ASSESSMENT OF A COLORECTAL CANCER SCREENING PROJECT USING FAECAL OCCULT BLOOD TEST (FOBT) KIT IN PENANG STATE, MALAYSIA

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by

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DEDICATION

بسم الله'لرحمن الرحيم

I dedicate this thesis to :

My Teachers,

My Families,

My Colleagues,

الحمدلله رب العالمين

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LIST OF ABBREVIATIONS

ACS	American Cancer Society
ASR	Age standardized rate
CFOBT	Chemical FOBT
CMS	Centre for Medicare and Medicaid Services
CPG	Clinical Practice Guidelines
CRC	Colorectal cancer
CT	Computed Tomography
FAP	Familial Adenomatous Polyposis
FDA	Food and Drug Administration (USA)
FIT	Faecal Immunochemical Test
FOBT	Faecal occult blood test
FOBT (+)	Participants with a positive result for FOBT
GFOBT	Guaiac faecal occult blood test
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
HPV	Human papilloma virus
IFOBT	Immunochemical FOBT
JEPeM	Jawatankuasa Etika Penyelidikan Manusia
MAHTAS	Malaysian Health Technology Assessment Section
MRI	Magnetic Resonance Imaging
NCDP-1M	Non-communicable Diseases Prevention 1 Malaysia
NCR	National Cancer Registry
NCSM	National Cancer Society of Malaysia
NGOs	Non-government organizations

NSAID	Non-steroid anti inflammatory drugs
OR	Odds ratio
PASW	Predictive analytics software
PN	Patient navigator
ROC	Receiver operating characteristics
SCS	Singapore Cancer Society
SGH	Singapore General Hospital
SEER	Surveillance Epidemiology and End Result
UiTM	Universiti Teknologi Mara
UK	United Kingdom
USA	United States of America
VIF	Variance inflation factor

PENILAIAN PROJEK SARINGAN KANSER KOLOREKTAL MENGGUNAKAN ALAT PENGESAN DARAH SAMAR DALAM NAJIS (PDSN) DI PULAU PINANG, MALAYSIA

ABSTRAK

Insidens kanser kolorektal (KKR) semakin meningkat di negara-negara membangun disebabkan oleh perubahan gaya hidup. Di Malaysia, KKR berada pada tahap kedua daripada semua jenis kanser dengan insidens tertinggi berlaku dalam kalangan kaum Cina. Saringan berkala untuk KKR menggunakan alat pengesan darah samar dalam najis (PDSN) telah diketahui dapat menurunkan kejadian kematian dan kesakitan akibat gejala penyakit ini. Tujuan kajian ini adalah untuk menilai suatu program saringan kanser KKR menggunakan alat PDSN di Pulau Pinang, Malaysia. Sebanyak 970 alat PDSN telah diedarkan antara bulan Jun hingga November 2009 semasa ceramah kesihatan mengenai KKR diselenggarakan. Data dikumpulkan melalui borang soal selidik yang diisi sendiri oleh peserta dan temu bual melalui telefon. Semua analisis dilakukan menggunakan perisian analisis ramalan (PAR) versi 18 untuk statistik deskriptif dan juga analisis regresi logistik binari untuk mengetahui faktor-faktor yang berkaitan dengan pengetahuan mengenai KKR dan keperluan mengembalikan semula alat PDSN. Seramai 617 orang peserta telah melengkapkan borang soal selidik (63.6%). Hanya sedikit peserta (3.8 %) yang menyatakan mereka menghadapi kesukaran untuk menjalani ujian ini. Tahap kesedaran peserta mengenai ujian najis dan pengetahuan mengenai KKR didapati rendah. Faktor yang berkaitan dengan rendahnya tahap pengetahuan peserta mengenai KKR ini ialah pendidikan yang rendah (OR = 3.07; 95%CI: 2.01-4.70) dan tiadanya sejarah keluarga yang menghidap kanser (OR = 1.71; 95%CI: 1.16-2.52). Kelompok umur yang lanjut (OR

= 3.31; 95%CI: 2.09-5.23), etnik Cina (OR = 2.35; 95%CI: 1.32-4.19), dan pendidikan yang lebih tinggi (OR = 2.26; 95%CI: 1.49-3.42) merupakan faktor yang berkaitan dengan pengembalian alat PDSN. Tiga puluh satu orang peserta mendapat hasil positif dan beberapa peserta merasa cemas (30%) dan takut (25%) selepas mengetahui hasil ujian. Lapan peserta menjalani kolonoskopi. Satu kes KKR disahkan dijumpai pada seorang peserta wanita berketurunan Cina berumur 61 tahun ; dua orang peserta menghidapi polip ; seorang peserta menghidapi kolitis berulser dan seorang lagi peserta menghidapi buasir. Sembilan perserta yang tidak menjalani kolonoskopi diwawancara dan 6 orang menyatakan bahawa mereka telah berjumpa dengan doktor tetapi doktor tidak mencadangkan mereka untuk menjalani kolonoskopi dan tiga orang peserta lainnya tidak menjumpai sebarang doktor. Sebagai kesimpulan, kajian ini menemukan kadar pengembalian PDSN sebesar 56.7% dan hanya seperempat peserta dengan KKR positif menjalani kolonoskopi. Meskipun projek saringan KKR ini menemukan satu pesakit menghidapi KKR, adalah disyorkan untuk mengambil langkah-langkah untuk meningkatkan kepatuhan dalam pengembalian alat PDSN dan menjalani kolonoskopi selepas mendapati hasil ujian positif.

ASSESSMENT OF A COLORECTAL CANCER SCREENING PROJECT USING FAECAL OCCULT BLOOD TEST (FOBT) KIT IN PENANG STATE, MALAYSIA

ABSTRACT

Incidence of colorectal cancer (CRC) has been increasing in many countries due to changes in life style. In Malaysia, CRC is the second most common cancer with the highest incidence among the Chinese ethnic group. Periodic screening for CRC with faecal occult blood test kit (FOBT) has been shown to reduce the mortality and morbidity from this disease. The objective of this study was to assess a CRC screening project using FOBT kit in Penang, Malaysia. A total of 970 FOBT kits were distributed between June and November 2009 during CRC public health talks. Data was collected using self-administered questionnaires and telephone interviews. Statistical analyses were carried out using PASW version 18 for descriptive statistics as well as for the binary logistic regression analyses to determine associated factors for CRC knowledge and return of FOBT. A total of 617 participants completed the first questionnaire with a response rate of 63.6 %. Few (3.8 %) reported encountering difficulties in doing the FOBT. The level of awareness of stool examination and knowledge of CRC were poor among participants. The factors associated with poor knowledge of CRC were low education (OR=3.07; 95%CI: 2.01-4.70) and not having family history of cancer (OR=1.71; 95%CI: 1.16-2.52). Older age (OR =3.31; 95%CI: 2.09-5.23), Chinese ethnicity (OR=2.35; 95%CI: 1.32-4.19) and higher education (OR=2.26; 95%CI:1.49- 3.42) were factors associated with the return of FOBT kit. Thirty-one participants had positive FOBT result and

some reported feeling anxious (30%) and frightened (25%) after knowing the result. Eight participants underwent colonoscopy. One case of CRC was found in a 61 year old Chinese female; two participants had polyps; one participant with ulcerative colitis and another with haemorrhoids. From the 9 participants who did not undergo colonoscopy, 6 reported seeing doctors for follow-up but were not advised colonoscopy and 3 did not seek any medical advice for the positive FOBT. In conclusion, this study found a return rate for FOBT of 56.7% and only a quarter of the positive FOBT cases underwent colonoscopy. Although the CRC screening project identified one case of CRC, it is recommended that steps be taken to increase the compliance in FOBT return and colonoscopy following a positive FOBT.

CHAPTER 1

INTRODUCTION

1.1 Background of the Study

Colorectal cancer (CRC) is now a major concern for many developed and developing countries. In the past, most cases of this cancer were found in developed countries and was considered a disease of western life style (World Health Sciences, 2010). In recent years, the incidence of CRC has been increasing in the developing countries, due to changes in life style, which include a more sedentary life style, obesity, alcohol intake and smoking habit (World Health Organization, 2007).

According to the National Cancer Registry Report 2011, CRC was the second most common cancer among males and females in Malaysia in 2007. There were 2,246 CRC cases or 12.3% of all cancer cases. The age standardized rate (ASR) for males was 13.4 per 100,000 population, while for females it was 10.2 per 100,000 population. The highest ASR was found among the Chinese ethnic group, with 19.4 per 100,000 population for males, and 14.6 per 100,000 population for females. Among Indian males, the ASR was 10.2 per 100,000 population; among Malay males, 10.1 per 100,000 ; among Malay females, 7.6 per 100,000 population; and the lowest ASR was among Indian females, 6.9 per 100,000 population (Omar, 2011).

This data showed that the Chinese had the highest risk of being diagnosed with CRC compared with other ethnic groups in Malaysia (Ministry of Health, 2009). Therefore, it is important to have a CRC screening programme in Malaysia especially among the Chinese ethnic group. Moreover, a CRC screening programme

has never been done before in Malaysia. Therefore, this study provides the first opportunity to screen the community for CRC.

Penang state has a population of 1.5 million, with a population breakdown showing a majority of Chinese ethnic group (46.5%), followed by Malays (42.1%), Indian and others (0.8 %). The number of cancer cases in Penang for the years 1999 to 2003 was 7,553 cases, of which 3,514 cases were males and 4,039 cases were females (Bina Rai, 2005). The CRC cases occurring in Penang state during that same time interval was 839 cases, with 458 males and 381 cases were females. From the 458 male cases, the highest number of cases were of Chinese ethinicity with 348 cases (76%), and from the 381 female cases, 284 cases (74.5%) were also among the Chinese (Bina Rai, 2005).

With a population that has a majority of Chinese ethnic group, Penang is somewhat similar to Singapore (Singstat, 2010). Based on the Singapore experience of CRC screening programme done in 2008, it could be expected that if 1000 FOBT kits are made available, at least one case of CRC would be identified (Singapore Cancer Society, 2009). Therefore, this study aimed to assess a CRC screening project in Penang state, to detect CRC cases or precancerous lesions (polyps) at an early stage. The benchmark for the success of the programme was set at finding at least one CRC case.

Many CRC screening programmes have been conducted in several other countries and only results of FOBT test, showing the number of positive and negative result are reported (Singapore Cancer Society, 2009-2011; Chew, 2009; Fu, 2009; Logan, 2012; Chong, 2013; Al Ahwal, 2013). There is still information which has not been described yet, for example, the feed back from participants regarding

the stool examination, reasons of noncompliance to FOBT and colonoscopy, knowledge of CRC and awareness of stool examination. Such information can be useful for the healthcare planners to formulate a screening programme. Therefore, it is timely to carry out this study to assess a community-based CRC screening project.

1.2 Objectives of the Study

The objectives of this study are as follows:

1. To assess a CRC screening project using FOBT kit by determining the return rate of FOBT kit and compliance rate for colonoscopy among participant with FOBT (+).
2. To assess the knowledge of CRC and awareness of stool examination and the associations with the demographic factors and to assess the usage of FOBT kit among participants.
3. To describe reasons for noncompliance for the FOBT and colonoscopy.

CHAPTER 2

LITERATURE REVIEW

2.1 Colorectal Cancer

Cancer or a malignant tumour refers to an abnormal and uncoordinated growth with proliferation of cells that can invade and destroy the tissue surrounding it and spread to other organs and cause death (Kumar, 2007).

Colorectal cancer (CRC) is cancer originating from cells of the colon and rectum. Most of the cancers are of the adenocarcinoma type (98%), with most precursor lesions originating from adenomas. Majority of CRC cases have occured among males compared to females (Kumar, 2007).

Most adenomas appear in the colon or rectum by the age of 50 years, and develop into cancer within 5 to 10 years (Rozen, 2006).

CRC is a treatable and curable cancer if it is detected at an early stage. Routine CRC screening will increase the detection rate of precancerous adenomas as well as CRC. Removing precancerous adenoma will reduce future incidence of CRC (Rozen, 2006).

2.2 Epidemiology

In the USA, CRC was responsible for 15% of the total number of cancer deaths and was the second most common cause of death among all cancer cases (Winawer, 2007). Every year at least 1 million people in USA are diagnosed with CRC. A total of 1,023,000 cases were found in USA in 2007, about 550,000 among males and 473,000 among females. The number of deaths was 278,000 males and

255,000 females (Winawer, 2007). It has been estimated that every person has a 5% chance of getting this disease (Kumar, 2007), and the highest incidence of CRC was among African Americans (Jandorf, 2005). From Surveillance Epidemiology and End Result (SEER) data for 1973-1989, the ASR for CRC among African American males was calculated to be 39% and among white American males was 11%. The ASR for the African American females was 26% and among white American females was 3%. In 1990, the ASR in USA reduced because of the successful prevention programme through polypectomy (Winawer, 2007).

In the United Kingdom, CRC was the third most common cancer occurring in both males (after lung and prostate cancer) and females (after breast and lung cancer). The incidence was found to be higher among males than among females. Every year, about 32,000 new CRC cases are diagnosed, especially arising in the rectum and sigmoid region (Garden, 2007). In Eastern and Southern Europe, the ASR has increased, but in the areas of North and Central Europe, it has levelled off (Winawer, 2007).

Other countries that have reported a high incidence of CRC were Canada, Australia, New Zealand, Denmark, and Sweden. In Australia, CRC was the second most common cause of death among all cancer cases. The risk for getting this disease was reported as 1:17 for males and 1:26 among females (Australia, 2004).

CRC also becomes the third most common cancer cases among males and females in Asia (Pourhoseingholi, 2012). Some Asian countries reported high incidence of CRC such as Japan, Singapore, South Korea, Taiwan, Hong Kong, and Iran (Kumar, 2007; Pourhoseingholi, 2012). In Japan, the incidence of CRC in people under the age of 50 years was very low, but it increased dramatically among

the population aged 50 years and older (Winawer, 2007). Incidence of CRC has increased two- to four-fold in recent decades in Singapore, China, Japan and South Korea (Pourhoseingholi, 2012). Incidence of CRC is higher among the Chinese compared to other ethnic groups in Asia, likewise to Chinese people who live in Malaysia (Pourhoseingholi, 2012). Furthermore, the incidence of CRC in Asia Pacific countries is now comparable to the incidence of CRC in western countries such as United States, Canada and European countries (Wong, 2011).

The incidence of CRC has also increased in the last decade in Malaysia (Bina Rai, 2005). Ten years ago, CRC was the third most common cancer among males and females in Malaysia, but it is now the second most common cancer (Bina Rai, 2005). Moreover, malignant neoplasm has become the third most common cause of death in the government hospitals in Malaysia after septicaemia and heart and pulmonary diseases (Ministry of Health, 2009).

2.3 Aetiology and Risk Factors

The cause of CRC is unknown (Allison, 2007). There is a complex relationship between environmental and genetic risk factors that contribute to the development of CRC. Age is one risk factor, as the incidence of CRC increases after the age of 50 years. Other risk factors found in many countries include diets with a high proportion of animal meat which have been cooked at high temperatures, a low portion of vegetables or fruits, and high consumption of alcohol. Gender, obesity, lack of exercise, smoking habits, diabetes, inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, adenomatous polyps, and cancer in other organs also have been implicated as risk factors (Rozen, 2006).

A person with a family history of CRC has a higher risk of getting the disease, compared with one with no family history (Rozen, 2006). This risk has been estimated as being two times higher than that of a person with a negative family history (American Cancer Society, 2008). The genetic factors which have been found to be important in CRC are Lynch syndrome (hereditary nonpolyposis colorectal cancer), familial adenomatous polyposis, familial juvenile polyposis, and Peutz-Jeghers syndrome (Rozen, 2006).

2.4 Diagnosis

Diagnosis of CRC is based on the signs and symptoms, laboratory, radiology, and endoscopic examination. The history taken from the patient should include questions on risk factors and past medical history such as ulcerative colitis and haemorrhoids to identify possible causes of blood in the stool.

2.4.1 Signs and Symptoms

The symptoms and clinical signs of CRC depend on the location of the tumour in the colon or rectum, and the presence of spread. If the tumour is in the right side of the colon, the patient usually complains of abdominal pain, or a feeling of a mass in the abdomen, or both. If the tumour is in the left side of colon, the patient commonly complains of abdominal pain, melaena, or fresh bleeding from rectum, and constipation. If the tumour is in the area of the rectosigmoid or rectum, patients usually experience melaena from rectum, constipation, tenesmus, and the diameter of the stool becomes smaller (Rozen, 2006). There may be a past medical history of ulcerative colitis, Crohn's disease, polyps, haemorrhoids, diabetes mellitus, as these are all risk factors for this cancer.

On physical examination in the case of an advanced stage of CRC, one may find signs of anaemia, weight loss, an enlarged liver, a mass in abdomen, especially if the cancer developed on the right side. There can be signs of intestinal obstruction, ascites, and symptoms of parietal pain if there is invasion to the wall of the abdomen, perianal pain or sciatic pain in the late stage of rectum cancer (Garden, 2007).

A patient with CRC may present with a history and physical examination similar to appendicitis or diverticulitis or even chronic perforation which produces symptoms of recurrent urinary tract infection and haematuria. There may also be signs of Peutz-Jeghers syndrome (hyperpigmentation of skin and mucous membranes).

Malignancies in the gastrointestinal tract have been known to produce symptoms of paraneoplastic phenomenon, for example, acanthosis nigricans, dermatomyositis, and hypercalcemia, but these are usually manifestations of CRC in its late stage (Berg, 2001).

2.4.2 Laboratory Examination

FOBT kit is used to detect blood in the stool. It has high sensitivity and specificity, 92% and 96% respectively in detecting CRC (Van Rossum, 2008; Park, 2010), but further examinations are needed to confirm if the positive FOBT is due to CRC (Berg, 2001).

2.4.3 Radiological Examination

Radiological examinations are used as diagnostic tools to detect CRC and metastases to other organs. Each type of radiological examination has its advantages and disadvantages when implemented in a screening programme.

2.4.3.1 Plain X-ray

Plain x-ray of abdomen can be carried out quickly, but it would not be a satisfactory screening modality as by the time a colorectal mass is visible on x-ray, it is already at a late stage and may have already produced symptoms. Furthermore, the disadvantages of x-ray examinations are radiation exposure and the need for bowel preparation before any abdominal radiological examination.

A plain x-ray of the chest can identify the presence of metastases to the lung. About 10% of patients with cancer of the rectum have metastases to the lungs at the time of diagnosis (Berg, 2001).

2.4.3.2 Barium Enema

A double contrast barium enema is widely available in many places (Winawer, 2007). This examination can detect 90% cases of CRC and 80% of polyps with diameter more than 1 cm, but it is less sensitive for polyps with diameter less than 1 cm (Rozen, 2006). This examination needs to be repeated every five years if polyps are not found (Cleveland, 2010). Barium enema can help in diagnosis, but it cannot facilitate a biopsy or polypectomy and it requires good bowel preparation (Berg, 2001).

2.4.3.3 Computed Tomography (CT) Scanning

Computed tomography scanning can be used to detect the spread of CRC to other organs, especially to the lung, liver, abdomen, chest, and pelvis. However, a contrast agent needs to be inserted to the vein before scanning, which makes this examination an invasive procedure (Berg, 2001). Exposure to radiation is higher than in a regular x-ray, while some patients have experienced an allergic reaction to the contrast agent (National Cancer Institute, 2012). This scanning is more useful for staging CRC rather than for a screening modality.

2.4.3.4 Computed Tomography (CT) Colonography

CT colonoscopy is also known as virtual colonoscopy, virtual endoscopy, or 3D-endoscopy. It can show a three dimensional figure by using multislice x-ray technology. This examination is less invasive compared with colonoscopy, and the patient does not need sedation. The disadvantage of this procedure is that a colonoscopy is still needed if polyps are found in the colon for polypectomy. The patient still needs colon cleansing before examination (Berg, 2001).

The sensitivity of this examination has been reported as between 45% and 97%, and the specificity is between 26% and 97% depending on the size of polyps. The examination is not satisfactory for polyps with the size 6 to 9 mm. The sensitivity and specificity increase to 93% and 97% for larger polyps with diameter of 10 mm or more (Winawer, 2007). Patients who undergo this examination will be exposed to ionizing radiation repeatedly, and the cost for this examination is expensive (Winawer, 2007).

2.4.3.5 Magnetic Resonance Imaging (MRI)

This examination (MRI) is usually carried out to detect relapse of CRC or if the liver has not been visualized adequately by CT scan. The advantages of MRI over a CT scan include the use of noniodine contrast agent to get clearer images and the lack of radiation exposure. The disadvantage of MRI is that it is an expensive procedure. In many countries, facilities for conducting MRI are limited. Furthermore, MRI cannot be used when patients have pacemakers or any metallic implants, therefore, this examination is not suitable for population screening (Rozen, 2006).

2.4.4 Endoscopic Examination

Endoscopic examination is an appropriate examination for detecting CRC, when applied in a CRC screening programme. To get maximum advantage and minimum disadvantage for patients, certain conditions and criteria have to be fulfilled, as will be described in the following subsections.

2.4.4.1 Rigid Proctosigmoidoscopy

This examination has been reported as capable of detecting between 25% and 30% of CRC cases. The advantage of this examination is that it does not need sedation or colon cleansing preparation, and is an outpatient procedure. One disadvantage of rigid sigmoidoscopy is that it only has an endoscope length of 20 cm, therefore it is only able to reach the rectosigmoid junction of the colon. The rest of the colon where 70% to 75% of CRC may develop, cannot be visualized. Proper training is also required to perform this examination (Rozen, 2006).

2.4.4.2 Flexible Sigmoidoscopy

The lengths of flexible endoscopes are 30 cm and 60 cm, and visualization of the sigmoid and descending colon is possible. About half to two-thirds of CRC cases can be detected by this examination. The examination can be carried out without sedation but requires bowel preparation (Rozen, 2006).

Complications including perforation can occur at a rate of 1:10,000. However, reports have shown that flexible sigmoidoscopy can reduce the mortality of colorectal cancer by 60% to 70% (Winawer, 2007).

The disadvantages of this examination are that it cannot reach the ascending and transverse colon, and thus CRC arising in those areas can be missed. Bowel preparation using enema is still needed. Furthermore, the examiner needs sufficient training to perform this examination (Rozen, 2006).

2.4.4.3 Colonoscopy

Colonoscopy can visualize the whole colon. It can be used as a diagnostic tool, for example, when doing a biopsy. It can also be used as a therapeutic tool because resection of the polyps (polypectomy) can be carried out. Colonoscopy can also detect small polyps with diameter less than 10 mm.

The sensitivity and specificity of colonoscopy has been reported as 95% in detecting polyps and CRC. The miss rate of colonoscopy for polyps is about 15% to 25% for adenomas with diameter less than 5 mm, and 0% to 6% for adenomas equal to 10 mm or bigger (Winawer, 2007).

Finding polyps by colonoscopy can help reduce the mortality of CRC by 60% to 80% and periodic colonoscopy with polypectomy has been estimated as being able to prevent 76% to 90% of cases of CRC (Benuzillo, 2009).

Colonoscopy is considered to be the gold standard examination in United States, after FOBT positive was found (Winawer, 2007).

The disadvantages of colonoscopy include the need for sedation and colon cleansing preparations. A highly skilled operator is needed to perform the examination, and the cost is expensive (Rozen, 2006).

The complication rate of colonoscopy is reported to be 1 to 2 among 1000 examinations, the complications that occur include severe haemorrhage and bowel perforation (Winawer, 2007).

2.5 Prevention of CRC

Prevention of CRC starts with the education of people regarding the importance of good diet and healthy lifestyles. The recommended good diet is to include more fibres, vegetables, fruits, fish, and low-calorie milk with sufficient daily supplements of calcium, iron, and folic acid. A healthy life style will include doing regular exercise, abstaining from smoking, reducing alcohol consumption, preventing obesity, and changing the pattern of cooking meat and fish by minimizing cooking with high temperature or by roasting with charcoal (Rozen, 2006).

A healthy man with genetic hereditary conditions such as Familial Adenomatous Polyposis (FAP) and Hereditary non-Polyposis Colorectal Cancer (HNPCC) or Lynch syndrome should undergo screening regularly from an early age.

For people with FAP, they need to have an annual sigmoidoscopy programme, and it should be started from the age of 10 to 12 years old. For people with HNPCC, colonoscopy examination has to be initiated 10 years earlier than the age of the youngest family member that had CRC (Winawer, 2007).

In Malaysia, some programmes have been implemented for cancer prevention, such as breast self-examination and mammography to detect breast cancer in early stage, hepatitis B immunization for babies, papanicolaou's smear and human papilloma virus (HPV) immunization for Malaysian girls aged 13 years old and above against cervical cancer, and anti-smoking campaign (Lim, 2002; Ministry of Health, 2009; Norbaya, 2010).

Ministry of Health Malaysia has launched The Non-Communicable Diseases Prevention 1Malaysia (NCDP-1M) programme in 2010 to detect individuals with non-communicable disease risk factors at an early stage (Omar, 2012). A National Cancer Registry (NCR) has been established in 2006 to collect data about cancers in Malaysia. The NCR facilitates in providing information regarding overall cancer incidence in Malaysia, which is useful for planning and evaluation for cancer prevention and control (Omar, 2012). A number of healthy lifestyles campaigns have been launched such as 'walking a 10,000 steps' and 'senam tari' activities (Omar, 2012). Collaboration between public, private sectors and non-governmental organizations in cancer prevention has been established (Lim, 2002) and some non-governmental organizations in Malaysia, such as National Cancer Society of Malaysia (NCSM), National Cancer Council (NCC) have been giving public education on CRC such as health talks and seminar, counseling for the patients and

their families. These programmes are implemented to reduce the burden of cancer in Malaysia in the future (Lim, 2012).

2.6 Screening of CRC

Screening is a process to detect a certain disease among healthy or asymptomatic people in the community (Rozen, 2006). CRC screening is very important, as CRC is known to be a curable cancer if it is found at an early stage. Furthermore, if polyps are detected and removed, it can reduce the incidence of having cancer in future. Therefore, screening is very useful to reduce the mortality and morbidity of CRC.

In some countries, CRC screening has been carried out routinely, but each country has a different method of screening. The choice of screening method depends on the resources, such as the financial support, the availability of health care services, and the number of trained professional health workers.

The success of any screening programme depends on several factors. These factors include awareness of the patient, approval from primary care clinic doctors, acceptance of participants, adequate funds, accurate risk group classification, sensitivity and specificity of the screening test, diagnosis and treatment in appropriate time, and appropriate follow-up (Winawer, 2007).

The Asia Pacific Working Group for CRC had formulated consensus regarding CRC screening for Asian countries in 2008. They stated that CRC sceening should be a national health priority due to the rapid increase of CRC cases in Asian countries, such as China, Japan, Korea, Hong Kong, Singapore and Malaysia (Sung, 2008).

In resource-limited countries, FOBT is recommended to be the first choice for CRC screening. A study by Lee et al. in Japan showed using immunochemical FOBT (IFOBT) decreased CRC mortality by 70% (Lee, 2007).

In 2008, Singapore conducted a CRC screening programme using IFOBT with a good response (Singapore Cancer Society, 2009). The Singapore Cancer Society carried out the programme and distributed 22,510 FOBT kits to the community. Free FOBT kits were distributed with each participant receiving 2 kits. The result would be considered a positive FOBT if either one of the sample was positive for occult blood. Participants with FOBT positive would undergo colonoscopy examination. Participants with FOBT negative were advised to repeat the FOBT examination annually. The FOBT kit used was the OC-Light Immunochemical FOBT, which was the same kit used in this study.

The screening programme in Singapore detected 32 cases of CRC and removed polyps from 128 patients, of which 91 were precancerous polyps. Singapore Cancer Society declared that the CRC screening programme in 2008 was successful and effective, and has saved the lives of 123 people (Lau, 2009).

2.6.1 CRC Screening in Malaysia

The Ministry of Health Malaysia has reported an increase in CRC incidence in Malaysia. The ASR was 8.1 per 100,000 population in 1987; 11.9 in 1998; 13.9 in 2002; and 18.4 in 2006 in Peninsular Malaysia (Azlie, 2011), but there has been no CRC screening implemented in Malaysia at national level. In August 2010, the Ministry of Health Malaysia conducted a CRC screening project in Negeri Sembilan, Malaysia and screened 310 people using IFOBT (Omar, 2012). In 2013, another

CRC screening project was carried out in Kedah state, Malaysia which targeted asymptomatic male and female populations, aged 50 years old and above (Radzi, 2013). According to the Clincal Practice Guidelines (CPG) for CRC screening in Malaysia 2001, the type of FOBT recommended for screening is Hemoccult II (SmithKline Diagnostic Inc., San Jose, CA) and colonoscopy is to be used for high risk individual (Qureshi, 2001). However, the Malaysian Health Technology Assessment Section (MAHTAS), under Medical Development Division Ministry of Health Malaysia has recommended the use of immunochemical FOBT (IFOBT) for CRC screening for general population in Malaysia (Azlie, 2011). As this study was carried out in 2009, one could consider this study as initiating the use of IFOBT in Malaysia.

2.7 Awareness of Stool Examination and Knowledge of CRC

Not many studies report on the awareness of stool examination and knowledge of CRC, especially in Malaysia. The majority of researchers did not report on the awareness of stool examination, knowledge of CRC or feedback regarding the use of FOBT. A study conducted by Harmy et al. among moderate risk patients in West Malaysia showed that the majority of patients had low knowledge and attitude towards CRC screening (Harmy, 2011). A study carried out by Bobryshev et al. among 300 university students in Malaysia showed the majority of the participants had no knowledge about faecal occult blood screening and colonoscopy (Bobryshev, 2013). Another study by Nahas et al. among university students in Penang reported that the majority of students had a lack of knowledge of CRC and dietary habits related to CRC (Nahas, 2013). A CRC screening project carried out by Chong et al. among 153 participants in Kuala Lumpur did not carry

out an assessment on the awareness of stool examination or knowledge of CRC (Chong, 2013).

Some studies from other countries had done assessment regarding knowledge of CRC. One example is a study by Wong, et al. in China which stated that high risk participants (male and smokers) had poor knowledge of CRC (Wong, 2013). Another study in Turkey carried out by Kaya et al. among 100 auxiliary healthcare personnel found some knowledge deficiency regarding early diagnosis, screening of CRC and potential causes of CRC among their participants (Kaya, 2013). This study would assess a CRC screening programme as well as the knowledge of CRC and awareness of stool examination in Malaysia for the first time.

2.8 FOBT Kit

FOBT kit is a kit to detect occult blood in human stool. Under normal conditions there should be no blood in the stool. Blood in stool can be caused by several conditions such as inflammatory bowel diseases, haemorrhoids, polyps, as well as cancer in the gastrointestinal tract. Further examinations such as colonoscopy, sigmoidoscopy, and barium enema are needed to confirm the diagnosis of those diseases and rule out cancer.

Two types of FOBT kits are available, a chemical FOBT (CFOBT) and an immunochemical FOBT (IFOBT) or FIT.

2.8.1 Chemical FOBT

The chemical FOBT is also called the Guaiac Test, as it uses guaiac acid. In principle, the examination detects the activity of peroxidase in haeme and guaiac will be oxidized and become blue. If a colour change occurs, then the result is positive, and this is an indication that bleeding has occured in the colon or rectum (Allison , 2007).

Some examples of guaiac kit test are Hemoccult II (Beckam Coulter Inc., Primary Care Diagnostic, LA, CA, USA); Hemoccult Sensa, Hema-screen (Immunostics, Ocean, NJ). However, Hemoccult II and Hemoccult Sensa have some disadvantages. Hemoccult II has low sensitivity and Hemoccult Sensa has low specificity in detecting cancer and significant polyps (>1cm). The low sensitivity will limit the effectiveness in reducing the mortality rate of CRC, and low specificity will increase the cost of screening by colonoscopy and the inconvenience for the patients who have to undergo the procedures (Allison, 2007).

False positive results can occur because haem is also found in red meat, peroxidase activity can also be found in fresh fruits and vegetables, such as broccoli and white radish. Vitamin C can also affect the result, because it can inhibit the reaction of guaiac. Therefore a test using guaiac needs restriction of certain foods prior to conducting the examination (Allison, 2007). This can lead to a low participation in screening programme and this has been shown in a study conducted in Australia on motivated volunteers who were asked to restrict certain foods before the test. Because of this restriction the number participation dropped by 13%, because in Autralia, red meat is a large part of the people's normal diet (Allison, 2007).

Moreover, stool samples for the guaiac test have to be in a dry state and must be smeared onto the kit impregnated paper with the wooden stick. This could also reduce the acceptance of the participants to do the test (Allison, 2007), hence these are the reasons why chemical FOBT was not used in this study, because it has many limitations, and currently chemical FOBT has been replaced in some countries by immunochemical FOBT because it has more advantages (Winawer, 2007).

2.8.2 Immunochemical FOBT

Immunochemical FOBT (IFOBT) or FIT is a new type of FOBT kit. Some examples of IFOBT that have been used for large number of people in the average risk group are FlexSure OBT, HemeSelect, Insure, MagStream 1000/Hem SP (Fuji Rebio Inc, Tokyo, Japan). Other examples are Hemoccult-ICT, Instant View, ImmoCare, MonoHaem, Clearview Ultra-FOB, OC Auto Micro 80, and Magstream Hem Sp (Allison, 2007).

The most commonly used IFOBT in the USA is Insure (Enterix Corporation, Falmouth, Maine). It has been approved by U.S. Food and Drug Administration (FDA) because it has higher sensitivity and specificity compared with guaiac FOBT or other immunochemical FOBT kits (Allison, 2003). IFOBT used in Japan is ImmudiaHem Sp (Fujirebio Inc, Tokyo). In the UK, IFOBT used is HemeSelect and FlexSure OBT from Smith Kline Diagnostic, San Jose, California (Allison, 2003).

In Malaysia, OC-Light IFOBT is available and distributed by Nagase Shd Bhd in Kuala-Lumpur. It is imported from Eiken company, Japan (Nagase, 2009a). This IFOBT had been used for this study, because of its benefits compared to guaiac test. Other IFOBTs available in Malaysia are VEDA LAB Hem Check-1 (France),

Chemtrue One-Step FOBT Test (China), and ACON FOB One Step Faecal Occult Blood (USA) (Azlie, 2011).

IFOBT was used in this study, because IFOBT are superior compared to guaiac FOBT. IFOBT uses specific monoclonal and polyclonal antibodies to detect human haemoglobin in the stool. These antibodies are labelled and these antibodies react with antigens of globin in the stool, a positive result will be produced (Allison, 2007).

IFOBT is more specific for detecting globin originating from the large bowel, because globin cannot survive the passage through the upper gastrointestinal tract (Allison, 2007).

Furthermore, IFOBT does not react with globin that is not of human origin, for example from meat, uncooked vegetables, or fruits that might contain peroxidase activity. Hence a restricted diet before the test is not needed (Allison, 2007).

IFOBT is not affected by drugs such as nonsteroid anti-inflammatory drugs (NSAID), and vitamin C. The procedure for sample collection is relatively simple compared with the guaiac test. IFOBT can be analysed by a machine provided by the manufacturer of the FOBT kit and the interpreter does not need special training to perform it. In 2004, USA Centre for Medicare and Medicaid Services (CMS) stated that IFOBT is a suitable and effective kit for CRC screening programmes. Its utilization to a huge population, can be adjusted according to the ability of the government or screening promoter to provide the budget and the human resources. In addition, it can achieve a good result (Allison, 2007).

The use of colonoscopy as a first line screening tool in the USA is inadequate, therefore, IFOBT has been recommended as the first line screening modality in the USA (Allison, 2007).

Malaysian Health Technology Assessment Section (MAHTAS), under Medical Development Section, Ministry of Health Malaysia has assessed accuracy, safety and efficacy of IFOBT and they have reported that IFOBT can be considered for CRC screening among general population in Malaysia (Azlie, 2011), hence IFOBT was chosen for this study.

2.9 National Cancer Society Malaysia, Penang Branch

National Cancer Society of Malaysia (NCSM) Penang Branch is a nonprofit, non-governmental organization. It is a branch of NCSM Kuala Lumpur, that was established in 1968 (National Cancer Society of Malaysia, 2010).

The organization has the following vision,

> ... to help reduce the cancer burden of the country through: dissemination of information on cancer, cancer prevention, early detection of cancer through screening, patient support, and supporting Penang based cancer register (National Cancer Society of Malaysia, 2010).

Since its inception in 1968, NCSM Penang branch has launched many activities related to combating cancer. The NCSM has organized activities such as screening of the cervical cancer, seminars, talks, courses, conferences about cancer, and so on. In 1989, the society launched a mammography centre and offered screening mammograms to the public for a small fee. In 1992, the society launched a "Hospice at Home Programme", and since 1995, the society has given cancer

education to the students in many schools in Penang. NCSM managed Rumah Hospice Penang from 2001 until 2009. In 2005, NCSM received the franchise of "Relay for Life" from American Cancer Society and has organized fund-raising events annually in Penang. The funds raised from the public have been used to finance the activities carried out by the society. In 2009, the society conducted CRC health talks in several senior citizen organizations in Penang state and assisted in the distribution and collection of the FOBT kits from the participant and sending the FOBT kits to the laboratory (National Cancer Society of Malaysia, 2010).

2.10 Conceptual framework

Screening for CRC was assessed in this study. The success of the screening would be influenced by the compliance of the participants to the FOBT testing. The higher the number of returned FOBT kits would imply good compliance to FOBT testing and a low number of returned FOBT kits showed low compliance to FOBT testing. Some factors that influence the compliance to FOBT testing will be explored. Participants with FOBT positive were encouraged to undergo colonoscopy examination and the compliance rate to colonoscopy as well as factors influencing it were identified.

The willingness to participate in screening could be affected by awareness of stool examination and knowledge of CRC among participants (Stokamer, 2005). Having good awareness and knowledge of CRC should increase the compliance to FOBT testing and colonoscopy. Some demographic factors were predicted to have significant associations with the participants' awareness of stool examination and knowledge of CRC. Identification of demographic factors that were predictors of good knowledge of CRC and awareness of stool examination could assist healthcare

planners in identifying priority areas to focus health education programme that in future would help ensure good compliance to screening activities.

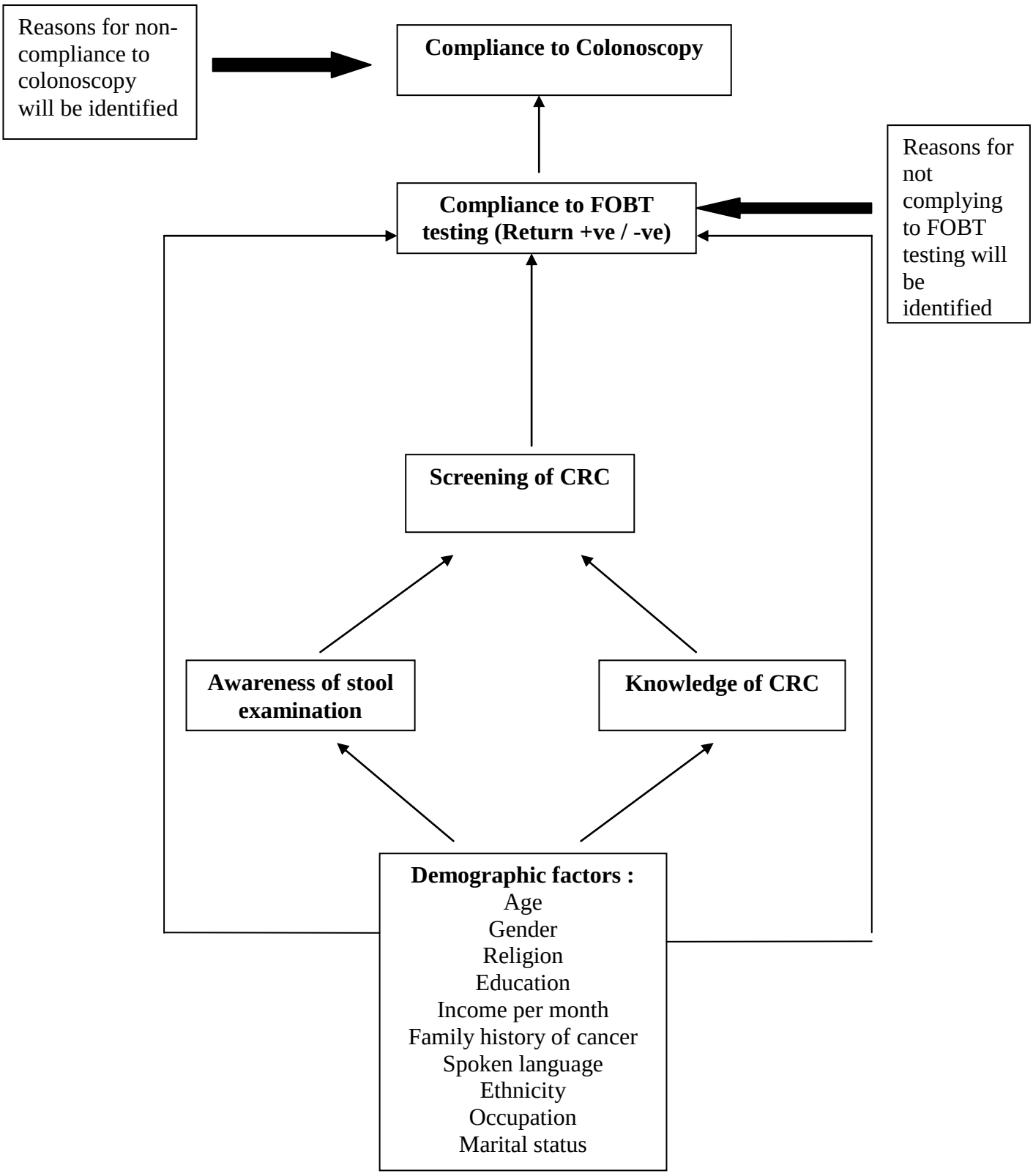

Fig. 2.1 Conceptual framework