descriptive analysis

Our study consisted of 210 participants (105 cases and 105 controls). Table 5.10 shows the characteristics of the study cases. The majority of our cases were colon cancer representing (92.4%) and only (7.6%) were rectal cancer patients. Most of our cases (77.1%) were living in the southern region (Hebron and Bethlehem). The mean age of our cases was 59.5 years with 24 years old was the youngest case and 81 was the oldest case. Males were more than females in our cases representing (54.3%) of the cases. The mean years since cancer diagnosis in the cases was 1.8 years. Cases whom were diagnosed with polyps were 29 which constitute of (27.6%) of the cases, and (25.7%) of the patient's having polyps removed them. (2.9%) of our cases were Crohn's positive, about (1%) of them were diagnosed with Ulcerative colitis, and (7.6%) of them were also diagnosed with Irritable bowel disease. None of our cases was diagnosed with Diverticular disease.

Table 5.11 shows that most of our cases have undergone colon or rectum removal operations (93.3% of cases, and (76.2%) of them removed it completely. (14.3%) of our cases were treated by radiotherapy and about (2%) of cases undergone bone marrow transplant. Only (12.4%) of the cases had diabetes, and (2.9%) of them were diabetes positive before cancer. In the BMI section we notice that most of our cases were overweight, and most of them were obese before cancer.

Table 5.10: Description of study cases characteristics, disease status and treatment.

Variable		Count	N %
Sex	Female	48	45.7%
	Male	57	54.3%
Age at diagnosis	Mean (SD)	59.49(11.81)	
	Min-Max	24-81	
Number of years since diagnosis	Mean (SD) Min-Max	1.84(1.58)	0-6 years
Location of cancer (Colon/Rectal)	Colon	97	92.4%
	Rectal	8	7.6%
Area of residence	Southern region**	81	77.1%
	Middle region*	24	22.9%
Polyps present	No	76	72.4%
	Yes	29	27.6%
Polyps present more than once	No	0	0.0%
	Yes	29	27.6%
	I don't have polyps	76	72.4%
Type of polyps	Benign	21	20.0%
	Malignant	8	7.6%
	I don't have polyps	76	72.4%
Removal of polyps	No	2	1.9%
	Yes	27	25.7%
	No polyps	76	72.4%
Polyps removed more than once	No	13	12.4%
	Yes	16	15.2%
	No polyps	76	72.4%
Familial Adenomatous polyposis	No	102	97.1%
	Yes	3	2.9%
Crohn's disease present	No	102	97.1%
	Yes	3	2.9%
Ulcerative colitis present	No	104	99.0%
	Yes	1	1.0%
Irritable bowel syndrome present	No	97	92.4%
	Yes	8	7.6%

*Middle region: Jerusalem, Ramallah, Jericho ** Southern region: Hebron, Bethlehem

Table 5.11: Description of study cases characteristics, disease status and treatment.

Variable		Count	N %
Remove colon or rectum	No	7	6.7%
	Yes	98	93.3%
Type of colon or rectum removal (Partial/Completely)	Completely removed	80	76.2%
	Partly Removed	18	17.1%
	Didn't remove	7	6.7%
First colon or rectum remove (Years)	In the past 1-2 years	90	85.7%
	In the past 3-6 years	8	7.6%
	Didn't Remove	7	6.7%
Remove colon or rectum more than once	No	35	33.3%
	Yes	64	61.0%
	Didn't remove	6	5.7%
Diabetes	No	92	87.6%
	Yes	13	12.4%
Diabetes before cancer	No	10	9.5%
	Yes	13	2.9%
	No Diabetes	92	87.6%
Radiotherapy	No	90	85.7%
	Yes	15	14.3%
Bone marrow transplant	No	103	98.1%
	Yes	2	1.9%
BMI	18-24.9 Normal	3	2.9%
	25-29.9 Overweight	63	60.0%
	>30 Obesity	39	37.1%
BMI before cancer	18-24.9 Normal	14	13.3%
	25-29.9 Overweight	22	21.0%
	>30 Obesity	69	65.7%

Univariate Analysis

5.2 Socio-demographic Data

Table 5.12 shows that our study has more males than females. It also shows that the mean age of our study subjects was 61 years old. No difference in marital status was observed between cases and controls with majority being married. Most of our cases were residents of cities (63.8%), whereas in controls majority were residents of villages (62.9%). In the education section, it was noticed that most of our controls (54.6%) were with no schooling while in cases (47.1%) were also with no schooling. There was no difference observed in the occupations section between cases and control with majority of were employed. The table also shows that cases have more yearly income in comparison to controls.

Comparing study cases and control group, table 5.12 shows that there are statistically significant differences ($P < 0.05$) in Residence section, yearly income and area of residence.

Table 5.12: Socio-demographic characteristics of the study subjects

Variable		Study cases N=105		Control Group N=105		P value of Chi Square
		Count	N %	Count	N %	
Sex	Female	48	45.7%	47	44.8%	0.890
	Male	57	54.3%	58	55.2%	
Age	Mean (SD) Min- Max	105	61.32(12.035) 22-89	105	61.12(13.1021) 22-89	P value of T test=0.783
Education	No Schooling	48	47.1%	56	54.4%	0.545
	School (Primary and High)	44	43.1%	37	35.9%	
	College and more	10	9.8%	10	9.7%	
Marital Status	Single	2	1.9%	4	3.8%	0.430
	Married	93	88.6%	95	90.5%	
	Divorced/Widowed/Separated	10	9.5%	6	5.7%	
Occupation	Not Work	14	13.7%	18	17.6%	0.441
	Work	88	86.3%	84	82.4%	
Yearly Income (Shekels)	Mean (SD) Min- Max	105	31503(21624) 6000-96000	105	23178(28985) 6000-96000	P value of T test= 0.001
Residence	City	67	63.8%	33	31.4%	<0.0001
	Village	32	30.5%	66	62.9%	
	Camp	6	5.7%	6	5.7%	
Area of residence	Southern region**	81	77.1%	102	97.1%	<0.0001
	Middle region*	24	22.9%	3	2.9%	

*Middle region: Jerusalem, Ramallah, Jericho

** Southern region: Hebron, Bethlehem

5.3 Medications and supplements

Table 5.13 shows that (16.2%) of our cases take Aspirin irrespective to period and duration compared to (37.1%) of the control group. Comparing study cases and control group, table 5.13 reveals statistically significant differences ($P<0.05$) in Aspirin, Frequency of taking Aspirin consumption, Taking Aspirin two years ago, and Duration of taking Aspirin. Other medications and supplements (Panadol, NSAIDs, Laxatives, Multivitamins, Folic Acid, Calcium, and Antacids) showed no significance and their tables are presented in the Appendix.

Table 5.13 Association between study cases and control group by Aspirin intake

Variable		Study cases N=105		Control group N=105		P Value of Chi Square
		Count	N %	Count	N %	
Aspirin	Yes	17	16.2%	39	37.1%	0.001
	No	88	83.8%	66	62.9%	
Frequency of Taking Aspirin per Week*	<7 Times	10	9.5%	25	23.8%	0.003
	≥ 7 Times	7	6.7%	14	13.3%	
	Don't Take Aspirin	88	83.8%	66	62.9%	
Take aspirin two years ago	Yes	12	11.4%	34	32.4%	<0.000
	No	93	88.6%	71	67.6%	
Aspirin duration (Years)*	≤ 1 Year	4	3.8%	7	6.7%	0.007
	2-5 Years	10	9.5%	26	24.8%	
	≥ 6 Years	3	2.9%	6	5.7%	
	Don't Take Aspirin	88	83.8%	66	62.9%	

*Aspirin level categorization and cut off value were according to the studies(García Rodríguez et al., 2017; Gray, Coleman, Hughes, Murray, & Cardwell, 2018)

5.4 Health Status

Table 5.14 shows that (12.4%) of our cases have diabetes compare to (15.2%) of controls. About (9%) of our cases and (6.7%) of our control were diagnosed with high cholesterol levels. On the other hand, we have (8.6%) of our cases and (6.7%) who were diagnosed with high Triglycerides level. Most of our cases and controls were overweight with (60%) and (70.5%) respectively.

Comparing study cases and control group, table 5.14 reveals that there are no statistically significant differences ($P < 0.05$) in any of the Health status sections.

Table 5.14: Association between study cases and control group by Health status

Variable		Study Cases N=105		Control Group N=105		P value of Chi Square
		Count	N %	Count	N %	
Diabetes present	Yes	13	12.4%	16	15.2%	0.548
	No	92	87.6%	89	84.8%	
First Diabetes Diagnosis (Years)	<10 years	10	9.5%	9	8.6%	0.427
	>10 years	3	2.9%	7	6.7%	
	No Diabetes	92	87.6%	89	84.8%	
Take Diabetes medications	Yes	13	12.4%	16	15.2%	0.548
	No diabetes	92	87.6%	89	84.8%	
Type of diabetes medication taken*	Pills	7	6.7%	3	2.9%	0.121
	Insulin injections	6	5.7%	13	12.4%	
	No diabetes	92	87.6%	89	84.8%	
Frequency of taking Diabetes medication per week	1-7 times	8	7.6%	11	10.5%	0.770
	8-14 times	5	4.8%	5	4.8%	
	No Diabetes	92	87.6%	89	84.8%	
Take Diabetes medications two years ago	Yes	10	9.5%	15	14.3%	0.287
	No diabetes	95	90.5%	90	85.7%	
Overall period of taking diabetes medications (years)	<5 years	7	6.7%	3	2.9%	0.121
	>5 years	6	5.7%	13	12.4%	
	No Diabetes	92	87.6%	89	84.8%	
High Cholesterol level	Yes	9	8.6%	7	6.7%	0.603
	No	96	91.4%	98	93.3%	
First high Cholesterol diagnosis (years)	<5 years	4	3.8%	3	2.9%	0.872
	>5 years	5	4.8%	4	3.8%	
	No Cholesterol	96	91.4%	98	93.3%	
High Cholesterol medications	Yes	9	8.6%	7	6.7%	0.603
	No cholesterol	96	91.4%	98	93.3%	

Table 5.14.... continues

Variables		Study Cases N=105		Control Group N=105		P value of Chi Square significance
		count	N %	count	N %	
High Triglycerides level	Yes	9	8.6%	7	6.7%	0.580
	No	99	94.3%	97	92.4%	
First high Triglycerides diagnosis (years)	<5 years	3	2.9%	5	4.8%	0.771
	>5 years	3	2.9%	3	2.9%	
	No Triglycerides	99	94.3%	97	92.4%	
High Triglycerides Medication	Yes	6	5.7%	8	7.6%	0.580
	No triglycerides	99	94.3%	97	92.4%	
BMI	18-24.9 Normal	3	2.9%	4	3.8%	0.201
	25-29.9 Overweight	63	60.0%	74	70.5%	
	>30 Obese	39	37.1%	27	25.7%	
Remove gallbladder	Yes	20	19.0%	16	15.2%	0.464
	No	85	81.0%	89	84.8%	

*none of the participants had a combined therapy for diabetes.

5.5 Screening and Intervention

Table 5.15 shows that about (75.2%) of our cases have performed occult blood test and all of them (100%) have performed colonoscopy. On the other hand, only (3.8%) of the controls performed the occult blood test while only (10.5%) of them have undergone colonoscopy. Most of the cases did the occult blood test in the past 1-2 years and the majority of them did it for the reason to investigate new health problem. In the colonoscopy section, most of the cases undergone the test in the past 1-2 years and for the reason to investigate new health problems. In the control group, the number of the controls who performed the occult blood test and undergone colonoscopy were very low in comparison to the cases.

Comparing study cases and control group, table 5.15 reveals that there are statistically significant differences ($P<0.05$) in the occult blood.

Table 5.15: Association between study cases and control group by Screening and Intervention

Variable		Study Cases N=105		Control Group N=105		P Value of Chi Square
		Count	%	Count	%	
Occult Blood test	Yes	79	75.2%	4	3.8%	<0.0001
	No	26	24.8%	101	96.2%	
First Occult blood test (years)	In the past 1-2 years	70	66.7%	1	1.0%	<0.0001
	In the past 3-6 years	9	8.6%	3	2.9%	
	Didn't do the Test	26	24.8%	101	96.2%	
Reason for Occult blood test	To investigate new problem	76	72.4%	1	1.0%	<0.0001
	Follow up of previous problem	2	1.9%	3	2.9%	
	Didn't do the test	27	25.7%	101	96.2%	
Occult Blood Separate Testes	1-2 times	68	64.8%	3	2.9%	----
	3-5 times	7	6.7%	1	1.0%	
	> 6 times	4	3.8%	0	0.0%	
	Didn't do the test	26	24.8%	101	96.2%	
Last occult test (Years)	In the past 1-2 years	64	61.0%	2	1.9%	<0.0001
	In the past 3-6 years	15	14.3%	2	1.9%	
	Didn't do the Test	26	24.8%	101	96.2%	
Colonoscopy	Yes	105	100.0%	11	10.5%	---
	No	0	0.0%	94	89.5%	
First Colonoscopy (Years)	In the past 1-2 years	86	81.9%	6	5.7%	---
	In the Past 3-6 Years	19	18.1%	5	4.8%	
	Didn't do the Test	0	0.0%	94	89.5%	
Reason for colonoscopy	To investigate new problem	73	69.5%	9	8.6%	---
	Follow up of previous problem	32	30.5%	96	91.4%	
	Didn't do the test	0	0.0%	0	0.0%	
Colonoscopy Separate times	1-2 times	93	88.6%	10	9.5%	---
	3-5 times	12	11.4%	1	1.0%	
	Didn't do the test	0	0.0%	94	89.5%	
Last colonoscopy (Years)	In the past 1-2 years	92	87.6%	6	5.7%	---
	In the past 3-6 years	13	12.4%	5	4.8%	
	Didn't do the Test	0	0.0%	94	89.5%	

5.6 Family History

Table 5.16 shows that (37.1%) of our cases and (15.2%) of our controls were born for parents who had a family relationship of some kind before marriage. Being a multiple birth sibling was more in the control group (28.6%) compared to (16.2%) in the cases. History of CRC in the family was in (8.6%) of cases and in (1.9%) of controls. In the other family cancers section, (12.4%) of the cases and (2.9%) of the controls have a family member whom was diagnosed with cancers other than CRC.

Comparing study cases and control group, table 5.16 reveals that there are statistically significant differences ($P<0.05$) in the consanguinity, multiple birth siblings, and family history of CRC and other cancers.

Table 5.16: Association between study cases and control group by Family history

Variable		Study Cases N=105		Control Group N=105		P Value of Chi Square
		Count	N %	Count	N %	
Consanguinity	Not Related	66	62.9%	89	84.8%	<0.0001
	Related	39	37.1%	16	15.2%	
Are you a twin, triplet or other multiple birth siblings?	Twin or other multiple	17	16.2%	30	28.6%	0.031
	No	88	83.8%	75	71.4%	
Family colorectal cancer	Yes	9	8.6%	2	1.9%	0.030
	No	96	91.4%	103	98.1%	
Relation with family colorectal cancer patient	First degree relative	6	5.7%	1	1.0%	0.090
	Second degree relative	3	2.9%	1	1.0%	
	No cancer	96	91.4%	103	98.1%	
Other family cancers	Yes	13	12.4%	3	2.9%	0.009
	No	92	87.6%	102	97.1%	
Type of other family cancers	Lung Cancer	2	1.9%	1	1.0%	0.029
	Other Cancers	11	10.5%	2	1.9%	
	No other Family Cancers	92	87.6%	102	97.1%	
Relationship with family other cancer patient	First degree relative	9	8.6%	2	1.9%	0.034
	Second degree relative	4	3.8%	1	1.0%	
	No other family cancers	92	87.6%	102	97.1%	

5.7 Lifestyle factors

5.7.1 Smoking

Table 5.17 shows that (24.8%) of our cases are smokers compared to (9.5%) of our controls. (84.6%) of the smoking cases compared to (90%) of the smoking controls are current smokers. Most of our smoking cases and controls started smoking at childhood (57.7%) and (66.7%) respectively. Manufactured cigarettes were the most used type of smoking followed by hand rolled cigarettes.

Comparing study cases and control group, table 5.17 reveals that there are statistically significant differences ($P < 0.05$) in the Smoking, Smoking status, age of smoking initiation, years since smoking started, and type of smoking. Pipe full of tobacco, cigars and non-smoked tobacco products were found to be non-significant can be found in the appendix

Table 5.17: Association between study cases and control group by Smoking

Variable		Study cases N=105		Control group N=105		P value of chi square
		Count	N %	Count	N %	
Smoking	No	79	75.2%	95	90.5%	0.003
	Yes	26	24.8%	10	9.5%	
Current Smoker	No	83	79.0%	96	91.4%	0.011
	Yes	22	21.0%	9	8.6%	
Age of Smoking initiation	Childhood	15	14.3%	6	5.7%	0.014
	Adulthood	11	10.5%	4	3.8%	
	Don't smoke	79	75.2%	95	90.5%	
Years since smoking started	<20 years ago,	3	2.9%	3	2.9%	0.007
	≥ 20 years ago,	23	21.9%	7	6.7%	
	Don't smoke	79	75.2%	95	90.5%	
Manufactured cigarettes smoked (Weekly)	<100 cigarettes	16	15.2%	4	3.8%	0.008
	≥100 cigarettes	10	9.5%	6	5.7%	
	Don't smoke	79	75.2%	95	90.5%	
Hand-Rolled Cigarettes smoked (Weekly)	<20 cigarettes	5	4.8%	2	1.9%	0.045
	≥ 20 cigarettes	7	6.7%	1	1.0%	
	Don't smoke	93	88.6%	102	97.1%	
Shisha sessions smoked (Weekly)	<3 sessions	8	7.6%	4	3.8%	0.492
	≥3 sessions	3	2.9%	3	2.9%	
	Don't smoke	94	89.5%	98	93.3%	
Quit smoking last 12 months	No	8	7.6%	2	1.9%	0.019
	Yes	14	13.3%	6	5.7%	
	I don't smoke	83	79.0%	97	92.4%	
Advice to quit smoking from doctor	No	4	3.8%	1	1.0%	0.010
	Yes	8	7.6%	5	4.8%	
	No doctor visits in the past 12 months	14	13.3%	3	2.9%	
	Don't Smoke	79	75.2%	96	91.4%	

5.7.2 Diet

Table 5.18 shows that (87.6%) of the controls compared to (49.5%) of the cases consume fruit meals twice or more a week. It also shows that (69.5%) of the cases and (86.7%) of the controls consume vegetable meals twice a week or more. Consumption of red meat weekly was lower than fruits and vegetables with (53.3%) of the cases compared to (37.1%) of the controls whom eat two or more meals of red meat weekly. If the red meat was grilled the consumption of it also lowers with (49.5%) of the cases compared to (30.5%) of the controls whom eat grilled red meat twice or more weekly. Eating two or more meals of chicken weekly was more in controls (54.3%) in comparison to (48.6%) in the cases. Most of our cases and controls preferred the outside appearance of the red meat and chicken to be lightly browned, while they preferred the inside appearance of the red meat to brown (well done).

Comparing study cases and control group table 5.18 shows that there are statistically significant differences ($P<0.05$) in the Fruit, Vegetables, Red meat, and Grilled red meat consumption between cases and controls. While Chicken didn't show any significance.

Table 5.18: Association between study cases and control group by Diet

Variable		Study cases N=105		Control Group N=105		P value of chi Square
		Count	N %	Count	N %	
Fruit	<2 Weekly	53	50.5%	13	12.4%	0.000
	≥2 Weekly	52	49.5%	92	87.6%	
Vegetables	<2 Weekly	32	30.5%	14	13.3%	0.003
	≥2 Weekly	73	69.5%	91	86.7%	
Red Meat	<2 Weekly	49	46.7%	66	62.9%	0.018
	≥2 Weekly	56	53.3%	39	37.1%	
Grilled Red Meat	<2 Weekly	53	50.5%	73	69.5%	0,005
	≥2 Weekly	52	49.5%	32	30.5%	
Red Meat outside appearance	Lightly browned	71	67.6%	80	76.2%	0.512
	Medium browned	22	21.0%	16	15.2%	
	Heavily browned or blackened	5	4.8%	5	4.8%	
	Don't eat grilled red meat	7	6.7%	4	3.8%	
Red Meat inside appearance	Red	45	42.9%	55	52.4%	0.057
	Pink	9	8.6%	16	15.2%	
	Brown	45	42.9%	27	25.7%	
	I don't eat red meat	6	5.7%	7	6.7%	

Table 5.18....Continues

Variable		Study cases N=105		Control Group N=105		P value of chi Square
		Count	N %	Count	N %	
Chicken	<2 Weekly	54	51.4%	48	45.7%	0.686
	≥2 Weekly	51	48.6%	57	54.3%	
Grilled Chicken	<2 Weekly	94	89.5%	88	83.8%	0.223
	≥2 Weekly	11	10.5%	17	16.2%	
Chicken outside appearance	Lightly browned	76	72.4%	88	83.8%	0.134
	Medium browned	21	20.0%	12	11.4%	
	Heavily browned or blackened	0	0.0%	0	0.0%	
	Don't eat grilled chicken	8	7.6%	5	4.8%	

5.7.3 Physical Activity

We used WHO's Global Physical activity questionnaire (GPAQ) to collect physical activity data from our study's participants. METs (Metabolic Equivalent) are commonly used to express the intensity of physical activities performed. The formula we used to measure the MET-min/Week includes the resting hours in each week.

Table 5.19 concludes that the control group had no significant difference in the average MET-min/Week. However, Table 5.20 showed that when physical activity was classified as groups (low physical activity group and moderate physical activity), cases had lower physical activity (96.2%) compared to controls (86.7%). Even though, there was no subjects that had high physical activity or no physical activity at all.

The table also shows that there are statistically significant differences ($P < 0.05$) between cases and control group in Physical activity.

Table 5.19: MET-mins/Week of the study subjects

Variable		N	Mean	Std. Deviation	Std. Error Mean	P value T test
Physical activity MET- Mins/Week	Study Cases	105	251.91	164.370	16.041	0.287
	Control Group	105	277.99	188.854	18.430	

Table 5.20: Association between study cases and control group by Physical activity

Variable		Study Cases		Control Group		P value of Chi Square
		Count	N %	Count	N %	
Physical Activity	Low Physical Activity (<600 MET-Min/Week)	101	96.2%	91	86.7%	0.014
	Moderate Physical Activity (600-1500 MET-Min/Week)	4	3.8%	14	13.3%	

5.3 Multivariate analysis

All the significant variables at ($p < 0.05$) in the univariate analysis were included in the multivariate analysis except for the variables with small numbers such as family history of CRC, other family cancers, relationship with family CRC or other cancers and other smoking variables.

Table 5.21 shows that living in villages was protective against CRC risk compared to cities and camps. It also shows that living in the southern area of the West Bank increases the risk of CRC by 1243% in comparison to the northern region of the West Bank. The analysis shows that consanguinity is a risk factor for CRC and increases its risk by 288%. On the other hand, being a multiple birth sibling, consuming fruits and taking aspirin all showed a protective pattern against CRC. In spite of that, smoking showed high risk for CRC with 550% increase in risk among smokers compared to non-smokers. Consuming grilled red meat twice or more weekly, was also associated with increased risk of CRC by 280% compared to those who consume less.

Table 5.21: Multivariate Forward conditional model analysis of the associated variables with colorectal cancer*

Variable	Sig.	AOR**	95% CI***		
			Lower	Upper	
Residence	City		Ref	Ref	
	Village	.212	.343	.064	1.841
	Camp	.619	1.536	.283	8.331
Area of residence	Middle region		Ref	Ref	
	Southern region	.001	12.439	2.724	56.809
Consanguinity	Not Related		Ref	Ref	
	Related	.021	2.887	1.171	7.118
Are you a twin, triplet or other multiple birth siblings?	Twin or other multiple		Ref	Ref	
	No	.010	.282	.109	.735
Smoking	No		Ref	Ref	
	Yes	.002	5.503	1.866	16.227
Fruit	<2 Weekly		Ref	Ref	
	≥2 Weekly	.000	.082	.032	.206
Grilled Red Meat	≥2 Weekly		Ref	Ref	
	<2 Weekly	.010	2.847	1.289	6.287
Aspirin	No		Ref	Ref	
	Yes	.003	.248	.099	.621

*All variables that were significant ($p < 0.05$) in univariate analysis were included in a multivariate model (P value 0.05): i.e. Residence, area of residence, Consanguinity, Aspirin (intake, frequency, and duration), smoking, diet, and physical activity**Adjusted odds ratio. ***Confidence interval.

Chapter Six: Discussion, conclusion and recommendations

6.1. Introduction

In this chapter, study results are summarized and compared to other studies results worldwide. Also, the results are interpreted and discussed. In the final part of the chapter study conclusions and recommendations are presented.

6.2 Summary of the results

The univariate analysis of the study data showed significant differences between study cases and control group in residence, area of residence, and yearly income. It also showed significance in Aspirin (intake, frequency, and duration). In the health status section diabetes and dyslipidemia didn't show any significance between cases and controls.

In the lifestyle, smoking, years of smoking, consuming fruit, vegetables, red meat, grilled red meat, and physical activity also showed significance in the univariate analysis. Family history of cancers, family history of colorectal cancer, and consanguinity were significant.

On the other hand, the multivariate analysis of the study data showed that living in the villages lowers the risk of CRC compared to living in cities or camps. Living in the southern region of the West Bank increases the risk of CRC by 12 folds compared to the middle region of the West Bank. Also smoking increases the risk of CRC by 5.5 folds. Consuming fruits, grilled red meat, and taking aspirin lowers the risk of CRC.

6.3 Socio-demographic variables and colorectal cancer

Gender: Males composed (54.6%) of our study sample and gender was matched between cases and controls to eliminate any confounding effect gender may cause to the study results. Despite that, literature states that CRC occurs more in females, and females are at more risk of developing CRC than males (Betes et al., 2003; Kolligs et al., 2011; Regula et al., 2006; Rex et al., 1993).

Residence: Our study showed no statistical significance in the residence section, but it showed difference in the risk levels in its sub-categories villages, camps and cities. The risk of CRC was inversely associated with living in villages compared to camps and cities. However, this result is inconsistent with results revealed by other studies that living in rural areas increase the risk of colorectal cancer (Kinney, Harrell, Slattery, Martin, & Sandler, 2006; Zahnd et al., 2018). Those studies stated that living in the rural areas increase cancer risk due to lack of screening behaviors and due to increased modifiable risk factors in those populations compared to the urban areas. In our study this decreased risk may be due to the lifestyle of the people living in the villages compared to the other areas. The villager's lifestyle in Palestine is healthier compared to other areas. A cross sectional study was conducted in Jordan, Lebanon, Syria, and Palestine showed that smoking in the rural areas is low compared to urban areas (Abdulrahim & Jawad, 2018). Also, the people in the villages work mostly in farming which needs more physical activity and physical activity lowers the risk of CRC as literature indicated (Aicr & WCRF, 2007; Golshiri et al., 2016; Morikawa et al., 2013; Slattery et al., 2003; Thune & Lund, 1996; Wolin et al., 2010). Dietary patterns in the Palestinian villages are healthier and based on more natural foods and its main source is from their harvest or the animals they pet. A study was conducted on the dietary patterns of the Palestinian population in 1999 showed that villages rely most on their animal and their food is more natural (Stene et al., 2000). This also could explain this protective pattern in the villages compared to camps and cities.

Area of residence: Our study showed that living in the southern area of the West Bank increases the risk of CRC by 12 folds when compared to people living in the middle region of the West Bank. This result is consistent with the Palestinian cancer report that indicates that cancer is more spread in the southern regions of Palestine compared to the middle and

northern regions (Abu-Rmeileh et al., 2016). No study indicated the reason of this cancer spread in the south. This high increased risk in our study is because 77.8% of our cases and 97.8% of our controls are from the southern region. It is also because of the high population of the southern governorates which comprise almost half of the Palestinian population (PHIC,2016).

6.4 Lifestyle variables and colorectal cancer

Smoking: The univariate analysis of our study shows that about 25% of our cases were smokers compared to 9.5% of the control group were also smokers. Smoking showed effect in the occurrence of CRC in both univariate and multivariate analysis. Our study showed that smoking increases the risk of colorectal cancer by 5.5 folds. This result is consistent with literature and international studies. Two case control studies conducted to determine the relationship between smoking and CRC one in the US (Zhao et al., 2010) and one in Germany (Verla-Tebit et al., 2006), showed that smoking increases the risk of CRC. The results were also consistent with two prospective cohort studies of (Hannan et al., 2009, and Parajuli et al., 2014).

Diet: In the diet section, fruit and grilled red meat consumption were the only categories that showed significance in our study. Consuming two or more meals of fruits weekly was negatively associated with the risk of CRC, meaning that it lowers the risk of CRC by 82%. This result is consistent with the literature (Nashar & Almurshed, 2008; van Duijnhoven et al., 2009; Vogtmann et al., 2013) which concludes that consuming fruits and vegetables lowers the risk of CRC.

Our findings also showed that consuming two or more meals of grilled meat weekly increases the risk of CRC by 2.8 folds. This result is consistent with the literature that supports that grilled meat increases the CRC risk. Literature (Bener & Bener, 2011; Cross & Sinha, 2004; Joshi et al., 2015; Kotake et al., 1995; Potera, 2016). Also literature suggests that grilling meat releases carcinogens that increases the risk of cancers (Potera, 2016). Our result is consistent with the literature and international studies.

Physical activity: The physical activity in our study showed significance in the univariate analysis but didn't show any in the multivariate analysis. Literature have shown that physical activity plays a major role in the protection against colorectal cancer (Aicr & WCRF, 2007; Golshiri et al., 2016; Hagggar & Boushey, 2009; Slattery et al., 2003; Thune & Lund, 1996; Wolin et al., 2010). This insignificance in physical activity in our study is due to that none of our study population showed a high physical activity index per week and most of our population (86.7%) reported that they have a low physical activity index per week. This could also be attributed to that when we calculated the total MET-min/Week we included the resting hours and sedentary activities. In addition, it can also be attributed to reporting bias from the patients themselves.

6.5 Family History, consanguinity and colorectal cancer

Family history: Family history showed significance in the univariate analysis. It wasn't included in the multivariate model because of the small numbers among cases and controls. Family history is known to be a strong risk factor for CRC (Beebe-Dimmer et al., 2017; Kotake et al., 1995; Negri et al., 1998). In our study, the number of cases and controls who had a positive family history to CRC or other cancers was very small. Those small numbers will affect the multivariate model power and are not enough to establish an association. Taking a look at the numbers, we notice that there is more positive family history to CRC or other cancers among cases compared to controls.

Consanguinity: Our findings show that being born to a consanguineous parent increases the risk of developing CRC by 2.9 folds. Very few studies worldwide addressed this issue. A case control study in Qatar aimed to examine whether parental consanguinity affects the risk of cancer in a local Arab highly inbred population. The study concluded that consanguinity has no effect on the overall cancers incidence(Bener et al., n.d.). This is the opposite to our study's findings. This is may be due to the high rate of consanguinity marriage in Palestine which accounts for 44% of total registered marriages (PCBS, 2017).

This percentage is high compared to the surrounding countries like Jordan 23%, Egypt 35.3%, and Lebanon 29.6% (Tadmouri et al., 2009). In our study, related parents in the study cases were 37.1% compared to 15.2% of the control group.

Twin, triplet or other multiple birth siblings: Our results shows that being a twin or a multiple birth increases the risk of CRC. This result is consistent with the literature that stated that being a twin or a multiple birth increases the risk of cancer (Mucci et al., 2016 ; Cnattingius, Lundberg, & Iliadou, 2009). The reason for this increase is not yet known and all the explanations are theories and assumptions.

6.5 Medications and colorectal cancer

Aspirin: Our results show that aspirin was negatively associated with CRC risk. Consuming aspirin lowers the risk of CRC by almost 28%. Literature states that aspirin intake reduces the risk of CRC. A pooled analysis of five cardiovascular-prevention RCTs linked to cancer outcomes, daily aspirin use at any dose reduced the risk of CRC by 24% and of CRC-associated mortality by 35% after a delay of 8–10 years (Garcia-Albeniz & Chan, 2011). A prospective cohort study was conducted in the US to assess the risk of CRC and aspirin intake among 47363 men found out that regular and long-term aspirin use reduces risk of colorectal cancer among men (Chan et al., 2008). Other studies show the same outcome are mentioned in the literature review (García Rodríguez et al., 2017; Gray et al., 2018; Zhang et al., 2006).

There is no policy for aspirin use or dose in Palestine. Aspirin in Palestine is prescribed for high risk people or people of family history of any cardiovascular diseases and given freely from the MOH and UNRWA. Cardiovascular diseases are the main cause of mortality in Palestine so there is a large high risk group of people in Palestine(PCBS, 2017), which suggests why so many people use it.

Diabetes and other diseases: Diabetes mellitus increases the risk of CRC (Deng, Gui, Zhao, Wang, & Shen, 2012; Tan et al., 2016). Our study showed no significance between CRC and diabetes. This is attributed to the close numbers of diabetic study cases and controls.

Our study also showed no significance between dyslipidemia (Cholesterol and Triglycerides) and the risk of CRC, while literature suggests that there is an increased risk for CRC among dyslipidemia patients (Agnoli et al., 2014). This is may be attributed that the numbers were small it failed to establish a statistical significance.

6.6 Limitations and obstacles

Our study showed similar results compared to international studies, but there were small contradictions of some of the study results with other studies that may be attributed to the relatively small number of the studied population. In addition to some biases that might affect the results like information bias, recall bias, and selection bias especially in the variables that require memorizing such as food frequency and physical activity. The study was limited in terms of time and finance, which in role prohibited more investigation and tests. Data provided from the patient's records was limited to oncological status of each patient and the lack of reporting of other medical conditions the patients have. Also, the medical records data was very difficult to use to calculate the survival data of the patients. Some limitations of this study derived from the nature of the case-control study. The participants were asked about their lifestyle. Most of the participants were patients who were under the effect of some medications, in addition to the old age of most of the participants, all these factors result in a recall bias.

The reporting bias may be present in our study as some of the participants might be trying either to deny the role of their lifestyle or to blame any other factors except themselves for their disease, so some participants answered some questions in a way to achieve their perception or to show that they live a better lifestyle than they do.

Moreover, the data of family history of malignancy in the patient were missing in most of the cases; therefore, we could not extract reliable family history. To compensate the defect in participant's medical record each participant was asked about his family history of colorectal cancer and this might be exposed to recall bias or information bias.

6.7 Conclusion

This study is the first one in Palestine that investigated the possible association between different factors whether protective or risk and colorectal cancer occurrence. A case control study design was used to answer the study questions. The study has identified the possible risk factors associated Colorectal cancer patients attending the oncology department or the daycare clinics at Beit Jala Governmental hospital.

Most results of this study were expected and comparable to other international studies results, while some others were unexpectedly contradicted the literature. Residence, area of residence, fruit consumption, grilled red meat consumption, aspirin consumption, smoking, consanguinity marriage and being a multiple birth, appeared to be associated with colorectal cancer either positively or negatively. Other factors showed no significance in our study such as vegetables consumption, red meat consumption, supplements and physical activity.

6.8 Recommendations

Recommendations for people at risk of colorectal cancer

- Living in a healthy lifestyle that helps preventing developing diseases that increase the risk of CRC such as bowel diseases.
- Increase the consumption of fruits and decrease the consumption of grilled red meat.
- Encourage people at risk to stop smoking.
- Since low numbers of controls undergone screening so, perform a screening for colorectal cancer on a regular basis after the age of 40 years as age is a risk factor for CRC.

Recommendations for policy makers and health care team:

- Providing more attention for colorectal cancer especially in people over 40 by policies designed for them.
- Establishing national initiatives for the encouragement of early detection of colorectal cancer.
- Modifying the national cancer registry to include more details related to each cancer type.
- Considering colorectal cancer detection when dealing with over 40 years old patients.
- Giving more attention to the groups at risk of colorectal cancer to enable the early detection.
- Work more on the modifiable lifestyle factors which eventually affect the risk of colorectal cancer.

Recommendations for public health researchers:

- Conducting more detailed researches with larger sample size and including more hospitals and health care facilities.
- Considering the type and the stage of colorectal cancer (histopathology) and the date of first diagnosis.

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Appendices

Appendix 1: Approval letter from the Palestinian MOH.

State of Palestine
Ministry of Health - Nablus
General Directorate of Education in Health

دولة فلسطين
وزارة الصحة - نابلس
الإدارة العامة للتعليم الصحي

Ref.:
Date:

الموضوع: تسهيل مهمة طلاب

الأخ مدير عام الإدارة العامة للمستشفيات المحترم،،،
تحية واحترام،،،

تماشياً مع سياسة وزارة الصحة المتعلقة بتعزيز التعاون مع الجامعات والمؤسسات الأكاديمية بإتاحة فرص التدريب أمام الطلبة والخريجين والباحثين في المؤسسات الوطنية وإسهاماً في تنمية قدراتهم. يرجى تسهيل مهمة الطالب: عيسى الغروز - ماجستير الصحة العامة - جامعة القدس، في عمل بحث الماجستير بعنوان: " محددات/ مسببات الإصابة بمرض سرطان الأمعاء والاثني عشر في فلسطين"، لذا يرجى تسهيل مهمته في الحصول على المعلومات اللازمة من خلال مقابلة مرضى (بعد اخذ موافقتهم على المشاركة في البحث) ومراجعة ملفاتهم في مستشفى بيت جالا الحكومي، علماً بأنه سيتم الالتزام بمعايير البحث العلمي والحفاظ على سرية المعلومات.

مع الاحترام،،،

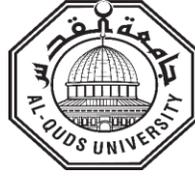
د. أمل عويض
مدير عام التعليم الصحي

نسخة: عميد كلية الصحة العامة المحترم/ جامعة القدس

P.O. Box: 14
Tel/Fax: 09-2333901

E-mail: pramoh@palnet.com

ص.ب. 14
تلفاكس: 09-2333901



جامعة القدس
Al-Quds University

الدراسات العليا

كلية الصحة العامة

ماجستير صحة عامة

عنوان البحث: محددات سرطان القولون والمستقيم عند مرضى السرطان في مستشفى بيت جالا الحكومي

شكرا على وقتك. سيتطلب استكمال الاستبيان 30 دقيقة تقريبا. إذا كنت لا ترغب في المشاركة بالدراسة لا تتردد بقول ذلك. هذا الاستبيان هو عبارة عن اداة لتحقيق اهداف الدراسة والتي تتلخص في معرفة محددات سرطان القولون والمستقيم في المرضى اللذين يتعالجون في مستشفى بيت جالا الحكومي. ومن خلال ذلك نسعى لفهم أفضل للعلاقة بين عوامل الخطر المختلفة وعلاقتها بسرطان القولون والمستقيم في المجتمع الفلسطيني ولماذا نسب هذا السرطان عالية في فلسطين مقارنة بالدول المحيطة.

اقرأ التالي بتمعن ثم وقع باخر الورقة:

إذا كنت تحتاج أي توضيح لا تتردد بسؤال الباحث. كن متأكدا ان جميع اجاباتك ومعلوماتك ستكون سرية ولن تنشر او تعطى لأي أحد. لأغراض الدراسة انه لمن الضروري ان توافق على التالي:

- أؤكد على انني قرأت المعلومات واني افهم هدف هذا البحث.
- اعطي الاذن للحصول على معلوماتي من قبل الباحث.
- اعطي الاذن للباحث لاستخدام ملفي الطبي لأغراض الدراسة.
- افهم انه لا يوجد أي مخاطر من المشاركة بهذه الدراسة.
- افهم انه لا يوجد أي فوائد من المشاركة بهذه الدراسة.
- افهم ان الاشتراك بهذه الدراسة هو تطوعي وغير اجباري.
- توقيعي بالأسفل يعني انني موافق على المشاركة بالدراسة.
- اعلم انني أستطيع الانسحاب من الدراسة وقتما اشاء من دون أي مشاكل.

_____ التوقيع:

_____ التاريخ:

_____ رقم ملف المريض:

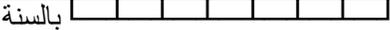
الباحث : عيسى خالد غروز جوال : 0599428481 وايميل : issa_ikg2006@hotmail.com

اشراف : د. نهى الشريف

Appendix 3: Determinants of Colorectal cancer questionnaire

القسم أ : معلومات المريض	
هل أنت؟	0 مريض 1 ضابط

معلومات المريض		
الترميز	الاستجابة	الأسئلة
A1	0 ذكر 1 انثى	الجنس
A2	يومشهرسنة □□□□□□□□□□	ما هو تاريخ ميلادك ؟ اذا لا تعلم 99 99 99
A3	سنوات □□	كم عمرك ؟
A4	0 لم ادرس بمدرسة 1 اقل من الابتدائية 2 المدرسة الابتدائية 3 المدرسة الثانوية 4 توجيهي 5 شهادة دبلوم/ جامعة 6 دراسات عليا 99 ارفض الإجابة	ما هو اعلى مستوى تعليمي وصلت له ؟

A5	0 غير متزوج 1 متزوج 2 منفصلين 3 مطلق 4 أرمل 99 ارفض الإجابة	الحالة الاجتماعية
A6	0 موظف حكومي 1 موظف غير حكومي 2 عمل خاص 3 غير مدفوع الاجر 4 طالب 5 اعمل في المنزل 6 متقاعد 7 عاطل عن العمل (قادر على العمل) 8 عاطل عن العمل (غير قادر على العمل) 99 ارفض الإجابة	أي من التالي يصف عملك خلال ال 12 شهر الماضية؟
A7	-----	ما هو عمالك؟
A8	بالسنة  ارفض الإجابة 99	ما هو معدل دخلك السنوي خلال العام الماضي؟
A9	0 مدينة 1 قرية 2 مخيم 99 لا اعرف	هل تعيش في؟
A10	-----	مكان السكن؟
A11	0 لا قرابة 1 أقرباء درجة أولى (أبناء عم، أبناء عمّة، أبناء خالة) 2 من نفس عائلة الام او الاب 99 لا اعلم	هل يوجد صلة قرابة بين والدك ووالدتك؟

A12	0 نعم 1 لا 99 لا اعلم	هل انت توأم او توأم ثلاثي؟
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القسم ب : التاريخ الطبي

التاريخ الطبي		
الترميز	الاستجابة	السؤال
B1	0 نعم 1 لا (اذهب لـ B2) 99 لا اعرف (اذهب لـ B2)	هل سبق وقمت بعمل فحص للدم في البراز (الدم المخفي بالبراز)؟
B1a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة عملت فيها هذا الفحص؟
B1b	1 للكشف عن مشكلة جديدة 2 تاريخ عائلي بوجود سرطان القولون 3 فحص روتيني 4 لمتابعة مشكلة سابقة 5 غير ذلك ----- 99 لا اعرف	ما هو السبب او الأسباب التي جعلتك تقوم بالفحص؟ (اختر المناسب)
B1c	لـ عدد المرات (اذا مرة واحدة فقط اذهب لـ B2) لا اعرف 99	كم مرة قمت بعمل هذا الفحص؟
B1d	و لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اخر مرة قمت فيها بعمل هذا الفحص؟

B2	0 نعم 1 لا (اذهب ل B4) 99 لا اعرف (اذهب ل B4)	هل سبق وقمت بعمل منظار للقولون؟
B2a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة عملت فيها هذا الفحص؟
B2b	1 للكشف عن مشكلة جديدة 2 تاريخ عائلي بوجود سرطان القولون 3 فحص روتيني 4 لمتابعة مشكلة سابقة 5 غير ذلك ----- 99 لا اعرف	ما هو السبب او الأسباب التي جعلتك تقوم بالفحص؟ (اختار المناسب)
B2c	لـ عدد المرات (اذا مرة واحدة فقط اذهب ل B4) لا اعرف 99	كم مرة قمت بعمل هذا الفحص؟
B2d	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اخر مرة عملت فيها هذا الفحص؟
B3	0 نعم 1 لا (اذهب ل B5) 99 لا اعرف (اذهب ل B5)	هل اخبرك طبيبك يوما انه يوجد لديك لحميات في قولونك لو في المستقبل؟
B3a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك طبيبك بذلك؟
B3b	0 نعم 1 لا (اذهب ل B4c) 99 لا اعرف (اذهب ل B4c)	هل اخبرك طبيبك بان لديك لحميات بالقولون او المستقبل اكثر من مرة؟

B3c	<p>1 حميدة</p> <p>2 ممكن ان تصبح سرطانية</p> <p>3 خبيثة</p> <p>4 غير ذلك -----</p> <p>99 لا اعرف</p>	هل كنت تعرف ما نوع تلك اللحميات ؟
B3d	<p>0 نعم</p> <p>1 لا (اذهب ل B5)</p> <p>99 لا اعرف (اذهب ل B5)</p>	هل فمت بإزالة تلك اللحميات؟
B3d(1)	<p>0 نعم</p> <p>1 لا</p> <p>99 لا اعرف</p>	هل فمت بإزالة اللحميات اكثر من مرة واحدة ؟
B4	<p>0 نعم</p> <p>1 لا (اذهب ل B6)</p> <p>99 لا اعرف (اذهب ل B6)</p>	هل اخبرك طبيبك يوما انك تعاني من مرض يسمى داء السلائل ؟ (هي حالة تحصل بعض الأحيان في العائلات بحيث يعاني الشخص من كثير من الأورام في القولون)
B4a	<p>او لـ العمر</p> <p>او لـ السنة</p> <p>او لـ قبل سنوات</p> <p>لا اعرف 99</p>	متى كانت اول مرة اخبرك طبيبك انك تعاني من مرض داء السلائل ؟
B5	<p>0 نعم</p> <p>1 لا (اذهب ل B7)</p> <p>99 لا اعرف (اذهب ل B7)</p>	هل اخبرك طبيبك يوما انك تعاني من مرض كرون ؟
B5a	<p>او لـ العمر</p> <p>او لـ السنة</p> <p>او لـ قبل سنوات</p> <p>لا اعرف 99</p>	متى كانت اول مرة اخبرك طبيبك انك تعاني من مرض كرون ؟
B6	<p>0 نعم</p> <p>1 لا (اذهب ل B8)</p> <p>99 لا اعرف (اذهب ل B8)</p>	هل اخبرك طبيبك يوما انك تعاني من التهاب القولون التقرحي ؟

B6a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك طبيبك انك تعاني من التهاب القولون التقرحي؟
B7	0 نعم 1 لا (اذهب لـ B9) 99 لا اعرف (اذهب لـ B9)	هل اخبرك طبيبك يوما انك تعاني من القولون العصبي؟
B7a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك طبيبك انك تعاني من القولون العصبي؟
B8	0 نعم 1 لا (اذهب لـ B10) 99 لا اعرف (اذهب لـ B10)	هل اخبرك طبيبك يوما انك تعاني من داء الرتوج؟
B8a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك طبيبك انك تعاني من داء الرتوج؟
B9	0 نعم 1 لا (اذهب لـ B11) 99 لا اعرف (اذهب لـ B11)	هل سبق وقمت بعملية ازاله للأمعاء الغليظة لو القولون او جزء منها؟
B9a	1 تم ازالته كاملا 2 ازالة جزء منه فقط 99 لا اعرف	هل قمت بإزالة الأمعاء الغليظة او القولون كاملا ام جزء منه؟
B9b	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة قمت بإزالة قولونك او امعاءك الغليظة؟
B9c	0 نعم 1 لا 99 لا اعرف	هل قمت بإزالة قولونك او امعاءك الغليظة اكثر من مرة؟

B10	0 نعم 1 لا (اذهب ل B12) 99 لا اعرف (اذهب ل B12)	هل سبق وقمت بإزالة المرارة؟
B10a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى قمت بإزالة المرارة؟
B11	0 نعم 1 لا (اذهب ل B13) 99 لا اعرف (اذهب ل B13)	هل اخبرك طبيبك انك تعاني من مرض السكري؟
B11a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك طبيبك انك تعاني من السكري؟
B11b	0 نعم 1 لا (اذهب ل B13) 99 لا اعرف (اذهب ل B13)	هل تأخذ ادوية للتحكم في مرض السكري؟

الرمز	كم المدة بالمجموع كنت تأخذ بها هذا الدواء بانتظام؟	هل كنت تأخذه بانتظام قبل سنتين؟	عندما كنت تأخذ هذا الدواء، كم مرة كنت تأخذه؟	ما نوع الدواء الذي تأخذه؟
B11c(1)	حبوب؟ ----- اشهر ----- سنوات 99 لا اعرف	حبوب؟ 0 نعم 1 لا 99 لا اعرف	حبوب؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	حبوب؟ 0 نعم 1 لا (اذهب للواء التالي) 99 لا اعرف (اذهب للدواء التالي)
B11c(2)	حقن انسولين؟ ----- اشهر ----- سنوات 99 لا اعرف	حقن انسولين؟ 0 نعم 1 لا 99 لا اعرف	ا حقن انسولين؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة	حقن انسولين؟ 0 نعم 1 لا (اذهب للواء التالي) 99 لا اعرف (اذهب للدواء التالي)

			99 لا اعرف	
B11c(3)	مضخة انسولين؟ ----- اشهر ----- سنوات 99 لا اعرف	مضخة انسولين؟ 0 نعم 1 لا 99 لا اعرف	مضخة انسولين؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	مضخة انسولين؟ 0 نعم 1 لا 99 لا اعرف

B12	0 نعم 1 لا (اذهب ل B14) 99 لا اعرف (اذهب ل B14)	هل اخبرك طبيبك يوما انك تعاني من ارتفاع الكوليسترول؟
B12a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك بها طبيبك انك تعاني من ارتفاع الكوليسترول؟
B12b	0 نعم 1 لا 99 لا اعرف	هل تأخذ علاجاً للتحكم في مستوى الكوليسترول؟
B13	0 نعم 1 لا (اذهب ل B15) 99 لا اعرف (اذهب ل B15)	هل اخبرك طبيبك يوما انك تعاني من ارتفاع في الدهون الثلاثية؟
B13a	او لـ العمر او لـ السنة او لـ قبل سنوات لا اعرف 99	متى كانت اول مرة اخبرك بها طبيبك انك تعاني من ارتفاع في الدهون الثلاثية؟
B13b	0 نعم 1 لا 99 لا اعرف	هل تأخذ علاجاً للتحكم في مستوى الدهون الثلاثية؟

B11	0 نعم 1 لا (اذهب ل B15d) 99 لا اعرف (اذهب ل B15d)	هل اخبرك طبيبك يوما انك تعاني من السرطان؟
B14a	الأول ----- الثاني ----- 99 لا اعرف	ما كان نوع ذلك السرطان؟
B14b	او [] العمر او [] السنة او [] قبل سنوات 99 لا اعرف	متى اخبرك طبيبك انك تعاني من هذا النوع من السرطان؟
B14c	0 نعم 1 لا 99 لا اعرف	هل تم علاجك باستخدام الاشعة؟ (تشمل كافة أنواع الاشعة)
B14d	0 نعم 1 لا 99 لا اعرف	هل سبق وخضعت لعملية زراعة نخاع عظم؟
B15	0 نعم 1 لا 99 لا اعرف	هل سبق وان تم تشخيص احد افراد عائلتك بسرطان القولون او المستقيم؟
B15a	0 قرابة درجة أولى 1 قرابة درجة ثانية 99 لا اعرف	ما صلة القرابة اللي تجمعك مع الشخص الذي تم تشخيصه بسرطان القولون او المستقيم؟
B16	0 نعم 1 لا 99 لا اعرف	هل سبق وان تم تشخيص أحد افراد عائلتك باي نوع من أنواع السرطانات الأخرى؟
B16a	----- 99 لا اعرف	ما نوع هذا السرطان
B16b	0 قرابة درجة أولى 1 قرابة درجة ثانية	ما صلة القرابة التي تجمعك مع الشخص الذي تم تشخيصه بسرطانات أخرى؟

	99 لا اعرف	
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الرمز	السؤال			
B17	في هذا السؤال سنسالك عن بعض الادوية التي ربما اخذتها. نحن فقط نهتم بالادوية التي اخذتها وانت بالغ ليست تلك التي بالطفولة			
	هل سبق واخذت احد الادوية التالية مرتين اسبوعيا لمدة شهر او اكثر ؟	هل كنت تأخذ هذا الدواء بانتظام قبل سنتين ؟	هل كنت تأخذ هذا الدواء، كل كم مرة كنت تأخذه ؟	ما هي المدة التي اخذت فيها هذا الدواء بانتظام ؟
B17a	الاسبرين بأنواعه ؟ 0 نعم 1 لا 99 لا اعرف	الاسبرين بأنواعه ؟ 0 نعم 1 لا 99 لا اعرف	الاسبرين بأنواعه ؟ 0 نعم 1 لا 99 لا اعرف	الاسبرين بأنواعه ؟ 0 نعم 1 لا 99 لا اعرف
B17b	اكامل، بانادول واسيتامنوفين بانواعها ؟ 0 نعم 1 لا 99 لا اعرف	اكامل، بانادول واسيتامنوفين بانواعها ؟ 0 نعم 1 لا 99 لا اعرف	اكامل، بانادول واسيتامنوفين بانواعها ؟ 0 نعم 1 لا 99 لا اعرف	اكامل، بانادول واسيتامنوفين بانواعها ؟ 0 نعم 1 لا 99 لا اعرف
B17c	مضادات الالتهاب غير الستيرويدية مثل ايبروفين وانواعه ؟ 0 نعم 1 لا 99 لا اعرف	مضادات الالتهاب غير الستيرويدية مثل ايبروفين وانواعه ؟ 0 نعم 1 لا 99 لا اعرف	مضادات الالتهاب غير الستيرويدية مثل ايبروفين وانواعه ؟ 0 نعم 1 لا 99 لا اعرف	مضادات الالتهاب غير الستيرويدية مثل ايبروفين وانواعه ؟ 0 نعم 1 لا 99 لا اعرف

B17d	ادوية مسهلة بأنواعها ؟ ----- أشهر ----- سنوات 99 لا اعرف	ادوية مسهلة بأنواعها ؟ 0 نعم 1 لا 99 لا اعرف	ادوية مسهلة بأنواعها ؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	ادوية مسهلة بأنواعها ؟ 0 نعم 1 لا (اذهب للواء التالي) 99 لا اعرف (اذهب للدواء التالي)
B17e	حبوب الفيتامينات ؟ ----- أشهر ----- سنوات 99 لا اعرف	حبوب الفيتامينات ؟ 0 نعم 1 لا 99 لا اعرف	حبوب الفيتامينات ؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	حبوب الفيتامينات ؟ 0 نعم 1 لا (اذهب للواء التالي) 99 لا اعرف (اذهب للدواء التالي)
B17f	حبوب حمض الفوليك ؟ ----- أشهر ----- سنوات 99 لا اعرف	حبوب حمض الفوليك ؟ 0 نعم 1 لا 99 لا اعرف	حبوب حمض الفوليك ؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	حبوب حمض الفوليك ؟ 0 نعم 1 لا (اذهب للواء التالي) 99 لا اعرف (اذهب للدواء التالي)
B17g	حبوب الكالسيوم ؟ ----- أشهر ----- سنوات 99 لا اعرف	حبوب الكالسيوم ؟ 0 نعم 1 لا 99 لا اعرف	حبوب الكالسيوم ؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	حبوب الكالسيوم ؟ 0 نعم 1 لا (اذهب للواء التالي) 99 لا اعرف (اذهب للدواء التالي)
B17h	مضادات حموضة ؟ ----- أشهر ----- سنوات 99 لا اعرف	مضادات حموضة ؟ 0 نعم 1 لا 99 لا اعرف	مضادات حموضة ؟ ----- مرة في اليوم ----- مرة في الاسبوع ----- مرة في الشهر ----- مرة في السنة 99 لا اعرف	مضادات حموضة ؟ 0 نعم 1 لا 99 لا اعرف

التدخين		
السؤال	الاستجابة	الرمز
هل تدخن التبغ او أي من منتجاته مثل السجائر، الغليون والنارجيلة ؟	0 نعم 1 لا (اذهب ل C8)	C1
هل انت حاليا مدخن للتبغ او أي من منتجاته ؟	0 نعم 1 لا	C2
كم كان عمرك عندما بدأت التدخين ؟	العمر بالسنوات <input type="text"/> لا اعرف 99	C3
منذ متى وانت تدخن ؟ 99 لا اعرف	او <input type="text"/> سنوات او <input type="text"/> اشهر <input type="text"/> اسابيع	C4
كم من المنتجات التالية تدخن أسبوعيا/ يوميا ؟	اسبوعيا ↓↓ يوميا	
	سجائر جاهزة <input type="text"/>	C5a/C5aw
	سجائر محضرة يدويا <input type="text"/>	C5b/C5bw
	غليون <input type="text"/>	C5c/C5cw
	سيجار <input type="text"/>	C5d/C5dw
	نارجيلة <input type="text"/>	C5e/C5ew
	غير ذلك <input type="text"/>	C5f/C5fw
هل فكرت بترك التدخين خلال ال 12 شهر الماضية ؟	0 نعم 1 لا	C6
خلال زيارتك للطبيب خلال ال 12 شهر الماضية ، هل نصحك بترك التدخين ؟	0 نعم 1 لا 2 لا زيارات للطبيب خلال ال 12 شهر الماضية	C7

C8	0 نعم 1 لا (اذهبل C12)	في الماضي، هل سبق وان دخنت أي نوع من أنواع التبغ؟
C9	0 نعم 1 لا	هل سبق لك وان دخنت بشكل يومي بالماضي؟
C10	العمر بالسنوات <input type="text"/> 99 لا اعرف	كم كان عمرك عندما توقفت عن التدخين؟
C11	او <input type="text"/> سنوات او <input type="text"/> اشهر او <input type="text"/> اسابيع لا اعرف 99	منذ متى وانت متوقف عن التدخين؟
C12	0 نعم 1 لا (اذهبل C14)	هل سبق لك وان استخدمت أي من منتجات التبغ الغير مدخنة مثل الممضوغة وعلكة التبغ وغيرها؟
C13	0 نعم 1 لا	ها تستخدم منتجات الدخان الغير مدخنة بشكل يومي؟
C14	0 نعم 1 لا (اذهبل C16)	هل سبق لك وان استخدمت أي من منتجات التبغ الغير مدخنة في الماضي؟
C15	0 نعم 1 لا	هل سبق لك وان استخدمت أي من منتجات التبغ الغير مدخنة بشكل يومي في الماضي؟
C16	0 نعم 1 لا	خلال ال 30 يوما الماضية، هل دخن احد داخل منزلك؟
C17	0 نعم 1 لا 2 لا اعمل في منطقة مغلقة	خلال ال 30 يوما الماضية، هل دخن احد بقربك في منطقة مغلقة مثل العمل؟
تناول الكحوليات		
الترميز	الاستجابة	السؤال
D1	0 نعم 1 لا	هل سبق لك وان شربت أي مشروب كحولي مثل البيرة، الخمر او المشروبات الروحية؟
D2	0 نعم 1 لا	هل شربت أي مشروب كحولي خلال ال 12 شهرا الماضية؟

D3	0 نعم 1 لا	هل توقفت عن شرب الكحوليات لأسباب صحية او لان الطبيب اخبرك بذلك ؟
D4	0 يوميا 1 5-6 أيام في الأسبوع 2 3-4 أيام في الأسبوع 3 1-2 أيام في الأسبوع 4 1-3 أيام في الشهر 5 اقل من مرة في الشهر	خلال ال 12 شهرا الماضية كم عدد المرات التي تناولت فيها كاسا كحوليا واحدا ؟
D5	0 نعم 1 لا	هل شربت أي مشروب كحولي خلال ال 30 يوما الماضية ؟
D6	عدد <input type="text"/> 99 لا اعرف	خلال ال 30 يوما الماضية، ما عدد المناسبات التي شربت فيها مشروبا كحوليا واحدا على الأقل ؟
D7	عدد <input type="text"/> 99 لا اعرف	خلال ال 30 يوما الماضية، ما عدد المرات التي شربت فيها مشروبا كحوليا واحدا خلال المناسبات التي شربت فيها ؟
D8	اكبر عدد <input type="text"/> 99 لا اعرف	خلال ال 30 يوما الماضية، ما هو اكبر عدد من المشروبات الكحولية التي شربتها خلال مناسبة واحدة ؟
D9	عدد <input type="text"/> 99 لا اعرف	خلال ال 30 يوما الماضية ، ما هو عدد المناسبات التي شربت فيها 6 او اكثر مشروبات كحولية ؟
D10a	السبت <input type="text"/>	خلال ال 7 أيام الماضية ، كم مشروبا كحوليا شربت في اليوم ؟
D10b	الاحد <input type="text"/>	
D10c	الاثنين <input type="text"/>	
D10d	الثلاثاء <input type="text"/>	
D10e	الأربعاء <input type="text"/>	
D10f	الخميس <input type="text"/>	
D10g	الجمعة <input type="text"/>	
	99 لا اعرف	

التغذية		
الترميز	الاستجابة	السؤال
E1	<p>للا وجبة يوميا</p> <p>للا وجبة أسبوعيا</p> <p>للا وجبة شهريا</p> <p>99 لا اعرف</p>	قبل سنة منذ تم تشخيصك بالسرطان، كم وجبة من الفواكه كنت تأكل؟
E2	<p>للا وجبة يوميا</p> <p>للا وجبة أسبوعيا</p> <p>للا وجبة شهريا</p> <p>99 لا اعرف</p>	قبل سنة منذ تم تشخيصك بالسرطان، كم وجبة من الخضروات كنت تأكل؟
E3	<p>للا وجبة يوميا</p> <p>للا وجبة أسبوعيا</p> <p>للا وجبة شهريا</p> <p>98 لا اكل لحوم حمراء</p> <p>99 لا اعرف</p>	قبل سنة منذ تم تشخيصك بالسرطان، كم وجبة من اللحم الاحمر كنت تأكل؟ (لا يشمل الدجاج او السمك)
E3a	<p>للا وجبة يوميا</p> <p>للا وجبة أسبوعيا</p> <p>للا وجبة شهريا</p> <p>98 لا اكل لحوم حمراء مشوية</p> <p>99 لا اعرف</p>	قبل سنة منذ تم تشخيصك بالسرطان، كم وجبة من اللحم الأحمر المشوي كنت تأكل؟
E3b	<p>0 بنية قليلا</p> <p>1 بنية بشكل معتدل</p> <p>2 بنية كثيرا او مسمر</p> <p>99 لا اعرف</p> <p>98 لا اكل لحما احمر مشويا</p>	عندما كنت تأكل لحما احمر مشويا، كيف كان مظهرها من الخارج؟

E3c	0 حمراء 1 زهرية 2 بنية 99 لا اعرف	عندما كنت تأكل لحما احمرًا مشويًا، كيف كان مظهرها من الداخل؟
E4	وجبة يومية وجبة أسبوعيا وجبة شهريا 98 لا اكل الدجاج 99 لا اعرف	قبل سنة منذ تم تشخيصك بالسرطان، كم وجبة من الدجاج كنت تأكل؟
E4a	وجبة يومية وجبة أسبوعيا وجبة شهريا 98 لا اكل دجاج مشوي 99 لا اعرف	قبل سنة منذ تم تشخيصك بالسرطان، كم وجبة من الدجاج المشوي كنت تأكل؟
E4b	1 بنية بشكل معتدل 2 بنية كثيرا او مسمر 99 لا اعرف 98 لا اكل دجاجا مشويا	عندما كنت تأكل دجاج مشويًا، كيف كان يبدو مظهرها؟

القسم ه : النشاط البدني

النشاط البدني		
الترميز	الاستجابة	الأسئلة
P1	0 نعم 1 اذهب إلى إذا لا P4 لا	هل نمط العمل يتوجب نشاطا شاقا يسبب زيادة كبيرة في التنفس وإسراع ضربات القلب مثل (الحمل الثقيل، الحفر، ورشة بناء) لمدة عشرة دقائق متواصلة على الأقل؟
P2	لا عدد الأيام	كم من أيام الأسبوع العادي يتوجب عليك النشاط الشاق كجزء من عملك؟

P3 (a-b)	ساعة : دقيقة ساعة دقيقة	ساعة دقيقة	كم من الوقت في اليوم العادي تستغرق لإنجاز هذا النشاط الشاق؟
P4	0 1 اذهب إلى إذا لا P7	نعم لا	هل يشمل عملك أنشطة متوسطة الجهد التي تسبب زيادة طفيفة في التنفس ونبضات القلب مثل (المشي السريع حمل أشياء خفيفة الوزن) لمدة عشر دقائق على الأقل؟
P5	عدد الأيام	عدد الأيام	كم من أيام الأسبوع العادي يتوجب عليك بذل نشاط متوسط كجزء من عملك؟
P6 (a-b)	ساعة : دقيقة ساعة دقيقة	ساعة دقيقة	كم من الوقت في اليوم العادي يستغرق منك القيام بنشاط متوسط كجزء من عملك؟
P7	0 1 اذهب إلى إذا لا P10	نعم لا	هل تسير على الأقدام أو تركب دراجة من وإلى أماكن معينة لمدة عشر دقائق متواصلة على الأقل؟
P8	عدد الأيام	عدد الأيام	كم يوماً في الأسبوع العادي تستعمل الدراجة أو تسير من وإلى أماكن معينة؟
P9 (a-b)	ساعة : دقيقة ساعة دقيقة	ساعة دقيقة	كم من الوقت في المجموع تستغرق للتنقل بالدراجة أو سيراً على الأقدام في اليوم العادي
P10	0 1 اذهب إلى إذا لا P13	نعم لا	هل يتضمن وقت الفراغ نشاطاً شاقاً سواء كان للرياضة أو اللياقة البدنية أو النشاط الترفيهي ويتسبب في زيادة في التنفس وعدد ضربات القلب مثل (الجرى أو كرة القدم) لمدة عشرة دقائق متواصلة؟
P11	عدد الأيام	عدد الأيام	كم يوماً في الأسبوع العادي تقوم بنشاط شاق كجزء من وقت فراغك؟
P12 (a-b)	ساعة : دقيقة ساعة دقيقة	ساعة دقيقة	كم ساعة في اليوم العادي تستغرق لإنجاز هذا النشاط؟
P13	0 1 اذهب إلى إذا لا P16	نعم لا	هل يشمل وقت فراغك أنشطة متوسطة الجهد، مثل (المشي السريع، ركوب دراجة أو حمل أشياء خفيفة الوزن - سباحة - كرة اليد) لمدة عشر دقائق على الأقل؟ استخدم الأمثلة والنماذج التوضيحية
P14	عدد الأيام	عدد الأيام	كم يوماً في الأسبوع تقوم بأنشطة معتدلة كجزء من وقت الفراغ؟
P15 (a-b)	ساعة : دقيقة ساعة دقيقة	ساعة دقيقة	كم من الوقت تستغرق للقيام بهذا النشاط في يوم عادي؟

P16 (a-b)	: □□ □□ ساعة دقيقة	ساعة دقيقة	كم من الوقت أمضيته جالساً أو مستلقياً في اليوم العادي؟
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القسم و : الطول والوزن

الترميز	الاستجابة	السؤال
G1	□□□□ سم	الطول
G2	□□□□ كغم	الوزن
G3	□□□□ كغم	كم كان وزنك قبل سنتين من الان
G4	□□□□ كغم	كم كان وزنك قبل سنتين من تشخيصك بالسرطان

Appendix 4: Panadol, NSAIDs, Laxatives, Multivitamins, Folic Acid, Calcium, and Antacids tables

		Study cases N=105		Control Group N=105		P value of Chi Square
		Count	Column N %	Count	Column N %	Significance
Panadol	Yes	15	14.3%	20	19.0%	0.355
	No	90	85.7%	85	81.0%	
NSAIDs	Yes	11	10.5%	13	12.4%	0.664
	No	94	89.5%	92	87.6%	
Laxatives	Yes	9	8.6%	4	3.8%	0.152
	No	96	91.4%	101	96.2%	
Multivitamins	Yes	11	10.5%	12	11.4%	0.825
	No	94	89.5%	93	88.6%	
Folic Acid	Yes	0	0.0%	2	1.9%	0.155
	No	105	100.0%	103	98.1%	
Calcium	Yes	4	3.8%	10	9.5%	0.097
	No	101	96.2%	95	90.5%	
Antacids	Yes	1	1.0%	2	1.9%	0.561
	No	104	99.0%	103	98.1%	

Appendix 5: Smoking status, age of smoking initiation, years since smoking started, and type of smoking. Pipe full of tobacco, cigars and non-smoked tobacco products

		Study cases		Control Group		P value of Chi Square
		Count	Column N %	Count	Column N %	Significance
Pipe full of tobacco smoked (Weekly)	<2 pipes	1	1.0%	0	0.0%	0.341
	≥2 pipes	1	1.0%	0	0.0%	
	Don't smoke	103	98.1%	105	100.0%	
Cigar smoked (Weekly)	<5 cigars	1	1.0%	2	1.9%	0.361
	≥5 cigars	4	3.8%	1	1.0%	
	Don't smoke	100	95.2%	102	97.1%	
Past Smoking	No	6	5.7%	2	1.9%	0.283
	Yes	7	6.7%	5	4.8%	
	Non Smoker	92	87.6%	98	93.3%	
Past daily smoking	No	2	1.9%	1	1.0%	0.274
	Yes	12	11.4%	6	5.7%	
	Non smoker	91	86.7%	98	93.3%	
Non Smoked tobacco	No	105	100.0%	104	99.0%	0.316
	Yes	0	0.0%	1	1.0%	
Non Smoked tobacco daily	No	105	100.0%	104	99.0%	0.316
	Yes	0	0.0%	1	1.0%	
Ever used Non smoked tobacco	No	105	100.0%	104	99.0%	0.316
	Yes	0	0.0%	1	1.0%	
Ever used Non Smoked tobacco daily	No	105	100.0%	104	99.0%	0.316
	Yes	0	0.0%	1	1.0%	
Indoor smoking	No	98	93.3%	103	98.1%	0.088
	Yes	7	6.7%	2	1.9%	
Work Smoking	No	61	58.1%	75	71.4%	0.121
	Yes	26	24.8%	19	18.1%	
	Don't work in a closed area	18	17.1%	11	10.5%	