



Gastrointestinal Cancer Update

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July 2006
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NATIONAL BOWEL CANCER SCREENING
PROGRAM: STARTING SOON

SCREENING FOR HNPCC BY IHC
TESTING IN EARLY AGE ONSET CRC

Q&A ON THE DHS INTEGRATED
CANCER SERVICES (ICS)

COLORECTAL CANCER FAMILY REGISTRY

ASCO MEETING REPORT

Produced by the Gastrointestinal Cancer Committee
of the Victorian Cooperative Oncology Group
Centre for Clinical Research in Cancer



GASTROINTESTINAL CANCER UPDATE

July 2006

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CONTENTS

Editorial	3
National Bowel Cancer Screening Program: Starting Soon	4
Participant's Screening Pathway	5
Prevention the best cure for bowel cancer	6
Screening for HNPCC by immuno-histochemistry testing for loss of mismatch repair proteins in early age onset colorectal cancer	7
Clinical Practice Guidelines on Familial Aspects of Cancer	8
Questions and Answers on the DHS Integrated Cancer Services (ICS)	9
The Colorectal Cancer Family Registry: An International Resource for Studying the Genetic and Molecular Epidemiology of Colorectal Cancer	14
Book available to families with a family history of colorectal cancer	20
Report of the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO)	21
TROG 01.04	24
The Sir Edward Dunlop Clinical Research Fellowship	25
Dunlop Fellowship: Development of Targeted Therapies for Cancer	25
Report of The Cancer Council Australia	27
Clinical Oncological Society of Australia (COSA) Report	28
The National Cancer Control Initiative (NCCI) Report	29
Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer (2nd Ed)	30
Australian Cancer Network (ACN) Activities	30
Cancer Council Events Calender	30
Key Published Articles Listing—Gastrointestinal Cancer	31
Key Published Articles Listing—General	31
Forthcoming Meetings	32

This newsletter is produced by The Cancer Council Victoria's Gastrointestinal Cancer Committee and sent to health professionals interested in management of gastrointestinal cancer(s). The Victorian Cooperative Oncology Group's advisory committees on breast, gynaecological, lung, skin and urological cancers also produce twice yearly cancer updates.

If you would like to have your name removed from the distribution list, or if you are interested in receiving any of the other updates please contact Mrs Noellyn Ngo, Ph: (03) 9635 5265.

* * * * * **Last Issue – No. 45 – December 2005** * * * * *

The articles in the Gastrointestinal Cancer Update have been published to contribute to professional debate and exchange. The opinions expressed are not necessarily those of The Cancer Council Victoria.

Editorial

*Mr Ian Faragher
Surgeon
Western Hospital*

*Mrs Susan Fitzpatrick
Executive Officer, CCRC-VCOG
The Cancer Council Victoria*

This issue is bursting with a number of excellent articles on colorectal cancer and other informative pieces.

The first, heralds the much-awaited introduction of FOBT screening – the first population-based early detection program for bowel cancer in Australia. Fin Macrae discusses the issue of consent for testing tumours for MMR proteins in CRC patients <50years of age, and potential for a hereditary bowel cancer diagnosis. Fin is to be congratulated on the recently published book for patients and families that simply answers questions about the hereditary nature of colon cancer. And, still on family cancer, Mark Jenkins describes the Colon Cancer Family Registry, a multi-national consortium, which has enrolled over 12,000 families.

Jeremy Shapiro has written a detailed report from ASCO, covering the leading presentations in GI cancer. And a summary of the complete accrual for the “RCT of preoperative radiotherapy for stage T3 adenocarcinoma of the rectum” is provided by Sam Ngan, PI for this TROG trial.

The guidelines for the management of colorectal cancer (2nd edition) are now available (see reference on page 29).

Elise Davies, provides an insight into the Integrated Cancer Services and the resources behind the development of this new structure for cancer services in Victoria.

Grant McArthur acknowledges the support by The Cancer Council Victoria’s Sir Edward Dunlop Clinical Research Fellowship, and provides details of his research program.

To conclude this issue there are a number of update pieces from The Cancer Council Australia, COSA and the last adieu from NCCI.

Happy Reading!

Contributions Welcome

The Gastrointestinal Cancer Update welcomes contributions – conference reports, review of an area of interest, reviews of recent journal articles, clinical trial updates.

	Deadline	Issue Date
Mid-year issue	1 June	1 July
Year-end issue	1 November	1 December

Contributions should be forwarded to:

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National Bowel Cancer Screening Program: Starting Soon

*Ms Alison Peipers
Manager, Cancer Education Programs
The Cancer Council Victoria*

Australia will become one of the first countries to introduce organised bowel cancer screening when the Australian Government launches the National Bowel Cancer Screening Program in August this year. Over the next two years nearly a million people will receive a free faecal occult blood test (FOBT) in the mail, as the program invites 55 and 65 year olds to participate in bowel cancer screening. In time, the program will expand to include all Australians aged 55 years and above. Re-screening will occur every two years.

Participants will be asked to take tiny (400mcg) samples from two bowel motions for laboratory testing using a Bayer Detect FOBT. Samples will be analysed by Dorovitch Pathology. People who have samples testing positive for blood will be encouraged to visit their general practitioner (GP) for further investigations, usually colonoscopy.

Health professionals will play a critical role in the program by:

- highlighting the program to those eligible and encouraging participation;
- arranging investigations for patients with positive results;
- returning information to the central register; and
- managing people not involved in the national program.

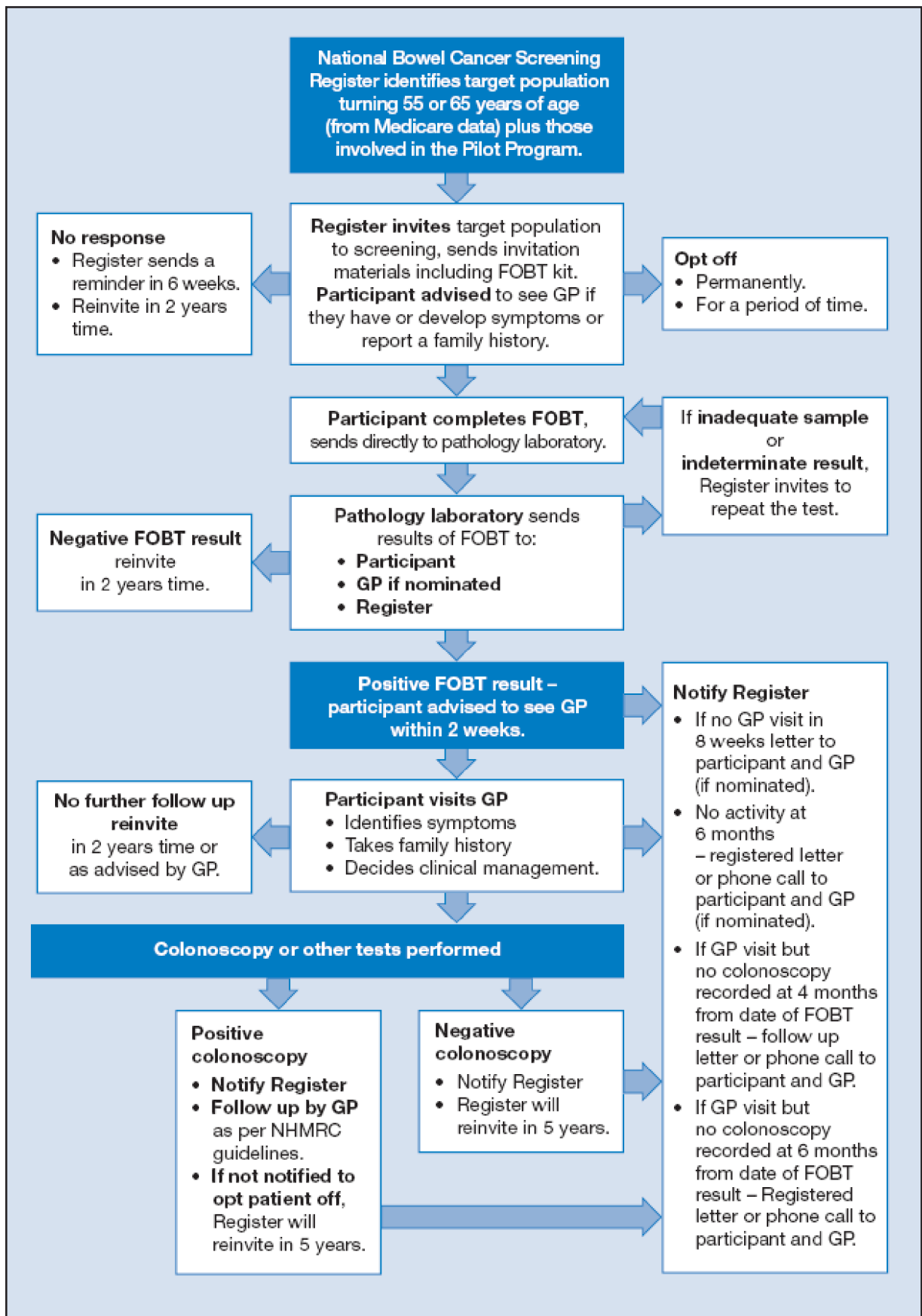
A central National Screening Register will support the program and manage all invitations and reminders, as per the Program Pathway. It is vital for the functioning and monitoring of the program that GPs, endoscopy services and histopathology services dealing with program participants, return information to the central Register.

A Victorian Implementation Plan is currently being developed for the screening program and an information kit will be sent to all general practitioners and endoscopy services before the program begins in their region.

The Cancer Council encourages health professionals to support the new screening program and to begin discussing its implications. Bowel cancer is the second most common cause of cancer-related death in Australia. When fully implemented, this screening program should save 1000 or more lives per year.

Further information on the National Bowel Cancer Screening Program can be found at www.cancerscreening.gov.au/bowel. For information on bowel cancer call the Cancer Information and Support Service on 13 11 20.

Participant's Screening Pathway



National Bowel Cancer Screening Program Information Line – 1800 118 868

Prevention the best cure for bowel cancer

The Cancer Council Victoria Media Release – 5 June 2006

June 5–9 is Bowel Cancer Awareness Week and The Cancer Council Victoria is reminding Victorians that prevention is the best cure for Australia's most common internal cancer affecting men and women.

While more than 12,000 Australians are diagnosed with bowel cancer each year, latest research indicates that many of these cancers could be avoided through simple lifestyle changes.

"By following a healthy diet, being physically active and maintaining a healthy weight range, research indicates that the number of Australians diagnosed with bowel cancer each year could be reduced by almost 25%," says The Cancer Council Victoria's Manager of Cancer Education Programs Alison Peipers.

Research conducted by the International Agency for Research on Cancer shows that 11% of bowel cancer is attributable to overweight and obesity, and another 13–14% is attributable to physical inactivity.

Ms Peipers says that slightly less than half of Australians meet the current physical activity recommendation of 30 minutes of moderate-intensity activity each day. Even less adults do not eat any fruit on a given day—indicating many Australians are either unaware of, or are ignoring the need, to protect themselves against obesity-related health issues such as cancer.

To remind Victorians that simple changes can make a big difference to their risk of bowel cancer, the Cancer Council's *Avoid the Cure* community service announcement will be broadcast on radio and television throughout the month of June.

During Bowel Cancer Awareness Week, the Cancer Council is also reminding Victorians about the importance of early detection of bowel cancer.

"More and more people are surviving cancer and with an early diagnosis, the cure rate for bowel

cancer is around 90%," says Ms Peipers. "So when it comes to bowel cancer, being aware of changes in your bowel actions and conscious of your bowel cancer risk really is a matter of life and death."

While bowel cancer is most common in people over the age of 50, The Cancer Council Victoria recommends that all Victorians watch for warning signs. These signs include blood after a bowel motion, a persistent change in bowel habits, a feeling that the bowel does not empty completely, abdominal pain, unexplained tiredness, weakness, breathlessness or unexplained weight loss.

Bowel cancer survivor and Cancer Connect volunteer John Scott knows all too well the importance of early detection.

"If I had paid attention to the warning signs and discussed them with my doctor sooner, I could have alleviated the pain and suffering both myself and my family have had to endure," said Mr Scott.

"My message is simple—take care of your body, listen to your body and don't be ashamed to talk about bowel cancer symptoms with your doctor. It could save your life."

The Cancer Council also recommends people over the age of 50 participate in regular bowel cancer screening, by using the Faecal Occult Blood Tests (FOBT) that can be accessed through their GP. A national bowel cancer screening program will be phased in by the Australian Government from mid-2006. People turning 55 or 65 will be the first group able to participate in this program and will receive further information about the screening program in the post.

People with a family history of bowel cancer or symptoms associated with bowel cancer should talk to their GP.

For more information on bowel cancer and bowel cancer prevention, call the Cancer Helpline on 13 11 20, or visit www.cancervic.org.au.

Screening for hereditary non-polyposis colorectal cancer (HNPCC) by immuno-histochemistry testing for loss of mismatch repair proteins in early age onset colorectal cancer

Professor Finlay Macrae
Chair, VCOG Hereditary Bowel Cancer Clinical Group
The Cancer Council Victoria

After passing through multiple committees in The Cancer Council Victoria, a policy to endorse routine screening of all patients presenting with colorectal cancer under 50 years of age has been launched to stakeholders. The aim is to ascertain more patients whose colorectal cancer has developed on a background of an inheritable mutation in one of the mismatch repair genes. It can be argued now that such testing is a standard of practice in colorectal oncology. It has substantial potential for identifying other family members at risk for colorectal cancer through predictive DNA testing in appropriate at risk family members. This approach is supported by research done through the Centre for Molecular, Epidemiological, and Genetic Analysis (MEGA) at the University of Melbourne, which identified that half the people with an inheritable mutation did not have a family history of colorectal cancer. A family history of three colorectal cancers over at least two generations, including at least one member diagnosed under 50 years, is the usual trigger for recognition of the possibility of such a mutation, embodied in the Amsterdam criteria (the 3:2:1 rule). Instead, simply early age of onset of the cancer was the signal in the Jenkins et al study. This led to editorial comment in the prestigious *Journal of Clinical Oncology* entitled "**First Amsterdam** (the initial set of criteria used to identify HNPCC), **then Bethesda** (the next internationally agreed criteria used to determine the need for consideration of the possibility of a mismatch repair carrier in an individual) **and now Melbourne** (from the results of the Jenkins et al. study)".

The Jenkins et al. study data is quoted in the Position Statement: A policy of screening all patients presenting with colorectal cancer under 50 years of age for loss of MLH1, MSH2 and

MSH6 (and now in contemporary practice PMS2) would require testing of about 240 cases per annum in Victoria, of which 10–15% would carry a germline mutation. This strategy would capture 80–100% of HNPCC (95% confidence limits of sensitivity) in this age group, which would be the majority of all HNPCC cases in the population. This would represent undeniable cost benefit in overall colorectal cancer management in these families.

The policy has met with some discussion from colorectal surgeons and pathologists, encapsulated by a meeting at The Royal Melbourne Hospital. The concern is around the recommendation that patients should consent to IHC testing before it is done. The RMH meeting minuted the following:

"Discussion focussed on the practicality of consenting patients pre-operatively, given the recommendation that the following statement is included in consent pre-operatively:

'The tissue removed at surgery will be tested by a pathologist for further information about the tumour. If you are under the age of 50 years, this testing may include a particular type of examination that may indicate the possibility of an underlying genetic (inherited) predisposition for your cancer. While this is not a genetic test, this may have implications for you and your family.'

Ian Jones (Head of Colorectal Surgery) expressed the view that this is a difficult call at this time in the patient's progress, and he would have been comfortable with proceeding with the testing without consent at that stage. However, the statement from the Cancer Council makes this not a standard of practice, so some other mechanism would be needed. He was concerned that a two-tier system might emerge – one for public and one for private.

Tony Landgren (Director of Pathology) considered that the duty of the pathologist was to maximise the information that could be obtained from the tumour, which included IHC for MMR proteins regardless of preliminary consent. (This position is shared by world leading pathologist in this domain, Professor Jeremy Jass.) Indeed, it was his practice to proceed with IHC for MMR proteins if there was an indication from histopathological features that the tumour was MMR deficient (TILs, Crohnoid features, mucinous, right sided etc) regardless of age. Professor Landgren considered the recommendation to secure consent inhibited the efficiency and possibly the quality of his practice, given the logistics and cost of addressing the issue on a second (post-consent) occasion. He stated that all pathology testing has genetic and sometimes familial implications, so he was uncertain as to why this particular scenario has been singled out. Many have commented on the familial implications of a standard pathology report of FAP from a colectomy specimen, which has more implications for inheritance than the less specific MMR protein loss. (Note that even for hMSH2, a large Belgium study has reported a 17% false positive rate for germline findings from loss of MSH2 in the tumour.) Tony also commented that the cost of initial testing on the number of cases that would present under 50 years was not an issue, especially as the costs were greater for a second accession to the tumour for post-consent testing.

Finlay Macrae thought that the societal benefits from routine testing of patients with colorectal cancer under 50 years were so strong as to override the weaker case to ensure routine pre-test consent always, given that the test is essentially phenotypic and not a test of inheritance, and given the Belgium data noted above.

Under the constraints of the guideline, it was decided that a process would be implemented at RMH whereby the FCC team would scan the pre-admission lists for colorectal cancer admissions diagnosed under 50 years, and introduce consent at the pre-admission visit, along the lines of the Cancer Council recommendation. This consent would need to be passed on to the pathologists pre-operatively. It was also agreed that MMR positive results would be copied to the FCC to provide a safety net for interpretation and determination of the need for genetic counselling, and germline testing."

It was also agreed at the meeting that there should be continuing discussions aimed at developing a position that did not require such consent pre-operatively, allowing the pathologist uninhibited discretion to do immuno-histochemical testing of the mismatch repair proteins where appropriate, particularly in early age onset colorectal cancer, and where there were recognisable features suggesting mismatch repair deficiency in the tumour.

It should be noted that the Cancer Council Position Statement is a recommendation only; consent practices could be varied according to local consensus, and practicalities. Some clinicians and hospitals in Australia and New Zealand are already performing immuno-histochemistry for MMR protein loss in routine assessment of colorectal cancers, especially where there is early age of onset.

Dr Peter Gibbs has suggested that the Australian Cancer Grid may be utilised to monitor the efficiency of the policy in identifying patients with colorectal cancer across Victoria having mismatch repair protein testing, and for those showing loss, referral to the state's familial cancer centres. This approach has the support of the VCOG Hereditary Bowel Cancer Group.

Participants in the state's Integrated Cancer Service - Colorectal cancer tumour streams are encouraged to address this issue.

Clinical Practice Guidelines on Familial Aspects of Cancer

This document is being developed with Associate Professor Judy Kirk as Chair. It is a revision of a 1999 document. It will be completed late this year. A question of publishing a revised Familial Aspects of Bowel Cancer Guide is being discussed as there is significant demand for it.

Reprinted from Wongi Yabber May 2006; 12(2): 2.

Questions and Answers on the DHS Integrated Cancer Services (ICS)

*Cancer & Palliative Care Section
Department of Human Services Victoria*

Following endorsement of the *Cancer Services Framework for Victoria* in November 2003, five regional and three metropolitan Integrated Cancer Services (ICS) have been established.

The purpose of the ICS is to develop service delivery structures that provide coordinated cancer planning and care provision across specified geographical areas, and to support the delivery of cancer care through the application of agreed best practice frameworks in ten defined tumour streams.

A program of cancer service improvement is being implemented by ICS, funded through the Department of Human Services. Those involved in the breast cancer redevelopment process will be familiar with the concept of funded service improvement initiatives, but for other areas of cancer care, this type of work is quite new.

Progress in establishing new service systems can be challenging and time consuming, and many clinicians are wondering when the results of these initiatives and the funding spent to date will flow on to improvements in care for patients.

Here Elise Davies and the Cancer and Palliative Care Section in the Department of Human Services answer some questions regarding Integrated Cancer Services, and outline plans for the future of cancer care in Victoria.

1. What do you consider to be the most valuable achievements of the first year of the ICS?

In their first year of operation, the main focus for the ICS has been to develop functional relationships between participating health services, to establish representative governance structures and processes for decision-making, to appoint staff to support the work of the ICS, and to map current service provision.

All ICS have appointed a Director (funded on a sessional basis), a Strategic Planner/Program Manager (1 EFT) and project staff (some part time, some full time). In rural regions, a Regional Cancer Nurse Coordinator has been employed (1 EFT).

A comprehensive service mapping process to identify service strengths and gaps has been undertaken. These data have informed the development of a three year Cancer Services Plan for each ICS, which were submitted to DHS in December 2005.

The ICS are establishing local collaborating tumour groups (LCTGs), and have each selected priority tumour streams for their initial focus. This has involved the identification of clinical leaders for each tumour group and a process for the group to advise on and implement the Patient Management Frameworks (championed by the Ministerial Taskforce for Cancer). Tumour groups will provide opportunities for clinical networking, multidisciplinary team development and service development with a tumour specific focus.

2. What have been the major stumbling blocks?

The configuration of some of the ICS has been challenging, with groupings based on geography and population size rather than pre-existing relationships between health services. In some cases, long-standing competition between health services initially constrained the early formation of good relationships. These issues have now been largely overcome, and ICS

Executive Groups are beginning to take up their roles in cancer planning and service improvement.

The authority and accountability of the ICS has been a big issue, with emerging tensions between the status of ICS decisions versus the directions of individual health services within ICS. The reasons for this include competing organisational priorities and pressures on health services, and the variable commitment of stakeholders to the development of a new and sustainable system model in cancer. It also relates in part to the lack of clarity about the permanency of funding for ICS, which has now been resolved (see question 4). Strong clinical and managerial leadership, capable of reaching across organisational boundaries is essential if the ICS model is to flourish. The authority and accountability of ICS will be strengthened in the near future through the establishment of a new Victorian Integrated Cancer Services Committee. This high-level group will oversee statewide ICS activities and directions, and will include health service executive level and senior clinical representation.

3. What do you believe will be achieved during the next 12 months?

The next twelve months will see:

- The establishment of the local collaborating tumour groups (LCTGs) in the priority tumour streams, with translation to other tumour streams. This will initially involve examination of the service mapping data against the patient management frameworks (PMFs), identification of gaps and the prioritisation of service improvement initiatives to be implemented.
- Monitoring implementation of initiatives and outcomes
- Achievement of agreements between health services and health care providers for the provision of the multidisciplinary (MD) approach to cancer care. This will include an increase in MD team formation, MD meetings, development of team protocols and commencement of multidisciplinary team and meeting audit processes.
- Utilising the PMFs, LCTGs will determine agreed optimal referral pathways in priority

tumour streams in their ICS, including the communication mechanisms required between the treatment team (including GP) and the patient.

- The development of multidisciplinary psychosocial and supportive care networks to scope the requirements for a coordinated and collaborative supportive care service within the ICS. This may include identification of referral pathways, determination of protocols to ensure appropriate referral and access, supportive care training for cancer teams, implementation of mentoring and supervision programs across the ICS, shared appointments, etc.
- Commencement of a statewide quality framework that will support service delivery and improvement via tumour streams.

4. It is clear that the funds provided by the ICS programs are non-recurrent and intended for development work. Many BSEP initiatives (supported by similar non-recurrent project funds) have resulted in innovations that no longer exist due to lack of continued funding, because of no ongoing funding by health services. How do you plan to prevent this from happening with the ICS process?

The ICS acknowledge the need to implement service improvements across the system and patient pathway to achieve coordinated quality care. They have also identified that certain ongoing core service improvement roles are critical to ensuring sustainable change and continuing engagement and commitment of key stakeholders.

The Minister for Health has recently approved a package of recurrent funding for ICS, which includes funding to support:

- ICS leadership and management;
- tumour stream development (including the capacity to fund sessional payments for the lead clinicians in each tumour stream);
- MD care coordination and development; and
- initiatives to improve coordination of care.

Funding allocated against these items in 2006–07 is \$1.2 million per metropolitan ICS and \$0.77

million per regional ICS (Total metropolitan ICS = \$3.6 million, total regional ICS = \$3.85 million).

In addition, in 2006–07 the ICS will receive development funds of \$0.25 million (each metro ICS) and \$0.18 million (each regional ICS) to support quality improvement and the development of psychosocial and supportive care models.

DHS will continue to discourage ICS from utilising their change management funds to plug service delivery gaps (such as core nursing or medical staff), which would yield minimal service development and improvement outcomes. For example, the conversion of the metropolitan ICS funding to WIES would equate to approximately 470 WIES to be distributed across a number of health services. Instead, ICS are being encouraged to utilise their program funds:

- to identify opportunities for service improvement;
- to engage health service management in the review and allocation of core inpatient and outpatient funding for cancer services; and
- to develop evidence for funding requirements to address gaps in services.

5. It appears that much of the involvement of medical staff in the ICS program is expected to be donated. What is being done to re-dress this situation?

There are considerable time and management pressures on specialist cancer clinicians. This is particularly evident in regional Victoria where there are limited numbers of medical and radiation oncologists and supportive care oncology workforce to meet increasing demand. In addition, in rural and regional Victoria the majority of surgeons are generalists rather than specialists. The capacity of Regional ICS to establish tumour specific LCTGs is limited, and in some regional ICS one clinical reference group has been established to undertake the work of a LCTG across a number of tumour streams. The ICS have clearly indicated a requirement for funds to support tumour stream development, including project staff to implement service improvement initiatives and remuneration for lead clinicians. Following concerns raised by ICS on their capacity to support the ongoing work

of the LCTGs, each ICS will receive recurrent funding from 06/07 specifically allocated to address the above issues.

6. What is being done to support the provision of basic care to patients (which is clearly considered to be inadequately funded in many situations) to allow clinicians to participate in projects looking at “adding the icing to the cake”?

Improving the provision of basic care to cancer patients is at the heart of all cancer reforms. The ICS initiatives aim to improve service provision through four key outcome areas: implementing MD care, improving care coordination, addressing psychosocial and supportive care needs and reducing variations in care.

The PMFs, which are guides to consistent care, will enable clinicians across the state to review how they can contribute to ensuring that cancer care and delivery of cancer services are coordinated, multidisciplinary, high quality, accessible and equitable for all Victorians with cancer.

The identification of gaps in service delivery will enable quantification of the need for service redesign and additional resources, including the case for further funding.

7. How is the Victorian Cancer Agency expected to contribute to cancer research in Victoria?

The new Victorian Cancer Agency has been funded to build research capacity and to connect research and clinical services through collaborative cancer research networks.

The key functions of the agency are:

- To build and fund cancer research capacity across Victoria, including the development of a comprehensive translational research program.
- To align cancer research and cancer services, and to connect clinical academic and cancer research organisations through the development of collaborative cancer research networks and clinical trials capacity. The networks will comprise of ICS, research

institutes, universities and peak bodies such as the Cancer Council of Victoria.

- To fund and coordinate cancer research development and innovation, including support for new platform technologies and research and development functions such as the Victorian Cancer Research Tissue Bank and the new Australian Cancer Grid.

Establishment of the new Victorian Cancer Agency will commence in 2006–07. The Agency will work closely with ICS to provide a clear alignment between cancer research and cancer services and to foster translational research.

8. Are there plans to provide recurrent funding for MD care and co-ordination of care for health services? Are these to be earmarked for this purpose?

MD care has been a key focus for the ICS and is internationally recognised as best practice for treatment planning and care of cancer patients. The Cancer and Palliative Care Section has developed a MD care toolkit for use by the ICS, and a MD care policy is being developed in consultation with the ICS. Metropolitan ICS have used some of their funding to purchase essential equipment to support MD care development.

From 2006–07 the ICS will be provided with recurrent funds to support MD care development. The Australian Government, through the Australian Better Health Initiative is to introduce an MBS item for multidisciplinary meetings in November this year.

The development of information/data systems to support clinical management of patients including MD care is being progressed through the proposed appointment of a consultant to scope the issues and needs of ICS, for consideration by the Ministerial Taskforce for Cancer.

Recurrent funds have also been made available to the ICS to support care coordination. Care coordination is seen as requiring a whole of system approach that incorporates the system, health service, team and individual health provider and consumer levels, not just the development of care coordination roles. This multifaceted approach recognises the inherent interface of care coordination with other priority

areas and strategies including MD care, the development of routine psychosocial assessment, clinical protocols, referral pathways and information provision. A policy on cancer care coordination is being developed in consultation with the ICS

9. What is envisaged for the ICS in the future: is this structure to be a continuing agency for cancer care, or like BSEP, a short term body expected to effect change?

Cancer reforms in Victoria are not a short-term strategy. It is recognised that changes as significant as these will take considerable time to establish and embed into practice. The recurrent funding that has been approved supports this premise and it is envisaged that the ICS will remain the infrastructure to enable delivery of the cancer reforms.

Establishment of a Victorian ICS Committee is being proposed. The Committee will provide a mechanism to provide a consistent statewide approach to cancer reform, and strengthen ownership and leadership of the cancer reform process at a local and statewide level. It will also foster decision making and working across organisational boundaries and over time will allow the ICS to develop as the key planning and decision making bodies for cancer services delivery in their geographic regions.

10. Are there any plans to change the mechanisms for funding of cancer care?

A number of options have been proposed about the longer term mechanisms for funding cancer care including possible per capita payments to support best practice and options for ICS fund holding for chemotherapy or other specified treatments. Review of options for funding reform will continue to be progressed in the context of the impact of such changes on the broader health funding system, although no early changes to current policy are anticipated.

However the DHS has been conducting a cost weights review in radiotherapy and chemotherapy. In radiotherapy the cost weights review will inform on requirements for updating the weights to reflect changes in technology and

practice since the model was implemented in 1998. It will also advise on how funding for the Single Machine Unit Radiotherapy services in Ballarat, Bendigo and Traralgon could be mainstreamed. Services will be expected to shadow fund against the new cost-weights in 2006–07, with a view to their implementation in 2007–08.

In chemotherapy, a number of recommendations have been made regarding funding reform. Further consideration of these proposals is required, with any changes to be made to the existing funding for chemotherapy likely to be several years away.

11. What is planned for the provision of appropriate psychosocial care for cancer patients, which is very poorly provided at present?

Assessment of psychosocial and supportive care needs, along with timely referral and access to psychosocial and supportive care services, have been identified as areas of significant concern across the State. The limited number of existing dedicated and skilled personnel necessitates the development of a broader and multifaceted approach that incorporates staff training in assessment of need and the development of referral pathways and protocols – both of which are linked to the implementation of the Patient Management Frameworks (PMFs). Detailed service mapping will enable identification of service provision gaps and areas in need of improvement.

A staged approach to addressing all interlinked factors impacting on the provision of timely and appropriate psychosocial and supportive care will support the development of sustainable and supported service delivery models to meet the needs of patients, carers and health professionals. This will be undertaken at both the statewide and ICS level.

12. How is the DHS planning to provide appropriate data collection mechanisms? Does the DHS support the development of a statewide (and ideally national) data collection system? What is being done to facilitate a coordinated approach?

The DHS recognises the challenges faced by the ICS regarding the lack of a statewide data collection system and the pressing need to develop such a system for quality improvement, to facilitate multidisciplinary and continuity of care, to better support research and population initiatives and assist clinicians in their management of cancer patients.

The Victorian Cancer Outcomes Network (VCN) is an initiative of the Ministerial Taskforce for Cancer and Cancer Council Victoria to trial and develop systems for the statewide collection of the NCCI Clinical Cancer Core Dataset (CCCD). The system is currently being piloted at RWH and Barwon Health.

Through the Data and Information Workshop and Cancer Service Plans, health services and ICS have identified major cancer data and information issues. It was identified that a system is needed to improve clinician access to patient data to support clinician decision-making and facilitate:

- information management of MD care, including documentation of MD meetings and recommendations;
- the clinical management of cancer patients;
- timely feedback from data systems to clinicians;
- identification of common practices and treatment pathways; and
- the provision of data for existing and future research and public health initiatives.

The DHS is working with ICS and the Ministerial Taskforce For Cancer to progress the work required to ensure the development of a statewide system to address the above issues.

A national approach to data collection, analysis and usage may become possible through the establishment of Cancer Australia.

The Colorectal Cancer Family Registry: An International Resource for Studying the Genetic and Molecular Epidemiology of Colorectal Cancer

Mark Jenkins¹, Finlay Macrae², Joanne Young³, Melissa Barker³, Barbara Leggett^{3,4}, Jack Goldblatt⁵, Judy Kirk⁶, Kathy Tucker⁷, Graeme Suthers⁸, Graeme Young⁹, Susan Parry¹⁰, Julie Arnold¹⁰, Ingrid Winship², Judi Maskiell¹, Graham Giles¹¹, Jeremy Jass¹², John Hopper¹
(refer to end of article for organisational affiliation)

Abstract

Created in 1997, the Colorectal Cancer Family Registry (Colon CFR) is an international consortium of six centres in North America and Australasia dedicated to the establishment of a comprehensive data resource to facilitate interdisciplinary studies on the aetiology, prevention, and clinical management of colorectal cancer. Standardised protocols were used to recruit colorectal cancer families and to collect information regarding colorectal cancer risk factors using questionnaires, DNA samples, and tumour samples. Tumours have undergone pathology review and have been tested for microsatellite instability, expression of mismatch repair proteins and DNA hypermethylation. DNA extracted from donated blood samples have been tested for germline mutations in the mismatch repair genes *MLH1*, *MSH2* and *MSH6*. Recruitment is ongoing, as is follow-up of all participants 5 years after recruitment to update

cancer and exposure data. The Colon CFR has enrolled over 12,000 families. Researchers are encouraged by the National Cancer Institute (USA) and the Colon CFR investigators to apply for access to this unique resource of data and biospecimens for collaborative research. Details of the Registry and application instructions are available at <http://epi.grants.cancer.gov/CFR/>.

Background

Recognising the importance for colorectal cancer of characterising known genetic pathways for and identifying additional susceptibility genes and environmental risk factors, the National Cancer Institute (NCI) funded the Colorectal Cancer Family Registry (Colon CFR) in 1997. The Colon CFR is composed of a multi-disciplinary team of international investigators that lead a consortium of six registries, and an Informatics Support Centre which stored centralised data (Table 1).

Table 1. Registries (sites) comprising the Colon CFR.

Colon CFR Registries	Principal Investigators	Recruitment
Australasia (University of Melbourne)	Prof John Hopper Prof Jeremy Jass	Population-based (early onset) and clinic-based
Seattle (Fred Hutchinson Cancer Res Ctr)	Prof John Potter Dr Polly Newcomb	Population-based (all ages)
USC Consortium (University Southern California)	Prof Robert Haile Prof John Baron	Population-based (stratified by ethnicity) and clinic-based
Mayo Clinic (Mayo Clinic)	Dr Laney Lindor Dr Stephen Thibodeau	Population-based (stratified by family history) and clinic-based
Ontario (Cancer Care Ontario)	Dr Steven Gallinger Dr Michelle Cotterchio	Population-based (stratified by family history)
Hawaii (University of Hawaii)	Dr Loic LeMarchand Dr John Grove	Population-based (stratified by family history)

The Australasian Colorectal Cancer Family Registry comprises central administration, a laboratory, a population-based recruitment site and six clinic-based sites throughout Australia and New Zealand (Table 2).

Infrastructure of the Colon CFR

The Colon CFR is led by a multi-disciplinary team of investigators composed of epidemiologists, statisticians, medical and surgical clinicians, molecular biologists, pathologists, and behavioural scientists. The Colon CFR is governed by the Steering Committee. A Scientific Advisory Committee provides overall advice on the research agenda and reviews and approves applications to use the resource. Working groups coordinate the work of the Colon CFR in various areas.

Methods

Recruitment

All six Colon CFR sites enrolled families with incident CRC identified through population-based cancer registries in defined geographic areas; however, at each study site, sampling probabilities differed according to age at diagnosis, ethnicity, and family history of

colorectal cancer. Following enrolment of the proband, his/her permission and assistance was sought to contact eligible and available relatives. Controls were either randomly sampled from the general population living in the relevant recruitment area. The selection of family members for recruitment was site-specific, ranging from first-degree only to the inclusion of second- and third-degree relatives.

Three sites enrol families with multiple or early-onset cases of CRC through family cancer clinics. Eligibility was typically based on either a strong family history, early-age of onset or known or high likelihood of segregating a mutation in a mismatch repair gene. The rationale for collecting HNPCC families was to facilitate studies of mismatch repair genes and the rationale for collecting other families was to facilitate gene-hunting studies.

Following proband enrolment, permission and assistance were sought to contact eligible and available relatives.

Questionnaires

Family history and environmental exposures was consistently collected for joint analyses. Each participant completed a family history

Table 2. Sites, lead investigators and roles of sites comprising the Australasian Colorectal Cancer Family Registry.

Site	Lead Investigators	Role
University of Melbourne	Prof John Hopper Prof Jeremy Jass	Principal Investigators
Queensland Institute of Medical Research	Dr Joanne Young Ms Melissa Barker	Bio-specimen repository and testing
Royal Melbourne Hospital	Prof Finlay Macrae	Clinic-based recruitment
Royal Brisbane Hospital	Prof Barbara Leggett	Clinic-based recruitment
South Australia Familial Genetics Service	Dr Graeme Suthers Prof Graeme Young	Clinic-based recruitment
University of Western Australia	Dr Jack Goldblatt	Clinic-based recruitment
Prince of Wales Hospital, Sydney Westmead Hospital	Dr Kathy Tucker Dr Judy Kirk	Clinic-based recruitment
University of Auckland	Dr Susan Parry Dr Julie Arnold	Clinic-based recruitment
University of Melbourne & Victorian Cancer Registry	Dr Mark Jenkins Ms Judi Maskiell Prof Graham Giles	Population-based recruitment

questionnaire on the, sex, birth dates, vital status and cancer history of first-degree relatives (parents, siblings, and children). Pedigrees were expanded to second- and third-degree relatives in several centres, depending on site-specific protocols and the reported family history.

Confirmation of cancer diagnoses was sought for all reported colorectal cancers and, at some sites, for other reported invasive cancers pathology reports, cancer registry reports, medical records or death certificates. Pathology reports for all probands' qualifying colorectal cancers were reviewed, recording site, stage, histology, grade, distant spread, nodular involvement, etc.

Participants also completed a risk factor questionnaire to capture information on established and suspected risk factors for CRC, including: medical history and medication use; reproductive history; physical activity; demographics; alcohol and tobacco use; ethnicity; and dietary data.

Four Colon CFR sites asked participants to complete a self-administered diet-history questionnaire to collect information on the frequency of food consumption and portion size.

Bio-specimens

For hypothesis-driven research to be based on this resource, extensive characterization of the families in the resource and of their cancers was required. Bio-specimens (blood and paraffin-embedded tumour tissue) were obtained from cases and selected relatives and controls.

Blood or buccal-cell collection - A standardised protocol was employed to collect and process blood samples. In general, 40mL blood was collected and stored as whole-blood spots, plasma and buffy coat, and white blood cells for eventual EBV-transformation to a lymphoblastoid cell line. For subjects who did not consent to a blood draw, some sites sought a buccal-cell sample. Germline DNA has been extracted, undergone a panel of quality control measures, concentrations standardised, aliquoted, and is stored at -70°C at each site.

Cell lines - To provide an unlimited supply of this valuable DNA, as well as RNA, lymphoblastoid cell lines of selected key individuals from each family were transformed and maintained using Epstein Barr virus using standard protocols.

Tumour - Paraffin-embedded colorectal tumours and diagnostic pathology reports from colorectal cancer affected probands and relatives were obtained from treating institutions, following informed consent. A standardised protocol to select and section representative blocks was developed. In general, sections were cut from each tumour and normal tissue block, and stained then reviewed by site pathologist(s) who selected a CRC tumour block and a block consisting of normal tissue for further sectioning. For planned immuno-histochemistry (IHC) and future protein-based studies, ten sections were prepared and mounted on slides. For microsatellite instability testing and other future tumour DNA-based studies, ten sections were prepared and either mounted on glass slides or stored in microfuge tubes at -70°C. When available, ten 5-micron normal tissue sections were similarly prepared and stored. DNA extractions from tumour and normal tissue were completed for microsatellite instability testing, with remaining DNA stored.

Because research of nearly any type of colorectal cancer would require first characterising participants' tumours according to DNA mismatch repair competency, registry-wide characterisation of tumours by tumour microsatellite instability, the phenotypic indicator of MMR competence was completed. Microsatellite instability testing was performed on all available colon CFR tumours collected to 2002 using 10 markers: four mononucleotide markers, four dinucleotide markers and 2 complex markers.

In addition to the MSI testing, the Colon CFR performed immuno-histochemistry (IHC) to establish the presence or absence of protein expression for MLH1, MSH2 and MSH6, and PMS2, the primary genes thought to be responsible in the MMR pathway.

The Colon CFR evaluated the methylation status of *hMLH1* gene promoter in tumours using methylation analysis in the laboratory of Dr Peter Laird (USC).

Mismatch repair gene germline mutation detection

Molecular characterisation was conducted across the Colon CFR, guided by the results of

the previous MSI and IHC tumour testing. Germline mutation status of the three MMR genes most commonly mutated in HNPCC, *MSH2*, *MLH1* and *MSH6*, has been determined using dHPLC followed by sequencing for selected case probands and selected relatives (both affected and unaffected). Testing was conducted for: all clinic-based families, all population-based families in which the proband has an MSI tumour, and a random sample of population-based families in which the proband did not have an MSI tumour. In addition, analysis of DNA for large genomic rearrangements (deletions, duplications) was conducted by the technique of MLPA.

Resource

Between 1996 and 2006 the Colon CFR has recruited over 12,000 families including participation from more than 40,000 individuals. Table 3 shows the number of questionnaires and bio-specimens collected to date. The Colon CFR has been funded at least till September 2007 and intends to continue to recruit families, as well as follow-up registered families.

Table 3. The Colon CFR participants, questionnaires and bio-specimens as of early 2006.

Resource	Approximate Number
Population-based families	11,000
Clinic-based families	1,200
Risk factor questionnaires	42,000
Blood samples	20,000
Tissue blocks	7,500
MMR mutation carrying families	230

Current Research

Highlighted below are examples of the diversity and quality of work that has been conducted using the Colon CFR. These examples are provided to illustrate the extremely diverse types of studies that the current infrastructure is capable of supporting. Examples of published research include:

Evaluation of new technologies: In a report entitled, "Conversion analysis for mutation detection in *MLH1* and *MSH2* in patients with colorectal cancer", Casey et al., (JAMA, 2005) conducted a blinded study comparing a new technology to

standard DNA sequencing and demonstrated a 56% increase in diagnostic yield in genetic testing of DNA mismatch repair genes due to detection of large deletions and splice site variants. Young et al. (Pathology, 2002) described their experience with a denaturing high-pressure liquid chromatography system for exon-by-exon scanning of tumour suppressor genes in colorectal cancers.

Understanding cancer prevention: Cotterchio M et al. (Cancer Causes and Control, 2005) demonstrated that cancer screening is associated with reduced colorectal cancer risk. Ramji F et al. (Cancer Detect and Prev, 2005) evaluated characteristics of subjects who underwent CRC screening and showed that family history of CRC, increased age, higher household income, and use of hormone replacement therapy were associated with ever having had colorectal cancer screening. Newcomb et al. (JNCI, 2003) reported on the long-term efficacy of sigmoidoscopy in reducing colorectal cancer incidence.

Defining new clinical risk groups: Lindor et al. (JAMA, 2005) separated families that met Amsterdam Criteria according to DNA mismatch repair status and proposed a new category, Familial Colorectal Cancer Type X, that has demonstrably lower cancer risks than families with DNA mismatch repair deficiency.

Defining risks for MYH gene mutation carriers: Croituro et al. (JNCI, 2004) and Jenkins et al. (Cancer Epidemiol Biomarkers Prev, 2006) estimated risk for CRC in both monoallelic and biallelic *MYH* gene mutation carriers in population-based studies in the CFR.

Identifying barriers to CRC screening: Madlensky et al. (Prevent Med, 2004) studied reasons given by relatives of colorectal cancer patients for not undergoing screening and proposed tailored interventions based on those findings.

Behavioural considerations arising from genetic testing: Esplen et al. (J Psychosomatic Res, 2003) assessed impact of genetic testing for hereditary colon cancers and suggest a subgroup will experience sufficient distress to warrant further interventions. Ramsey et al. (Community Genet, 2003) used focus groups to explore attitudes towards genetic screening for predisposition to colon cancer among cancer patients, their relatives, and members of the community.

Pathology-genotype-phenotype correlations: Jass et al. (Journal of Clinical Pathology, 2003) studied APC mutations and tumour budding in colorectal cancer. Wright et al. (Annals of Surgery and Oncology, 2003) studied lymph node retrieval and assessment in staging colorectal cancer in a population-based study.

Validation of methodologies: Madlensky et al. (Cancer Epidemiol Biomarkers Prev, 2003) compared self-reported colorectal cancer screening with medical records while Nadalin et al. (Chronic Disease Can, 2003) compared agreement between proxy- and case-reported information obtained using a self-administered epidemiologic questionnaire.

Surgical issues: Easson et al. (Annals of Surgical Oncology, 2002) studied the extent of surgical resection across different providers in a population-based study.

Microsatellite instability in clinical practice: Lindor et al. (J of Clinical Oncology, 2002) addressed the correlation between immuno-histochemistry and microsatellite instability testing in phenotyping colorectal tumours.

Statistical analysis issues: Siegmund and Langholz (American J of Epidemiol, 2002) studied ascertainment bias in family-based case-control studies, and stratified case sampling and the use of family controls (Genetic Epidemiology 2001).

Gene environmental interactions: Kim et al. (Cancer Epidemiol Biomarkers Prev, 2001) studied the vitamin D receptor polymorphism and the risk of colorectal adenomas, showing evidence of interaction with dietary vitamin D and calcium. This led to submission of R01 (funded) on this topic.

Risk of cancer in carriers of germline mutations in mismatch repair (MMR) genes: Jenkins et al. (Clin Gastro Hepatol, 2006) estimated, for individuals with a germline mutation in a mismatch repair (MMR) gene, the cumulative risks of colorectal and other cancers using family data from population-based probands with germline mutations in MMR genes and their relatives unselected for family history. They found that, for carriers, the age-specific incidence of colorectal cancer was high to age 50 but close to population incidence at older ages. Lifetime risks in carriers were about half those of previously published estimates.

Major ongoing studies include these projects

Research by Colon CFR investigators and by researchers external to the Colon CFR – all using the Colon CFR resource include:

- MSI prevalence versus family history
- Sensitivity/Specificity and predictive values of MSI and IHC for MMR mutations
- Mechanism of the second hit in *MSH2* tumours
- Penetrance in MMR carriers
- Base Excision Repair *MYH* gene and Colorectal Neoplasia
- MSI and prognosis
- Pathology as a predictor of MMR status
- Center for Disease Control Family History Project evaluating the CDC-developed familial risk assessment tool (Family Healthware™) using the CFR families
- Attitudes and motivations concerning genetic testing, psychosocial functioning, and screening behaviours
- Randomised control trial of three counselling models for relatives of cancer patients
- Relationship between family history of CRC and screening behaviour
- CpG Island Methylator Phenotype (CIMP).

Accessing the Registry

The scientific community at large has fair and equitable access to this large and well-characterised resource for studies of the genetics and epidemiology of CRC. Colon CFR investigators have already participated in numerous projects with external researchers from throughout the world and have initiated Colon CFR projects that include new collaborators, including a number of young and promising investigators. Details of the Registry and application instructions are available at <http://epi.grants.cancer.gov/CFR/>.

Summary

The Colon CFR has established a unique, comprehensive and valuable resource for a wide variety of studies on the aetiology and prevention

of colorectal cancer. In an international collaborative environment, the world's largest collection of CRC families has been assembled, complete with epidemiologic data, bio-specimens, and tumour tissues. A thorough search for genetic, epigenetic, environmental, and other causes is being conducted for this disease. The Colon CFR has great research potential, with follow-up data on the original Colon CFR families, a sizable number of identified gene mutation carriers, enrolment of African-American and Asian families, and access to quality bio-specimens and data from all centres. This resource is available to the international community of scientists interested in studying colorectal cancer.

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Book available to families with a family history of colorectal cancer

*Professor Finlay Macrae
Head, Colorectal Medicine and Genetics
The Royal Melbourne Hospital*

Do you ever wonder about the relevance and importance of bowel cancer to the immediate and extended family of people with bowel cancer? What does it mean for the children, brothers and sisters and even more distant relatives in the family?

The book is written for people diagnosed with bowel cancer and their families. It focuses particularly on inheritable bowel cancer. It is unique in its field.

Chapters cover:

- the nature of inherited colorectal cancer
- risk factors
- the place of family cancer clinics and registers
- the experience of cancer patients after diagnosis
- stresses and strategies in disclosing the diagnosis to family members and others
- how to manage the risk of familial cancer
- engagement in research
- prospects for a cure for colorectal cancer, and
- special considerations for China and the Far East.

It also lists a wealth of websites and other information sources as well as a glossary.

The book was developed as an initiative by co-editors Professor Finlay Macrae, Head of Colorectal Medicine and Genetics at The Royal Melbourne Hospital and Terri Berk, Clinical Coordinator / Social Worker, Familial GI Cancer Registry, Mt Sinai Hospital, Toronto, Canada. It has already been acclaimed by many health professionals around the world, including the US National Institutes of Health Colon Cancer Registries and the worldwide InSiGHT associated registries.

The work carries a preface from Professor John Burn, Medical Director, Institute of Genetics, Newcastle upon Tyne, UK, and immediate past Chairman of the International Society for Hereditary Gastrointestinal Tumours (InSiGHT), to whose Council many of the chapter authors are elected. It also carries a foreword from Professor Henry Lynch, the name synonymous with Hereditary Non Polyposis Colorectal Cancer (HNPCC), which is known by many as the Lynch Syndrome. Both readily recognise the value of the book to families who have had experience with colorectal cancer.

The book can be purchased through the website – www.crcbook.com.

Report of the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO)

2–6 June 2006, Atlanta, Georgia, USA

Dr Jeremy Shapiro
GI Oncologist
Alfred and Cabrini Hospitals

ASCO 2006 was in Atlanta – perfect weather, first-rate presenters, and lots of new data, which more than compensated for the trans-US air travel, traffic jams, and a conference centre that took nearly 25 minutes to traverse. There were no groundbreaking GI papers this year, although lots of new data, confirmation of previous results, and some practice changes.

Oesophagus

Yu#4013 – This randomised Chinese study compared surgery to “modern” radiotherapy alone in 269 patients with oesophageal squamous cell carcinoma. Radiotherapy was conformal, late-course accelerated, and hyper-fractionated (45 Gy/25 + accel 24Gy / 8 days bd). Survival was similar: median OS (S vs R) 29 vs 31 months, with 5-year OS 35% vs 37%. Although the old RTOG 8501 study (RT +/- chemo, Cooper JAMA '99) was from a different era, no 5-year survivors were reported in that study in the RT alone arm. It is interesting to speculate whether the addition of chemotherapy would further improve these impressive, and somewhat unexpected, results.

Tepper#4012 – This CALGB study planned to randomise 500 patients to surgery alone or chemo-radiotherapy (cisplatin / 5FU + 50Gy) followed by surgery for oesophageal cancer (adeno + squamous). However this study closed after only accruing 56 patients in 3 years likely due to bias by US physicians for combined modality therapy. Despite the small numbers, a very large survival difference was seen favouring combined treatment (median OS 4.5 vs 1.8 years, 5-year OS 39% vs 16%, $p < 0.008$). This data will strengthen the US bias for tri-modality therapy, but is unlikely to sway the UK preference for chemotherapy alone prior to surgery.

Gastric – Early Stage / Adjuvant

Sasko#LBA4015 – This Japanese study (n=523) compared radical (D2) versus super-radical (D3) gastric cancer resection, with similar survival reported in both arms. This study was particularly notable for the excellent surgical outcomes reported. Although the trial had been designed expecting a 50% 5-year overall survival (NB 5-year OS in surgery alone arm in McDonald [NEJM 2004] and MAGIC [ASCO 2003] studies was <25%), in fact the 5-year overall survival was 70% in both arms, despite two thirds of patients being node positive. The average nodal yields were enormous – 54 (D2) and 74 (D3), and operative mortality was low (0.8% both arms). These surgical outcomes are yet again far superior to Western data, this time raising the bar even higher. How much of these results can be attributable to the surgery (rather than differing tumour biology) was not well understood.

Ychou#4026 – This study (n=224) confirmed the survival benefit for pre- and post-operative chemotherapy versus surgery alone, for operable gastric cancer first reported in MAGIC – similar magnitude of benefit was also reported in this study with cisplatin + 5FU / surgery versus surgery alone – 3-year DFS 40% vs 25%, 5-year OS 34% vs 17%.

Gastric – Metastatic

Cunningham#LBA4017 – The REAL2 trial was a large (n=1002) 4-arm, randomised phase III study of ECF, ECX, EOF, and EOX (E, C, X, O = Epirubicin, Cisplatin, Xeloda, Oxaliplatin). The study was powered for non-inferiority (of xeloda vs 5FU and oxaliplatin vs cisplatin). Both end-points were met (5FU vs xeloda arms 1-year OS 39% vs 45%), (cisplatin vs oxaliplatin arms 1-year OS 40% vs 44%). The EOX arm appeared

to have improved efficacy vs ECF (RR 48% vs 41%, 1 year 47% vs 38%, $p=0.02$). Although the REAL2 study does not confirm superiority, this data will likely see the eventual substitution of the protracted (and logistically difficult) 5FU infusion / ambulatory pump with oral capecitabine, although currently there is no reimbursement for this indication.

The REAL 2 conclusions were also supported by two other studies: *Al-Batran#4016* – improved RR and TTF with FLO (oxaliplatin) vs FLP (cisplatin) with reduced toxicity; and *Kang#LBA 4018* – improved RR, and trend to increased PFS with XP vs FP.

Pancreas – Adjuvant

Regine #4007 – This US Intergroup study (RTOG9704, $n=442$) compared gemcitabine to 5FU following pancreatic resection and post-operative chemo-radiotherapy (50.4Gy / PVI 5FU) which is still widely used in US despite the ESPAC1 data. Gemcitabine increased 3-year overall survival versus 5FU for pancreas head tumours (31% vs 21%, $p=0.04$). This study confirms the benefit of adjuvant chemotherapy previously reported in ESPAC1 and CONK01 (also updated at the meeting: 3-year OS 36% vs 21%). These data may pre-empt the results of our current study ESPAC3, which has nearly completed accrual (adjuvant 5FU vs gemcitabine, without RT).

Pancreas – Advanced

The routine use of chemo-radiotherapy for inoperable, locally advanced disease has been questioned by the results of this study – *Chauffert #4008*. Patients were randomised to gemcitabine +/- chemo-radiotherapy (60Gy + PVI 5FU+ 20m² daily cisplatin weeks1+5). The trial was stopped early due to inferior survival in the RT arm (median OS 8 vs 14.5 months, 1-year OS 24% vs 51%, $p=0.03$), likely due to toxicity.

On the other hand, an Australian multi-centre phase II study – *Goldstein#4104* – showed that more modern chemo-radiotherapy (3D conformal + PVI 5FU) allows safe delivery of chemo-radiotherapy in this setting, with encouraging efficacy. Several new targets and multiple chemo-biologic regimens continue to be evaluated in metastatic disease without any particularly encouraging data.

Disappointing results also from the 3-arm phase III study comparing gemcitabine to FDR (fixed dose rate) gemcitabine, and FDR gemcitabine-oxaliplatin – *Poplin#4004*. At best, a very marginal benefit was seen in both experimental arms at the expense of more toxicity [median OS 5.0, 5.6, 6.0 months, $p=ns$]. In discussing this data, even Margaret Temporo (a long time advocate of FDR-gemcitabine) concluded that administering gemcitabine in standard dose and schedule remained a reasonable approach.

Resectable Colorectal Metastases (Liver / Lung)

Nordlinger#3501 – evaluated the difficult clinical problem of what to do with resectable liver metastases that have resolved fully on radiological imaging following neo-adjuvant chemotherapy. In a retrospective review of 586 patients, there were 66 metastases that fully resolved in 38 patients. In 9 of these patients (20/66 mets) there was persisting disease at surgery. A further 15 patients had no obvious evidence of cancer, and underwent resection – of these 12/15 still had residual microscopic viable cancer. The remaining 14 patients (31 mets) did not undergo surgery, but by one year, 11 (23/31 mets) had recurred locally. ie there was persisting microscopic cancer in (32/38) 82% patients, and (55/66) 83% metastases suggesting that even if a CR is achieved, cure is unlikely, and surgical resection of the metastasis should still be considered. Use of biologics and functional imaging will hopefully improve these figures in the future.

Gruenberger#3500 – A little more data from EORTC40983, the adjuvant study of pre- and post-operative Folfox chemotherapy versus liver resection alone. Toxicity was presented last year (low) and this year further clinical response data in the 364 patients was reported. The average tumour shrinkage was 30% (3% CR, 35%PR), with only 8% of patients progressing during neo-adjuvant Folfox. The long-awaited survival data should be available in early 2007.

Yan #3502 – The St George, NSW group presented their experience in treating lung metastases with radiofrequency ablation. Although this technique appears feasible, with limited side-effects and can control lesions <3 cm, controlled clinical trials evaluating the impact of this local control measure on survival and

QOL are needed. It may be a technique to consider in patients unwilling or medically unsuitable for resection of limited pulmonary metastases, particularly for small, non-hilar lesions.

Advanced Colorectal Cancer – Chemotherapy

Falcone#3513 – This study compared triplet upfront chemotherapy (FOLFOXIRI) to FOLFIRI, reporting increased RR (41% vs 66%), PFS (6.9 vs 9.8 months), OS (16.7 vs 22.6 months), and Ro resection of metastases (12% vs 36%) (all with $p < 0.05$). The authors' currently recruiting study is evaluating all five drugs (including bevacizumab and cetuximab) – a pento-drug regimen that is already being offered off study in some US centres. We sorely need predictive (and prognostic factors) to try to target those most likely to benefit from this prohibitively expensive approach.

CFIs – Chemotherapy free intervals – were the subject of three studies. All three suggesting that patients can take drug holidays, and “stop and go” treatment strategies can be employed after response to initial chemotherapy, provided patients are carefully monitored.

Maindrault-Goebel et al.#3504 – This large phase II study “Optimox2” follows on from the Optimox1 study (JCO, 2006) which demonstrated that maintenance 5FU following three months of Folfox7, and subsequent reintroduction was as active and better tolerated than Folfox4 until progression. In Optimox2, the maintenance arm from Optimox1 (Folfox7→LV5FU2→Folfox7) was compared to stopping Folfox7 chemotherapy after three months (with reintroduction at progression). Progression free survival was a little greater in the maintenance arm (36 vs 38 weeks) although duration of disease control was equivalent, supporting the CFI concept. In a second study – **Labianca et al.#3505** “Giscad” – CFIs did not impact adversely on survival in patients treated with first-line using alternating FOLFIRI (2 months on / 2 months off) vs continuous treatment, both until progression. Further support for this strategy also came from a retrospective review – **Plantade #3581**.

Fuchs#3506, n=900 – Folfiri has won out as the optimal schedule for irinotecan in first line, with

greatest activity and the most favourable toxicity versus Capiri and modified IFL. The current AGITG DaVinci study should answer whether the 5FU backbone (FOLFIRI) is also required in second-line irinotecan treatment.

Cassidy#3507 – Xaliproden, an oral neurotrophic agent was evaluated as a potential neuro-protectant in a randomised placebo-controlled trial in patients receiving first-line Folfox. Whilst there was a 5% reduction in grade 3 neuro-toxicity there were no differences in the number of patients developing cumulative neuropathy, nor was it able to increase the cumulative oxaliplatin delivered dose. Acute neurosensory symptoms were also unaffected. Although this agent was well tolerated, excess PE were seen in the Xaliproden arm without clear explanation, 10 (3.1%) vs 3 (0.9%).

Hochster#3510 – This study (TREE2) added bevacizumab to the three oxaliplatin schedules evaluated in the previous TREE1 multi-arm phase II study, and confirmed that bevacizumab increases the response rate by a further 10%. The median survival of all patients on TREE2 was an impressive, 24.4 months (and 27 months for the capecitabine-oxaliplatin + bevacizumab arm), passing an important 2-year milestone in CRC trials.

Saltz#3542 – Bevacizumab can be given safely over 10 minutes according to the Sloan-Kettering experience of 8250 doses delivered without any infusion reactions. All MSKCC patients are now treated over 10 minutes (for 5mg/kg dose). Only two minor reactions that did not interrupt treatment were reported in 1059 10-minute treatments delivered since November 2005.

Haller#3514 – An interesting poster demonstrating the variability in tolerance to fluoro-pyrimidines (both 5FU and capecitabine) between countries, utilising data from clinical trials and the Roche database (>3000 patients). The US in particular experienced the greatest toxicity (diarrhoea), and capecitabine dose reductions have been required in some studies (TREE2, **Bendall#3541**). Speculation was raised about inadequate dietary folate in the US.

Next year... Chicago!

Disclaimer: Jeremy Shapiro was sponsored by Roche to attend the ASCO meeting.

TROG 01.04 – A randomised trial of preoperative radiotherapy for stage T3 adenocarcinoma of rectum

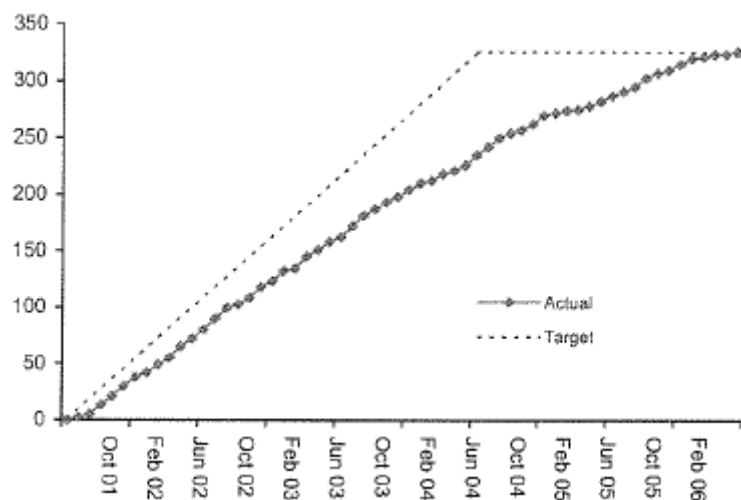
Dr Sam Ngan
Principal Investigator
Peter MacCallum Cancer Centre

Bev McClure
Trial Centre Data Manager
Peter MacCallum Cancer Centre

The trial was closed to accrual on 1 June 2006.

There will be another three years of follow-up and data collection before the main analysis. Please undertake follow-up, quality of life (QoL) assessment and late toxicity assessment according to the schedule in the protocol. It should also be noted that follow-up for local recurrence should continue in the event that distant metastasis is detected and visa versa.

Thank you very much for your support.



Target = 310 evaluable patients (equivalent to approx. 326 patients accrued)

Participating Centre	Accrual
NZ Auckland	4
Waikato	17
Wellington	0
ACT Canberra	1
NSW Campbelltown	0
Liverpool	6
Mater Newcastle	6
Nepean	1
Prince of Wales	13
Riverina Cancer Care	7
Royal North Shore	2
Royal Prince Alfred	27
Westmead	10
QLD East Coast Cancer Centre	6
Mater Adult - Brisbane	2
Mater Private - Brisbane	7
Princess Alexandra	25
Royal Brisbane	0
Townsville	6
SA Royal Adelaide / Queen Elizabeth	8
TAS Launceston	0
VIC Alfred	9
Ballarat Base	0
Ballarat St John of God	0
Box Hill	61
Frankston	15
Geelong	2
Monash Medical Centre	17
Murray Valley Private	0
Peter MacCallum - E Melbourne	53
Peter MacCallum - Bendigo	1
St Vincent's Melbourne	1
Western	0
WA Royal Perth	7
Sir Charles Gairdner	12
Subiaco St John of God	0
Total	326

The Sir Edward Dunlop Clinical Research Fellowship

This Fellowship is named in memory of Sir Edward 'Weary' Dunlop (1907–1993) to mark his contribution to Australia and, in particular, to the work of The Cancer Council Victoria.

The Dunlop Fellowship is the third prestigious Cancer Council fellowship recognising Sir Edward. It has been awarded to Associate Professor Grant McArthur who is Consultant Medical Oncologist, Head of the Translational Research Group and Head of the Molecular Oncology Laboratory at the Peter MacCallum Cancer Centre.

Dr McArthur's fellowship research program involves the development of targeted therapies for cancer. He will work on three different streams of research concurrently.

These streams of research all relate to the development of new treatments for cancer and encompass understanding the fundamental biology of the target and integrating this with

strategies to clinically develop novel targeted therapeutics. Dr McArthur's will also continue his clinical practice as a medical oncologist, specialising in targeted therapies and his work with patients will complement and enhance his research.

The Fellowship is for 5 years and commenced in January 2006. It will provide over \$700,000 to Peter MacCallum Cancer Centre to cover the fellowship salary and overheads as well as a conference travel allowance and research infrastructure support.

The overall aims of the fellowship are to develop and support medical researchers undertaking a program of clinical research and to provide the fellow with the mentorship and research environment to further develop their careers as leaders in cancer research.

The funding for these fellowships has been made available due to the generous donations from the Victorian public.

Dunlop Fellowship: Development of Targeted Therapies for Cancer

*Associate Professor Grant McArthur
Sir Edward Dunlop Clinical Research Fellow
The Cancer Council Victoria*

The development of imatinib and trastuzumab have changed the paradigm for the systemic therapy of cancer. Targeting specific molecular abnormalities in human cancer by identifying genomic abnormalities that activate oncogenes such as c-ABL, c-KIT or ERB-B2 has led to dramatic results fundamentally changing the clinical course of cancer in these patients. We are now on the verge of an explosion in novel targeted therapies, however significant challenges remain to develop these therapies in a rapid manner particularly identifying patients that will get greatest benefit from these costly therapies.

With the generous support of The Cancer Council Victoria's Sir Edward Dunlop Clinical Research Fellowship, my research program will encompass:

- Novel applications of targeted therapies to the treatment of neoplasia;
- The use of positron emission tomography in monitoring response to targeted therapies; and
- Development and application of biomarker assays to predict response to targeted therapies.

Novel Applications of Targeted Therapies to the Treatment of Neoplasia

A major goal of my teams research program is to develop novel applications of targeted therapies for both common and less common malignancies. The overall approach is not disease focused, but rather is focused on the target and the application of targeted therapies to a variety of diseases. As such the research program encompasses both haematological malignancies and solid tumours.

Although targeting oncogenes that are protein kinases that harbour activating mutations has been highly successful, there are a number of other interesting targets are not directly mutated that hold promise. For example agents that inhibit the vascular endothelial growth factor receptor have shown significant activity in renal cell cancer although the target is not mutated. This approach of identifying pathways important in cancer and targeting molecules that modulate activity of the pathway is a potential new application of targeted therapies.

Targeting c-MYC and Ribosome Biogenesis

High levels of protein synthesis characterize malignant cells, particularly tumours with dysregulated expression of the oncogene c-MYC. We have shown that the mTOR-inhibitor rapamycin can inhibit global protein synthesis, promoting cell cycle arrest and cell differentiation. Interestingly the c-MYC oncoprotein is selectively reduced in response to rapamycin and further research efforts will focus on combining rapamycin analogues with other agents to reduce activity of c-MYC.

Targeting DNA damage responses

The activity of both cytotoxic chemotherapy and ionising irradiation in malignant disease is dependent on altered checkpoint responses of malignant cells when compared to normal cells. We specifically hypothesise that further modulation of checkpoint responses through the use of agents that target checkpoints will enhance the response of malignant cells to cytotoxic chemotherapy and ionising irradiation. Two targets are being investigated: 1) CDK2 and 2) CHK1.

CDK2 is a cyclin-dependent kinase involved in the regulation of normal G1-S progression and

DNA replication. However its activity is also modulated during DNA damage responses. We have demonstrated a role of CDK2 in DNA repair and that cells with loss of function of BRCA1 or ATM display heightened sensitivity to small molecule inhibitors of CDK2. We now plan to extend these novel observations to evaluate small molecule inhibitors of CDK2 in a variety of preclinical models of combination with chemotherapy and irradiation.

CHK1 is a central protein kinase in regulation of the G2-checkpoint. In pre-clinical models we have demonstrated that a small molecule inhibitor of CHK1 modulates the G2-checkpoint following irradiation and cytotoxic chemotherapy enhancing DNA damage and increasing tumour responses.

The use of Positron Emission Tomography in Monitoring Response to Targeted Therapies

In partnership with Professor Rod Hicks our team have recently demonstrated the utility of using Positron Emission Tomography to monitor response of tumours in vivo to novel target therapeutic agents, both clinically and in animal models. Importantly our research strategy utilizes a variety of metabolic tracers that enable us to probe a number of biological process in vivo. Currently we utilise Fluoro-deoxyglucose (FDG), Fluorine-L-Thymidine (FLT), Fluoro-ethyltyrosine (FET) and Fluoro-azomycin-araboside (FAZA) to monitor glucose transport and metabolism, cell proliferation, amino acid transport and hypoxia respectively. This will have the greatest utility in the evaluation of targeted therapy agents that do not induce rapid tumour progression. This approach may significantly accelerate the development of these agents, as currently proof of biological activity of novel agents typically requires either demonstration of rapid tumour regression or improvements in longer-term clinical endpoints such as time-to-progression or overall survival.

Development and Application of Biomarker Assays to Predict Response to Targeted Therapies

One crucial component in the development of targeted therapeutics is to address whether the agent successfully modulates the target in vivo.

A second key component to the development of these agents is to determine if the molecular profile of the tumour can predict response to the agent. This issue was critically important in the development of Trastuzumab in breast cancer, where only ERB-B2 over-expressing tumours responded to this agent. Therefore successful development of targeted therapeutic agents requires access to biomarker assays such as assays that assess target phosphorylation for drugs that inhibit protein kinases, or mutation analyses that predict activation of the target.

Our initial approach is to validate biomarker assays using pre-clinical models and archival tumour specimens from the Peter MacCallum Cancer Centre and in the near future the Victorian Tissue Bank Initiative. Having validated

these assays we are extending these assays into clinical trials to demonstrate target inhibition and to address the hypothesis that activation of specific pathways in individual patients will lead to selective application of targeted therapeutics in subsets of patients.

Summary

The advent of targeted therapies for cancer is enabling us to use basic knowledge of the pathogenesis of cancer to develop new treatments for patients. In partnership with my basic and clinical research colleagues and our patients in Victoria, Australia and overseas we are entering an exciting new phase in the battle against cancer.

Report of The Cancer Council Australia

*Glen Turner
Communications Manager
The Cancer Council Australia*

Changing of the guard at The Cancer Council Australia

After eight years of running Australia's largest federated health charity, The Cancer Council Australia CEO Professor Alan Coates has retired and passed the baton to the former Chair of the organisation's Medical and Scientific Committee, distinguished ex-Adelaide oncologist, Professor Ian Olver.

President of The Cancer Council Australia, Mrs Judith Roberts AO, said the transition was a good opportunity to both celebrate Professor Coates's extraordinary contribution while welcoming Professor Olver as the ideal candidate to position the organisation to address the future challenges of leading national cancer control in the non-government sector.

"We are extraordinarily fortunate to have had eight years of service from a scientist, advocate and communicator of Professor Coates's calibre and then to be able to seamlessly anoint

Professor Olver as his successor," Mrs Roberts said.

"Under Professor Coates's stewardship, The Cancer Council Australia has evolved into one of the nation's most important peak bodies and has influenced a major increase in commitment to cancer control at the federal government level.

"Professor Olver is ideally placed to continue Professor Coates's invaluable work and to use his own unique skills and experience as one of the nation's leading oncologists and healthcare administrators to take the organisation forward to meet the challenges of an expected 30% increase in cancer incidence over the next five to 10 years as Australia's population ages."

"One-stop-shop" for primary care cancer resources

A new web-based directory of cancer resources for primary care professionals provides quick and easy access to national, state and territory

information. The new directory, developed by The Cancer Council Australia's General Practice Committee, will provide a single access point to a range of cancer resources including guidelines and advice on prostate, breast, bowel, ovarian and skin cancer, as well as issues associated with screening and psychosocial care for cancer patients.

The directory will be updated as new resources become available or revised resources are

released - ensuring that primary care professionals have access to the most current information.

The primary care resources directory can be accessed via The Cancer Council Australia website at www.cancer.org.au/primarycare.

Reprinted from Wongi Yabber May 2006; 12(2): 3-4.

Clinical Oncological Society of Australia (COSA) Report

*Ms Margaret McJannett
Executive Officer, COSA*

COSA has been continuing to move forward on a number of issues on behalf of its membership. Key activities include:

Annual Scientific Meeting (ASM)

The Australian Health & Medical Research (AH&MR) Congress, site of this year's COSA ASM, continues to gain momentum. The impressive confirmed speaker list now exceeds 150 speakers and many of them are speaking on cancer related topics.

Specifically within the COSA program, there is the normal range of symposia and sessions meeting the wide range of needs of the membership. We are in process of confirming the international speakers and COSA program. A draft program will be posted on the COSA website shortly. Please note this year's meeting will be held at the Melbourne Convention Centre, 29 November-1 December. There will be a Consumer Forum held on Tuesday 28 November.

Professional development packages for cancer professionals

The Commonwealth DoHA called for tenders late in 2005 to look at educational needs of cancer health professionals. A consortium involving Centre for Innovation in Professional Health

Education (CIPHE), COSA, TCCA, NBCC, and the RACGP successfully tendered for Phase 1 of the project, scoping current cancer professional development resources and associated needs of cancer professionals, GPs and counsellors.

A reference group is guiding the project, which includes an online survey targeting relevant professionals.

COSA Enabling Grant

Working parties have been convened to make recommendations about how to allocate funds for each component of the grant:

- Protocol Development, Information Systems and Quality Assurance. Scoping exercises for each component are in progress. The protocol development working party has developed its recommendations and will be reviewed by the Steering Committee in due course.
- Executive Committee has been established to oversee the work of this grant and meet more frequently than the Steering Committee. Members include: Dr Steve Ackland, Chair, Professor Alan Coates, CEO TCCA, Ms Haryana Dhillon, Project Coordinator, Ms Margaret McJannett, EO, TCCA / COSA, and Dr John Seymour and Associate Professor Martin Stockler.

- Responses have been made on behalf of the Cooperative Groups through COSA to NSW Health regarding the Policy Directive on Clinical Trials – Risk Management, Insurance and Indemnity, and to the Cancer Institute NSW regarding Streamlining of Ethical Review of Cancer Research in NSW.

Alan Coates honoured for scientific leadership

COSA joins the chorus of clinicians and health professional groups congratulating Professor Alan Coates for winning the prestigious

Distinguished Service Award for Scientific Leadership, bestowed by the American Society for Clinical Oncology (ASCO). We have particular reason to celebrate, as ASCO is our US counterpart and the conferring of this award on Professor Coates, a member of our Executive, builds on the already strong relationship between our two organisations.

We are fortunate that Professor Coates will remain active within COSA and in cancer research after he retires from his Cancer Council Australia career later this month.

Reprinted from Wongi Yabber May 2006; 12(2): 3.

The National Cancer Control Initiative (NCCI) Report

*Professor Mark Elwood
Director
National Cancer Control Initiative*

This is the last report from the National Cancer Control Initiative. The NCCI is disbanding, sadly, on the 31 May 2006. Since its inception in 1997, NCCI has contributed greatly to strategic developments in cancer in Australia, and has during this process produced some 36 reports based on wide consultation, and about 75 peer-reviewed papers. NCCI conducted the largest consultation to yield a national consensus on cancer priorities, developed a practical core clinical data set, produced the first evidence-based rationale for the requirements for radiotherapy, set up implementation programs based on the lung cancer and psychosocial guidelines, developed a primary care program in cancer, and jointly produced the 'Optimising Cancer Care in Australia' report. The closure of NCCI is very regrettable, and I do not think we are being conceited if we say that this is not only unfortunate for those of us who have worked with and supported NCCI, but also for the progress of effective cancer strategies in Australia. NCCI has made a major contribution and has developed considerable expertise and resources that are highly relevant to ongoing issues in cancer care. Inevitably, much of this

experience will be lost. Our position all along has been that while we support the development of Cancer Australia as a larger and more comprehensive focus for strategic efforts in cancer, it would have been simple and inexpensive to ensure that NCCI continued until it could be incorporated into or linked with Cancer Australia in an effective way. However there has been no action to ensure linkage. Some of the NCCI staff have accepted other positions, while for others there is still some uncertainty. We are making what arrangements we can to allow some aspects of continuity, for example we are trying to ensure that the NCCI website (www.ncci.org.au) continues for a reasonable time as a portal through which people can still get access to published reports and other material produced by NCCI. A final report is being prepared for the Department of Health and Ageing.

ACN would like to thank Professor Mark Elwood and his staff for their generous cooperation with a number of projects over the last nine years and wish them well for the future.

Reprinted from Wongi Yabber May 2006; 12(2): 2.

Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer (2nd Edition)

These revised guidelines, which already provide the curriculum for surgical Fellows doing advanced work in colorectal surgery, are also to have an updated aide-memoire type desk guide prepared for General Practitioners. It is also planned to revise the consumer document based on the new version of the clinical practice guidelines.

Copies of the revised clinical practice guidelines are now limited, however, they can be viewed / downloaded from the ACN website at www.cancer.org.au/guidelines.

It is encouraging to note that the Guidelines are being introduced to undergraduates in a number of instances.

Reprinted from Wongi Yabber May 2006; 12(2): 2.

Australian Cancer Network (ACN) Activities

Work is continuing with discussion and dissemination of **Accreditation** and **Credentiailling** documents. There will be further fine tuning necessary.

The Draft **Guidelines Implementation** document has met with significant approval after being piloted in Victoria. Its distribution is being planned by the National Institute of Clinical Studies (NICS). The generous support of Dr Heather Buchan of NICS has been integral to progress and is appreciated by ACN.

There is to be a major meeting with NICS in October when all three documents will be featured in discussion and decision-making, which should further embed guidelines and the evidence-based approach and hopefully further eradicate unnecessary variation in practice.

Reprinted from Wongi Yabber May 2006; 12(2): 1.

Cancer Council Events Calender

AUGUST

25 Volunteer on Daffodil Day
www.daffodilday.com.au

26 Daffodil Ball
www.daffodilday.com.au



SEPTEMBER

1 Cancer Council Mazda Raffle tickets on sale – [Ph: 1300 65 6 585](tel:1300656585)

20 Sep – 4 Oct Tour for a Cure – Trek Mont Blanc
www.tourforcure.org.au

OCTOBER



Host a Girls Night In Month
www.girlsnightin.com.au

Relay for Life – Carlton, Swan Hill
www.relayforlife.com.au

14–27 Tour for a Cure – Race Around Asia
www.tourforcure.org.au

23 Pink Ribbon Day
www.pinkribbonday.com.au



21–22 Relay for Life – Shepparton
www.relayforlife.com.au

28–29 Relay for Life – Echuca, Murrumbena
www.relayforlife.com.au

NOVEMBER



Relay for Life – Ararat, Ballarat, Bass Coast, Dandenong Ranges, Frankston, La Trobe Valley, Whitehorse
www.relayforlife.com.au

10–22 Tour for a Cure – Trek India
www.tourforcure.org.au

12–25 Tour for a Cure – Cycle Vietnam
www.tourforcure.org.au

DECEMBER

6 Cancer Council Mazda Raffle drawn

Shop online at www.cancervic.org.au/shop

For information on our events or other ways to help, such as our regular giving or bequester club programs, call 1300 65 65 85 or visit www.cancervic.org.au

Key Published Articles Listing—Gastrointestinal Cancer

Title	Author & Journal
Measures of familial aggregation depend on definition of family history: Meta-analysis for colorectal cancer	Baglietto L, Jenkins MA, Severi G, et al. Journal of Clinical Epidemiology Feb 2006; 59(2): 114–124.
Systematic review of microsatellite instability (MSI) and colorectal cancer prognosis	Popat S, Hubner R & Houlston RS. Journal of Clinical Oncology Jan 2005; 23(3): 609–618.
Risk of colorectal cancer in monoallelic and biallelic carriers of MYH mutations: A population-based case-family study	Jenkins MA, Croitoru ME, Monga N, et al. Cancer Epidemiology Biomarkers & Prevention Feb 2006; 15(2): 312–314.
Cancer risks for mismatch repair gene mutation carriers: A population-based early onset case-family study	Jenkins MA, Baglietto L, Dowty JG, et al. Clinical Gastroenterology & Hepatology Apr 2006; 4(4): 489–498.
Consumer choice and the National Bowel Cancer Screening Program [Editorial]	Salkeld GP, Young YM & Solomon MJ. The Medical Journal of Australia 5 June 2006; 184(11): 541–542.
A comparison of colorectal neoplasia screening tests: A multicentre community-based study of the impact of consumer choice	The Multicentre Australian Colorectal-neoplasia Screening (MACS) Group. The Medical Journal of Australia 5 June 2006; 184(11): 546–550.

Key Published Articles Listing—General

Title	Author & Journal
Public illness: How the community recommended complementary and alternative medicine for a prominent politician with cancer	Lowenthal RM. The Medical Journal of Australia Dec 2005; 183(11/12): 576–579.
Religious perspectives on withdrawal of treatment from patients with multiple organ failure	Ankeny RA, Clifford R, Jordens CFC, et al. The Medical Journal of Australia Dec 2005; 183 (11/12): 616–621.
Clinical Cancer Advances 2005: Major research advances in cancer treatment, prevention and screening – A report from the American Society of Clinical Oncology	Herbst RS, Bajorin DF, Bleiberg H, et al. Journal of Clinical Oncology 1 Jan 2006; 24(1): 190–205.
Promoting the implementation of best-practice guidelines using a matrix tool	Luxford K, Hill D & Bell R. Disease Management & Health Outcomes 2006; 14(2): 85–90.

Forthcoming Meetings

Date / Place	Meeting / Contact
28 June – 1 July 2006 Barcelona, Spain	8th World Congress on Gastrointestinal Cancer Organised by the European Society for Medical Oncology (ESMO). Secretariat: Imedex, 70 Technology Drive, Alpharetta 30005, Georgia USA Ph: +1 770 751 7332 Fax: +1 770 751 7334 E-mail: meetings@imedex.com Website: www.worldgicancer.com
1–4 July 2006 Budapest, Hungary	19th Meeting of the European Association for Cancer Research (EACR) EACR 19 Conference Secretariat, Federation of European Cancer Societies, Avenue E. Mounier 83, B-1200 Brussels Ph: +32 2 775 02 05 Fax: +32 2 775 02 00 E-mail: EACR19@fecs.be Website: www.fecs.be
8–12 July 2006 Washington DC, USA	UICC World Cancer Congress – <i>Bridging the gap: Transforming knowledge into action</i> American Cancer Society, 1599 Clifton Road, NE, Atlanta Georgia 30329-4251 USA Ph: +1 404 417 5998 Fax: +1 404 728 0133 E-mail: secretariat2006@cancer.org Website: www.worldcancercongress.org
14–15 July 2006 Adelaide, SA, Australia	9th CNSA Winter Congress Pre-conference workshop on 13 July Ph: (02) 9280 0577 E-mail: cnsa@pharmaevents.com.au Website: www.cnsa.org.au
9–12 August 2006 Sanctuary Cove, QLD, Australia	Annual Scientific Meeting of the Medical Oncology Group Australia (MOGA) MOGA Conference Secretariat c/o Pharma Events, PO Box 265, Annandale NSW 2038 Ph: (02) 9280 0577 Fax: (02) 9280 0533 E-mail: moga@pharmaevents.com.au
24–26 August 2006 Honolulu, Hawaii, USA	4th International Conference on Gastroenterological Carcinogenesis Organized by the University of Texas, MD Anderson Cancer Center, Houston, Texas, USA Ph: +1 713 792 2222 Fax: +1 713 794 1724 E-mail: register@mdanderson.org Website: www.mdanderson.org

Date / Place	Meeting / Contact
25 August 2006 Melbourne, VIC, Australia	Australian Liver Foundation / Australian Liver Association Combined Single Topic Conference – <i>Liver Tumours</i> Contact: Dr Stuart Roberts / Dr William Kemp E-mail: S.Roberts@alfred.org.au / W.Kemp@alfred.org.au
3–9 September 2006 Sunshine Coast, QLD, Australia	The Australia and Asia Pacific Clinical Oncology Research Development (ACORD) Workshop – <i>A Workshop in Effective Clinical Trials Design</i> ACORD Workshop, Level 6, 52 Phillip Street. Sydney NSW 2000 Ph: (02) 8247 6207 Fax: (02) 9247 3022 E-mail: mog@racp.edu.au
14–16 September 2006 Adelaide, SA, Australia	8th Annual Scientific Meeting of the Australasian Gastrointestinal Cancer Trials Group (AGITG) Website: www.gicancer.org.au
21–23 September 2006 Arlington, Virginia, USA	3rd Annual Meeting of the International Society of Gastrointestinal Oncology (ISGIO) International Society of Gastrointestinal Oncology, 200 Broadhollow Road, Suite 207, Melville, NY 11747 Ph: +1 631 390 8390 Fax: +1 631 393 5026 Website: www.isgio.org
27 Sep – 1 Oct 2006 Toronto, Ontario, Canada	14th International Conference on Cancer Nursing Organised by the International Society of Nurses in Cancer Care (ISNCC), Cheshire, UK Ph: +44 11 6270 3309 Fax: +44 11 6270 3673 E-mail: conference@isncc.org Website: www.isncc.org
29 Sep – 3 Oct 2006 Istanbul, Turkey	31st Annual Congress of the European Society for Medical Oncology (ESMO) ESMO Head Office, Via la Santa 7, 6962 Viganello-Lugano, Switzerland Ph: +41 91 973 1900 Fax: +41 91 973 1902 Website: www.esmo.org
8–12 October 2006 Leipzig, Germany	European Society for Therapeutic Radiology and Oncology (ESTRO) Ph: +32 2 775 9340 Fax: +32 2 779 5494 E-mail: info@estro.be Website: www.estro.be/estro/index.html
9–14 October 2006 Adelaide, SA, Australia	Australian Gastroenterology Week Website: www.gesa.org.au

Date / Place	Meeting / Contact
18–21 October 2006 Venice, Italy	8th World Congress of Psycho-Oncology – <i>Multidisciplinary Psychosocial Oncology: Dialogue and Interaction</i> Organised by the International Psycho-Oncology Society (IPOS). Contact: Luigi Grassi Ph: +39 053 223 6409 Fax: +39 052 121 2240 E-mail: luigi.grassi@unife.it Website: www.ipos2006.it
19–20 October 2006 Melbourne, VIC, Australia	NICS Using Evidence: Using Guidelines Symposium National Institute of Clinical Studies, Level 5, 499 St Kilda Road, Melbourne VIC 3004 Ph: (03) 8866 0400 Fax: (03) 8866 0499 E-mail: info@nicsl.com.au Website: www.nicsl.com.au / www.usingevidence.com.au
26–29 October 2006 Christchurch, New Zealand	57th Annual Scientific Meeting of the Royal Australian and New Zealand College of Radiologists (RANZCR) Website: www.ranzcr.edu.au
1–4 November 2006 Rome, Italy	5th Biennial International Sentinel Node Society Meeting – <i>Sentinel Node Biopsy: New Boundaries</i> Conference Secretariat: CQ Travel SRL, Via Pagliano, 3-20149 Milano, Italy Fax: +39 02 4391 1650 E-mail: infoeventi@ieo.it
5–9 November 2006 Philadelphia, Pennsylvania, USA	48th Annual Meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) American Society for Therapeutic Radiology and Oncology (ASTRO), 12500 Fair Lakes Circle, Suite 375, Fairfax Virginia 22033 USA Ph: +1 703 227 0170 Fax: +1 703 502 7852 E-mail: meetings@astro.org Website: www.astro.org
7–10 November 2006 Prague, Czech Republic	18th International Conference on Molecular Targets and Cancer Therapeutics Jointly organised by EORTC, NCI and AACR. EORTC-NCI-AACR Conference secretariat, Federation of European Cancer Societies, Avenue E. Mounier 83, B-1200 Brussels Ph: +32 2 775 02 01 Fax: +32 2 775 02 00 E-mail: ENA2006@fecs.be Website: www.aacr.org

Date / Place**Meeting / Contact**

29 Nov – 1 Dec 2006

Melbourne, VIC, Australia

33rd Annual Meeting of the Clinical Oncology Society of Australia (COSA)

COSA Office, Medical Foundation Building, Level 5, 92 Parramatta Road, Camperdown NSW 2011

Ph: (02) 9036 3100

Fax: (02) 9036 3101

E-mail: cosa@cancer.org.auWebsite: www.cosa.org.au**29 Nov – 2 Dec 2006**

Venice, Italy

13th Congress of the European Society of Surgical Oncology (ESSO)

ESSO 2006 Conference secretariat, Federation of European Cancer Societies, Avenue E Mounier 83, B-1200 Brussels

Ph: +32 2 775 0205

Fax: +32 2 775 0200

E-mail: ESSO2006@fecs.beWebsite: www.fecs.be

The Cancer Council Victoria

The Cancer Council Victoria is a public institution set up by an Act of Parliament in 1936. It operates as a charity, relies heavily on volunteer support, and raises and spends \$3-\$4 per head of population annually. It is governed by the Council and Executive and other committees. It's mission is to lead, coordinate and evaluate action to minimise the human cost of cancer for all Victorians. The Cancer Council houses three research divisions (behavioural science, clinical research, epidemiology) and units undertaking public and professional education, cancer registration, cancer information and support services, anti-smoking campaign (QUIT), finance, administration and fund raising. It employs about 300 staff. The Cancer Council also auspices a cooperating network of cancer specialists through the Victorian Cooperative Oncology Group and resources an expert Medical & Scientific Committee to dispense studentships, scholarships, fellowships and research grants to other academic, research and medical institutions.

Centre for Clinical Research in Cancer — Victorian Cooperative Oncology Group

The Centre for Clinical Research in Cancer (CCRC) formed in 1997, provides a coordinated and effective resource for collaborative clinical research and development in Victoria. The Centre provides administrative and research support for the Victorian Cooperative Oncology Group, which brings together Victoria's cancer specialists. The Centre fosters and facilitates the development and promotion of a range of collaborative clinical measures to optimise cancer management.

The Victorian Cooperative Oncology Group (VCOG) established in 1976, provides advice to the Cancer Council Victoria, through the CCRC, on all clinical aspects of cancer control, in particular research, screening, diagnosis, treatment, palliative medicine, cancer genetics and professional education. The strategic role of VCOG is to have a 'parliament' of clinical cancer specialists with a view to promoting a range of cooperative measures to optimise cancer treatment in Victoria. VCOG consists of a primary committee, 9 cancer-site and 3 task-specific advisory committees, and 5 trial research sub-committees. These committees bring together in regular meetings approximately 400 key specialist health care professionals and scientists, representing the various treatment disciplines and centres in Victoria. VCOG has established unique linkages between public and private health care professionals, institutions and governments.

