Colorectal Cancer Screening

Workshop Report

Sheraton Gateway Hotel
Toronto, Ontario ~ March 28, 2006

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

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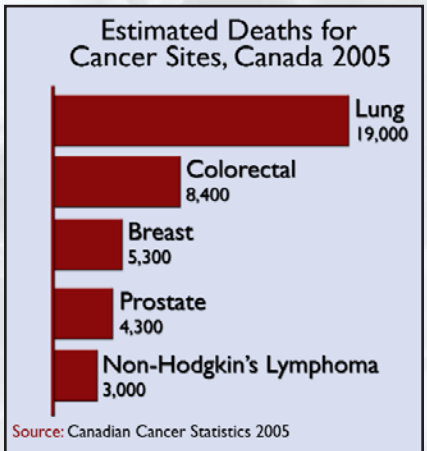
Executive Summary

Background

Canada has one of the highest incidences of colorectal cancer in the world. It is the third most diagnosed cancer in Canada after prostate and lung cancer in men, and breast and lung cancer in women. Overall, colorectal cancer is second only to lung cancer in the number of deaths caused.

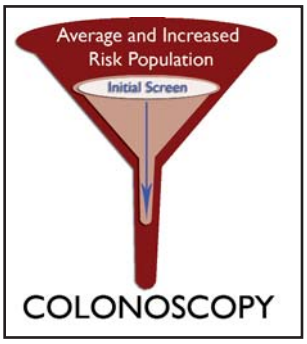


Overall, colorectal cancer is second only to lung cancer in the number of deaths caused.

Regular screening for colorectal cancer can diagnose the disease at an early stage and screening using fecal occult blood testing (FOBT) has been proven to reduce mortality. Early screening can also prevent the disease through the detection of pre-cancerous polyps which can be removed during a procedure called colonoscopy. However, Canada has no population-based screening programs and uptake of available screening procedures by the population occurs on an ad-hoc basis. Although the National Committee on Colorectal Cancer Screening, established by Health Canada in 1998, recommended population-based screening programs for all Canadian adults between the ages of 50 and 74, such a program has never been implemented. Recently some provinces (Alberta and Ontario) have mounted pilot studies and have plans for provincially-based colorectal screening programs. In addition, British Columbia recently approved the provincial coverage of FOBT as a screening test, as well as coverage for other related technologies (colonoscopy, sigmoidoscopy, etc.) for diagnostic follow-up of positive screens.

There has been lower compliance with screening in Canada than in the UK or the US which is probably due to the relative lack of publicity given to these screening tests. One reason given for the low public compliance rate with available screening tests is the embarrassment that surrounds discussion of the subject among health care providers and the public and the fact that most currently available screening tests are done on stool samples. The current 'gold standard' diagnostic test of colonoscopy is not available for screening on a routine basis and has never been proven efficacious as a screening test in randomized controlled trials.

In order to make rapid reductions in colorectal cancer mortality, we need more research on how best to implement, at a population level, the tests that are currently available to us for screening and diagnosis. Secondly, new screening tests are required that not only have the necessary specificity and sensitivity to accurately predict risk, but that are also suited to the operational considerations of population screening.



Ideally, after being subjected to a non-invasive screening test, only patients suspected or known to have a suspicious polyp(s) or mass, would advance to the next screening stage: colonoscopy. Identification of high-risk patients for more frequent screening and a minimal risk group for less intensive screening would significantly reduce the potential for population harm and also the resources needed for implementation of the colonoscopy component of population-based screening programs.

The Institute of Cancer Research (ICR) of the Canadian Institutes of Health Research (CIHR) has identified early detection of cancer as one of its strategic research priorities. Colorectal cancer screening falls within this priority. To date, the Institute has launched two Pilot Project initiatives on screening in preparation for a larger initiative aimed at providing the evidence required for the design and implementation of successful Canadian colorectal screening programs. As part of the process in developing a Request for Applications (RFA), the Institute hosted a one-day invitational workshop on March 28th 2006, in Toronto, to determine what new technologies exist, what other countries are doing to address this important health issue and to identify the outstanding research questions.

Colorectal Cancer Screening Workshop

The workshop provided the opportunity for knowledge exchange between individuals with a common interest and expertise in colorectal and cancer screening in general. A number of presentations described the state of the art in terms of innovative screening modalities, such as virtual colonoscopy, and the new generation of gene-based screening tests. Participants also shared some of the lessons learned during the early development of existing screening programs in Canada (provincial) and the UK (national).

The Colorectal Cancer Screening Workshop was held at the Sheraton Gateway Hotel in Toronto, Ontario

Break-out group discussions focused on the **research questions** in three main areas - basic/biomedical; clinical; and population/health services. Full details of these discussions are described in the Workshop Report, but **several common themes emerged** from the three groups, including:

- ***Research is needed that compares both new and existing screening tests, including new imaging techniques, in terms of specificity, sensitivity, practicality and cost effectiveness;***

- ***Research is required on what kind of information health professionals, the public and the government needs in order to accelerate the implementation of a national screening program and increase patient compliance with screening programs already in place. Research is also needed on the best and most effective way to get this information to the public and health professionals;***

- ***Research is needed to develop new screening tests, preferably blood-based, which would provide the necessary specificity and sensitivity to stratify patients into high, low and medium risk groups. Information would be required on the optimal order in which such tests should be administered. An overriding requirement for any screening test should be that it has very low potential for harm;***

- ***In order to facilitate rapid evaluation of new tests, research is required on the best way to access both tissue (mucus, stool, serum, polyps, tumours) and comprehensive patient data. Wherever possible links should be made to existing infrastructure such as Canada's Tumour Repository Network and national and international biomarker initiatives currently in development;***

- ***Research should not be limited to stool and blood-based assays but should include evaluation of new imaging modalities such as virtual colonoscopy and the development of improved agents for tagging and contrast studies; and***

- ***Research should be incorporated as an integral part of any natural experiments occurring in Canada. Examples would be the screening programs currently being developed in Alberta and Ontario.***

The Path Forward

Based on the recommendations of the workshop participants, ICR staff will work with the original steering committee members to draft an RFA for launch in June 2006. ICR will commit a minimum of $1 million per year for five years to this initiative. It is possible that this amount will increase through partnerships. Eligible research areas will include any topic documented in the Workshop Report, that is likely to lead to improvements in the process and uptake of colorectal cancer screening in Canada. It is hoped that some studies will prepare the way for larger randomized controlled trials in the future. Emphasis will be placed on novel ideas that will have significant impact and add to the existing knowledge on population-based colorectal cancer screening in a new way.

The program tool will be the CIHR Emerging Team Grant which is intended to support multidisciplinary teams and encourage networking between groups with complementary expertise and/or resources. These grants are eligible to receive up to $500,000 per year for up to five years.

In addition ICR may, at a later date, include the topic of colorectal cancer screening as an eligible research area in other CIHR programs, including the Partnerships in Health System Improvements Program and the Collaborative Health Research Projects Program, which is a joint program between CIHR and the Natural Sciences and Engineering Research Council (NSERC).

Workshop Report

Welcome and Introductions

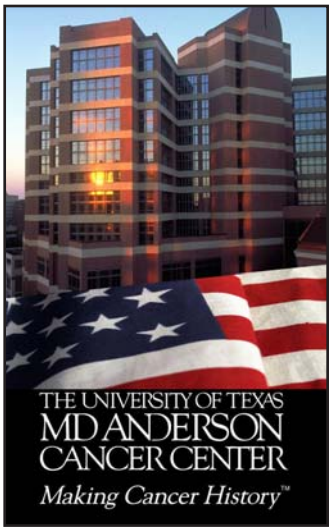
Dr. Philip Branton, Scientific Director of the Institute of Cancer Research (ICR) of the Canadian Institutes of Health Research (CIHR), welcomed participants and thanked the speakers from the UK and US for finding the time to attend the meeting and share their experiences in colorectal cancer screening (see Workshop Participants, Appendix 2). Dr. Branton briefly explained the structure of CIHR and the role of the Institutes. From the beginning, ICR has recognized the importance of early detection as a preventative measure in colorectal cancer and applauds the advocacy and commitment of the two Canadian colorectal foundations - the Colorectal Cancer Association of Canada and the National Colorectal Cancer Campaign. The purpose of this workshop is to define the outstanding research questions that need to be addressed if Canada is to have effective colorectal cancer screening programs. The objective is to use the information and recommendations from the workshop to drive the design of a research initiative that will be launched in June 2006.

Dr. Philip Branton, Scientific Director of ICR with Dr. Heather Bryant ICR Advisory Board Chair

Dr. Heather Bryant added her thanks to the group and described two small initiatives previously launched by ICR to pave the way for a more significant Request for Applications (RFA). Dr. Bryant encouraged participants to think of the bigger picture and focus on multidisciplinary projects likely to move the field of colorectal cancer screening forward at an accelerated pace.

The workshop began with a series of presentations to set the stage and provide information and guidance for small group discussions later in the day (see Workshop Agenda, Appendix 1). Drs. Bryant and Rabeneck introduced the speakers (see Speaker Biographies, Appendix 3).

SETTING THE STAGE



DR. BERNARD LEVIN, MD ANDERSON CANCER CENTRE, US

"What Are Pressing Research Questions to Advance Colorectal Cancer Screening?"

Highlights of the Presentation and Discussion

The incidence and mortality of colorectal cancer remains a significant health problem world-wide. Canadian estimates for 2005 suggested that 19,600 Canadians would be diagnosed with colorectal cancer and 8,400 would die of it. The natural history of non-inherited colorectal cancer is generally characterized by a slow progression from early histological changes to neoplasia. This timeline, which can be as long as 15 years, allows ample opportunity for interventions. Effective and timely colorectal cancer screening can prevent the development of colorectal cancer.

Current screening methods include:

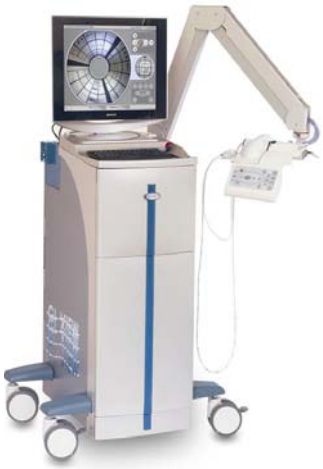
- ***Fecal occult blood tests;***
- ***Flexible sigmoidoscopy;***
- ***Double contrast barium enema; and***
- ***Fiberoptic colonoscopy.***

Methods under development include virtual colonoscopy and molecular detection of gene abnormalities in stool or blood. Of these tests, only endoscopy and virtual colonoscopy are able to detect changes at the early adenoma stage, although new stool DNA tests show some promise as a non-invasive marker of pre-malignant disease. In North America, there has yet to be a randomized control trial (RCT) on what is currently referred to as the gold standard diagnostic test - colonoscopy. The fact that this has not been done is surprising given the disease burden on the health service system and the continuing demand for data. However, at this point, it is probably impossible to randomize people to an RCT comparing colonoscopy to a "no-screening" group.

The objective of a colorectal screening program is to prevent cancers and reduce mortality by detection and resection of adenomatous polyps and/or detection of surgically curable (stages I and 2) colorectal cancers. Barriers to uptake of conventional screening technologies centre around the decision making processes of public health care providers (including primary care physicians) and policy makers and the ability to effectively assess and communicate risk.

Coupled to this is the perception that current screening tests are both inconvenient and embarrassing, a view often shared by the public, media and health care professionals. It is possible to estimate risk using a web-based model that can predict an individual's ten year and life-time risk based on the answers to a series of questions. Mathematical modeling also has a role in linking screening, treatment and prevention goals to mortality goals.

It would seem likely that screening using colonoscopy could prevent colorectal cancer by removing adenomatous polyps, but the procedure is expensive, uncomfortable, and not without risk of serious adverse events, such as perforation of the colon. For this reason, specific and sensitive screening tests are required to limit the number of colonoscopies to those at high risk of disease. Current screening tests, including the more recent gene-based tests using stool or blood samples, suffer from a lack of sensitivity and compliance rates tend to be low for studies requiring stool samples. Gene-based testing however may be the way of the future as genetic abnormalities are inherent to tumorigenesis. Currently, multi-target gene-based testing in stool offers high specificity (although disappointingly low sensitivity), is non-invasive and does not require dietary restrictions or bowel preparation - all factors likely to increase the rate of compliance. The current cost of these tests is not insignificant, however, and projections suggest that stool-based tests may not fall below a cost of $100 (US) per test. We have yet to determine the frequency at which such tests should be given and the differences between males and females in terms of age and frequency of testing.

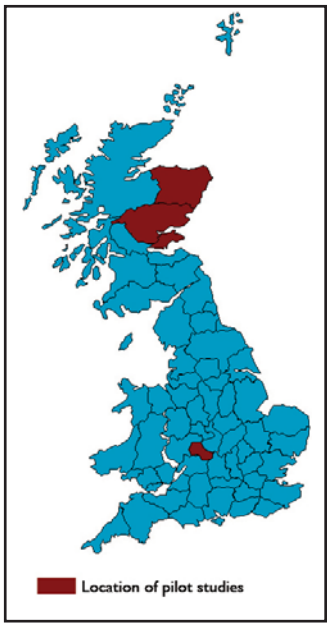


It is hoped that in the future, combinations of gene-based markers can be used in a simple blood test which will select patients requiring colonoscopy. Novel endoscopic approaches include self-propelling, self-navigating colonoscopy (Aeroscope) and sigmoid stiffener to enhance passage. Virtual colonoscopy is another relatively new technique which some perceive to be more "user friendly" than colonoscopy and which may provide a means to determine the natural history of polyps, although optical colonoscopy will still be required for polyp removal. A novel method involving NMR spectroscopy of stool is currently yielding very high sensitivity and specificity on a limited sample size. Further clinical validation is needed.

It will be important to help the media, legislators and public understand the role and value of novel screening technologies and their potential impact on clinical practice and health policy so that access can be improved at the population level.

Dr. Neil Haslam, Greater Manchester Strategic Health Authority, UK

"Cancer Screening Programmes: NHS Bowel Cancer Screening Programme"



Highlights of the Presentation and Discussion

In 2000, the UK introduced a series of pilot projects in England (Warwick and Coventry) and Scotland (Dundee) to prepare for the roll-out of a national colorectal screening program, beginning in 2006. The primary screening test was the fecal occult blood test (FOBT), which was offered every two years to individuals between the ages of 50 and 69. Uptake in the pilot projects was 56.8% with a 2.0% positivity rate. Of the 2% that tested positive, 45% progressed to a diagnosis of adenoma or cancer following colonoscopy. The organization of the full screening program for England will centre around five program hubs each connected to a series of service centres.

The program hubs will have the following functions:

- ***Responsibility for up to 20 screening centres;***
- ***Call/re-call of population for initial screening;***
- ***Assembly and dispatch of kits to invited population;***
- ***Laboratory - test the returned kits;***
- ***Dispatch of test results to individuals within 48 hours of receipt;***
- ***Book appointments at nurse positive clinics at local screening centre with result letter within one week of result;***
- ***Provide a help line;***
- ***Have overview of screening centres/clinic space; and***
- ***Facilitate polyp surveillance for screening patients.***

Each screening centre will have the following roles:

- ***Nurse positive clinics and follow up clinics;***
- ***Colonoscopy clinics: 1 to 2 per week per 500,000 people (will double in time with polyp surveillance);***
- ***Radiology;***
- ***Pathology (histology);***
- ***Refer to local hospital for treatment;***
- ***Collect outcome data;***
- ***Education of and liaison with primary care and public health; and***
- ***Promotion of the service locally.***

Screening centres will be selected based on a global rating scale with emphasis on waiting times and patient experience, adequate number of accredited colonoscopists to provide timely colonoscopy, maintenance of colonoscopists' workload at 200 colonoscopies per year and ability to offer all patients a colonoscopy within two weeks of a nurse positive clinic appointment. Quality control of the colonoscopy procedure will be an important component to ensure that the benefits consistently exceed the capacity for harm. To achieve this goal, a system of accreditation will be introduced that includes an intense evaluation component. Competence and performance of colonoscopists will be evaluated by submission to a regular audit of practice that will include observation of two colonoscopies by tri-split video. Quality indicators will include a completion rate greater than 90%, an adenoma detection rate of at least 35%, polyp recovery of over 90% of those excised, and correct identification of tumour location in more than 95% of cases. In terms of safety measurement, indicators will include a perforation rate less than 1:1000, low post-polyectomy complications such as bleeding and perforation, and low rate of complications requiring hospital admission (less than 3:1000). Based on the global rating scale for the pilot projects, there has been a significant improvement between April and October 2005 in all areas, including equality, timeliness, choice, privacy, aftercare and feedback.

Screening centres will link not only to the program hubs but also to local hospitals and cancer centres where the planning will take place for associated treatments such as pathology, surgery, further imaging, oncology and palliative care. The primary care trusts will be critical for the development and commissioning of screening services for their local population and will be responsible for promotion of screening and monitoring of coverage and uptake in 'hard to reach' groups. When the program is initially rolled out in 2006/2007 it is expected to cost the equivalent of approximately $25 million (Can.). As enrollment expands this cost is projected to rise by year two to around $50 million (Can). Full national coverage is anticipated by 2009. In preparation for the full roll-out, a national Information Technology system, including electronic patient records that incorporate family data, is under development along with the training of additional endoscopists, including nurse endoscopists and expansion of the overall workforce required for implementation of the project. Once in place, the national screening program, which hopes to enroll 2.5 million individuals between the ages of 60 and 69 per year, will provide an excellent research platform as all the information will be on a single database. Although the pilot projects have proved that the system works, launch of the full program may be delayed due to the current funding freeze in the National Health Service (NHS).

Dr. Perry Pickhardt, Univ. of Wisconsin Medical School, US

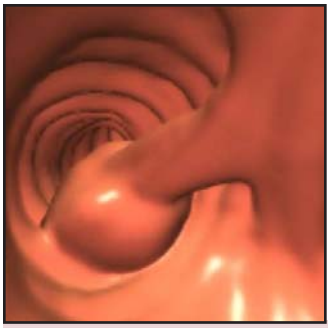
"Key Research Questions in Colorectal Cancer Screening: Imaging Perspective"

Highlights of the Presentation and Discussion

Virtual colonoscopy, or CT colonography (CTC), is a relatively new imaging technique that is far less invasive, and therefore safer, than standard optical colonoscopy. Virtual colonoscopy involves the preparation and distension of the colon (using carbon dioxide - which is absorbed much faster than room air and causes less discomfort), administration of an oral contrast agent and CT scanning along the length of the colon combined with the specialized software necessary to produce a 3-D image. In contrast to optical colonoscopy, imaging does not require insertion of a tube into the colon. Virtual colonoscopy has been under study at the University of Wisconsin Medical School for about two years, where the following research questions have been addressed:

- ***Performance characteristics;***
- ***Target lesions;***
- ***Surveillance intervals;***
- ***Effect on overall compliance;***
- ***Cost effectiveness;***
- ***Minimal prep approaches;***
- ***Computer-aided detection; and***
- ***Combined CTC-PET evaluation.***

Standard CTC produces a 2-D image as a series of colon "slices" which can be scrolled through to detect polyps. The procedure can be difficult, time consuming and exhausting, with polyps (especially smaller ones) being difficult to find. With virtual colonoscopy and a 3-D image the location of polyps is much faster and easier and has proven, in a trial of 1200 asymptomatic patients, to be comparable to optical colonoscopy in terms of both the specificity and sensitivity of detection of clinically relevant polyps. One advantage is that patients diagnosed with a large (over 10mm) or medium sized (6-9mm) polyp can be sent for an optical colonoscopy and polyp removal the same day so that only one bowel preparation is required. Continual improvement in the software means that it is now possible to obtain virtual colonoscopy results within two hours. The current referral rate for colonoscopy following virtual colonoscopy is 12% (all patients with lesions greater than 6mm diameter).



Virtual Colonoscopy showing a large polyp

This technique provides an excellent mechanism for the study of the natural history of polyps. There are four major classes of polyps: diminutive lesions, medium sized polyps, large polyps and masses. The detection and removal of advanced adenomas of greater than 1cm. diameter (prevalence approx. 2-5% among healthy adults) is the key to the prevention of colorectal cancer. Of particular interest is the progression rate of medium sized polyps and whether they should necessarily all be removed by follow-up colonoscopy or whether a 'wait and see' policy with follow-up virtual colonoscopy is adequate. Available data suggest that very few medium sized polyps grow to 1 cm. and in fact the overall tendency is for regression. Therefore the risks of optical colonoscopy and polyp removal may well outweigh the benefits for this class of polyp. For diminutive lesions the current view is that these very common lesions are of no clinical significance and in fact should not be reported following virtual colonoscopy in order to reduce patient anxiety.

Virtual colonoscopy promises to be the way of the future for colorectal imaging, although few centres currently have either the expertise or software to be able to implement a virtual colonoscopy program. In Canada, there is not much capacity for virtual colonoscopy which can be difficult to read compared to standard CT scans, even for trained radiologists. Hopefully this will change in the future as techniques and software continue to evolve and as novel biomarkers become available for tagging and improved contrast.

Dr. Steven Gallinger, Samuel Lunenfeld Research Institute, Toronto, Canada

"DNA Testing for Colorectal Cancer and Polyps, How Far are We Away?"

Highlights of the Presentation and Discussion

Current recommendations for colorectal cancer screening for the over 50 population, including FOBT, flexible sigmoidoscopy and colonoscopy, are not being met for a variety or reasons. These reasons include inadequate communication of risk to the population and primary care physicians and people's reluctance to comply with tests that are perceived to be embarrassing, uncomfortable and in some cases dangerous. A stronger focus is needed on education and behavioural changes among the population at risk. In addition, improved screening tests are required to reduce the number of colonoscopies and identify those patients most at risk at an

early stage of disease or with pre-cancerous lesions. Currently the available tests, all of which require stool samples, lack both adequate specificity and sensitivity. However, they have several advantages over colonoscopy as they require no bowel preparation, medication or dietary restrictions and have better patient compliance. However, they do not negate the need for colonoscopy as patients with a positive stool test progress to colonoscopy for confirmation and polyp resection.

Current molecular biology research is providing new information on the genetic changes that accompany neoplastic transformation, beginning with the earliest precursor stages such as aberrant crypt foci. It is now known that there are at least two molecular pathways leading to the development of colorectal cancer: the chromosomal instability pathway (85%) and the microsatellite instability pathway (15%). Many genetic mutations have been identified in the progression from normal to carcinoma, some of which can be detected in stool early in the disease process. Although no single mutation has proven to be effective as a screening test, when grouped together as multi-marker panels, genetic markers show considerable promise. These multi-marker tests, such as the PreGen-Plus produced by Exact Sciences, though expensive at an estimated $695 (US) compared to $75 (US) for FOBT, have several advantages over FOBT. Polyps growing in the colon continuously shed cells and DNA into the stool stream. As time progresses some of these polyps acquire additional mutations leading to the development of cancerous growths which also shed DNA into the stool stream. Unlike bleeding that may occur intermittently, if at all, DNA shedding occurs continuously. In the PreGen-Plus test, stool containing altered DNA is collected and sent to the laboratory. Here, sophisticated laboratory techniques are used to extract, purify and amplify the human DNA and isolate specific DNA targets associated with colorectal cancer. If an abnormality is found, a further test such as a colonoscopy is recommended.

Current trends indicate a consistent rise in specificity and sensitivity of DNA tests and a corresponding decrease in cost, making them perhaps a primary screening test for the future particularly if, as recent studies indicate, these markers can be isolated from blood or serum. These early markers of cancer may also prove to have predictive value for treatment allowing patients to be stratified into those who will respond to certain treatments and those who will not.

Dr. Heather Bryant, Alberta Cancer Board, Calgary, Canada

"CRC Screening Overview Canada/Alberta"

Highlights of the Presentation and Discussion

Screening tests for colorectal cancer have been shown to be effective in preventing disease. For example, in one study in which about 27,000 people (aged 50-80) were randomly assigned to annual FOBT, biennial FOBT or usual care, there was a 17-20% reduction in colorectal cancer in the screened group. In 2002, the Canadian National Committee on Colorectal Cancer Screening released a technical report that acknowledged that there would be potential benefits to a national colorectal cancer screening program with possibly as many as 7,700 deaths being prevented over a 10 year period. However the committee also recognized that there are potential risks with colonoscopy, forecasting perhaps as many as 611 colon perforations and 75 deaths over the same 10 year period. Because of similar projections, a New Zealand National Screening Committee did not recommend a national FOBT screening program as it was felt that the risk of the follow-up diagnostic tests was not tolerable for a population-based screening program. One challenge is to weigh the risks and benefits and to strike an acceptable balance between the two. Canada's National Committee eventually recommended that colorectal cancer screening should be made available to Canadians in an organized and structured environment and under the following conditions:

- ***Clear, concise and understandable information for patients and physicians on the risks and benefits of screening and on the administration of the test;***
- ***Informed consent following personal consultation with family practitioner or equivalent;***
- ***Standardized protocols and procedures with a single entry test and options for follow-up; and***
- ***Systematic tracking and evaluation of all screening invitations (if used), testing frequency, results (including false positive and false negative rates), follow-up, and outcomes.***

It was further recommended that population-based screening programs for colorectal cancer in individuals between the ages of 50 and 74 be adopted on a province by province basis depending upon available resources. It was agreed that an unrehydrated Hemoccult II test, or its equivalent, be used as the entry test initially with an ongoing evaluation of new screening tests as they arose.

In Alberta, statistics show a steady increase in the number of invasive cases of colorectal cancer, with over 1400 new cases being diagnosed in 2002 and 530 deaths - making colorectal cancer second only to lung cancer as the leading cause of cancer deaths. The lifetime probability of developing colorectal cancer is one in 16.4 for women and one in 14.7 for men. Recent estimates indicate that fewer than 20% of Albertans aged 50-74 are being screened. In order to implement the recommendations of the National Committee, the Alberta Cancer Board has hosted an expert panel involving representatives from several disciplines, including representatives from Alberta Health and Wellness and the two large regional health authorities in the province.

To date, the Expert Group that was created to develop a working model of a screening program has accomplished the following:

- ***Developed background documents including a proposed model for a screening program;***
- ***Held meetings to look at topics such as recommendations for screening, components of other screening programs and different screening tests;***
- ***Held discussions with gastroenterology groups in Alberta;***
- ***Held meetings with Statistics Canada staff regarding POHEM data;***
- ***Contacted other groups working on colorectal cancer screening pilots in order to obtain information on aspects of their screening programs; and***
- ***Initiated development of a database.***

Next steps will depend on the availability of adequate financial resources, an increase in diagnostic and human resources and promotion of the program in the population at large. It was acknowledged that Alberta is in a good position compared to some other provinces with respect to provincial funding commitments. It is anticipated that other provinces will benefit from the lessons learned during the roll-out of a pilot program in Alberta.

Dr. Linda Rabeneck, Toronto Sunnybrook Regional Cancer Centre, Canada

"Colorectal Cancer Screening in Ontario"

Highlights of the Presentation and Discussion

There is huge burden of disease in Ontario with almost half the cancer cases in the country being in this province. In 2005, for example, there were 7,500 new cases of colorectal cancer and 3,050 deaths. These numbers have a significant impact on health care resources with over 100,000 hospital bed days in 2001 for colorectal cancer as compared to around 20,000 each for prostate and breast cancer. Despite the recommendation by Health Canada in 2002 that all individuals over age 50 years should have a FOBT test every two years, the reality for Ontarians is that only about 20% of the population actually has any kind of screening test and there are no organized screening programs, so uptake of screening is low. Only about 6% have endoscopic tests (colonoscopy or flexible sigmoidoscopy). The current challenge for Ontario is that, of the 2.8 million people in the 50-74 year age range, less than 20% are being screened and there is inadequate capacity to offer colonoscopy as the initial screening test for those at average risk. A study by the Institute for Clinical Evaluative Sciences (ICES) on patterns of colonic evaluation procedures in Ontario from 1992-2001 revealed that there has been an increase in the rate of colonoscopies for both men and women but overall, the proportion screened is very low. In terms of distribution across the province, analysis shows that many more colonoscopies are performed in small, community hospitals than in the large teaching hospitals.

In March 2006, Toronto launched a program to train nurses to perform flexible sigmoidoscopy. This technique can be performed as an office procedure, requires no sedation, and has an easier preparation and lower perforation rate than colonoscopy. So far the program has trained six nurses at two sites in Toronto. In addition, the report from a one-year pilot project on FOBT has recently been submitted to the Ministry of Health and Long-Term Care (MOHLTC) with a request for funding for a provincial FOBT screening program. The design of the program is similar to that in the UK with a central program office, regional offices and colonoscopy hubs.

There are also plans for linked information systems and quality assurance and ongoing monitoring of participation rates, positivity rates, referral rates, adverse events and evaluation of outcomes.

The primary barrier to full implementation of a screening program in Ontario is a funding commitment from the MOHLTC.

Members of the Clinical Research Group discuss current colorectal screening tools

Break-out Session and Plenary Reports

Participants were asked to align themselves with one of three smaller working groups to discuss, in more depth, the research questions around colorectal cancer screening and the opportunities for advancing a national colorectal cancer screening program in Canada. The groups were: Basic/Biomedical; Clinical; and Population /Health Services. Following the working group sessions, participants were asked to re-convene and present the results of their discussions and any recommendations to the whole group.

Potential Funding Tools

Prior to the break-out sessions, Dr. Judith Bray, Assistant Director of the CIHR Institute of Cancer Research took a few minutes to describe some of CIHR's funding mechanisms to the group. (details on these programs can be found in Appendix 4). Participants were asked to consider the suitability of these various programs in addressing the research questions identified in the small group sessions.

Reports from Break-out Groups

Population / Health Services Group

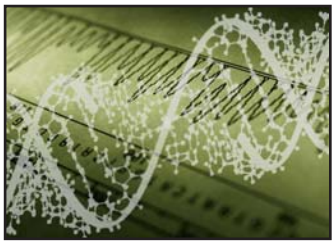
Facilitator: Angela Brooks-Wilson

Participants: Angela Brooks-Wilson, Jean Marie Berthelot, Heather Bryant, Andy Coleman, Neil Haslam, Desmond Leddin, Amy Lerman-Elmaleh, Julian Little, Deborah Marshall, Elizabeth McGregor, Gail McKewown-Eyssen, Howard Morrison, Larry Paszat, Brenda Payne, Paul Ritvo, Maida Sewitch, Hartley Stern

Presentation:

The presentation from this group focused on the following areas:

- *Determination of the best tests:*



Currently there is little definitive evidence on which screening tests are best and with new technologies and genetically based tests becoming available the baseline is constantly shifting. Research on new markers and screening methods is needed and also on the effectiveness of the various tests by disease stage and the order in which they should be delivered. An overriding principle should be the development of tests that do the least possible harm to the individual.

- *Implementation of Tests:*

Research is required on the feasibility of available tests, particularly those requiring stool samples. Some tests may simply not be implementable at a provincial or national level because of a lack of public and political acceptance and inadequate resources. Any screening program should be highly flexible in order to incorporate new techniques and technologies as they evolve and should be tailored to individual risk. Colonoscopy, as a screening test, has not been evaluated, in Canada, by randomized controlled trials nor has it been compared with other imaging methods such as virtual colonoscopy and flexible sigmoidoscopy.

- *Behaviour*

Knowledge translation research is needed to identify the kind of information required by the public, health care workers and government bodies and the best way to deliver this information to encourage maximum uptake of available screening tests. The current information disseminated by advocacy groups and physicians should be evaluated for effect, content and complexity.

- *Economic Evaluation*

Research is needed on how to design programs that could evaluate changes in technology and relate it to budget impact and health economics, i.e. cost effectiveness vs. utility.

- *Capacity building*

It was noted that capacity building is needed across the spectrum including primary care physicians, radiologists, imaging personnel, lab services etc. Training programs that focus on alternate labour sources such as non-medical personnel might provide one solution to the resource problem.

The group recommended multidisciplinary team programs that could build networks and capacity (such as the Emerging Team Grant program) and lead eventually to clinical trials to compare and evaluate different screening tests, or to further knowledge in population-based implementation of the technologies currently known to reduce mortality. There was also support for the Partnerships in Health System Improvement program (PHSI) as a way to involve provincial centres and health services researchers and administrators. For new imaging modalities, the Collaborative Health Research Program (CHRP) operated by CIHR and NSERC might be an effective way to access new discoveries in the physical sciences and apply them in imaging, e.g. virtual colonoscopy.

Basic /Biomedical Research Group

Facilitator: Ian Smith

Participants: Philip Branton, Steven Gallinger, Doug Horsman, John McLaughlin, Ian Smith, Barry Stein, Isabella Tai

Presentation:

This group focused on research to improve screening methods and usage in colorectal cancer and pre-cancerous disease (polyps). Emphasis was placed on evaluation of novel biomarkers and panels comprised of the new generation of genetically based markers as effective screening tools. It was noted that there is a great deal of activity currently in this area through the international biomarker initiative led by Lee Hartwell in Seattle. It was suggested that perhaps Canada could join this initiative with a focus on colorectal screening targets. Closer to home, the Ontario Cancer Research Network (OCRN) has also initiated a biomarker network that has some links to Lee Hartwell's. It was pointed out that one of the biggest obstacles in screening new markers is access to samples - blood and fecal - and the corresponding tumour tissue. Ideally Canada needs a tissue repository similar to that created for the Canadian Tumour Repository Network (CTRNet), funded by ICR, that is linked to comprehensive patient data. However collection of stool and tumour samples does not have the 'glitzy' aura of an exciting research project and it takes time - perhaps too much time to appeal to a researcher in the early career path who needs rapid results.

The group suggested that in order to bring research teams together some infrastructure would be required that provided links to the existing tumour network. Emphasis should be placed on sample collection including polyps, mucosa, blood, stool, serum and tumours. This could be best accomplished at a major hospital centre. It was proposed that up to $500,000 would be required per team and that there might already be existing groups working in other areas that could turn their attention to colorectal screening.

Dr. Dan Sadowski presented discusssions from the Clinical Research Group

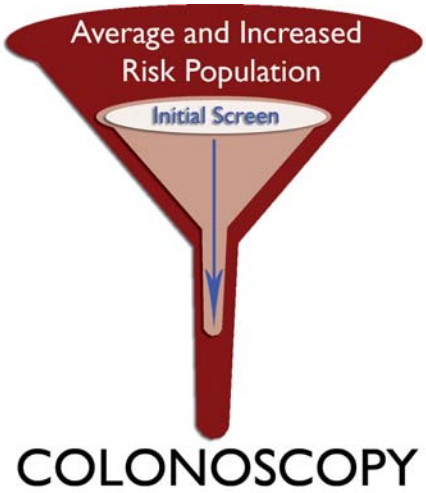
Clinical Research Group

Facilitator: Neil Berman

Participants: Neil Berman, Bob Hilsden, Rachel Jiang, Bernard Levin, Jacob Louw, Paul Moayeddi, Perry Pickhardt, Linda Rabeneck, Nancy Baxter, Terry Rooney, Dan Sadowski

Presentation:

This group emphasized the importance of being able to stratify the population into risk categories by understanding the biology and natural history of polyps. A biomarker test that could discriminate between 'benign' and 'dangerous' polyps would be ideal. Basic research is needed on the biological determinants that predispose a polyp to progress to cancer. Follow-up of polyps using an endoscopic approach however would take too long and it is doubtful that the average length of a research grant (3-5 years) would be adequate to observe and evaluate changes. Ethics approval might also present a challenge.



Concern was expressed about using colonoscopy, which is a therapeutic test, as a screening test. Better screening tests are needed that can stratify patients in terms of risk, reducing the need for unnecessary interventions. However none of the currently available stool-based screening tests have adequate specificity and sensitivity and it is hard to predict if or when new biomarkers may become available. It was suggested that prospective collection of material and population-based data was needed so as to be ready for analysis when technology catches up. Obtaining ethics approval might prove to be a barrier to this kind of study however. The idea of RCTs to evaluate pre-screening tests and colonoscopy was dismissed as being too expensive and too long-term for the current funding opportunity. An RCT also requires large numbers of patients and given the current lack of resources it might be unethical to offer RCTs if colonoscopies cannot be offered to everyone.

Attention was drawn to natural experiments already happening in the country, such as the pilot studies described in Alberta and Ontario. It would make sense to take advantage of these experiments by building-in a research component and gathering all the information together.

The group recommended that any projects in the clinical area should be large collaborative ones, such as the Emerging Team Program that might lead to future RCTs. Pilot Projects could be appropriate for studies on quality assurance, information issues, safety and cure maps for example.

Recommendations and Next Steps

Dr. Heather Bryant very briefly summarized the group presentations and explained the next steps. An RFA will be launched by ICR in June 2006. Based on the recommendations from the three break-out groups, it is likely that the primary funding tool will be the Emerging Team Grant. Applications will be eligible from any relevant and original research area that is likely to lead to improvements in colorectal cancer screening Potential applicants will be strongly advised to consult the report from this workshop for information on the discussions that took place and the recommendations that came out of it before preparing an application. One of the primary objectives of this initiative will be to indicate how to implement currently available technologies at a population level in order to reduce colorectal mortality as soon as possible in Canada. Another critical objective is to develop screening tests for colorectal cancer that are capable of stratifying patients into low and high risk groups and do minimal harm in the process. It is hoped that the results of some of the funded projects will lead to large RCTs, perhaps to compare different screening modalities. It will be important that applicants clearly indicate in their application the way in which their proposed research provides impact, reduces harm and adds significantly to the body of current research in a new way.

It is also possible that, contingent on available funds, this area of research might be included in a subsequent launch of the PHSI and CHRP programs to facilitate implementation of research results and engage relevant partners.

Appendix 1 - Workshop Agenda

Colorectal Cancer Screening Workshop

Location: Sheraton Gateway, Toronto International Airport (Terminal 3)
Room: Zermatt Room

Participants: Nancy Baxter, Neil Berman, Jean-Marie Berthelot, Erik Blache, Philip Branton, Judith Bray, Angela Brooks-Wilson, Heather Bryant, Andy Coldman, Amanda Devost, Steven Gallinger, Neil Haslam, Bob Hilsden, Mary Hodges, Doug Horsman, Rachel (Yuchong) Jiang, Desmond Leddin, Amy Lerman-Elmaleh, Bernard Levin, Julian Little, Jacob Louw, Deborah Marshall, Elizabeth McGregor, Gail McKeown-Eyssen, John McLaughlin, Paul Moayyedi, Howard Morrison, Lawrence (Larry) Paszat, Brenda Payne, Perry Pickhardt, Linda Rabeneck, Paul Ritvo, Terry Rooney, Daniel Sadowski, Maida Sewitch, Ian Smith, Barry Stein, Hartley Stern, Isabella Tai

Time	Agenda Item	Location
8:00 - 8:30	**BREAKFAST**	Zermatt Foyer
8:30 - 8:40	*Philip Branton & Heather Bryant* Welcome and Introductions: 1) Aim of the workshop is to generate ideas by the end of the day in order to stimulate research in this field 2) Format for the day	Zermatt Room
8:45 - 9:05	*Bernard Levin* Topic: What are pressing Research Questions to Advance Colorectal Cancer Screening ?	Zermatt Room
9:10 - 9:30	*Neil Haslam* Topic: Cancer Screening Programmes: NHS Bowel Cancer Screening Programme	Zermatt Room

Appendix 1 - Workshop Agenda

CIHR IRSC

Colorectal Cancer Screening Workshop

Time	Agenda Item	Location
9:35 - 9:55	*Perry Pickhardt* Topic: Key research Questions in Colorectal Cancer Screening: Imaging Perspective	Zermatt Room
9:55 - 10:15	**BREAK**	Zermatt Foyer
10:15 - 10:35	*Steven Gallinger* Topic: DNA Testing for Colorectal Cancer and Polyps, How Far are we away?	Zermatt Room
10:40 - 10:55	*Heather Bryant* Topic: CRC Screening Overview Canada/Alberta	Zermatt Room
11:00 - 11:15	*Linda Rabeneck* Topic: Colorectal Cancer Screening in Ontario	Zermatt Room
11:20 - 11:30	*Judith Bray* Topic: Examples of types of grants as background to discussions	Zermatt Room
11:30 - 11:40	*Linda Rabeneck* Small groups and format for the discussions	Zermatt Room
11:40 - 12:40	**LUNCH**	Zermatt Foyer
12:40 - 1:40	Small group discussions	Group A: Rm 344 Group B: Rm 346 Group C: Zermatt
1:40 - 2:00	**BREAK**	Zermatt Foyer
2:00 - 2:30	Reports from the small groups	Zermatt Room
2:30 - 4:10	*Linda Rabeneck & Heather Bryant* Large group discussion	Zermatt Room
4:10 - 4:25	Summary	Zermatt Room

Appendix 2 - Workshop Participants

Colorectal Cancer Screening Workshop

Toronto, ON ~ March 28, 2006

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Appendix 2 - Workshop Participants

Colorectal Cancer Screening Workshop

Toronto, ON ~ March 28, 2006

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Colorectal Cancer Screening Workshop

Toronto, ON ~ March 28, 2006

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Appendix 2 - Workshop Participants

Colorectal Cancer Screening Workshop

Toronto, ON ~ March 28, 2006

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Members of the Organizing Committee
Speakers

Appendix 3 - Speaker Biographies

Colorectal Cancer Screening Workshop

Speakers Biographies

Philip E. Branton, Ph.D.

Scientific Director, Institute of Cancer Research, Canadian Institutes of Health Research
Gilman Cheney Professor of Biochemistry, McGill University; Fellow of the Royal Society of Canada

Phil Branton obtained his Ph.D. in 1972 in Medical Biophysics at the Ontario Cancer Institute, University of Toronto. Following post-doctoral studies at MIT with Phillips W. Robbins he became an Assistant Professor in the Department of cellular biology at the University of Sherbrooke. In 1975 he moved to the Cancer Research Group at McMaster University where he became Associate and then Full Professor of Pathology, and in 1987 he was named the Group's Coordinator. He moved to McGill University as Chair of the Department of Biochemistry (1990-2000), and in 1996 was named Gilman Cheney Professor of Biochemistry. In December, 2000 he was named the first Director of the Institute of Cancer Research of the CIHR and was made a Fellow of the Royal Society of Canada in 2002. He has served many agencies in Canada, the USA and Europe in several capacities, and has been a highly productive cancer researcher. He is co-Founder of GeminX Biotechnologies Inc. of Montreal, and is known for basic research on viruses, cell death and tumour suppressors, and for applied work on new cancer therapies.

Heather Bryant

Chair of the Institute of Cancer Research Advisory Board
Clinical Professor, Departments of Community Health Sciences and Oncology, University of Calgary

Heather Bryant studied medicine at the University of Calgary, and took her first residency certification in family medicine followed by a Fellowship in Community Medicine and Ph.D. in epidemiology at the University of Calgary. She is now Vice President and Chief Information Officer (C.I.O.) of the Alberta Cancer Board and Director of the Division of Population Health and Information. She oversees the Cancer Registry, screening and prevention programs, and an active research unit in cancer epidemiology and prevention, as well as leading the electronic health record implementation for the ACB. Dr. Bryant has been active on many national committees, and chaired the National Committee on the Breast Cancer Screening Initiative (Health Canada), the Advisory Committee on Cancer Control (National Cancer Institute of Canada), the Population Health Committee (Medical Research Council), and the National Colorectal Cancer Screening Committee for a number of years; she currently chairs the Institute Advisory Board for the Institute of Cancer Research for CIHR (Canadian Institutes for Health Research). She is also a Clinical Professor in the Departments of Community Health Sciences and Oncology at the University of Calgary.

Bernard Levin

Professor of Medicine and Vice President for Cancer Prevention
The University of Texas, M.D. Anderson Cancer Centre

Dr. Levin earned his medical degree in 1964 from the University of the Witwatersrand Medical School in Johannesburg, South Africa. He moved to Chicago for an internal medicine residency and then completed a research fellowship in biochemistry in the Department of Pathology and a clinical fellowship in gastroenterology at the University of Chicago. He held academic appointments at the University of Chicago from 1972 until 1984, when he joined the faculty at the University of Texas M. D. Anderson Cancer Center. He served as chairman of the Department of Gastrointestinal Medical Oncology and Digestive Diseases until 1994 before assuming his role in Cancer Prevention as Vice-President, a newly created position for the Cancer Center. The Division of Cancer Prevention at M. D. Anderson comprising four Departments, has grown to one of the most comprehensive programs of its

Appendix 3 - Speaker Biographies

Colorectal Cancer Screening Workshop

Speaker Biographies

kind in the USA, embodying innovative interdisciplinary research in molecular epidemiology, chemoprevention, behavioral science and health disparities research.

Dr. Levin was the first recipient of the Betty B. Marcus Chair in Cancer Prevention, which was established to promote professional excellence in cancer prevention. He is included in "Who's Who in America" and has been listed in "The Best Doctors in America" since 1993. In 2001, Dr. Levin was the recipient of the Partners in Courage Achievement Award - American Cancer Society (Houston Unit) and the American-Italian Cancer Foundation Award for Scientific Excellence in Medicine. In 2004, Dr. Levin was the recipient of the Emanuel G. Rosenblatt Award for Scientific Achievement - Israel Cancer Association and the American Society of Clinical Oncology/American Cancer Society Award. In May 2005, he received the Masters Award in Gastroenterology from the American Gastroenterology Association.

Dr. Levin has published more than 252 articles, and edited 10 books. He served as an editor of Prevention and Early Detection of Colorectal Cancer, which was published in 1996 and Colorectal Cancer in Clinical Practice: Prevention, Early Detection and Treatment which was published in 2002 with a second edition of the book that was published in 2005. He is co-editor of the textbook Gastrointestinal Oncology published in 2002 and a second edition will be published in late 2006. He is lead editor of a new book entitled "American Cancer Society's Complete Guide to Colorectal Cancer" that was published in Dec, 2005. He currently serves on the editorial board of the Journal of the National Cancer Institute, and Cancer Epidemiology, Biomarkers & Prevention.

Dr. Levin is chair of the American Cancer Society's National Advisory Task Force on Colorectal Cancer and was chair of the National Colorectal Cancer Roundtable from 1998-2005. He serves as a consultant to the National Cancer Institute and as an investigator on NCI-funded research programs. He co-chaired the NCI's Program Review Group on Colorectal Cancer and currently serves as chair of the Network Consulting Team for the Early Detection Research Network. Dr. Levin is Co-PI for the Multinational PRESAP Trial, sponsored by Pfizer, to evaluate the role of a specific cyclooxygenase-2 inhibitor in the prevention of sporadic adenoma recurrence. He served as chair of the American Society of Clinical Oncology's Committee on Cancer Prevention from 2002-2004 and also served as a committee member on the UT Task Force on Prevention in 2004. Dr. Levin will serve as President of the International Society of Gastrointestinal Carcinogenesis from 2005-2006.

Dr. Levin's research interests include seeking molecular markers for detection of colorectal cancer, chemoprevention of colorectal adenomas and better methods for enhancing public awareness of colorectal cancer prevention.

Neil Haslam

Consultant Physician and Gastroenterologist,Greater Manchester, Clinical Lead for Endoscopy

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Neil qualified as a doctor in 1988 from of Manchester University Medical School. Following general training he moved to Bristol and the South West of England as a Gastroenterology trainee. He completed his 12 year period as a trainee and was appointed Consultant Physician and Gastroenterologist at Bury General Hospital.

In five years at Bury he has developed his interest in Endoscopy training becoming a Faculty member of the Mersey School of Endoscopy as well as establishing Bury as an independent training centre.

Neil was appointed as Greater Manchester Strategic Health Authority Clinical Lead for the Endoscopy Programme in 2003. He has worked closely with the Bowel Cancer Screening Programme helping develop a quality assurance framework for the roll out of screening in 2006.

Neil is currently on a four month career break snowboarding in Fernie, BC.

Appendix 3 - Speaker Biographies

Colorectal Cancer Screening Workshop

Speaker Biographies

Perry J. Pickhardt

Associate Professor of Radiology, Abdominal Imaging Section, University of Wisconsin Medical School

Dr. Perry J. Pickhardt graduated from the University of Wisconsin-Madison, his hometown school, in 1991 with a B.S. in Physics (class rank: 1 out of 3,274). Beginning in 1991, Dr. Pickhardt attended the University of Michigan Medical School on the HPSP Scholarship Program and graduated in 1995 (Hewlett-Packard Award as a top 5 graduate). From 1995-1999, he was a resident in diagnostic radiology at the Mallinckrodt Institute of Radiology at Washington University in St. Louis. During his residency, Dr. Pickhardt co-edited a textbook on body CT and published a number of scientific papers and book chapters. During the next four years after residency training, Dr. Pickhardt served in the U.S. Navy, spending one year as the Department Head of Radiology, U.S. Naval Hospital Guantanamo Bay, Cuba and three years as the head of GI-GU Imaging at the National Naval Medical Center in Bethesda, MD (twice named Teacher of the Year). He also served as an Assistant Professor of Radiology at the Uniformed Services University of the Health Sciences in Bethesda. Among other projects at NNMC, Dr. Pickhardt organized a large multi-center screening trial evaluating CT colonography (virtual colonoscopy) and served as the PI. Among other awards and honors, Dr. Pickhardt completed a Figley Fellowship at the AJR Editorial Office in Winston-Salem, NC in 2002.

Dr. Pickhardt joined the Abdominal Imaging Section at the University of Wisconsin Medical School in 2003 as an Associate Professor of Radiology. CT colonography and colorectal cancer screening continue to be Dr. Pickhardt's primary clinical and research interests. His work has resulted in over 100 scientific publications, 6 book chapters (with more in press), and 1 text book (with another in progress).

Steven Gallinger

Senior Investigator, Samuel Lunenfeld Research Institute, Mount Sinai Hospital
Professor, Department of Surgery, University of Toronto

Dr. Steven Gallinger is a Senior Investigator in the Program in Molecular Biology and Cancer at the Samuel Lunenfeld Research Institute (SLRI) of Mount Sinai Hospital (MSH), and Professor in the Department of Surgery at the University of Toronto. He is also Co-Director of the Fred A. Litwin Centre for Cancer Genetics, SLRI. Dr. Gallinger is an active Staff member in Surgical Oncology, Princess Margaret Hospital, Toronto General Hospital, and General Surgery, Mount Sinai Hospital.

Dr. Gallinger's research interests' center on studying both inherited and acquired molecular aspects of gastrointestinal cancer. His group is well known for work on the prognostic and predictive features of microsatellite instability in colorectal cancer.

Dr. Gallinger is Head of the Ontario Familial Colorectal Cancer Registry (OFCCR), which collects data and tissue samples from approximately 2,000 colorectal cancer patients, and family members, across the province.

Appendix 3 - Speaker Biographies

Colorectal Cancer Screening Workshop

Speaker Biographies

Linda Rabeneck

Regional Vice President, Cancer Care Ontario
Vice President, Toronto Sunnybrook Regional Cancer Centre

Linda Rabeneck, MD, MPH, FRCPC, is Regional Vice President, Cancer Care Ontario, and Vice President, Toronto Sunnybrook Regional Cancer Centre. Dr. Rabeneck, who is Professor of Medicine and Professor of Health Policy, Management and Evaluation at the University of Toronto is the former Director of the Division of Gastroenterology at the University of Toronto. Dr. Rabeneck is a Senior Scientist at the Institute for Clinical Evaluative Sciences (ICES) in Toronto and is a Senior Investigator with the Cancer Quality Council of Ontario (CQCO).

Dr. Rabeneck received her undergraduate and medical degrees at the University of British Columbia, where she also completed her residency training in Internal Medicine. Dr. Rabeneck received her Gastroenterology training at the Universities of Toronto and British Columbia. She spent the first 7 years of her career in full-time private practice in Gastroenterology at St. Paul's Hospital in Vancouver, BC. Because of her interest in clinical investigation, she closed her successful practice in 1988 to pursue formal research training. From 1988-90 she trained under the mentorship of Dr. Alvan Feinstein as a Robert Wood Johnson Clinical Scholar at Yale University School of Medicine in New Haven, CT, where she received her MPH degree. From the fall of 1990 until her move back to Canada in the spring of 2002, Dr. Rabeneck served on the full-time faculty at Baylor College of Medicine in Houston, Texas, where she held joint appointments in the Sections of Gastroenterology and Health Services Research. While in the US Dr. Rabeneck received funding from the National Institutes of Health (NIH) and the Department of Veterans Affairs (VA) to support her research. Dr. Rabeneck's major research interest is colorectal cancer screening, for which she currently holds CIHR funding. Dr. Rabeneck has served the professional societies and funding agencies in various capacities including the Editorial Board of Gastroenterology, the Board of Trustees of the American College of Gastroenterology (ACG), the Scientific Advisory Committee of the Glaxo Institute for Digestive Health (GIDH), and NIDDK Special Committee C, an NIH study section.

Appendix 4 - CIHR Funding Options

Colorectal Cancer Screening Initiative
CIHR Funding Options

CIHR Team Grants

The objective of the CIHR Team Grant program is to strengthen Canadian health research by supporting teams of talented and experienced researchers conducting high-quality research and providing superior research training and mentorship. The program emphasis is on the production of new knowledge, and the translation of research findings into improvements in the health of Canadians and the Canadian health care system. These results will be realized more rapidly and more efficiently through the CIHR Team Grant program than if the components were to be funded as a series of separate operating grants. There is no upper limit on the amount requested, but only applications of exceptional merit and scope will receive over $2 million per year. CIHR Team Grants program will provide support for a maximum duration of five years. The final 2 years of funding are subject to a satisfactory progress review in the third year of funding. ***The next opportunity for this tool will be launched in June 2006.***

Collaborative Health Research Projects (CHRP)

The CHRP program supports focused collaborative research projects involving any field of the natural sciences and engineering and the health sciences. It represents a collaboration between the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council. Successful projects will lead to health benefits for Canadians, more effective health services, or economic development in health-related areas. The proposed projects may range from fundamental knowledge creation to research on knowledge application relevant to industry or public policy. The objectives of the CHRP program are to:

- Translate the research results to end users/stakeholders;
- Encourage the NSERC and CIHR communities to collaborate and integrate their expertise and research activities;
- Advance interdisciplinary research leading to knowledge and technologies useful for improving the health of Canadians;
- Train highly qualified people in collaborative and interdisciplinary research of relevance to health.

The participation of two or more independent researchers with complementary expertise is required. Team composition must include expertise in the natural sciences and engineering, and in the health sciences. New and genuine collaborations between researchers in the natural sciences and engineering and medical researchers, clinicians, social scientists, and humanists are strongly encouraged. Typically, support will be for up to three years for defined projects with milestones, a beginning, an end, and clear decision points. The average annual award of during the last competition was $116,304. *The next* ***deadline for letter of intent submission is in May, 2006.***

Emerging Team Grants

This program is intended to fund the creation or development of research teams undertaking collaborative research relevant to a significant health problem or issue. Eligible teams will consist of at least three independent investigators who will form an integrated and effective research team and who have not worked together on the same problem or issue for more than five years. It is expected that this grant will enable such teams to build capacity and add expertise, develop strategies for knowledge translation, provide superior training and mentoring environments and achieve research excellence, so that at the end of the funding period they are competitive for funding through other major funding competitions. Funding for Emerging Team Grants is for a period of up to five years. The maximum amount of funding will not exceed $500,000 per application. Funding is subject to a satisfactory review of progress before the end of the third year. Emerging Team grants are non-renewable. ***This opportunity is launched every year in June.***

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Operating Grants

An operating grant provides support for a research project by an individual or small group of investigators. The objective is to support the highest quality investigator-initiated health research projects, in any area of health research. These grants cover supplies, technical assistance, small items or equipment, specialized services, and stipends for research trainees. Grants will usually be awarded from two to five years. ***Deadlines for registration are in August and February.***

Partnerships for Health System Improvement (PHSI)

The purpose of this initiative is to support teams of researchers and decision-makers interested in conducting applied health research useful to health system managers and/or policy makers over the next two-to-five years. More specifically, successful applicant teams will conduct health services, systems and policy research projects of up to three years in length, in thematic areas identified as high priority in recent national consultations conducted by the Institute of Health Services and Policy Research (IHSPR), Canadian Institutes of Health Research (CIHR) and its partners.

The maximum CIHR contribution to each project is $150,000 over the life of the project (up to a maximum of 3 years). Applicants are required to find matching funding (though a 1:1 funding ratio is the acceptable minimum, there is no limit on partner contributions that can be applied to a project). This funding mechanism is a good vehicle for knowledge translation. ***This opportunity is launched every year in October.***

Pilot Project Grants

Pilot Project grants support innovative, high risk, pilot or feasibility research. Grants will allow investigators with novel ideas and observations to conduct pilot studies and /or gather evidence necessary to determine the viability of new research directions. It is anticipated that applicants who validate their pilot hypothesis will then continue their research by applying to regular funding opportunities. Funding for Pilot Project grants will be provided for a period of up to two years. The maximum amount of funding will not exceed $100,000 per application. ***This opportunity can be launched in December or June.***

Randomized Control Trials

A randomized controlled trial (RCT) is an experiment in which investigators randomly assign eligible subjects (or other units of study, e.g. classrooms, clinics, playgrounds) into groups to receive or not receive one or more interventions that are being compared. The results are analyzed by comparing outcomes in the groups. Applications will be examined for the relevance of the question posed, and the appropriateness of the methodology and of gender representation in the study design and selection of research subjects. ***Deadline dates for Outline submission: August 1, October 1, January 15, and March 1.***

CIHR IRSC

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