A STUDY ON KNOWLEDGE, ATTITUDE AND PRACTICE ON COLORECTAL CANCER SCREENING AMONG AVERAGE RISK MALAY PATIENTS ATTENDING SELISING HEALTH CLINIC

By

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LIST OF ABBREVIATIONS

APC	Adenomatous poliposis coli
BMI	Body mass index
CRC	Colorectal cancer
DCBE	Double contrast barium enema
FAP	Familial adenomatous polyposis
FOBT	Fecal occult blood test
HINTS	Health Information National trends Survey
HNPCC	Hereditary non polyposis colorectal cancer
IBD	Inflammatory bowel disease
KKM	Kementerian Kesihatan Malaysia
NSAIDs	Nonsteroidal anti inflammatory drugs
RR	Relative risk
SD	Standard deviation

ABSTRAK

TAJUK: Kajian mengenai Pengatahuan, Sikap dan Amalan terhadap Saringan Kanser Kolorektal Dikalangan Pesakit Melayu berisiko sederhana di Klinik Kesihatan Selising.

PENGENALAN: Di Asia, kanser kolorektal sedang meningkat secara mendadak. Di sebalik peningkatan dari segi insiden dan mortaliti, kadar saringan kanser kolorektal masih rendah di kebanyakan negara-negara Asia. Penerimaan untuk melakukan saringan kanser kolorektal dipengaruhi oleh pengetahuan dan sikap manusia. Kajian ini adalah bertujuan untuk menilai tahap pengetahuan, sikap dan amalan dikalangan pesakit Melayu terhadap saringan kanser kolorektal.

OBJEKTIF: Objektif kajian ini adalah untuk mengenal pasti tahap pengetahuan, sikap dan amalan, serta faktor-faktor yang berkaitan dengannya, dikalangan pesakit Melayu berisiko sederhana terhadap ujian saringan kanser kolorektal. Selain itu, kajian ini juga bertujuan untuk mengenalpasti hubungan diantara pengetahuan dan sikap, serta pengetahuan dan amalan terhadap saringan kanser kolorektal.

METODOLOGI: Ianya adalah kajian keratan rentas yang dijalankan bermula Oktober 2009 sehingga Disember 2009 di Klinik Kesihatan Selising. Kajian ini menggunakan borang soal selidik yang memerlukan peserta menjawab sendiri soalan tersebut. Ianya

melibatkan 262 peserta Melayu berumur 50 tahun dan ke atas. Soalannya terdiri daripada tiga bahagian yang melibatkan pengetahuan, sikap dan amalan terhadap saringan kanser kolorektal.

KEPUTUSAN: Keputusan daripada kajian ini menunjukan hanya 6.1% daripada responden mempunyai pengetahuan yang baik dan 31.7% daripada responden mempunyai sikap yang baik terhadap saringan kanser kolorektal. Seterusnya, kadar saringan kanser kolorektal adalah teramat rendah dikalangan responden dimana hanya dua daripada 262 responden telah menjalani ujian saringan kanser kolorektal. Selain itu, keputusan kajian ini juga menunjukan terdapatnya hubungan(korelasi) diantara pengetahuan dan sikap terhadap saringan kanser kolorektal. Seterusnya, kajian ini juga menunjukkan bahawa lelaki, tahap pendidikan yang rendah dan jenis pekerjaan bukan profesional adalah faktor-faktor yang mempengaruhi tahap pengetahuan terhadap saringan kanser kolorektal.

KESIMPULAN: Keputusan dari kajian ini menunjukan responden Melayu yang berisiko sederhana mempunyai pengetahuan yang tidak mencukupi, sikap dan amalan yang kurang memuaskan terhadap saringan kanser kolorektal. Ianya juga menunjukan bahawa dengan peningkatan pengetahuan akan mengurangkan sikap yang negatif terhadap saringan kanser kolorektal. Selain itu, didapati tahap pendidikan yang rendah adalah faktor yang menentukan tahap pengetahuan dan sikap, manakala jenis pekerjaan pula mempengaruhi tahap pengetahuan dan amalan terhadap saringan kanser kolorektal.

ABSTRACT

TITLE: A STUDY ON KNOWLEDGE, ATTITUDE AND PRACTICE ON COLORECTAL CANCER SCREENING AMONG AVERAGE RISK MALAY PATIENTS ATTENDING SELISING HEALTH CLINIC

INTRODUCTION: Colorectal cancer is rapidly increasing in Asia. Despite the rising trend in incidence and mortality, colorectal cancer screening rates are still low in most Asian countries. The acceptability of CRC screening is influenced by people's knowledge and attitude. This study was conducted to evaluate the knowledge, attitude and practice of Malay people toward CRC screening.

OBJECTIVES: The objectives of the study are to determine the level of knowledge, attitude, practice and their associated factors on colorectal cancer screening among average risk Malay patients. It also to determine the relationship between knowledge and attitude score, and knowledge and practice score on colorectal cancer screening.

METHODOLOGY: It was a cross sectional study conducted from October 2009 to December 2009 at Selising Health Clinic. The study used a self administered questionnaire which involved 262 Malay participants aged 50 years and above. The questionnaire consisted of 3 parts, which dealt with knowledge, attitude and practice on colorectal cancer and screening.

RESULTS: There were only 6.1% respondents had good knowledge and 31.7% of the respondents had good attitudes on colorectal cancer screening. Consequently, colorectal cancer screening uptake was extremely poor with only two out of 262 of the respondents had CRC screening. There was moderate to good positive correlation between knowledge and attitude score. In addition, the results show male gender, low education level and non professional group are the associated factors for low level of knowledge on colorectal cancer screening.

CONCLUSION: These findings indicate that average risk Malay patients had inadequate knowledge, poor attitude on colorectal cancer screening together with extremely poor practice on colorectal cancer prevention. This study also concluded that increasing knowledge on colorectal cancer screening may encourage less negative attitudes about colorectal cancer screening. Other than that, educational level appears to be the major determinant on the level of knowledge and attitudes. While, type of occupation affects the level of knowledge and practice on colorectal cancer screening.

CHAPTER 1

INTRODUCTION

1.1 Epidemiology of colorectal cancer

Colorectal cancer (CRC) is a worldwide problem, with an annual incidence of approximately one million cases and an annual mortality of more than 500,000 worldwide(WHO, 2003). In the United States and other Western countries, colorectal cancer ranks the fourth most common malignant neoplasm and the second leading cause of death(Ahmedin *et al.*, 2008). During the last decades, there was a dramatic increase in the incidence of colorectal cancer in Asia. Moreover, data from this region indicates that this incidence had already approximates those reported from the West, especially among the more affluent populations(Sung *et al.*, 2008).

In Peninsular Malaysia, colorectal cancer is the first among male and the second most common among female after breast cancer. In 2006, there were 2866 cases of colorectal cancer which represented 13.2 % of all cases registered with National Cancer Registry. The incidence was highest among Chinese with age-standardized rates was 21.4/100 000 population and were lower in Indian and Malay where the age-standardized rates were 11.3/100 000 and 9.5/100 000 respectively(MOH, 2006).

1.2 Risk factors

At present, the cause of colorectal cancer is not completely understood. However, it is thought to involve many factors developing over a long period of time. The risks for colorectal cancer vary from country to country and even within countries and also among individual based on diet, lifestyle and hereditary factors.

Migrant studies which was among one or two generations of immigrants moving from low-incidence of colorectal cancer countries to host countries of high incidence showed they have a higher burden from colorectal cancer(Melissa *et al.*, 2007). It was concluded that acquired environmental and lifestyle factors including a diet low in fiber and vegetables but high in fat, red meat and alcohol, sedentary occupation and cigarette smoking could be the major modifiable etiologic causes.

Among non modifiable risk factors for colorectal cancer include age more than 50 years old, a family history of colorectal cancer, a personal history of colorectal cancer and adenoma, a hereditary history non polyposis colorectal cancer syndrome, Turcot's syndrome, Gardner's syndrome or inflammatory bowel disease of the colon such as ulcerative colitis and Crohn's disease.

The population age of more than 50 years is the only risk factor considered to be of "average risk," whereas those with other risk factors such as personal or family history of colorectal cancer, adenomas or inflammatory bowel disease are considered to be at "high risk". Approximately 70 to 80 % of CRC's arises among population at the average risk(U.S.Preventive Services Task Force, 2008).

1.3 Pathogenesis of colorectal cancer

Colorectal cancer is a genetic disorder which can be acquired or inherited. The inherited syndromes only accounts for less than 5% of all colorectal cancer cases. Therefore, majority of the cases (95%) are often considered sporadic(Burt *et al.*, 1995).

According to genetic model, colorectal cancer develops through a process termed multistep carcinogenesis in which progressive genomic instability affects the function of genes that are important in oncogenesis which includes oncogenes (K-ras), tumor suppressor genes (APC, DCC/DPC4, P53), DNA mismatch repair genes (hMLH1 and hMLH2), cell adhesion molecules (epCam), angiogenic factors (VEGF), as well as epigenetic changes (DNA menthylation) and microsatellite instability(Burt *et al.*, 1995).

The development of colorectal cancer occurring in stages result in transformation of a normal epithelial cell into adenocarcinoma. The abnormal colonocytes with certain genetic alterations was able to proliferate excessively. As this process continues, the

cells assume malignant characteristics of invasiveness and metastatic potential. In addition to genetic predisposition, environmental factors are believed to be associated with an increased colorectal cancer risk(Pignatelli *et al.*, 2008).

Colorectal cancer is a slow growing disease that may present without symptoms for several years. In most of the cases, cancer of the colon and rectum arise from the formation of a small, non cancerous growth called polyps. These polyps, or precancerous lesions, are an early warning sign that colorectal cancer may develops. The average time from onset of a polyp to onset of carcinoma, termed the "dwell time," is about ten to fifteen years. However, dwell time appears to vary with the location of the cancer. It is longer in the distal colon than in the proximal colon, and it is shortest in the recto sigmoid segment(Launoy *et al.*, 1997).

1.4 Clinical Manifestation

The key clinical features of large bowel cancers are alteration in bowel habit and per rectal bleeding. The presenting signs and symptoms are also influenced by the location of the tumor. If it occurs at the caecum and ascending colon, usually it presented late with palpable mass, right iliac fossa discomfort or hypochromic microcytic anemia due to chronic occult blood loss. Since the left colon is narrower and holds more solid content compared to right colon, the obstruction, alteration of bowel habit and perectal bleeding are common presentation. While if the tumor is in the rectum, bleeding is often the main symptom and the patient may believe that he has piles. A feeling of incomplete evacuation of the rectum is common after defecation and the patient may

experience urgency and the frequent passage of slime and blood. As the rectum is capacious, obstruction is unusual(Forrest *et al.*, 1995).

1.5 Prognosis

The outcome of colorectal cancer depends on how advanced the disease when it was first diagnosed. Therefore, the diagnosis of early stage cancer results in better survival. Curtbert Dukes described a pathological staging system for colorectal cancer based on invasion through the bowel wall and lymph nodes involvement. It has major prognostic implications. In early stages (Dukes A-invasion of muscularis propia), survival is excellent through surgical intervention with 62% to 98% of 5 years survival. While in those presenting late (Dukes C- Lymph nodes involvement) the chances of cure is less than 30%(David *et al.*, 2008).

Apart from that, the TNM classification according to the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC) which depends on the depth of cancer invasion into the bowel wall, lymph nodes involvement and distant metastasis showed a correlation between stage at diagnosis and survival. For stage 0 and 1, the survival rate was up to 100% while in stage 4, it was only 3%(Paul *et al.*, 2006).

However, earlier symptomatic diagnosis was difficult to achieve since majority of them were asymptomatic at early stage, even if this could be achieved, the overall improvement in survival was likely to be small. Therefore, screening is the option to detect CRC during its pre symptomatic phase which results in improvement of the survival rate.

1.6 Treatment

The treatment for colorectal cancer depends on the stage of the cancer. At early stage, it was almost curable. However, when it was detected at a late stage with distant metastases, it was less likely to be curable.

Surgery is the mainstay of treatment for colorectal cancer as it offers a higher chance of cure. Surgical resection with anastomosis is the treatment of choice in more than 85% of patients with colon cancer while locoregional resection is for rectal cancer. The majority of resections done with curative intent where the affected segment bearing tumor is first resected with adequate margins of normal appearing tissue together with its vascular pedicle and lymphatic drainage, then an anastomosis or colostomy is performed. In case of multiple metastases, palliative (noncurative) resection of the primary tumor is still offered to reduce further morbidity caused by tumor bleeding, invasion or obstruction(Paul *et al.*, 2006).

Chemotherapy is used to reduce the likelihood of metastasis developing, shrinking tumor size or slowing tumor growth. Chemotherapy is often applied after surgery (adjuvant), before surgery (neoadjuvant), or as the primary therapy (palliative). In colon cancer, usually chemotherapy after surgery is given only if the cancer has spread to the lymph nodes (Stage III)(Paul *et al.*, 2006).

Radiotherapy is not used routinely in colon cancer, as it could lead to radiation enteritis and it is difficult to target specific portions of the colon. It is more common to be used in rectal cancer, since the rectum does not move as much as the colon and is thus easier to target(Paul *et al.*, 2006).

1.7 Colorectal cancer screening

The American Cancer Society has recommended people aged more than 50 years to undergo CRC screening as most of sporadic CRCs in developed countries occur in patients above 50 years old. CRC screening test enables early detection and cure of early-stage disease cost effectively. Individuals who undergo regular FOBT are shown to have significant reduction in CRC mortality(Kronborg *et al.*, 1996; Mandel *et al.*, 2000). Further reduction can be achieved by performing sigmoidoscopy and colonoscopy followed by colonoscopic polypectomy. However many studies showed the obstacle for implementing CRC screening program were limited by knowledge on CRC, inconvenient and embarrassing nature of the test and lack of physician recommendation.

CHAPTER 2

LITERATURE REVIEW

2.1. Risks factors

Notwithstanding, the important of age and genetic influences which are non modifiable risk factors, several lines of evidence support the substantial role of lifestyle or environmental factors in the etiology of colorectal cancer. By knowing the risk factors for colorectal cancer, it may motivate and remove barriers for colorectal screening.

2.1.1 Non modifiable risk factors

2.1.1.1 Age

The single greatest risk factor for development of CRC is advancing age. The incidence of the colorectal cancer increases exponentially with age and become plateaus in the sixth decade. Thus, ninety percent of colorectal cancer occurs at the age of above 50 years old and peak at the age of 60 years(Jaffer *et al.*, 2005). However, only 5% of cases reported in those under the age of 40 years old. Colorectal cancer is also common in men and this is true of all countries and races(Reis *et al.*, 2007). Recent data from National Cancer Registry showed similar finding among Malaysian population where more than half of the total cases reported at the aged 60 years and above(Radzi *et al.*, 2009). More males were recorded compared to females. Due to the estimated 10 year timescale for the adenoma-carcinoma sequence, most experts agree that screening should target those over 50 years(Radzi *et al.*, 2009).

2.1.1.2 Familial risk factors

Colorectal cancer is the most familial of all human cancers. Between 10% to 30% of colorectal cancer patients have a family history of colorectal cancer but do not belong to a known inherited syndrome(Burt, 1996). First-degree relatives of persons with colorectal cancer have a twofold to threefold increase in the risk of colorectal cancer in comparison with control or population incidence(Johns and Houlstan, 2001). Moreover, the risk increases with the number of relatives with colorectal cancer, the closer the relatives are to the patient, and with the age of colorectal cancer in family members(Burt, 1996).

There are several conditions which have a significant predisposition for colorectal cancer. The first is Familial Adenomatous Polyposis (FAP) responsible for 0.5% to 1% of all colorectal cancer(Rustgi, 1994). Genetically, FAP is an autosomal dominant condition caused by APC (adenomatous polyposis coli) gene mutations of tumor suppressor gene on chromosome 5q21(Kinzler *et al.*, 1991). Spontaneous mutations account for approximately 20% of cases in which no prior family history is present(Hamilton, 1993). Persons with FAP develop hundreds to thousands of colon polyps in adolescence, and nearly in all patients with untreated FAP there is malignant transformation in at least one of these polyps by the fifth decade. The incidence of malignancy in these cases approaches 100%(Strate and Syngal, 2005). Gardner's syndrome is a phenotypic variant of FAP. In addition to colonic polyposis, other manifestations may be seen, such as benign soft tissue tumors, osteomas, duodenal

adenomas, periampullary tumors, desmoids tumors and congenital hypertrophy of the retinal pigment epithelium.

The other condition is hereditary non polyposis colorectal cancer (HNPCC) or Lynch syndrome. HNPCC is the most common inherited disorder accounting for 2% to10% of colon cancer cases and lifetime risk of 80%. It is characterized by the development of colorectal cancer and an increased susceptibility to numerous other cancers. HNPCC is also an autosomal dominant inherited disorder and is caused by a mutation in one of the mismatch repair genes (MLH1, MSH2, MSH6 or PMS2)(Haq *et al.*, 2008). Persons with Lynch I syndrome develop a small number of proximal polyps at the young age, which often progressed rapidly to the development of colon cancers. Persons with Lynch II syndrome develop the characteristics of Lynch I syndrome together with extra colonic cancers such as endometrial, ovarian, small bowel, transitional cell of the ureter or bladder, and gastric cancer.

In Malaysia, there was no accurate data available on prevalence of hereditary colon cancer, since there was no customized registry exists to collect such information. Thus, the burden of the disease could not be estimated in our community. But, making the diagnosis of hereditary form of colon cancer is important not just for the individual but also for the sake of other family members who may be affected. In these conditions, screening plays an important role to detect the lesion earlier before cancer develops.

Another endogenous factor associated with an increased risk of colorectal cancer is inflammatory bowel disease. Early studies of patients with Crohn's disease and ulcerative colitis demonstrated a risk of 20 to 30 times the average population risk(Jaffer *et al.*, 2005). Chronic and extensive inflammatory bowel disease (IBD), which therefore leads to an increased turnover of epithelial cells, is associated with an increased risk for bowel cancer. The risk is greater for ulcerative colitis than for Crohn's colitis. Moreover, it become more great with the longer the duration of the disease, which is more than eight years and more extensive the area of inflammation, which is more than rectosigmoid. However, with intensive and systematic medical therapy and earlier surgery, the cancer risk and mortality from colorectal cancer have decreased(Paul *et al.*, 2006).

2.1.2 Modifiable risk factors

2.1.2.1 Diet

International variations in diet and colorectal cancer rates from one country to another suggest that diet is an important preventable risk factor for colorectal cancer. The dietary recommendations to reduce gastrointestinal cancer risk include lowering fat intake, avoidance of grilled and smoked foods and increasing fruits, vegetables and fiber(Thomson *et al.*, 2003).

Both polyps and colon cancer occur more frequently due in part to diets of low in fruits, vegetables, vegetable protein and fiber. An extensive meta-analysis has confirmed the significant reduced risk for colorectal cancer with high consumption of fruits and

vegetables(Riboli and Norat, 2003). In 1993, Burkitt proposed that high fiber intake could be protective for colon cancer, based on the very low rate of this malignancy observed in Africa, where high quantities of fiber were consumed in their population(Burkitt, 1993). The strongest evidence was from a multinational European Study among 500 000 persons, which demonstrated a significant reduced risk for cancer in those having the highest fiber intake(Bingham *et al.*, 2003). Similarly, in large United State screening study showed dietary fiber, independently of source was significantly associated with a reduced risk for colonic adenoma(Peter *et al.*, 2003).

Increased intake of fiber, on the other hand, shortens the intestinal transit time, which in turn reduces the exposure of the colon and rectum epithelium to mutagens present in the stool. However, fiber supplementation in form of vitamins was not recommended as a chemopreventive to decrease the risk of colorectal cancer. There is no evidence of benefit(Wilkins and Reynolds, 2008).

Epidemiologic data from 27 countries showed a strong correlation between colorectal cancer incidence and average per capita meat consumption(Ognjanovic *et al.*, 2006). This is supported by the consensus of the World Health Organization which concluded that the high consumption of red meat increases the colorectal cancer risk(Scheppach *et al.*, 1999). This finding is consistent with a systematic review that reports an increased risk of colorectal cancer in those in the highest red and processed meat consumption categories compared with the lowest(Norat *et al.*, 2002). High red meat intake is also associated with colonic adenomatous polyps(Yoon *et al.*, 2000).

There have been several biologic explanations for this apparent association. Meat contains a substance called creatine and heme iron. High amount of heme iron can be cytotoxic and cause hyperproliferative of colonic mucosa(Cross *et al.*, 2003). High temperature cooking methods used by grilling, frying and charring of high protein foods have been associated with increased colon cancer risk. At high temperatures, creatine reacts with amino acids to form heterocyclic aromatic amines which are potent mutagens, formed on the surface of beef, chicken and fish when these foods are exposed to high temperatures(Nowell *et al.*, 2002).

In addition to that, consistent intake of processing meat has also been associated with an increased risk for large bowel cancer. These contain nitrites, which reacts with amino acids to form nitrosamines, another class of cancer-causing chemical(Franceschi *et al.*, 1998).

A diet high in saturated animal fat, particularly dairy products and red meat increases colorectal cancer risk. The digestion of fats requires the activity of normal bile acids that irritate and damage cells lining of the colon. Consequently, bile acids activate factors associated with abnormal growth of these cells, resulting in an increased risk of colorectal cancer(Glinghammar *et al.*, 1999).

For micronutrients such as folate, calcium and vitamin A, C, D, and E, there are still limited evidence to support the protective action against colorectal cancer(World Cancer Research Fund international, 2011). Their anticarcinogenic roles seem to be minor, acting on the intraluminal contest and by strengthening the resistance of the large bowel epithelium to carcinogens and by correcting genetic damage(Thomson *et al.*, 2003). Furthermore, it was not recommended for the use of vitamin and mineral supplements as a prevention to colorectal cancer. Those supplements did not replace or add to the benefit of eating fruits and vegetables. Although, we could not rule out the benefits of supplements such as improved quality of life but the concern on their long term safety still in doubt(Emma, 2011).

2.1.2.2 Obesity

There is a consistent association between Body Mass Index (BMI) and risk of colorectal cancer. A systematic review(Bergstrom *et al.*, 2001) identified 19 papers which consist twelfth cohort and seven case-control studies that evaluated the association between BMI and risk of colorectal cancer with fifteen reporting a statistically significant positive relationship. Overall there was a 1.03 relative risk (RR) of colorectal cancer for every unit increase in BMI. A similar association exists between waist to hip ratio and colorectal cancer risk. In a Framingham study, a large waist circumference was associated with RR for colon cancer of 4.4 for middle age adult and 3.0 for older sedentary adults(Moore *et al.*, 2004). Another recent study also had a similar finding. Indeed, this finding suggests measures of central adiposity was more informative for risk of colon cancer than BMI alone(Pischon *et al.*, 2006).

2.1.2.3 Smoking

Cigarette smoking has been shown to be a significant risk factor for colorectal Cancer particularly long term smoking(Tsong *et al.*, 2007). It has been estimated that 20% of colorectal cancer in men and 15% in women may be associated with smoking(Heineman *et al.*, 1994). Thus, the results of a recent study suggest that smokers presented with colorectal cancer at a younger age than nonsmokers(Zisman *et al.*, 2006). There were multiple studies estimated the number of years of tobacco use required to increase the risk for large and advanced adenomas. Therefore, a study suggests that it may take 25 years for the risk of advanced adenomas to be increase(Giovannucci, 2004). A recent study showed patients who have smoked more than 30 pack-years had a more than two fold increase for significant colorectal neoplasia as compared with nonsmokers(Anderson *et al.*, 2009).

2.2 Colorectal cancer symptoms

Actually, once the symptoms develop it seems that survival is determined by the invasive nature of each tumor and cannot be related to the duration of symptoms(Terhaar Sim Dreste *et al.*, 2010). However, the delay in diagnosis and treatment may be a particular disadvantage to those patients in whom emergency surgery becomes necessary. Emergency surgery is associated with hospital mortality of 10% whilst elective surgery carries a mortality of only 3.5%(Sio *et al.*, 2009). Therefore early recognition of symptoms has a role in improving colorectal cancer mortality.

A study showed early education of patients about breast cancer has lead to early consultation. However, this would be difficult to achieve for colorectal cancer, since most people experience minor variations in bowel habit. According to a study among 200 colorectal cancer patients, ninety nine patients were ignorant of the implications of their symptoms and sixty six patients did not regard them as being serious. About 30% of patients thought they had piles(Holiday and Hardcastle, 1979). Furthermore, though rectal bleeding and alteration in bowel habit carry an increased risk of distal neoplastic lesions, most lesions are detected among asymptomatic subjects. This finding suggests that screening represents the optimal strategy to detect CRC or large adenomas in the distal colon in the targeted age range.

2.3 Population screening

Screening is a process of identifying a disease or pre disease condition in a person without signs or symptoms, considered as healthy individuals. A Screening test did not provide a definitive diagnosis. Instead, they help stratify screened subjects into those who are likely to have disease and those at higher risk are then candidates for further diagnostic testing. Ideally, a screening test should be cheap, safe, quick, well accepted and well tolerated.

Average risk group is defined as asymptomatic persons who are 50 years of age without family history or other diseases known to increased risk of colorectal cancer(Paul *et al.*, 2006). In this population, the only factor indicating risk is age.

Colorectal cancer is in increasing trend and is expected to become the first cause of death in Asia. There is strong evidence that population screening and early treatment reduces colorectal cancer mortality(Pignone *et al.*, 2002). Reports from the American Cancer Society, where colorectal cancer screening program have been implemented, showed that the incidence has decreased in two straight years and this has been largely attributed to the remarkable success of screening programs for colonic polyps and colorectal cancer in the United State.

The screening was increased from 38% in year 2000 to 53% in year 2008(Ahmedin *et al.*, 2008). A recent meta-analysis of studies evaluating screening using fecal occult blood tests estimated the mortality reduction to be 15% to 33%(Hewitson *et al.*, 2007). The UK Flexible Sigmoidoscopy Trial is examining the efficacy of a single Flexible Sigmoidoscopy screen offered to asymptomatic individuals aged 55 to 64 years, and data on the effect on mortality showed 43% reduction and confers a substantial and long lasting benefit(Atkin *et al.*, 2010).

Subsequently, as the biology of colorectal cancer has a latern phase, where most of it develops from benign polyps over a period of several years, it provides a window of opportunity to intervene(Paul *et al.*, 2006). Furthermore, the cancer development process consists of multiple step, from polypoid adenomas to shedding of cell component and occult bleeding which is presymptomatic or preclinical phase that are potentially detectable by appropriate screening techniques(Paul *et al.*, 2006). Therefore, screening is an ideal strategy, as the detection and removal of premalignant lesions can

prevent the subsequent development of colorectal cancer. Thus, surgical resections of pre cancerous stage or early stage of colorectal cancer offer a chance of cure(Jaffer *et al.*, 2005).

In fact, all standard options for colorectal cancer screening in average-risk individuals are cost effective compared to cost of treating the colorectal cancer(U.S.Preventive Services Task Force, 2008). They are as cost-effective as mammography(Frazier *et al.*, 2000). The cost of treating colorectal cancer is significantly high. According to National Cancer Institute in United State, it is estimated that the direct medical expenditure annually approached $ 6.5 billion. This was second in cancer treatment costs only to breast cancer, at $6.6 billion per year(National Cancer Institute, 2010).

2.3.1 Screening tools

The recognized standard examinations for colorectal cancer screening have included digital rectal examination, fecal occult blood test (FOBT), sigmoidoscopy, double contrast barium enema and colonoscopy.

Digital rectal examination is generally no longer recommended as a colorectal cancer screening because alone it has not proven effective. The seven to eight centimeter reach of the examining finger could detect at best only 10% of colorectal cancers. Nonetheless, digital rectal examination remains a part of sigmoidoscopy, colonoscopy and barium enema examination(Paul *et al.*, 2006).

Fecal Occult Blood Test checks for occult or hidden blood in the stool. The effectiveness of fecal occult blood test has been established. Evidence from several randomized controlled trials suggests that annual or biennial fecal occult blood test (FOBT) screening reduces mortality by 16 percent to 33 percent (Kronborg *et al.*, 1996; Mandel *et al.*, 2000).

Although the use of annual fecal occult blood test with a lower sensitivity has been demonstrated to reduce both colorectal cancer cases and colorectal cancer mortality, the number of life years gained will be greater using higher sensitivity test(U.S.Preventive Services Task Force, 2008).

High sensitivity fecal occult blood test means the test with sensitivity more than 70% and its specificity more than 90%. Currently the available tests that meet both specifications include SENSA guaiac testing and fecal immunochemical tests(U.S.Preventive Services Task Force, 2008).

FOBTs are based on two principal techniques, Guaiac tests and immunochemical test. The Guaiac test is a conventional stool test for stool occult blood. For accurate test results, it required 3 different days sample from bowel movement with a strict diet. For three days before stool collection period, they have to avoid red meat, vitamin C, citrus fruits and juices.

The Guaiac test used a chemical method that was designed to detect fecal hemoglobin via the oxidize chromogenic material in the presence of hydrogen peroxide. The chemical test may give rise to a false positive when reacts with dietary fresh vegetable components which posses peroxidase-like activity, as well as with hemoglobin contained in meat, myoglobin or bleeding from benign lesions (David *et al.*, 2008). Hence, high false positive rate leads to unnecessary anxiety and unnecessary performance of invasive tests.

Despite that, FOBT can also lead to false negative result. Diet contains vitamin C will inhibit the peroxidase reaction caused false positive result. (David *et al.*, 2008). In case of a negative FOBT, it could falsely reassure patients and lead to delay response to the development of colorectal symptoms. Therefore, dietary restrictions are mandatory to ensure accurate tests for fecal occult blood.

To overcome this problem, fecal immunochemical test has been introduced. Recently, fecal immunochemical tests for hemoglobin have been shown to be more sensitive than the guaiac test for cancer and adenomas(Hoepffner *et al.*, 2006). Immunological fecal occult blood test uses immunochromatography technique to detect human hemoglobin. The sensitivity was around 69% to 88% and the specificity was 99%(Lohsiriwat *et al.*, 2007). The test was not interfering with the dietary intake. Immunochemical stool tests are more expensive than guaiac-based tests, but it has the potential to be more cost effective if fewer colonoscopies are needed for post screening follow-up. Fecal occult blood test is more practical as primary screening tool since the test is non invasive,

inexpensive and can been rolled out in the community without much involvement from the hospital setting.

For double-contrast barium enema (DBCE), a series of X-rays of the entire colon and rectum are taken after the patient is given an enema with barium solution and air is introduced into the colon. The barium and air help to outline the colon and rectum on the X-rays. The use of barium enema as a screening tool has been considered to be cost effective(Winawer S *et al.*, 2003). Furthermore, the procedure rarely cause complication and it does not require any sedation. However, the consequences of repeated radiation dose are unclear, but are of concern(Sung *et al.*, 2008). In addition, it has lower sensitivity where the test may not detect some small lesions and does not permit removal of polyps or biopsy of the lesion. In the National Polyps Study, DCBE detected only 53% of adenomatous polyps six to ten mm in size and 48 percent of those more than ten mm in size compared with colonoscopy(Winawer *et al.*, 2000). Because of its lower sensitivity, the Asian Pacific Consensus Group does not recommend DCBE as a first-line option for colorectal screening in average risk group(Sung *et al.*, 2008).

As approximately three-quarters of all colorectal cancers are in the rectum or sigmoid colon, it seems reasonable to use flexible sigmoidoscopy with a 60 cm instrument as a screening tool, particularly as the finding of a significant distal adenoma may act as an index of proximal disease. Based on these premises it has been proposed flexible sigmoidoscopy as an effective modality for colorectal cancer screening(Atkin *et al.*, 2001). Sensitivity of this test varies from 73.3% for small polyps to 96.7% for cancer

and large polyps and the specificity ranges from 92% for small polyps to 94% for cancer and large polyps.

Screening by flexible sigmoidoscopy appears to be safe, the bowel perforation rate is only 1 in every 5000 procedure and complications associated with biopsy and polypectomy are unlikely if the bowel has been prepared or carbon dioxide insufflations is available(David *et al.*, 2008). The examination can be conducted without sedation and with only enema preparation, rather than taking an oral bowel preparation.

However, the limitations of flexible sigmoidoscopy include the length of the scope. Since up to two thirds of proximal advanced lesions in Asians are found in the absence of distal lesions, it creates a false sense of security using flexible sigmoidoscopy for screening.

Colonoscopy appears to be the most effective screening tool. A colonoscopic examination provides better visualization of the entire rectum and colon. Because of that it can be considered as a gold standard test for colorectal cancer screening. It's also had the advantages of removing the polyps and biopsy during the procedure itself. The sensitivity is ranging between 78.5% to 96.7%, and it's specificity is 98%(Markowitz and Winawer, 1999).

However the procedure is not without risks and complications. Furthermore, it is also costly. In a study of 16318 individuals age 40 years and older undergoing colonoscopy between 1994 to 2002, the rate of serious complications was 0.5% with perforations occurred in 0.09% of colonoscopies(Levin *et al.*, 2006). However, the benefit of colonoscopy must also be measured against risk of perforation and procedure-related deaths.

In addition, colonoscopy is an operator dependent procedure. A study done comparing colonoscopies with mean withdrawal times of less than six minutes to those with withdrawal times of six minutes or more shows those with withdrawal times longer had higher rates of detection of any neoplasia. Thus, it also has been shown that 15% to 27% of adenomas were missed by a single colonoscopy and 6 % of adenomas larger than one centimeter were missed(Hixson *et al.*, 1991).

In recent years, some groups have also proposed newer screening technologies such as stool DNA and computed tomographic colonography (CT)(Smith *et al.*, 2009). Virtual colonoscopy refers to examination of computer-generated images of colon constructed from data obtained in an abdominal CT examination. These images simulate the effect of an optical colonoscopy. A bowel preparation is required to cleanse the bowel before examination, and the colon insufflated with carbon dioxide by insertion of rectal tube.

The performance of virtual colonoscopy depends heavily on the size of the lesion. The accuracy of detection is also a reflection of the experience and training of the radiologist. A study done in asymptomatic adults underwent same day CT and optical colonoscopy showed virtual colonoscopy performed with excellent techniques compare favorably with optical colonoscopy. The sensitivity of virtual colonoscopy for adenomatous polyps was 93.8% for polyps at least 10 mm in diameter, 93.9% for polyps at least 8 mm and 88.7% for polyps at least 6 mm in diameter. The sensitivity of optical colonoscopy was 87.5%, 91.5% and 92.3% for the three polyps respectively. The specificity of virtual colonoscopy was 96%, 92.2% and 79.6% respectively(Pickhardt *et al.*, 2003).

Fecal DNA testing is promoted as a more accurate, non invasive alternative to FOBT for CRC screening. Briefly, many DNA mutations have been identified that are associated with the progression from normal colonic mucosa to adenomatous polyps and finally carcinoma. Recent advances in technology allow human DNA to be separated from bacterial DNA in the stool, amplified more than a billion fold by polymerase chain reaction (PCR), and then tested for mutations associated with colorectal neoplasia. The sensitivity of the test to detect colorectal cancer was 52% and specificity was 95%(Imperiale *et al.*, 2004). In a more recent study using two markers, the sensitivity of the test increased to 87.5%(Itzkowitz *et al.*, 2006).