National Committee *for* Clinical Research

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The NCCR bulletin aims to disseminate information on latest clinical research policies and guidelines as well as to feature articles on Malaysia's progress and pioneering attempts in this industry. The content is prepared by the members of the National Committee for Clinical Research (NCCR) who consist of Ministry of Health personnel, academicians and industry professionals actively involved in clinical research activities in Malaysia. The compilation of articles in each issue reflects the diverse range of clinical research areas and thus offers readers the opportunity to appreciate various perspectives on issues related to clinical research in Malaysia.

IN THIS ISSUE we cover two separate studies on satisfaction levels. Results from the first article suggested that almost all patients were satisfied with the services provided in traditional and complementary medicine units in public hospitals. The second study which was on colorectal cancer screening found significant variation in the acceptance levels of different screening approaches. We also include a thought-provoking review on Malaysia's involvements in major cardiovascular trials and their clinical significance. Finally, we highlight the superiority of cumulative sum (CUSUM) compared to conventional methods of assessing surgical performance. This research paper which analysed the performance of four cataract surgeons in Malaysia is the British Journal of Ophthalmology's Editor's choice article for April 2010.

CONTENTS

FOREWORD

by Director-General of Health, Malaysia

Collaboration is vital if we hope to progress in any field. This is especially true for clinical research where contribution from the various stakeholders is vital for its success and sustainability. Members of the National Committee for Clinical Research (NCCR) comprise several clinicians, experts and stakeholders with diverse backgrounds to ensure fair representation and feedback on issues pertaining to the conduct of clinical research especially in Malaysia. Our main aim, besides ensuring the proper conduct of clinical trials in Malaysia, is to position Malaysia as the region's preferred clinical research destination.

As a committee, we have accomplished a great deal since our pioneering years. We have published guidelines, developed curricula, conducted training courses, established accreditation procedures, carried out inspections, reviewed current practices and set up mechanisms to harmonise approval standard and procedures. Our role is necessarily a dynamic one and where necessary, all these guidelines, procedures and processes will be updated. As the NCCR, we have a heavy burden to bear and a great responsibility to shoulder as we have been honoured with the privilege of being the point of reference for the clinical research industry. We need to ensure that research is done ethically, our investigators are trained properly and our patients and public benefit from the research we undertake.

The best research and the most novel of ideas are futile if it remains hidden and unknown to the world. There is more good work in our midst than we know and the only way for this good work to be acknowledged is through publication in peer-reviewed journals. Obtaining valuable research findings is meaningless if one does not publish the data. Also, a researcher will not be acknowledged if he or she does not take the more challenging task of getting his or her work published. As they say, you either publish or perish! So it is our hope that clinicians will walk the extra mile to publish their work, if they feel strongly that the findings of their research will contribute to the medical and health fraternity.

On that note, let me take this opportunity to congratulate and thank all of you for contributing to this publication and I hope for more such thoughtful and informative articles for our subsequent issues.

Thank you

Tan Sri Dato' Seri Dr Haji Mohd Ismail bin Merican

A study on patient satisfaction in Traditional and Complementary Medicine Units

Research & Development Section, Traditional & Complementary Medicine Division.

Introduction

In line with the Ministry of Health's commitment to excellence and quality improvement activities in the public hospitals, the newly established Traditional and Complementary Medicine (T&CM) Unit considers patient satisfaction as one of its priorities. The Institute for Health Management conducted patient satisfaction survey in the public hospitals looking at patients receiving conventional treatment in the wards and outpatient clinics (1,2). However, such research has not been conducted on patients' assessments of traditional and complementary medicine treatment in Malaysia. Hence, this is a good opportunity for the Ministry of Health to gain information on patients' satisfaction in the T&CM Unit as based on findings that satisfied patients are more likely to comply with treatment (3), take active role in their own care (4), continue using medical care services and stay with a health provider and maintain a specific system (5).

Objective

The objective was to measure the level of patient satisfaction of services offered in the T&CM units.

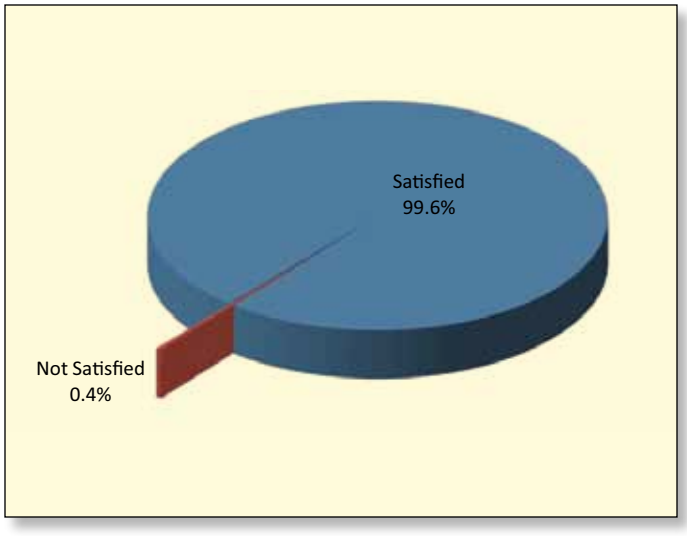

Figure 1: Overall satisfaction for services provided by T&CM Unit based on a single question

Methodology

This cross-sectional study involved 450 patients and was conducted between 2008 and 2009 in T&CM units at three Ministry of Health integrated hospitals. Questionnaires were distributed to registered patients and responses were analysed using ServQual software. The Servqual questionnaire has five dimensions and it measures tangibles, reliability, responsiveness, assurance and empathy. In this study, the instrument was modified to accommodate local setting, therefore a few additional areas (i.e. outcome, caring, teamwork and professionalism) were added.

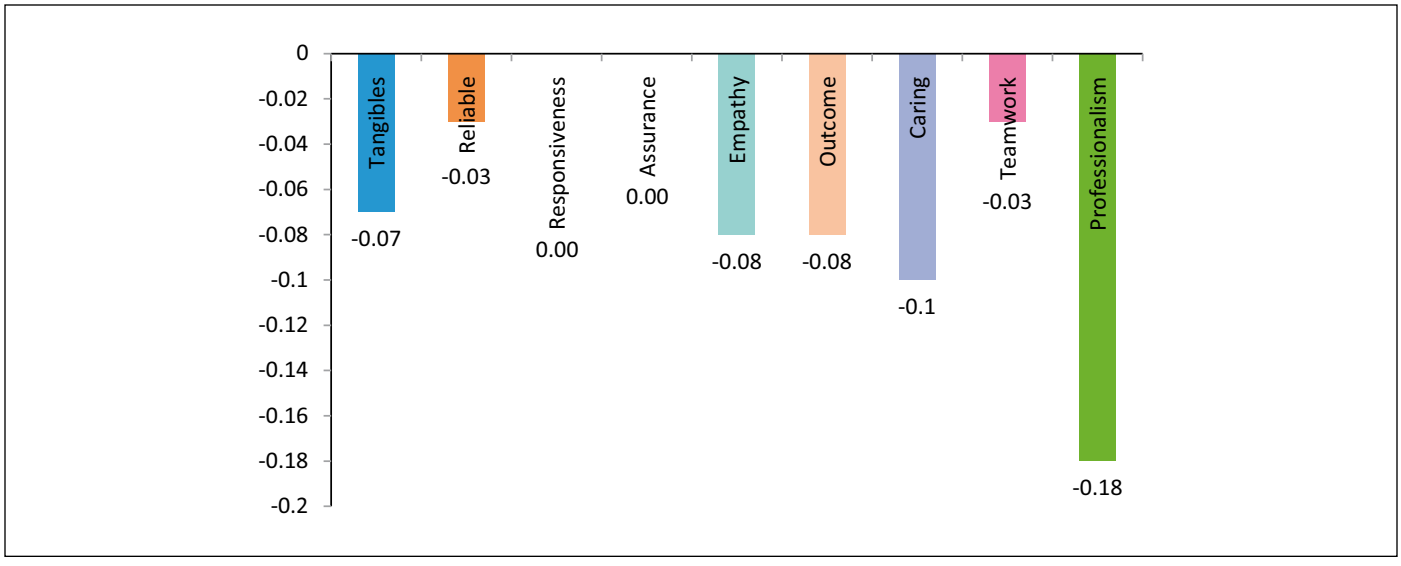

Figure 2: Service gap quality based on a single dimension

Results

The majority of respondents were between 40 and 55 years of age (43.8%), female (57.9%), Malays (73.6%), married (87.9%), and had education up to secondary level (46.8%). This study found that the age of respondents, ethnicity and education have significant relationship with patients' satisfaction ($p<0.05$). Overall, 99.6% (Figure 1) respondents were satisfied with the services provided. The results demonstrated that there is a negative quality gap in all dimensions except for responsiveness and assurance (Figure 2). The negative quality gaps mean patients' expectations are greater than their perceptions, and this indicates dissatisfaction.

Conclusion

Although 99.6% respondents were happy with the services offered, further improvements are needed across all Servqual dimensions especially for professionalism.

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4. Donabedian A. The quality of care: How can it be assessed? Journal of American Medical Association 1998; 260:1743- 1748.

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Review on the use of magnet for pain management

Research & Development Section, Traditional & Complementary Medicine Division.

Introduction

Magnets have been used for many centuries to treat pain. A 1999 survey of patients who had rheumatoid arthritis, osteoarthritis or fibromyalgia reported that 18% of these patients had used magnets or copper bracelets. Magnets come in all shapes and prices and have been touted for a variety of health purposes. There are static magnets and permanent magnets. Static magnets are usually made from iron, steel, rare-earth elements or alloy. Magnets come in different strengths and most often measured in units called gauss (G). Products that have magnets include mattress pad, belts, bracelets and other types of jewellery, headwear etc. In view of its increasing popularity, a review on magnet's effectiveness and safety is essential.

Studies

A review by the Health Technology Assessment of the Ministry of Health of Malaysia in 2008 involving "Bio-Magnetic Therapy" indicated that there were no evidence substantiating the use of bio-magnet therapy to treat chronic low back pain (1). In addition, evidence of pain reduction in the treatment of knee pain is somehow poor. This review focused on three main issues of magnet use; the effectiveness, safety and legal implication. Latest scientific evidences from systematic reviews, randomised controlled trials and experimental studies from year 2000 until 2008 are reviewed. One editorial of the International Anesthesia Research Society (Magnet Therapy: Healing or Hogwash) (2) stated that even a well designed study (Cepeda *et al.* "Static magnetic therapy does not decrease pain or opioid requirements: a randomized double blind trial) showed that magnet fails to decrease pain in postoperative patients. It also stated that there is no evidence that magnetic fields have any significant effect, therapeutic or otherwise, on human tissue. In terms of legal implication, both the review and the editorial above stated that magnetic therapy in the form of band or bracelet is not a registered medical device with the U.S. Food and Drug Administration (U.S. FDA). The FDA has authority to regulate magnets only if specific medical claims are made. To skirt the requirements of the law, magnet promoters often make only the vaguest of claims. And sadly, pain therapy does not count as a significant claim to trigger FDA enforcement. The National Center for Complementary and Alternative Medicine (NCCAM), NIH, USA (3) stated in their report "Question and Answers About Using Magnets to Treat Pain" that *Overall, the research findings so far do not firmly support claims that magnets are effective for treatment of pain*. They also concluded that "Scientific research has yet to firmly support a conclusion that magnets of any type can relieve pain. However, some people do experience some relief.

Conclusion

The use of magnet for pain management is not supported by current scientific evidences. Clinical trials in this area have produced conflicting results. However, it is considered safe to be used when applied to the skin and yet, it is not a replacement for a standard medical treatment.

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1. Health Technology Assessment, Ministry of Health Malaysia, Bio-Magnetic Therapy"; February 2008, 002/08.

2. Flamm BL. Magnet Therapy: Healing or Hogwash? International Anesthesia Research Society 2007; 10 4 doi : 10.1213/01.ane.0000250925.20995.a1.

3. National Center for Complementary and Alternative Medicine (NCCAM) research report "Questions and Answers about Using Magnets to Treat Pain".

Four major recent outcome trials in cardiovascular medicine – four important contributions from Malaysia

Professor Dr Abdul Rashid Abdul Rahman

Medicine, particularly cardiovascular medicine, is constantly changing, especially as one considers the therapeutic aspects. Drugs unheard of some years ago have become medical 'household' names (e.g. the statins) today. Drugs which were once contraindicated have become 'must use' drugs few years down the road (e.g. beta blockers for heart failure). Drugs which were hyped as potential blockbusters and aggressively sold worldwide were withdrawn from the market a few years later (e.g. mebafradil, rofecoxib, rimonabant). The reason for these is the therapeutic element in medicine which is driven by good scientific evidences and this is an evolving science. While it is a necessity for new drugs to go through the pre marketing drug development process, it is only after large multicentre outcome trials are performed, do we really know how good a drug is compared to established treatment. That is when the position of a particular drug in the big therapeutic puzzle becomes clearer.

Until recently Asia in general and Malaysia in particular had been 'neglected' in major clinical outcomes trials. Even in Japan where many new drugs were discovered, the region's involvement in clinical outcome trials was negligible. Things are poised to change for the better in future. Over the last decade, China with its huge population has performed major indigenous cardiovascular outcome trials. Five years ago, Japan announced a series of indigenous cardiovascular outcome trials. Some of these trials have been completed and recently published, while others are in the pipeline. For the rest of Asia, Malaysia included, major indigenous outcome trials is still a feat yet to be accomplished. However, Asia's involvement as important sites in multinational multicentre trials has become evident of late and the future looks promising.

Within the last two years, four major cardiovascular outcome trials were published in major medical journals; all included Malaysia as a centre.

- The ADVANCE (Action in Diabetes and Vascular disease: Preterax and Diamicron MR Controlled Evaluation) trial is the largest clinical trial ever performed in patients with type 2 diabetes.

- The ONTARGET (The Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial) is the largest ever cardiovascular trial.

- The RE-LY (Randomized Evaluation of Long term anticoagulation Therapy: dabigatrin vs warfarin) is a very important advancement in the field of oral anti-coagulation in 50 years.

- The HEAAL (Heart Failure endpoint Evaluation of Angiotensin 11 Antagonist Losartan) addressed a 10-year-old issue.

In the ADVANCE trial, 11,140 patients from 20 countries were randomised according to a two-by-two factorial design to determine whether an ACE inhibitor driven (perindopril plus indapamide), intensive BP control and a sulphonylurea-driven (diamicron MR) intensive sugar control can improve clinical outcomes in patients with established type 2 diabetes. Before ADVANCE, recommendations on tight BP control in type 2 diabetics (< 130/80 mmHg) were made from subanalysis of earlier trials, small 'prove of concept trials' or expert consensus only. The trial proved for the first time that lowering BP in diabetics to a mean of 135/75 mmHg is beneficial with significant reduction in all cause mortality and significant reduction in combined macrovascular and microvascular events. In terms of glycaemic control, recommendations were less clear cut prior to ADVANCE. Some guidelines recommended an HbA_1C < 7 while others < 6.5%.

This was despite that the best available clinical trial evidence prior to ADVANCE; the UKPDS (the United Kingdom Prospective Diabetic Study) only managed to lower HbA_1C in the tight sugar control group to 7.1%. It is also worth remembering that UKPDS studied newly diagnosed diabetes and a recent trial called ACCORD (Action to Control Cardiovascular Risk in Diabetes) showed that in patients with long standing diabetes, bringing down HbA_1C to < 7% produced more harm than good. The ADVANCE trial showed for the first time that tight sugar control (mean HbA_1C of 6.5%) in chronic diabetics is safe and leads to significant microvascular disease reduction and positive trends in macrovascular mortality/morbidity and total mortality reduction. More than a third (37%) of the 11,140 patients was from Asia (India, Malaysia, China and the Philippines) with Malaysia contributing 236 patients. It is interesting to note that at the point of randomisation, Malaysian diabetics had one of the best BP control (142/89 mmHg) but one of the worst glycaemic control (HbA_1C 8.3%).

In ONTARGET, 25,620 high risk cardiovascular patients from 39 countries were randomised. Asian patients were from China, Hong Kong, Malaysia, Philippines, Singapore, South Korea, Taiwan, Thailand and the UAE. Malaysia contributed about 450 patients. The ONTARGET addressed a question which has not been answered conclusively for the last 10 years; is Angiotension Receptor Blockers (ARB) as good as Angiotensin Converting Enzyme Inhibitors (ACE I) in patients with high cardiovascular risk? Another research question in ONTARGET was whether ARB plus ACE I is better than either alone in such patients. The ONTARGET reaffirmed what has been shown in three other smaller 'head to head' ARB vs ACEI trials; ARB is not better than ACEI (although ARB was meant to be better when it was first launched). However, ARB is 'non-inferior', or in other words 'maybe as good' as ACEI. 'Maybe' because 'non-inferior' is not identical to 'equivalence'. Non-inferior also implies that ARB is 'superior to placebo'. However, in TRANSCEND (Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular

Disease); a study done parallel to ONTARGET, with 5,776 patients, Telmisartan failed to show that it is better than placebo in the primary composite outcome of CV death, non-fatal stroke and non-fatal myocardial infarction and hospitalisation for congestive heart failure. The ONTARGET also showed that ARB should not be combined with ACEI because such combination not only failed to produce any added advantage on cardiovascular outcome compared to ACEI or ARB on their own, but it produced more adverse events.

In RE-LY, 18,113 patients with atrial fibrillation were randomised to receive either dabigatrin or warfarin. Dabigatrin is a novel oral anticoagulation which acts by directly inhibiting thrombin. The primary study endpoint was prevention of stroke and systemic embolic episodes. Two fixed doses of dabigatrin were used (110 mg and 150 mg daily) compared to an INR titrated warfarin dosing regime. The trial was designed to prove that dabigatrin was 'non-inferior' to warfarin. After two years, the lower dose of dabigatrin proved to be non-inferior to warfarin but the higher dose was shown to be superior to warfarin both for primary efficacy endpoint and bleeding complications. The higher dose also showed reducing total mortality compared to warfarin (p=0.051). The RE-LY trial signifies a potential major shift in the way we treat these patients in future. Before RE-LY, warfarin was the 'gold standard' oral anticoagulation not only in stroke prevention associated with atrial fibrillaton, but other clinical conditions requiring long term anticoagulation. Although backed by good scientific evidence, haemorrhage risk and tedious monitoring process required made it one of the most under prescribed drugs in medicine.

The HEAAL trial's importance lies in the fact that ARBs had undergone a chequered history since it was first launched just over a decade ago. One of the proposed reasons for the less than convincing performance of ARBs in randomised control trials was that the doses used in earlier trials were inadequate. As a result it failed to show superiority against established treatment especially ACEI. In HEAAL, 3,846 patients with heart failure who were intolerant to ACEI were randomised to receive either 50 mg losartan (the dose used in earlier trials) or a supra-high dose of 150 mg losartan. The primary endpoint was a composite of total mortality and admissions to hospital for heart failure. Losartan at the higher dose significantly reduced the primary endpoint by 10%. The main benefits seen were in reduction in hospitalisations by 13% with a non-significant 6% reduction in total mortality. Importantly, the safety profile of high dose losartan was acceptable with no significant differences in side effects profile or in the discontinuation rate. Although HEAAL did not change the way we use established heart failure treatment especially ACEI, it gives us the confidence and evidence to optimise the dose of ARB in ACE I intolerant patients with heart failure.

The ADVANCE, ONTARGET/TRANSCEND, RE-LY and HEAAL were not the first major outcome cardiovascular trials to have hit Malaysian shores. They were, however, the largest trials that Malaysia have ever been involved in a relatively short period of time.

They were also trials with far reaching clinical implications. Malaysian investigators involved in these four mega trials had derived invaluable experience in participating. With the credible performance of the Malaysian investigators in these trials, more major trials have been and will be coming our way. We, however, still dream of our very own indigenous major outcome trials, which we hope will not be too far off in the future.

References available on request.

National Pharmaceutical Control Bureau Compliance Monitoring Programme for Good Laboratory Practice

Dr Hasenah Ali and Dr Kamaruzaman Saleh

The National Pharmaceutical Control Bureau (NPCB) of the Ministry of Health Malaysia was appointed together with the Department of Standards Malaysia (STANDARDS MALAYSIA), Ministry of Science, Technology and Innovation Malaysia by the Malaysian Government as the National Compliance Monitoring Authorities (CMAs) for monitoring compliance to Organization for Economic Co-operation and Development (OECD) Principles of Good Laboratory Practice (GLP). For NPCB, the decision by the Government of Malaysia is enforced by the issuance of a Directive under Regulation 29 of the Control of Drugs and Cosmetics Regulations 1984 in June 2009. Ministry of Health is also appointed as the coordinator for the GLP Compliance Program (CP) in Malaysia.

The NPCB acts as the CMA for the nonclinical safety testing of test items contained in pharmaceutical products, cosmetics products, veterinary drugs and food additives while STANDARDS MALAYSIA is the CMA for the non-clinical safety testing of test items contained in industrial chemicals, pesticides, feed additives, and biotechnology (non-pharmaceuticals).

As GLP CMA, the NPCB has adopted the OECD GLP principles. The structure, policies and procedures under which NPCB operates are documented to ensure implementation of these policies and procedures are administered independently and impartially to ensure the smooth operation of all compliance activities. The NPCB's quality system has been established, documented, implemented and maintained to give confidence in its ability to effectively operate the compliance process.

The NPCB GLP CP is a voluntary programme open to Test Facilities, intended to ascertain whether these facilities have implemented requirements as described in the OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring. Test Facilities requesting for verification and certification of compliance to Principles of GLP, and subsequent inclusion into the CMAs GLP CP need to make the relevant application to the CMAs.

Type of studies/area of expertise on test item subjected to NPCB GLP CP includes physical-chemical testing, toxicity studies, mutagenicity studies, analytical and clinical chemistry testing and other studies (where applicable).

There are two mechanisms by which a Test Facility can enter into the programme. They can either submit an application to NPCB; or through request of inspection received from national or international authority. In this case, the Test Facility will be invited to submit the application form. In both cases the Test Facility shall be

entered into NPCB CP only after the Test Facility has received GLP compliance certificate. The procedure for application (NPCB/GLP/200/003) and Application Form (NPCB/GLP/300/001) can be obtained and downloaded from NPCB GLP Compliance Programme webpage.

The NPCB GLP CP includes pre-inspection, inspection, surveillance inspection and extra ordinary inspections (where applicable) and/or study audits. The NPCB shall inspect, register and monitor a Test Facility within two years since the last inspection, in accordance with the Master Register of CP. The NPCB shall establish and maintain a Master Register which shall contain information on the name of Test Facility, the date of inspection, scope, the area of studies/expertise, compliance status and remarks.

During the inspection, the inspection team may come across areas/issues which are not in compliance with the NPCB's CP. Such non-compliances are classified into major and minor categories. Within one week after the conduct of inspection and/or study audit, the inspection team shall prepare an inspection report. The copy of the inspection report shall be submitted to the Test Facility visited for their record and action. Test Facility in compliance will be issued a certificate with statement of GLP compliance to show that the Test Facility has been inspected and found to be operating in compliance with the Principles of GLP. Detailed information and condition regarding NPCB GLP CP procedures is available in the NPCB GLP Compliance Monitoring Programme website, www.bpfk.gov.my

National Medical Research Register (NMRR) – Why the need to register?

Clinical Research Centre, Ministry of Health Malaysia

There is a global consensus that clinical trials need to be registered in order to address the problems of publication bias and *hidden* data. This led to the establishment of several regulations requiring clinical trials to be registered in publicly accessible research registers to ensure:

- transparency and to increase public trust in the conduct of clinical trial.
- prevention of concealment of negative data or unfavorable results.
- physicians and prospective volunteers are informed about ongoing research in which they may wish to enroll.

We need to exercise corporate accountability for the management of research performance throughout a research organisation. Accountability is *the requirement that organisation members to whom responsibility and authority are delegated be held answerable for their performance (results)* and research performance is accessed based on the quality and quantity of research output and that there is ethical and responsible research conduct.

On the local front, the National Institutes of Health, Ministry of Health (MOH) Malaysia with its responsibility of research governance, has developed a web based tool to support the conduct of research in the MOH. This web-based tool portal through which MOH research are registered and processed online is known as the National Medical Research Register (NMRR).

International guidelines and regulations requiring trial registration

1. International Committee of Medical Journal Editors (ICMJE) 2005: Trial registration as a condition for publication in journals affiliated with the ICMJE.

2. US Food and Drug Administration (FDA) Revitalization 2007; Act, 27: All drug trials, other than phase 1, regulated by the FDA and all device trials intended “to determine safety and effectiveness of a device” and regulated by the FDA.

3. Helsinki Declaration Seoul 2008; Paragraph 19: Every clinical trial must be registered in a publicly accessible database before recruitment of the first subject.

Why research protocols need to be registered to NMRR?

1. **Efficiency:** reduce the time to submit, review and approve research; enable users/ managers to track submission status.

2. **Research registration:** to ensure transparency and prevent concealment of negative data.

3. **Public information:** Inform physicians and prospective volunteers about research which they may wish to enroll.

4. **Research information:** Inform researchers about ongoing and completed research to avoid duplicate work.

5. **Accountability:** track progress and outcomes of research that has been approved; account for research that has received public funding.

6. **Policy & Management:** Information to manager and policy maker on the state of research.

7. **Research promotion:** Demonstrate our track record and identify experienced investigators; promote Malaysia as a research hub in Asia.

Feasibility study on population based colorectal cancer screening in Malaysia

Noriah B, Roslan J, Tahir A, Koh C N, Paul S, Amal N, Nor Saleha I, Zainudin M A, Alan Khoo S B, Rohani I

Abstract

A cross-sectional study was conducted to determine the feasibility of Fecal Occult Blood Test (FOBT) as a screening tool for colorectal cancer in terms of population acceptance, barriers for screening and the cost implication. Three approaches (house-to-house, awareness campaign and opportunistic testing) were used to recruit subjects in the District of Seremban. The sample size for each approach was calculated using Epi Info and the sample size estimated for the study was 2,354. A face-to-face interview using a validated questionnaire was carried out to obtain the knowledge, attitude and practice of respondents with regard to colorectal cancer. Informed consent was obtained from the respondents prior to enrolment in the study. All respondents were given the FOBT kits for stool screening. Colonoscopy was arranged for those who tested positive on FOBT screening and for high-risk respondents with family history of colorectal cancer or personal history of Inflammatory Bowel Disease such as Crohn's Disease and Ulcerative Colitis. A total of 605 patients took part in this study, which is a response rate of 26%. Results showed a significant difference ($p < 0.05$) in acceptance of the test between the recruitment approaches, the highest being house-to-house (151), followed by opportunistic testing (179) and awareness campaign (275). More than 90% of respondents returned the FOBT kits for testing. Out of 605 respondents, nine were found to be FOBT positive and was referred for colonoscopy. Patient barriers for FOBT screening include being unsure of taking the test, feeling well, having no symptoms and thinking that they understand about colorectal cancer. In terms of costing, the cheapest approach was the awareness campaign followed by opportunistic testing; house-to-house approach was the most expensive. In conclusion, it is feasible to conduct screening for early detection of colorectal cancer using FOBT because the acceptance rate was good. The respondents were enthusiastic even though the study was conducted during the fasting month and school holidays. Opportunistic testing was the best and most cost-effective approach. However, in the Malaysian setting, all three approaches may be necessary depending on the area and ethnicity.

Introduction

Colorectal cancer is the third most common cause of death among Malaysian males and females after lung and breast (1) cancers. The incidence of colorectal cancer has increased over the past decade; the age-standardised incidence was estimated to be 8.1 per 100,000 population in 1987; 13.9 in 2002 and 18.4 in 2006. The incidence of colorectal cancer

varies among the races, highest in the Chinese population, and lower among the Malays and Indians (2). Its incidence among the Chinese in Malaysia (23.1 per 100,000 population) is comparable to those in the western countries (23.7 per 100,000 population in Scotland, and 29.1 per 100,000 population among Caucasian Americans).

Several risk factors that would increase a person's chance of developing colorectal cancer have been identified. The risk factors include being over the age of 50 years, (90% of people diagnosed with colorectal cancer are older than 50 years), having personal history of colorectal polyps and inflammatory bowel disease (including ulcerative colitis and Crohn's Disease) as well as having family history of colorectal cancer (3).

Several methods have been identified as screening tools in detecting colorectal cancer. The most frequently used screening method is Fecal Occult Blood Test (FOBT), complemented with sigmoidoscopy, colonoscopy and double-contrast barium enema. The purpose of screening is to find cancers before they are large enough to cause any warning signs (4-5). Because finding cancer early means that it is more likely to be cured, it is important for patients to have appropriate screening tests. The aim of this study is to determine the feasibility of using Fecal Occult Blood Test (FOBT) as a screening tool for colorectal cancer in terms of the population acceptance and the cost implication.

Methodology

Three methods of approach were used to obtain the samples; house-to-house, awareness campaign and opportunistic testing. Depending on the method of approach, sampling size was calculated based on the number of population in the district of Seremban. The sample size was calculated using Epi Info version 6.

Sampling method and size

Minimum sample size for house-to-house was 168, based on estimation prevalence of 50% (rate of acceptance) and acceptable limit of 15%. For the awareness campaign, minimum sample size was 1,784 (number of pamphlets distributed) with estimation prevalence of 5% and acceptable limit of 4%. In the opportunistic campaign, the minimum sample required was 382 (pamphlet and health education) based on estimation prevalence of 20% and worst acceptable limit of 16%. The confident intervals of 95% were taken in all approaches. This estimation prevalence was obtained from the exploratory study done in Seremban Health District before the study was carried out.

Study procedure

In the house-to-house approach, the sample was selected randomly based on Enumeration Block provided by the Seremban Statistical Department. In the awareness campaign, 2000 pamphlets on colorectal cancer were distributed at supermarkets, bus stations and housing areas in Seremban. For opportunistic testing, patients would be invited by the health

care workers to take part in the study. These patients came to the health clinic for other treatments or for follow-up. Health education on colorectal cancer was given to the patients. The FOBT screening was conducted from 15th September 2007 until 31st December 2007. The cost was calculated based on the method of approach. These were costs for screening kits, banners, pamphlets, overtime compensation for personnel testing the kit and those involved in data collection for the house-to-house approach.

Inclusion and exclusion criteria

The respondents, either male or female, were 50 years and above, and able to perform the FOBT test. Group 1 and 2 were given the Hemocult ICT kit while Group 3 received the Hemocult SENSA kit for testing. The exclusion criteria were menstruation and active hemorrhoids for all groups. The exclusion criteria for Group 3 were patients on non-steroidal anti-inflammatory drugs such as ibuprofen, naproxen or aspirin.

Data collection tool

The data collection tool consists of one set of questionnaires, consent form and three stool collection kits.

Data analysis

Data analysis and cross-tabulation by proportion used the Statistical Package for Social Science (SPSS) program version 15.

Results

Out of 2,574 potential respondents that were approached, 605 agreed to take part in the study. This was a response rate of 24% (Table 1). The highest acceptance rate was for the house-to-house approach (86.8%), followed by opportunistic campaign (44.8%). More than 50% of the respondents were between the ages of 50-59 (Table 2). Males and females were almost equally distributed. Malays constituted 42.5% of the respondents followed by Chinese (38%) and Indians (18%). 'Others' in this context referred to the Orang Asli.

Ninety percent of the respondents returned the FOBT kit for screening. Nine respondents were found to be FOBT positive and referred for colonoscopy (Table 3).

House-to-house approach had the highest rate of acceptance of FOBT screening; followed by opportunistic and awareness campaign (Table 4).

Patient barriers for FOBT screening include being unsure of taking the test, feeling well, having no symptoms and thinking that they understand about colorectal cancer. In terms of costing, the cheapest approach was awareness campaign followed by opportunistic testing; house-to-house approach was the most expensive (Table 5).

Discussion

The Malaysian National Cancer Registry (2006) reported colorectal cancer as the second most

common cancer after breast. It is the most common type of cancer among males and second among females in Peninsular Malaysia. The incidence rate starts to rise after the age of 40 (2).

Early detection of colorectal cancer is critical as treatment success depends on the disease being diagnosed at a localised stage (6). Fecal Occult Blood Test has been recommended as a screening tool for colorectal cancer in patients at average risk (7) and shown to reduce mortality from colorectal cancer by 15 to 33 percent in a targeted population of 50 (8) to 74 year olds. The results of this study showed that the response towards FOBT screening was good even though the study was conducted during the fasting month and major festive holidays, when attendances were expected to be reduced compared to other months. Public acceptance is important because a population-based screening for colorectal cancer can be effective when the population acceptance is high. This study showed that the house-to-house approach recorded the highest acceptance rate followed by opportunistic testing and awareness campaign. It has been reported that understanding the risks and benefits of screening and the willingness of the physician to communicate this information to patients does have a positive influence on patient acceptance (9).

Table 1: Samples and response rate by methods of approach

Group	No. of samples required	No. of houses visited/ pamphlets/ health education given	No. of respondents agreed to take part in the study	Acceptance rate (%)
House to house	168	174	151	86.8
Awareness campaign	1784	2000	275	13.8
Opportunistic campaign	382	400	179	44.8
Total	2334	2574	605	23.5

Table 2: Socio demographic profile of respondents

Socio-demographic profile	N=605
Age group (years)	
50-59	310 (51.2%)
60-69	211 (34.9%)
70-79	70 (11.6%)
>80	14 (2.3%)
Gender	
Male	294 (48.6%)
Female	311 (51.4%)
Ethnicity	
Malay	257 (42.5%)
Chinese	229 (37.9%)
Indian	108 (17.9%)
Others	11 (1.8%)

Table 3: Response rate of screening

Participants	Number	Frequency
Questionnaires and FOBT	550	90.9%
Questionnaires only	55	9.1%

Table 4: Distribution of acceptance of FOBT screening

Participants	Acceptance by approach	Percentage
House-to-house	144/151	95.4%
Awareness campaign	241/275	87.6%
Opportunistic	165/179	92.2%
Total	550/605	90.9%

The Clinical Practice Guidelines of the Academy of Medicine Malaysia suggests that several factors are considered before screening is introduced nationwide. For instance, compliance among the general population will determine the success of the screening programme. Therefore, public awareness is vital to improve compliance, and media coverage of any screening program with the aid of national health agencies is essential. Furthermore patients should be taught that positive occult blood test requires further evaluation and a negative occult blood test does not rule out polyps or malignancy (10).

Those who refused the screening claimed, among others, that they are well, experienced no sign and symptoms of colorectal cancer, know when to go to hospital if they experience the sign and symptoms or lack the time. There were some who refused screening without any reason. According to the Washington State

Table 5: Costing per respondent by approach

Approach	House-to-house	Awareness campaign	Opportunistic
Cost per respondent	RM95.33	RM54.75	RM58.72

studies, 50% of the unscreened participants cited lack of awareness of the disease that led them not to volunteer for screening (11-12). Ninety-one percent of the total participants who agreed to participate in this study returned both the questionnaires and screening kits for analysis and 9% of the respondent only submitted the questionnaire, the highest percentage of returning the kits for testing were from house-to-house followed by opportunistic and lastly awareness campaign. In Taiwan, 81% returned the FOBT kits. Of those whose results were positive, two-thirds attended colonoscopy screening (13).

In terms of cost, the lowest was for the awareness approach, followed by opportunistic and house-to-house approaches. Many studies have suggested that individuals prefer to initiate test that they believe to be the most accurate (e.g. colonoscopy) or the least invasive (e.g. FOBT) (4-5). Screening with the fecal occult blood test has been shown in randomized control trials to be effective in reducing mortality from colorectal cancer. Compliance to this test recommendations among the general population is however, usually low (9).

Conclusion

This study showed that it is feasible to introduce the FOBT screening test for colorectal cancer in our community because the response and acceptance on the screening were good even though the study was conducted during festive and school holidays.

Awareness campaign incurred the lowest cost compared to opportunistic and house-to-house approaches. Nine out of 550 respondents (1.6%) tested FOBT positive.

The main reasons given by the patients for not agreeing to the screening were that they did not have any signs and symptoms, were feeling well or unsure.

Recommendations

The favorable public response and acceptance as shown by this study indicate that screening programmes for colorectal cancer can be introduced to the public. This move is essential as 13% of the total burden of cancer is contributed by colorectal cancer.

The best approach would be opportunistic screening with the health clinic as a one-stop centre for the programme. This approach

showed good acceptance rate compared to the cost generated by other approaches with comparable cost implications to the awareness campaign.

Fecal Occult Blood Testing is a non-invasive, cheap and easy method of screening, with reasonable levels of acceptability to the population. Protocol can be developed by the expert committee taking into consideration the cost effectiveness and the availability of manpower, material and money.

In the Malaysian setting, all three approaches may be necessary depending on the area and ethnicity. Screening can be focused on subjects aged 50 years and above but those with the signs and symptoms and family history of colorectal cancer should be screened earlier.

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Applying CUSUM to assess surgical performance

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Malaysian researchers recently published an article in the British Journal of Ophthalmology on the superiority of cumulative sum (CUSUM) compared to conventional methods of assessing surgical performance such as logbooks, progress interviews, peer reviews or direct supervision. CUSUM analysis, which is commonly used for quality control in the manufacturing sector has potential in healthcare as it is an objective evaluation of performances over a period of time and is compared to a set standard. CUSUM is not a new application in the medical field as it has been previously used to assess clinical performances in surgeries, anaesthetic procedures, interventional nephrology and diagnostic procedures. However, CUSUM is not suitable for all surgical procedures and the analysis need to be regularly performed to be efficient. Furthermore, there is the problem of incomplete data entry, which nevertheless, can be resolved by automated data mining from electronic medical records or patient registers.

Several reasons why CUSUM is a good assessment for clinical performances:

- Its analysis is presented in a simple and easy to understand chart. An upward trend indicates deteriorating performance.

- Compared to conventional methods which are subjective and time consuming, CUSUM analysis exposes poor performances early.

- Standards can be modified based on the level of training. A trainee who fails to achieve the learning curve after performing a set number of procedures, would need more supervision before he can move on to the next level of training.

- CUSUM can be used to determine the mean number of procedures that trainees need to perform before they can perform surgeries without supervision.

In an article in the British Journal of Ophthalmology, four cataract surgeons (three trainees and one senior consultant) who performed 20 cases of phacoemulsification were assessed using CUSUM. The set standard of performance was defined as the absence of posterior capsular rapture (PCR) or refracted visual acuity of 6/ 12 or better by 12 weeks postoperatively. The trainee charts started off with an upward trend and followed by a plateau; indicating the process of acquiring competency in phacoemulsification. The consultant's chart was a flat curve, which meant a continuous maintenance of competence.

The Ministry of Health has adopted the CUSUM competency monitoring in its ophthalmology programme since 2009. In an effort to be more efficient, surgeons can view their CUSUM charts online through the eCUSUM website. They can also send these charts to their supervisors via an automated email message.

eCUSUM website: https://app.acrm.org.my/eCUSUM/

Source

Salowi MA, Goh PP, Lim TO. CUSUM: A dynamic tool for monitoring competency in cataract surgery performance. Br J Ophthalmology 2009 (Epub ahead of print).

This paper is Editor's choice in the April 2010 issue of British Journal of Ophthalmology.

About NCCR

Established in 1997 to coordinate and encourage clinical trials in Malaysia, the National Committee for Clinical Research (NCCR) supports the enhancement and regulation of the quality of biomedical research as well as clinical research practice in Malaysia. The NCCR is headed by Tan Sri Dato' Seri Dr Hj Mohd Ismail Merican, Director-General of Health and it is managed by the Clinical Research and Compliance Section of the National Pharmaceutical Control Bureau, Ministry of Health Malaysia who acts as secretariat. The members of this committee consist of experts from Ministry of Health (MOH), various national universities, the Malaysian Pharmaceutical Society (MPS), the Pharmaceutical Association of Malaysia (PhAMA), the Malaysian Organisation of Pharmaceutical Industries (MOPI), and other non-governmental organizations. www.nccr.gov.my

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