Cancer Forum is the official journal of the Clinical Oncological Society of Australia (COSA), the peak multidisciplinary organisation for health professionals working in clinical oncology. To mark COSA’s 40th anniversary, this special edition of Cancer Forum features a retrospective on cancer treatment and care over the past 40 years. We review the progress made, obstacles yet to be overcome and future directions for cancer treatment and care in Australia. Our sincere thanks to Emeritus Professor Tom Reeve AC CBE, for bringing together many of the profession’s finest to give their perspective on the future of oncology and cancer care in this country.

Overview
Tom S Reeve 3

THE PATIENT
The many faces of preventative care in the practice of oncology
Alison Zucca, Rob Sanson-Fisher, Amy Waller 12
Promoting patient based care and consumer engagement
Karen Luxford 17
Psychosocial aspects of delivering cancer care: an update
Phyllis Butow, Afaf Girgis, Penelope Schofield 20
Medical and psychosocial challenges in caring for adolescent and young adult patients with cancer
Antoinette Anazodo and Jennifer Chard 23
Aboriginal and Torres Strait Islander Australians and cancer
John R Condon, Gail Garvey, Lisa J Whop, Patricia C Valery, David Thomas, Russell Gruen, Joan Cunningham. 27

CRAFT BASED
Continuity of cancer care: Where do primary care practitioners fit in?
Moyez Jiwa, Alexandra McManus, Ann Dadich 31
40 years of cancer nursing in Australia: The emergence of a specialty
Patsy Yates and Sanchia Aranda 35
Evolution of palliative care in Australia 1973-2013
David C Currow and Jane Phillips 38
Radiotherapy - a leap forward in cancer care
Lizbeth M Kenny, Lester J Peters, Michael Barton, Chris Milross 42
Surgery - a pillar of modern oncology
G Bruce Mann, Robert SJ Thomas, Tom S Reeve 47
Cancer risk assessment and screening: the need to take notice
Andrew G Penman 50

MOST COMMON CANCERS
Breast cancer
Alan Coates 54
Prostate cancer
Ian D Davis, James Lynam, Pavel Sluka 56
### Colorectal cancer
Eva Segelov

### Lung cancer
David Ball

Haematological malignancies - intractable obstacles and path finding breakthroughs over 40 years
James F Bishop

### Melanoma
John F Thompson and Alexander M Menzies

### Applied Sciences

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue banking and its role in clinical and biological advances in oncology</td>
<td>67</td>
</tr>
<tr>
<td>Targeted therapies, aspects of pharmaceutical and oncological management</td>
<td>70</td>
</tr>
<tr>
<td>Clinical trials – advancing national cancer care</td>
<td>80</td>
</tr>
<tr>
<td>Patient reported outcomes are important in oncology</td>
<td>88</td>
</tr>
</tbody>
</table>

### Articles

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public perceptions of cancer clusters, associated events, and appropriate institutional response</td>
<td>93</td>
</tr>
</tbody>
</table>

### Awards

<table>
<thead>
<tr>
<th>Award</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOGA Novartis Oncology Cancer Achievement Award 2012</td>
<td>100</td>
</tr>
<tr>
<td>The Tom Reeve Award for Outstanding Contributions to Cancer Care</td>
<td>103</td>
</tr>
</tbody>
</table>

### Reports

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support for research funding 2013</td>
<td>107</td>
</tr>
<tr>
<td>Australian behavioural research in cancer</td>
<td>125</td>
</tr>
<tr>
<td>Flinders Centre for Innovation in Cancer Survivorship Conference 2013</td>
<td>127</td>
</tr>
<tr>
<td>Cancer Council Australia</td>
<td>128</td>
</tr>
<tr>
<td>Clinical Guidelines Network</td>
<td>131</td>
</tr>
<tr>
<td>Clinical Oncological Society of Australia</td>
<td>132</td>
</tr>
<tr>
<td>Faculty of Radiation Oncology, RANZCR</td>
<td>133</td>
</tr>
<tr>
<td>Medical Oncology Group of Australia</td>
<td>134</td>
</tr>
</tbody>
</table>

### Calendar of meetings

<table>
<thead>
<tr>
<th>Event</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>136</td>
</tr>
</tbody>
</table>
The 40th anniversary of the Clinical Oncological Society of Australia (COSA) is a milestone for the society itself and to the many aspects of cancer control to which society members both contribute and continue to promote in Australia.

Forty years ago cancer control in a clinical sense was a relatively unconsidered entity. Patients consulted their local doctors who frequently oversaw their total management. There were few clinicians other than radiotherapists who were considered to be cancer doctors. Once patients were referred to a specialist, that clinician frequently looked to the care of the patient thereafter, and continued until absolutely nothing more could be done. This was the practice pattern and it limited patient care. There were few institutions dedicated to delivering active cancer care while cancer was still treatable; there was a general sense of patient ownership by clinicians. Within the referral process, patients often had to make appointments far from home. These were negotiated appointments and meant frequent treks between doctors’ rooms. Patients frequently had to meet heavy economic demands.

To be fair, governments were aware of cancer and contributed to funding of education at public and professional levels, but individual patients and their families were often bewildered in this area and felt short-changed during the course of their management and at what they felt were unsatisfactory outcomes.

However, changes occurred as they always do and there were strong minds and hearts belonging to skilful people who began to look more carefully at how cancer could be better controlled and managed. There were small groups exploring the way ahead, as new findings in cancer control and as new patterns of care were acknowledged. One such group became COSA.

COSA owes a great deal to three of its founders. Brian Fleming, a head and neck surgeon in Melbourne, had observed what was happening in the cancer arena overseas and thought it should happen here. Together with Leicester Atkinson, an English trained radiotherapist who was striving for more modern equipment, and Robert Melville, a Sydney surgeon interested delivering care in breast cancer. They gathered some like-minded people to start to address the issues facing cancer control. COSA became a reality in 1973, with Brian Fleming as its President. He was succeeded in turn by Atkinson and Melville. The first two presidents each had three years to ensure stability and since then a two year presidency has seen steady longitudinal and additive growth. The first medical oncologist and total academic was Martin Tattersall, who became President in November 1981. These early leaders have been followed by distinguished and skilful clinicians who have covered the spectrum of modern day skills in cancer control (table 1).

<table>
<thead>
<tr>
<th>President</th>
<th>Dates of service</th>
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<tbody>
<tr>
<td>Mr Brian Fleming</td>
<td>Nov 1973 – Nov 1976</td>
</tr>
<tr>
<td>Professor Leicester Atkinson</td>
<td>Nov 1976 – Nov 1979</td>
</tr>
<tr>
<td>Dr Robert P Melville</td>
<td>Nov 1979 – Nov 1981</td>
</tr>
<tr>
<td>Professor Martin HN Tattersall AO</td>
<td>Nov 1981 – Nov 1983</td>
</tr>
<tr>
<td>Professor Gordon Clunie</td>
<td>Nov 1983 – Nov 1985</td>
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<tr>
<td>Dr Malcolm Coppleson</td>
<td>Nov 1985 – Dec 1987</td>
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<tr>
<td>Dr John A Levi</td>
<td>Jan 1988 – Dec 1989</td>
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<tr>
<td>Professor Richard M Fox AM</td>
<td>Jan 1990 – Dec 1991</td>
</tr>
<tr>
<td>Professor William H McCarthy AM</td>
<td>Jan 1992 – Dec 1993</td>
</tr>
<tr>
<td>Professor Alan S Coates AM</td>
<td>Jan 1994 – Dec 1995</td>
</tr>
<tr>
<td>Professor Robert JS Thomas</td>
<td>Jan 1996 – Dec 1997</td>
</tr>
<tr>
<td>Professor Henry Ekert AM</td>
<td>Jan 1998 – Dec 1999</td>
</tr>
<tr>
<td>Professor John Zalcberg OAM</td>
<td>Jan 2000 – Dec 2001</td>
</tr>
<tr>
<td>Dr Lizabeth Kenny</td>
<td>Jan 2002 – Dec 2003</td>
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<tr>
<td>Professor Stephen Ackland</td>
<td>Jan 2004 – Dec 2005</td>
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<tr>
<td>Professor David Currrow</td>
<td>Jan 2006 – July 2006</td>
</tr>
<tr>
<td>Professor David Goldstein</td>
<td>Aug 2006 – Dec 2008</td>
</tr>
<tr>
<td>Professor Bruce Mann</td>
<td>Jan 2009 – Dec 2010</td>
</tr>
<tr>
<td>Professor Bogda Koziwara</td>
<td>Jan 2011 – Nov 2012</td>
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<tr>
<td>A/Professor Sandro V Porceddu</td>
<td>Nov 2012 -</td>
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The Presidents have been assisted in pursuing their goals by dedicated staff, initially by Lawrie Wright, who helped effectively establish and promote the Association. In 2003 Margaret McJannett became Executive Officer. Through her generosity and management skills she adopted changes and incorporated advances as they developed.
These moves cemented COSA as a leader in cancer control. She and her staff established a succession which works closely with all elements of COSA to ensure success across Australia.

No less than 27 groups have since joined COSA, with experimental oncology and head and neck leading in 1973, breast in 1974, and the remaining groups joining in an orderly fashion over time, and this is likely to continue. The significant input of nursing and psychosocial groups adds to COSA’s lustre and an inexhaustible future.

The forming of the individual groups (table 2) reveals the dates of their commencement and acts as a strong indicator of how individuals had made the decision to develop special skills and no longer work in isolation. Multidisciplinary groups interested in cancer care were aborning.

Table 2: COSA group history

<table>
<thead>
<tr>
<th>Group name</th>
<th>Dates</th>
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<tbody>
<tr>
<td>Breast Cancer</td>
<td>1974-2011</td>
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<tr>
<td>Cancer Biology</td>
<td>2011-2013</td>
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<tr>
<td>Cancer Research</td>
<td>1978-2010</td>
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<tr>
<td>Experimental Oncology</td>
<td>1973-1977</td>
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<tr>
<td>Cancer Nurses Society of Australia (CNSA)</td>
<td>2003-2013</td>
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<tr>
<td>Oncology Nursing (CNSA)</td>
<td>1980–2002</td>
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<tr>
<td>Cancer Pharmacists</td>
<td>1991-2013</td>
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<tr>
<td>Clinical Trials Research Professionals</td>
<td>2013</td>
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<td>Clinical Research Professionals</td>
<td>2006-2012</td>
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<tr>
<td>Data Managers</td>
<td>1991-2005</td>
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<tr>
<td>Epidemiology</td>
<td>1978-2013</td>
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<tr>
<td>Familial Cancer</td>
<td>2007-2013</td>
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<tr>
<td>Gastrointestinal</td>
<td>1977-2013</td>
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<tr>
<td>Gynaecology</td>
<td>1976-2013</td>
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<tr>
<td>Head and Neck</td>
<td>1973-2001</td>
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<tr>
<td>Lung</td>
<td>1982-2013</td>
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<tr>
<td>Medical Oncology (MOGA)</td>
<td>1979-2013</td>
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<td>Melanoma and Skin</td>
<td>1982-2013</td>
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<tr>
<td>Neuro-Oncology</td>
<td>2004-2013</td>
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<td>Nutrition</td>
<td>2008-2013</td>
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<tr>
<td>Paediatric and ANZCHOG</td>
<td>1974-2013</td>
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<td>Palliative Care</td>
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<td>Psycho-Oncology</td>
<td>1993-2013</td>
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<tr>
<td>Radiation Oncology</td>
<td>1997-2012</td>
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<tr>
<td>Regional and Rural</td>
<td>2002-2013</td>
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<tr>
<td>Social Work</td>
<td>1987-2013</td>
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<tr>
<td>Surgical Oncology</td>
<td>1997-2011</td>
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<tr>
<td>Urologic Oncology</td>
<td>1976-2013</td>
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These observations and the reality of the strength shown in the annual COSA meeting every November demonstrates that the truth and strength derived from association of focused minds are not evanescent.

This special issue of Cancer Forum acknowledges the 40 years of COSA and addresses a number of areas relevant to cancer control and how they are being impacted by wider cooperation and broadening of minds towards management of malignancy.

I have enjoyed the opportunity to pay deference to this special association which is rather unique in the Australian scene.

A wide range of endeavours is represented and the health of each segment, as expressed through leaders in each field, is self-evident. It was determined that the common cancers should be short presentations in the interest of the length of the issue.

The presentation has been broken into four parts to represent COSA’s activities - the patient, craft based, specific cancers and applied sciences. Each paper addresses a special subject and is complete in itself. While there will be some overlapping, all are directed at an element of cancer control.

The patient
The many faces of prevention in the practice of oncology – each a challenge to the clinician

Zucca et al outline that prevention in oncology is usually addressed towards progression of treated cancer or development of new cancer.1 The authors promote prevention in a holistic scenario.2 This approach features the prevention of suffering and the maintaining of quality of life. The health professionals in the cancer team are encouraged to promote healthy lifestyles for patients and for the relatives for whom the patients’ cancer (the patient and the cancer) pose risk.

The paper is presented in three parts and will reward those who read it in its entirety.

1. **Primary and secondary prevention in the practice of oncology.** The most important factor is to treat pain. Despite strong guidelines to assist in pain management, one in two patients have cancer associated pain which is frequently undertreated because its intensity is underrated by observers. Fatigue is overlooked and not addressed in 40% of cancer patients.3 These two factors deserve more frequent oversight, as do unmet psychological issues, as focused care can prevent adverse effects and help avoid poorer physical outcomes. The Institute of Medicine has recommended strong survivorship care, which should be facilitated between cancer and primary care providers (outlined by Jiwa in this issue) to better ensure recommended care for non-cancer conditions.4,5

2. **Prevention of family members for whom patients convey risk.** Risks for hereditary cancers are discussed and attention to published surveillance programs recommended. Spouses lifestyle behaviours involve
smoking, body mass and diet, hypertension and cardiac disease. There is no specific guide, but generally accepted lifestyle factors should apply. Families with suspected hereditary cancers should be referred to a familial cancer registry and enrol for surveillance.

3. System based prevention. The oncology service should anticipate and meet the needs of cancer patients in delivery of care, cementing better relations and trust with providers. This approach is elegantly summarised in figure 1 within Zucca et al’s paper. Anticipatory planning is reported as allowing advanced care planning, catalysed by shared care planning and promoting life expectancy discussion. These shared care factors should optimise the quality, effectiveness and productivity of the system, which must be subject to measurement of system function and for evaluation of quality improvement. Over time, this approach should eliminate the need for crisis management and become a system that involves patients at every step. May it happen sooner rather than later.

Patients play a part in their own care
Luxford makes the unambiguous observation that patients are entitled to receive respect and understanding of their values and preferences, established through courtesy, communication and trust. COSA has been a catalyst in promoting comprehensive approaches involving individuals in their own care, but also in research, governance and policy. COSA has worked with a number of groups promoting consumer involvement in clinical cancer research through “increased training, mentoring and collaboration across the 14 cancer cooperative trials groups”. The paper summarises the moves to rise above the ‘disease-based’ model of care and recognises that acceptance of evidence is upon us. In summarising consumer involvement, ‘nothing about me without me’.

Psychosocial aspects of delivery oncology care: an update – a win-win situation
Butow et al present a paper clearly stating the factors faced by oncology patients in relation to their psychosocial needs in the broad generality of their lives, and also the effects on those around them when being presented with a diagnosis of life threatening disease.

The practice of psychosocial care became established in the 20th century, but psycho-oncology emerged as a defined discipline only 40 years ago. The first psycho-oncology interest group in Australia was established within COSA in 1996 and merged with (PoPoG) in 2004 as one of the country’s 14 national cancer trial groups. Australia’s cancer researchers and consumers have joined to advance the field and together with many organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer and organisations have produced evidence-based guidelines for psychosocial care of women with breast cancer. These researchers have demonstrated that communication between health professionals and patients is a crucial element of quality health care despite being a challenge to all groups. In Australia, patients expect effective communication with their doctor and the opportunity to do so.

Downsides occur when patients are dissatisfied with communication; noncooperation or compliance and reversion to alternative medicines are important elements of failure. These trends have been clearly observed and Butow et al point to Australian randomised control trials, as being the first in the field. Trials have been extended to involve supportive care/psycho-educational interventions that are clinically feasible and can be demonstrated on strong evidence to have a positive impact on patients.

The authors also observe that some patients live longer and are ‘survivors’. Their special needs are being addressed across Australia with the formation in November 2012 of a cost approved survivorship group, from which it is certain high level evidence-based knowledge will emerge to aid clinical carers. Interventions, will undoubtedly flow and supplement cancer plans and priorities among psychosocial researchers. It is clear that Australia has now placed its own indelible mark on the cancer agenda in relation to psycho-oncological and survivorship issues.

Medical and psychosocial challenges in caring for adolescent and young adult patients with cancer
Anazodo and Chard are reporting on a very young speciality and address both clinical and healthcare delivery matters. Adolescent and young adult (AYA) patients with cancer are categorised as being between 15 and 25 years of age. The authors note that people in this age range have needs that differ from both younger children and adults, and are entitled to receive specialised services.

People with lower socioeconomic status have lower five year survival than those living in areas of higher economic status (90% v 85%) and are 1.3 times more likely to die if they live outside a big city. There is lack of improvement in survival figures between children and AYAs (survival gap) in specified tumour groups; this causes great concern among both professionals and carers and is not yet explained.

The authors are limited in providing reasons for lower survival rates, but outline a range of suggestions for study, including RCTs which are to be encouraged; tissue banking outlined in this group of papers should not be overlooked.

Psychosocial aspects are better developed and distress (a spectrum of clinical conditions from sadness and fear to depression and anxiety) is an area that should attract attention of all cancer healthcare workers. CanTeen’s psychosocial screening tool to guide psychological assessments has been in use in youth cancer services since May 2011. It is planned to validate this tool in international studies and it may be the key to better outcomes. Government has recognised the validity of this infant speciality and in 2010 provided CanTeen with supporting finance to administer the Youth Cancer Networks Program, leading to provision of services in mainland Australia. The effectiveness of this program is undergoing implementation research to ensure an evidence base. The issues that involve survivorship have been covered extensively in Cancer Forum, but further research in assessing and advising survivors has high priority. Fertility preservation, early diagnosis and better assessment has been guaranteed by COSA and CanTeen.
Specialisation at this early stage with a special oncology certificate in Adolescent Health and Welfare, was created at the University of Melbourne in 2011.

**Their care – our inheritance [healthcare of Indigenous people]**

Condon et al's paper is a challenge to our hearts and minds.22 Our hearts are easily in place with doing something to alleviate the problems outlined. Our minds have produced numerous approaches and extremely laudable work from dedicated people. Governments have given money and acronym-based management groups, but despite Reconciliation have yet to find ‘can do’ in the minds of all the populace, both Australian and Indigenous people.

After 225 years, Australia is a country where Indigenous people have a lower incidence of cancer than non-Indigenous people, but their prognosis is poorer. This most often is because diagnosis is later or too late. Furthermore, it is unfortunate that Indigenous people often do not live as long as the remainder of the population and this may accentuate what appear to be poorer outcomes of treatment. Patients may contribute to the cancer through their toxic lifestyle and are less likely to receive complete or curative treatment than non-Indigenous Australians, “particularly in the first year after diagnosis”.

The paper identifies that Indigenous people have some protective factors eg. greater levels of melanin in skin, earlier age pregnancy and longer breast feeding, whereas lower participation in cancer screening, higher prevalence of hepatitis B and higher risk of smoking are adverse factors. Smoking is the single most damaging risk factor for cancer and many other health problems.

A good report on significant reduction in smoking has been recorded recently and state Governments and anti-tobacco groups have had significant effect, yet 47.7% of Indigenous people aged 18 and over still smoke.23 It is important that governments and advocates continue to be supporters of anti-smoking programs.

Screening programs need encouragement in carefully planned approaches; maybe one cancer at a time would be worth trying. Teams need training and greater exposure of medical students to elective term research through good mentors and sound advisors; this approach might widen the committed pool required. I certainly observed strong interest in indigenous health by medical undergraduates when I was at James Cook University Medical School last year.

The National Health and Medical Research Council has established studies to discover indigenous strategies to improve cancer outcomes via engagement, research, translation and training (DISCOVER-TT). An educational network for practitioners, policy makers and researchers, the National Indigenous Cancer Network is being established through the Menzies School in Darwin and appropriate institutions to learn more about cancer in Indigenous people.

**Craft based**

**Primary care providers and specialists join together in patient care**

Jiwa, McManus and Dadich make a strong observation that primary care in Australia is "well positioned to support individuals diagnosed with cancer and their caretakers."76 Primary care providers have a number of impediments to address and overcome if they are to provide optimal quality and continuity of care. The authors performed a review of research available in this area and identified a paucity of evidence-based knowledge of practice, a hiatus that clearly needs to be addressed. Recommendations address the areas of deficiency and make persuasive suggestions for primary care providers involvement following specialists treatments and strategies, and for continuity of care to be planned before patient discharge.

**Forty years of nursing in Australia – the emergence of a specialty**

Yates and Aranda record the dramatic changes that have occurred in nursing in Australia from that of 40 years ago.24 While all areas in cancer care have experienced progress, perhaps nursing has incorporated more changes than any of those in health care over this period would have envisaged.

When the Government decided to move all nurse training from hospitals to universities in the 1980s, there were fiery discussions on the pros and cons of the magnitude of the changes. The Government was right. Nursing training was reset and became homogeneous over Australia by the time transfer was completed in 1944, in spite of those who denied change could happen in Australia.

Once there was a single entry required for practice as a registered nurse. The opportunity for nurses to advance through university-based processes of masters and doctorate degrees was a new beginning. Now nurses in special areas have defined their special needs and embarked on specialisation in various areas. For instance, nurses with a special interest in cancer have transitioned through COSA and, while maintaining strong links with the society have established the Cancer Nurses Society.

While being highly specialised, being a nurse conjures up strong images in the eyes of patients; maintaining a ‘nurse’ image will not detract in any way from the nurses ambition of fulfilling important specialist roles.

Papers by Butow, Koh, Luxford and Zucca carry strong messages for nurses, and indeed all health workers, to adopt supportive and innovative approaches to care which strengthen the capacity of patients to be involved in their own care.18,7,25 Such processes will strengthen patients’ capacity for involvement in their own management and make for better multidisciplinary, professional and inter-professional interaction and patient satisfaction. Nurses will have significant opportunities to ensure that patients receive optimal pain relief. Other papers refer to unrelieved pain,26,27 which could be an area where cancer nurses working with palliative care teams can help eliminate judgemental assessment once appropriate distractors are eliminated and pain relief administered.1 The nursing odyssey is another good news story in cancer care.
Evolution of palliative care in Australia 1973-2013 – an icon for compassionate care

Currow and Phillips relate the background of the development of palliative care in Australia and its association with the development of oncology services. They take into account the continuous development of sub-specialist groups in oncology. Early on, services for the dying were initially directed at the poor and the dying and included problems beyond cancer care. Initially, there were three major service groups and there were also smaller groups in suburbs and towns, mostly under religious operators. In most local areas, there were dedicated nursing staff who took care of these patients, usually assisted by local GPs. There were no formal discharge policies and as a consequence, patient numbers grew in spite of the nature of the facility.

The authors outline the changes that led to the important step to bring palliative care into existing health services, so hospices closed. Although not all agreed with the model developed by the Webster Committee, it prevailed, and has been very successful. Its spread was aided in no little part by associating with health care groups already interested to support palliative care: oncology primary care, anaesthesia, pain medicine, general medicine, geriatrics and psychiatry. Each of these specialties had their champions and contributed to progress on the basis that they would assist development of processes directed at ameliorating the lot of patients requiring palliative care services and their families. Government support in relation to Medicare agreements has increased service and increased geographical access.

National funding has also assisted research, much of it being at category 1 level. Research sources and access to evidence has been nationally facilitated.

The authors acknowledge and encourage efforts to get a handle on drugs traditionally used, but not proven effective by a range of phase III trials. Quality of care meeting benchmarks and review is a constant feature of palliative unit activity.

It is pleasing to see two iconic peers in the field in Australia recognised for their persistence and early success, the late Wally Moon and Fred Gunz. Fred himself lent on Cancer Society of Australia and COSA early in the piece to promote a palliative mind set.

Importantly, undergraduate education to entrench the overall skills required in palliative care as a part of medicine, and the outreach to ensure all graduates can engage and plug into a program which seamlessly enhances the essential dignity of patients and their care and totally frees them of pain, is a continuum commencing when appropriate to patients needs and not just seen as a terminal endeavour.

Radiotherapy a miracle of cooperative ingenuity

Kenny et al in their well stated paper, fully justify the avant-garde title. The authors strongly support the role radiotherapy contributes to integrated cancer care as now practised. The advances in the field would, it is thought, more than fulfill the aspirations of 40 years ago. They restate their credo that delivery of radiation therapy “is, always has been, and always will be” to treat cancer tissue and spare normal tissue at a maximal level. Progress has required massive organisation of technological resources and skilful integration with all elements of cancer care. Its importance in the cancer field far exceeds that of 40 years ago. Radiation oncology requires the near perfect symbiosis of basic scientific research, bioengineering and nuclear physics, combined with the highest level of oncology, medical and radiological training.

As essayed for the reader, radiation care is an example of what science can do when appropriately integrated into cancer care. Every component of this paper deserves special attention.

Aside: The only equivalent to collating all these technological resources was seen in the development of the atom bomb and demonstrates that some good can come from horrendous events.

Surgery becomes multidisciplinary

This paper stresses the need for strong support from surgery in areas where it has been regarded as the mainstay of cancer treatment for centuries, and where it still remains a central component of cancer management. Mann et al discuss the key elements of changes in surgery that have occurred during the last 40 years. They also encourage speculation on future changes. It is clearly noted that surgeons and surgery no longer stand alone and have shown leadership and flexibility in becoming involved in multi-disciplinary care. Surgeons have shown that in a multidisciplinary approach with committed expert personnel, together with multiple care modalities and where necessary, special technology can be vital to sound surgical practice. Sound decision making can lead to better selection of care and better and safer outcomes which boost current expectations, particularly when patients are involved in the planning process.

The surgeon’s approach to screening and early detection of malignant lesions are of importance in reducing the magnitude, deformity and disability which hitherto confronted patients after heroic or extended surgery. It is questioned as to whether or not some of this surgery was appropriate. Further challenges will, it is assumed, lead to a greater role for neo-adjuvant therapy in reducing the extent to which surgery is required in patient care.

Screening: a critical process for clinical practice

Penman discusses screening and addresses areas of success and areas where physician alertness needs to be maintained. He urges the development of guidelines that will catalyse physician motivation to appreciate the value of screening and early detection, and to optimise the response by taking notice of the results. COSA itself was born as efforts to screen for cancer was being pioneered, its particular effort being directed to the breast, an area of limited evidence at that time. Nor was time lost in promoting education on ‘the seven warning signs of cancer’ promulgated by the American Cancer Society.
of course, are interested in the results of individuals, particularly those that relate to themselves. The paper addresses the range of current screening activities and particular reference is made to hepatocellular cancer. This demands the attention of us all and support for local efforts is important.  

**Most common cancers**

**Breast cancer - the change to chronic disease**

Breast cancer has clearly been and remains the foremost malignancy in the public eye. Coates explains the breadth of change in its diagnosis and management and what a difference 40 years can make. No longer is the most massive surgical procedure a mark of capable management, and the move of diagnosis from palpability and possible spread of cancer to radiologically diagnosed minimal malignancy has been beneficial. Breast reconstruction has led to greater personal esteem as body image is restored. Endocrine and drug therapies are now better tailored and effective, while molecular therapy targeting specific molecular changes represents an exciting and possibly minimalistic approach in some patients.

Attention to the patient’s quality of life and self-evaluation has closed a deep gap from the past. The growth of breast caring supportive staff has significantly reduced patient anxiety. The Australia-wide support and conduct of clinical trials is now expected rather than doubted, and has strong patient and consumer advocates. Cancer of the breast is now more effectively treated and has an increasing survival rate.

**Prostate cancer – exciting news for men**

Prostatic cancer is the most common non-skin malignancy and a frequent cause of death in men. In this paper, Davis et all endorse that most men diagnosed with prostate cancer have localised disease and that prostatectomy or radical radiotherapy, in spite of a range of morbidity, have excellent cancer treatment outcomes. Relapsed or metastatic disease is treatable, but leads to the lethal form of disease, metastatic castrate-resistant prostate cancer (mCRPC) over variable lengths of time. Docetaxel was introduced 10 years ago and new treatments, which only became available in the last two-three years, are showing benefit. All depend on understanding the unique biology of prostate cancer and recognising of the important place played by signalling through the androgen receptor axis, which is still critical in many instances in mCRPC, even when androgen deprivation or receptor blockade have already failed. Among many positives is the development of a new generation of androgen receptor antagonists. A new cytotoxic drug, Carbazitaxel, is effective and is allowed for use and reimbursed for mCRPC post-docetaxel. Bone therapy has been expanded as targeted therapy with radium 223 chloride. Effective immunotherapy has shown advantage and is being extensively trailed in mCRPC.

Image-guided and robotic ablative surgery are being investigated. Imaging and its role in underpinning clinical confidence is discussed. The demand of each man with mCRPC to have tailored supportive treatment is endorsed. The authors’ encouragement for excitement in the new therapeutic targets to increase the benefits for men with mCRPC is inimical to better understanding the biology of this difficult disease, which should be of assistance to both clinicians and patients and lead hopefully to better outcomes.

**Colorectal cancer – an exemplar of clinician cooperation**

Over the last 40 years, the range of care of this common cancer has been a notable success for Australian clinicians and patients, particularly those contributing through local trial groups. COSA’s role in facilitating research, education and multidisciplinary interaction in an academic environment has further improved patient care. This broad spectrum of study, education, prevention and best clinical care is well stated in Segelov’s contribution. The additional role of COSA in supporting screening from its beginning, before becoming government funded (National Bowel Cancer Screening Program) is worthy of particular notice. More sophisticated diagnostic evaluation by MRI is now the standard of care. Another significant method of diagnosis, with PET and CT scanning, has led to better selection of patients with liver metastases who are suitable for appropriate hepatic resection. Australian and New Zealand surgeons have contributed to proving laparoscopic equivalence with open surgery (ALCCaS study) and are continuing trials with AGTIG (Australasian Gastro-Intestinal Group) (a la carte).

The importance of quality training for colorectal surgery, while at the same time promoting appropriate surgery for liver and lung metastases, has been clearly demonstrated. The value of multidisciplinary teams in these areas of progress together with chemotherapy, radiation therapy and psychosocial and survivor support underlies the strong moves that are being realised in personalised medicine. This needs to be built on better understanding of the genetic and molecular elements of the cell. The results of these efforts will be able to be translated to rural and regional centres and countries beyond our shores.

**Lung cancer – a continuing challenge and a public health victory**

Survival for lung cancer continues to be among the worst for any cancer. Ball outlines the quintessential problems that have faced those treating lung cancer over the last 40 years. It is noted that a nihilistic trial in 1971 discouraged and delayed active treatment of the disease and this view continued for some years. A most important advance however, resulted from public health advocacy and the active anti-tobacco campaigns, which have resulted in a fall in mortality from lung cancer. The public health campaign continues to gain acceptance and strength.

In 1973, stage and performance status were recognised as critical prognostic factors and CT screening of the chest was adopted in staging and radiotherapy planning. Each decade since 1970 has been marked by a significantly strong research effort and been rewarded with an improvement in outcomes resulting from newer therapeutic approaches, and confirmation that lung cancer can be detected earlier by CT scanning. Both small cell lung cancer and non-small
cell lung cancer require well directed and continuing research, to identify the best of many strategies available.

**Haematological malignancies – showing the way in oncology**

Bishop notes that the treatment of haematological malignancies introduced systemic treatment and combination therapy and reduction of either the need for or the extent of radiotherapy.43 These agents blazed a trail for oncology to follow. Although Paul Ehrlich was first to use the term ‘chemotherapy’, its human use was hastened by a very serious and serendipitous affair in war. It was serendipitous on two accounts, first the sinking of the liberty ship John Harvey in a Luftwaffe raid in Bari Harbour in Italy on 2nd December 1943. The ship was carrying a secret cargo of 2000 M47A1 mustard gas bombs, to be used if Germany used mustard gas as it had threatened in Italy. On sinking, the liquid sulphur mustard splashed into the water. The second serendipitous fact was that the water was contaminated by oil spilled from the damaged ships. The sailors who had abandoned their ships and became smeared with oil, an effective solvent for sulphur mustard. On triage, those damaged by blast and fire were treated and the oil smeared sailors were not given priority attention; sailors and hundreds of civilians were poisoned by a gaseous cloud of sulphur mustard vapour. The incident was kept secret by the military, but bone marrow failure led to a wider medical investigation and to the first chemotherapy drug, mustine. In a sense, these two serendipitous events led to an enormous breakthrough in medical care and set the scene for the birth of oncology.44

The author addresses the progress made in the areas of lymphoma and leukaemia and includes mention of the move towards personalised or precision therapy.16 The development of tyrosine-kinase inhibitor drugs introduces the possibility that they may have use as targeted therapies,16 and also be effective in other malignancies than chronic myeloid leukaemia. The importance of allogeneic haemopoietic cell transplantation remains as a durable way to eradicate chronic myeloid leukaemia. Monoclonal antibody development has played a significant part in therapeutic plans, some in association with other systemic drugs. Genetic studies and treatment may be of greater use as they draw on genomic resources.

A possible obstacle to progress in the general field of cancer arises as more defined subsets of malignancies indicate the challenges these create for large scale and clearly necessary clinical trials.

**Melanoma – the nemesis of sunshine...**

Thompson and Menzies make a clear statement on melanoma as at 40 years ago and pay appropriate respect to the efforts of two Australians, the late Gerald Milton and Neville Davis, who led the world in establishing dedicated melanoma treatment centres.45 The recognition of Oliver Lancaster’s epidemiological research revealing exposure to solar ultraviolet radiation in melanoma genesis, marked a huge Australian contribution to leading the charge on melanoma clinically.46 Breslow thickness of melanoma is recorded as the principal indicator of outcome, while indicating that ulceration and mitotic rate are significant factors. The Breslow thickness is discussed in relation to surgical clearance of lesions. In lesions 1-4mm thick, the sentinel node has, on the basis of interim trial (MSLT-1) results, provided accurate staging and substantial survival advantage if lymphadenectomy is performed when found to be positive.47 This trial has significant Australian input and the final analysis is expected in the middle of this year.

Increased understanding of molecular biology and immune regulation are continually changing systemic treatments to patients’ advantage and research continues. Immunological therapies in melanoma and their effects are described, but most including antibodies are under trial at present. Melanoma persists as a serious problem in Australia and is increasing worldwide. Multidisciplinary trials will play an important part in research at basic and clinical level. The development and contribution to well-planned trials continues to be an imperative if more definitive therapy is to be achieved.

**Applied sciences**

**Tissue banking and its role in clinical and biological advances in oncology – a reservoir for future research**

Gundara and Sidhu point to clinical and translational aspects of oncology and their exponential advancement over 40 years.17 The laboratory, “where rigorous scientific study of the biological milieu that is neoplasia has been undertaken,” is responsible for much of the progress that has paralleled advancement in informational technology systems and mathematical modelling facility in both in vitro and in vivo tissue experimentation. It is a given that cancer clinicians know that understanding of cancer can be derived from asking questions of cancer in human tissue samples. This process is a benefit derived from tissue banking, where tissue deposits yield material from study and provision of information to researchers. The authors refer to the history of this enlightened activity by Rudolf Klen in 1952, and while initially only cadaver tissue was banked, it has now expanded to involve living donor tissue.48 It is important that all clinical oncologists be aware of best quality of care and the ethics that relate to tissue banks and medical registries. The clinical responsibility towards patients are imperatives to be noted, understood and acted upon.49,50

The authors refer to their own units’ tissue bank and point to its value in stimulating international cooperation, especially when the cancer is rare.51,52 Electronic records will assist further in advancing translational research hubs and assist in linking tissue and clinical data. These factors are impacted in the age of personalised medicine, which is riding on the back of tissue banks and laboratories that are researching new methods and standards of diagnosis.12,16,18,53 They also allow review of old material at appropriate times.

Optimising tissue bank collection of clinical tissue and other appropriate body elements has been achieved in some sites.54 This requires that all cancer clinicians develop a prospective mindset to ensure materials are ethically collected, promote a bedside bench to and return to bedside attitude in practice and training, embracing the full force of demands as outlined in the authors’ ‘call to arms’.
Targeted therapies, aspects of pharmaceutical and oncological management

Brown and Burdett have submitted a comprehensive paper on targeted therapy, which is a new and complex subject. Surgery, radiotherapy and chemotherapy are the established modalities of cancer treatment. The authors suggest that immunotherapy is ready to be included as the fourth pillar of standard cancer therapy.

Each element of this paper conveys a clear message to the reader and carefully guides interpretation. Definition of the subject is clearly essayed. The aim of personalised cancer medicine is to deliver the right drug to the right person at the right time. However, there are distractors which, it is indicated, may not always allow for choosing the right drug, right cancer or right person. The scope of targeted therapy is to encompass “the complex biology intrinsic to most cancers”. While the aim to find the right target can be a protracted and difficult exercise, identifying an appropriate target mutation can be evident to the receptive researcher/clinician.

The Medical Benefits Schedule now reimburses the cost of genetic tests to allow determining use of targeted cancer therapies. While this will hasten research, challenges to drug access and reimbursement will still be hurdles to jump to achieve truly personalised cancer medicine.

The benefits of being on target are well outlined, and the importance of being well acquainted with the tumour biology and becoming aware of newer and emerging investigative tools such as functional cancer imaging should excite us all. The final sentences in the paper should encourage clinicians and researchers of all generations.

“Therefore work on providing electronic point of care services may help to mitigate the risks of polypharmacy. Ultimately however, the targeted therapies boom will oblige clinical oncology professionals to obtain new skills to control cancer.”

This paper was an exciting primer and will encourage clinicians to maintain close surveillance of the new literature as it appears, so that their cancer patients can receive the full measure of care.

Randomised clinical trials the core of the future in clinical practice

Over the last 40 years there has been a strong move to, where possible, incorporate evidence-base in medical practice. In most areas of practice, evidence is accrued through randomised clinical trials (RCTs). Sjoquist and Zalberg support this approach and outline various aspects of the process to achieve their titled outcome.

Establishing trials that are both recognised and trusted involves a wide range of tools that are to be embraced by developers of RCTs, whether they are based on an individual investigation or cooperative group. Initially, safety and efficacy of the tool chosen to answer the question, together with the special elements of psychological support, palliation and outcome, are expected by patients and their significant others. These factors must be addressed during the trial if patients are to accept the findings. Patients must be strong contributors to the trials process.

The authors outline some specific successes and make the point that in Australia, enthusiasm and collaboration have resulted in cooperative trial groups, which from the time of developing each trial makes literally enormous demands on all members of the trial group. They are unable to relax in their role without adversely affecting others who must “pick up the ball” for them. Seeing any trial through from concept to finalisation and presenting results in acceptable form can take focused effort over a period of years.

Investigator initiated trials have found significant trust as against industry sponsored trials. Investigator initiated trials must appear substantiated by evidence at every point to retain accolades and trust and the question asked must be seen as relevant by peers. These characteristics also apply to cancer cooperative trials groups and must exercise the minds of trial developers in selecting collaborators who can stay the distance. Australian trials groups have been rigorous in design and personnel and patient selection.

The importance of RCTs being biologically appropriate, readily interpreted, clinician accepted and having regulatory approval, means all have met high standards. Some barriers to trials development persist in relation to funding, total signing off of the nationwide ethics approval system, trials design and time involved by collaborators. These areas all continue to be evaluated.

There have been appropriate suggestions that the Pharmaceutical Benefits Scheme should consider funding local drug trials evaluation before listing. This seems a reasonable request. The careful planning and balance of Australian trials have received high recognition. The interest in trials is reflected in the Primary Care Collaborative Cancer Clinical Trials Group (PC4) founded in 2009; it has received many concepts and 34 are under development.

RCTs open the way to develop pathways to tolerable and less demanding care.

Outcomes are important in oncology – what patients expect

Patients have an interest in the outcome of their proposed management from the time they receive a firm diagnosis. Historically, mortality, survival and recurrence rates of cancer have been major factors in decision making, particularly as seen by the clinician. Koh et al report that significant change has occurred, with emphasis being placed on patient reported outcomes being seen as important both in research and clinical practice. Patient reported outcomes are any outcome measures reported by patients without interference or interpretation by any health care professional. The outcomes as perceived by the patient are often intangible to other people and so they are clearly complementary to traditional outcome measures.

Patients also show significant interest in their quality of life; the specifics of measuring quality of life are discussed in relation to health. Health related quality of life measurement needs to be relevant to the condition under care and each measure validated, as patient specific measures allow choice of outcome. Such an approach generates growth in the number of measuring instruments and commercial databases to assist in identifying health related quality of life, but costs are involved in the measuring and repetitive
processing of patient preference and decision making. These areas are still in the research field and the level of literacy to allow their valid use is still not clear.

The authors address cost-effectiveness against a range of health costs as a percentage of GDP, from 4.1% in the Netherlands, to 16% in the US, to 8.4% in Australia. The approach towards 20% presents political challenges. Despite differing costs, life expectancy and cancer outcomes are similar in all these countries. High cost drugs and their benefits, and whether there is fairness if money limits are capped, are matters under investigation.

Patient reported outcomes are becoming a feature of RCTs, but the uptake is slow.

The goal in patient reported outcomes research is to have the knowledge incorporated into practice and improve patient care and clinician capacity. Health related quality of life feedback to clinicians is invaluable in care and understanding of survivorship. If a financial incentive to collect data is effective, it should be pursued to the benefit of patients and perhaps survival of intelligence andfavoured carers for future studies.

References


The Patient

THE MANY FACES OF PREVENTATIVE CARE IN THE PRACTICE OF ONCOLOGY

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Abstract

Prevention in the oncology setting has traditionally focused on the progression of cancer, recurrence and development of new cancers. Increasingly, the focus has moved to a more holistic view of prevention that pursues prevention of suffering and maintaining quality of life. The cancer treatment team has the opportunity to play an active role in the promotion of healthy lifestyles for patients, and the relatives for whom the patient’s cancer conveys risk. Assisting patients to adhere to ‘non-cancer’ care is important for their mortality and morbidity. Given patient’s reluctance to disclose physical and emotional side-effects they may be experiencing, there is a need for health providers to regularly initiate discussions with their patients about their needs. Similarly, an oncology service that actively seeks to understand patient preferences will be better equipped to provide individualised care. A systems-minded approach to prevention may ensure that cancer care is organised to anticipate and to prevent of poor quality care. As the cancer treatment team will continue to play a more complex role in prevention, they must be supported by organisational factors that facilitate evidence-based practice.

An ounce of prevention is better than a pound of cure. This principle is as important in the practice of oncology as it is in primary care. The cancer treatment centre plays a leading role in the patient’s health care during diagnosis, treatment and post treatment follow-up care. Traditionally, ‘prevention’ in this setting has focused on preventing the progression of cancer, cancer recurrence and development of new cancers. However, the focus has moved to a more holistic view of prevention that pursues prevention of suffering and maintaining quality of life.1 This article examines the role of the cancer treatment centre in providing holistic preventative care to patients and their families across the cancer journey. Section one describes primary and secondary prevention of physical and psychosocial issues in cancer patients, including preventing comorbid non-cancer conditions. Section two explores the role of the treatment centre in preventing future cancer diagnoses of relatives for whom the patient’s cancer conveys risk. Section three proposes a systems-minded approach to prevention and explores organising cancer care in anticipation of patient needs and prevention of poor quality of care.

Primary and secondary preventative care

Is there a need to prevent physical co-morbidities?

Focusing on the long-term health of individuals diagnosed with cancer is essential, as almost 60% of those diagnosed live beyond five years post-diagnosis.2 Cancer patients are more likely to have pre-existing medical conditions and are also at risk for the development of comorbid conditions including cardiovascular conditions, osteoporosis and diabetes.3,4 Cancer patients have a 50% higher risk of mortality from non-cancer causes compared to the general population, primarily due to coronary heart disease and stroke.5 However, a cancer diagnosis may divert attention from non-cancer health problems.6 Cancer survivors are often undertreated for chronic medical conditions such as diabetes, heart failure, as well as receipt of recommended preventive services including cholesterol screening.
influenza vaccination, bone density measurements and cervical cancer screening.10

Cancer and other chronic medical conditions, such as heart disease, share many risk factors including smoking, poor diet and physical inactivity. Reducing risk factors by changing lifestyle factors may be protective against the development of other chronic disease, however only 20% of oncologists provide patients with guidance about lifestyle change.4 When comparing lifestyle risk factors between individuals diagnosed with cancer and the general population, Australian cancer survivors are more likely to be smokers (particularly those with tobacco related cancers),10 slightly more overweight or obese and have higher levels of alcohol consumption. Levels of physical inactivity and fruit and vegetable consumption are not different.10

Is there a need to identify patient side-effects early?

The vast majority of cancer patients undergoing treatment will experience one or more side-effects as a result of their cancer and treatments. Up to 90% will experience fatigue,11 33% of patients undergoing curative treatment and 64% of advanced cancer patients will experience pain,12 and 33-45% will experience psychosocial distress.13 Despite guidelines outlining optimal management of side-effects,14,15,16 almost one in two patients with cancer-associated pain is undertreated,17 fatigue is not addressed in almost 40% of cancer patients,11 and between 12-85% of cancer patients report unmet needs for psychological issues.18 Detection of patient concerns is the first step towards appropriate and effective management of issues, however health professionals do not accurately recognise the physical and psychosocial problems that their patients are experiencing.19,20 Patients may be reluctant to disclose issues without prompting from a health care provider.21 22 Undetected and untreated side-effects result in unnecessary suffering and may also escalate in intensity over time. Patients experiencing pain are significantly more likely to be depressed.23 Similarly, depressed patients are less likely to adhere to medical advice and treatment recommendations, which in turn can lead to poorer physical outcomes among patients.24

What can the cancer treatment team do?

The cancer treatment team have the opportunity to play an active role in health promotion across this cancer trajectory by taking advantage of the ‘teachable moment’ that a cancer diagnosis provides,4 and through better management of their patient’s non-cancer health care.25 Asking about current health behaviours is the first step to promoting a healthy lifestyle.26 Appropriate referral and/or provision of information should follow.26

To ensure that the survivor’s health needs are met, the Institute of Medicine has recommended that survivorship care should focus on coordination between the cancer treatment team and primary care providers.27 Survivors who are observed by both a general practitioner (GP) and their cancer treatment team are most likely to receive recommended care for their non-cancer issues.5,7 The cancer treatment team could be informed of their patient’s non-cancer medical history and emphasise to patients the importance of managing non-cancer illnesses. Asking the patient about their contact with other health care providers, such as GPs, may be the first step. When the cancer care is the only routine health care provided, the cancer treatment team should take action, by providing an appropriate referral. Documenting these activities in the patient’s medical record is important, and may serve as a prompt for future consultations.

Given patients’ reluctance to disclose their physical and emotional problems, there are benefits in health providers regularly initiating discussions with their patients about their needs. Health care providers may need to provide patients with ‘permission’ to discuss their issues by encouraging questions, and providing adequate information.28 One proposed way forward has been routine screening for psychosocial and physical issues via self-report surveys and providing summary data to the cancer treatment team. However, while routine screening systems have demonstrated efficacy, effectiveness of these interventions in regular clinical practice has not yet been established.29

Prevention of cancer in family members for whom the patient conveys risk

The patient’s cancer may implicate increased risk for their family members, as a result of a hereditary cancer predisposition or shared lifestyle factors. Key health promotion strategies for at-risk family members include cancer surveillance and targeting lifestyle factors for both patients and family members.

Is there a need to prevent cancer in the first degree relatives of patients?

While cancer risks are greater in the first degree relatives of cancer patients from a variety of cancer types,30 the survival benefits of surveillance are only evident for relatives of colorectal, breast and melanoma patients.31-33 First degree relatives of patients may be classified as average risk where surveillance recommendations correspond with the general population. Other relatives may be classified as moderate or high risk where more intensive surveillance is recommended.31-34 Screening for a genetic mutation may be appropriate when confirmation of a strong family history is obtained,34 however only a small subset of cancers (5%-10%) can be attributed to specific cancer causing genes.34

In Australia, there is no population-based approach to identify and target at-risk relatives of individuals diagnosed with cancer. Identifying at-risk family members depends on the actions of individual health professionals. This relies upon family history taking, yet incomplete records are a common occurrence.35 36 Colorectal screening rates remain low in Australia despite having the best evidence for reducing mortality, with only 18% of individuals aged over 50 tested using the faecal occult blood test (FOBT) within the last five years. Relatives of cancer patients are 20% more likely to be tested with FOBT.37 Only one-fifth of Australian family members with a strong family history of melanoma met National Health and Medical Research Council screening guidelines, with less than 60% ever having received a recommendation from a health professional to conduct skin self-examination or receive a clinical skin examination.38 Mammographic screening in high risk women is conducted according to guidelines in 74% of cases, with the remaining 16% being under-screened and 10% over-screened.39
Is there a need to prevent cancer in the spouses of patients?

Spouses’ lifestyle behaviours and physical health often correspond. Concordance has been found between spouses’ smoking status, body mass, diet and presence of high blood pressure.43, 44 There is modest evidence that spouses may share risk factors for lung, bladder and stomach cancers.45 While no specific guidelines exist for promoting lifestyle factors in the spouses of patients, general population lifestyle recommendations apply.

In the oncology setting, little is known about whether lifestyle interventions are routinely directed to patients only, or to the family unit. However, in the cardiovascular setting, dietary interventions are commonly targeted to both the patient and their spouse. To date, there is insufficient research about whether family-based interventions are any more or less effective than individually focused interventions at changing health behaviours.

What can the cancer treatment centre do?

A cancer diagnosis not only offers a teachable moment for the patient, but also for the family member for whom the patient’s cancer conveys risk.43 While it may be argued that relatives do not fall within the duty-of-care of cancer treatment centres, targeting relatives has the potential to indirectly benefit the patient and impact in a positive way on the lives of both patients and their families.

Given the potential survival benefits of surveillance for colorectal, breast, ovarian cancer and melanoma, attention should be paid to first degree relatives of these cancer patients. Risk levels may be readily identified based on the patient’s family history. Verbal and/or written information about cancer risk, and appropriate screening recommendations, could be provided to the relative or to the patient to pass on to their relatives. Families with suspected hereditary cancers should be referred to familial cancer services and encouraged to join their state-based hereditary cancer registry to facilitate surveillance. As patients often worry about whether their family member might be at risk,46 discussion with patients about risk levels of their first degree relatives may help to meet this unmet need. Furthermore, accessing an at-risk family member via the cancer patient will help to overcome some of the problems with inaccuracies in self-reported family history.47

For patients who have unhealthy lifestyles, it is possible that the spouse may share these risk factors. Therefore, promotion of healthy lifestyle behaviours to both the patient and spouse could double the reach of these important health messages.

System based prevention

The health care system is largely reactive, waiting for trouble before responding.1 Rather than a reactive health care system that responds at the point of crisis, the Institute of Medicine envisions a system that organises the delivery of care in anticipation of the needs of patients.1 It is argued that a health care system of this nature would be more patient-centered.1 Patient-centered care is a central aim of quality health care and is founded on the idea that health care should not simply cure disease, but relieve suffering and maintain quality of life. Patient-centred care must: a) support the provision of information, communication and education to enable patients to understand and make informed decisions about their care; b) attend to consumer needs, values and preferences; c) provide emotional support; d) relieve physical discomfort; e) allow for the involvement of family and friends; and f) be integrated and co-ordinated.48 While patient-centered care is important in and of itself, it is also associated with increased adherence to treatment plans, more efficient care, and improved quality of life.49-51

There are a number of ways we might ensure that the oncology service anticipates and meets the needs of cancer patients. The first is to actively understand the preferences and values of each individual patient in order to provide individualised care. Doing this is likely not only to meet patient needs, but also increase patient satisfaction and trust in their health provider, and the service that they receive.51, 52 The second approach is to prepare the patient for future problems or issues with which they will have to deal, by providing information and an explicit response plan to prevalent and treatable problems.53 The third approach focuses on the way in which the system is currently responding, and by gathering data, anticipate and respond so that any system deficits can be addressed.54 This third approach reflects the Institute of Medicine’s emphasis on optimising the quality and productivity of the health care system,55 whereby measurement of system functioning is essential for quality improvement activities.

What can the cancer treatment team do?

Oncology services should actively seek to understand patient preferences for future care delivery. Examples of scenarios where seeking patient preferences is fundamental to the delivery of quality cancer care include: 1) advanced care planning, which involves seeking patients preferences for end of life care; 2) shared decision making, whereby the clinical knowledge of the provider is considered alongside the preferences, values and needs of the patient, to arrive at the best decision for patient; and 3) life expectancy discussions, whereby patient preferences must be sought regarding the level of information they would like to receive. Figure 1, describing advanced care planning, has been used to illustrate the role of the oncology service in actively seeking a patient’s preferences to prevent poor delivery of care. This scenario contrasts a model of care that reacts during a crisis with an anticipatory model that seeks to understand patient preferences ahead of time. The benefits of the anticipatory model are evident for the patient, their family and the health system.
**Oncology services should anticipate and respond to system deficits at a systems-level.**

A quality cancer treatment centre is “one which is both organised around and responsive to the needs of the people who use it”.54 Patients should receive best practice cancer care, irrespective of the treatment centre they attend, or the health care provider they visit.1 However, if we wish to better meet the needs of future patients and reduce inequities in the delivery of care, first we must understand the current level of care being delivered to patients.1, 55 This information can be used to respond to system deficits.

Assessing delivery of care on a regular basis is essential for identifying deficits in best practice cancer care, and for monitoring progress towards clearly defined goals.1, 56 The Australian Commission on Safety and Quality in Health Care has recommended that systems be put in place to regularly collect information about patient-centred outcomes.56 The gold standard for assessing patient-centred outcomes is patient self-report.1 Most Australian states administer periodic pen-and-paper surveys to subsamples of patients to track quality of care over time. However these surveys are limited in their ability to provide feedback that is both timely and specific. These two essential ingredients would enable individual cancer treatment centres to target their quality improvement activities.57 One solution may be for cancer treatment centres to routinely survey their own patients.56 The use of information technology, such as tablet computers to collect and automatically analyse data, has the potential to provide real time feedback.

**Conclusion**

The practice of oncology in the 21st century has moved to a more holistic view of prevention. Not only can the oncology service successfully treat patients for their cancer, but by delivering optimal cancer care, can relieve their suffering. Cancer care has moved beyond the acute stage of cancer treatment, towards the long-term care of a growing number of survivors with a “chronic” cancer condition. Consequently, the cancer treatment team will continue to play a more complex and expanding role in the delivery of cancer care. To date, a focus on changing the behaviour of individual health care providers via single vector mechanisms, such as distribution of clinical practice guidelines or education seminars, has been insufficient to improve the delivery of care.58 The future of prevention in cancer care may look towards a systems-minded approach to improve the delivery of health care, whereby organisational factors, such as the structure and process of the cancer treatment, are modified to approximate evidence-based practice.53 Future research should be conducted to identify what environmental or system-based changes would facilitate better delivery of patient-centered care.

**Acknowledgements**

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5. Earle CC, Neville BA. Under use of necessary care among cancer survivors.

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**Table 1: Advanced care planning, an example of reactive versus anticipatory care.**

<table>
<thead>
<tr>
<th>Reactive care</th>
<th>Anticipatory care</th>
</tr>
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<tbody>
<tr>
<td>Intensive end of life cancer care provided to all patients.</td>
<td>End of life cancer care consistent with the patients preferences, values and beliefs.</td>
</tr>
<tr>
<td>Family members or health care providers make decisions about end of life care after the patient’s health has deteriorated.</td>
<td>Patients are consulted about their preferences ahead of time, before deterioration of health.</td>
</tr>
<tr>
<td>Patients asked once about their end of life preferences.</td>
<td>Continuous discussion between patient, family and health provider about end of life care, as preferences change over time.</td>
</tr>
<tr>
<td>Patient preferences not documented.</td>
<td>Patient preferences clearly documented.</td>
</tr>
<tr>
<td>Avoiding discussion about end of life care.</td>
<td>Promoting ongoing end of life care discussions that may include informal discussions with family and providers; formal legal documents, appointment of a substitute decision-maker.</td>
</tr>
<tr>
<td>Poorer patient quality of life</td>
<td>Higher patient quality of life.</td>
</tr>
<tr>
<td>Poorer bereavement outcomes for the caregiver.</td>
<td>Better bereavement outcomes for the caregiver.</td>
</tr>
<tr>
<td>Higher health care costs.</td>
<td>Lower health care costs.</td>
</tr>
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PROMOTING PATIENT BASED CARE AND CONSUMER ENGAGEMENT

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Abstract

Consumer engagement has blossomed in recent decades into a comprehensive approach, not only engaging people in their own care, but also in key health care system improvements at a range of levels including health services, research, governance and policy. These changes parallel international progress in patient based care and culminate in the recognition of the need for consumer partnerships in recent national and state frameworks. Striving to deliver patient-based care means that we need to rise above the ‘disease-based’ model of care. Consumer engagement to improve Australian cancer care has grown to support all aspects of the journey.

“Why would you want a consumer on the guidelines working group? This is about best clinical practice. We know the research evidence,” said the doctor. That statement was delivered over 15 years ago now. How things change! Recognising the importance of the patient’s perspective and engaging consumers in all levels of activity in health care has come a long way in Australia in a relatively short period of time.

While promoting consumer engagement in health care has been a more recent development, its origins can clearly be linked to grass-roots community engagement movements in the 1960s and 1970s and public engagement (particularly by UK governments) in the 1980s and 1990s. Initially, patient engagement in health care focused on individual patients and centred on ‘self-management’ of chronic conditions and ‘shared decision making’ for treatments. Equally, the broader social rights movement can be seen to have generated a focus on ‘patient rights’. In 1987, Consumers Health Forum of Australia was established to champion consumer issues. Prominent advocacy groups started to form centred on specific diseases such as HIV-AIDS and cancers.

Australia was recognised early on as leading the way for the world in consumer advocacy. Starting in the late 1980s, researchers worked to identify core components of ‘patient-centred care’, and in 1993 The Picker Institute (US) identified eight domains: respect for patient preferences and values; emotional support; physical comfort; information, communication and education; continuity and transition; co-ordination of care; involvement of the family and friends; and access to care.1 It was acknowledged that really understanding patient values and preferences required establishing a healing relationship between clinicians, patients and patients’ families, grounded in strong communication and trust.2 By 2001, recognition of ‘patient-centredness’ as an essential characteristic of high quality care by the US Institute of Medicine, cemented patient focus as a key domain of quality.3

Against a background of high profile inquiries in Australia highlighting harm to patients and the need improve patient safety,4 consumer engagement has increasingly focused on improving care delivery and on governance. Patient involvement has been recognised as a way to deliver safer care for individuals and to improve accountability in the health services, but requires a shift from provider-focused ‘paternalism’,5 to ‘patient empowerment’.

Recent innovation

Within the last six years, a growing body of evidence has emerged indicating that patient-based care – with patients as true partners – not only improves the patient care experience, but also results in clinical and operational-level benefits. This growing evidence includes decreases in mortality,6,7 rates of hospital-acquired infection,8 surgical complications,9 and improvements in patient functional status,8 and higher quality clinical care.10 The business case for patient-focused care highlights decreased malpractice claims, decreased staff turnover, reduced operating costs and increased market share.11 Leading health care services are those that are transforming their care delivery with a focus on patient and consumer engagement at all levels – from the ward to the Board.12

A systematic review by Doyle et al.13 has also highlighted the positive association between self-reported patient experience, clinical outcomes and resource utilisation (eg. impact on length of stay). Increasingly, patient feedback is being used at a service and systems level to drive patient-focused approaches to quality improvement, evidenced in Australia by state-based surveys of cancer patients. For example, when the Cancer Institute NSW conducted its inaugural patient experience survey in 2007, ‘discussing anxieties and fears’ and ‘pain management’ stood out as key aspects of care for improvement.14

Patient narratives and stories are also acknowledged as powerful drivers of change. The shared stories of people living with cancer have provided great insights and
motivated us to aim to ‘get it right’. Sharing his story of a diagnosis of prostate cancer, Ian Roos encapsulated the journey through diagnosis and treatment choices for many cancer patients – fear of cancer, confronting mortality, quality of life choices and the question of ‘why me’?15

Over the past 40 years, since the Clinical Oncological Society of Australia (COSA) was established, consumer engagement in cancer care has blossomed into a comprehensive approach, not only engaging people in their own care but also in key health care system improvements at a range of levels including health services, research, governance and policy. Australia has a proud history of consumer engagement and advocacy in the cancer field. Early leading groups included Breast Cancer Advocacy Groups (Vic – 1994 and NSW - 1997), Prostate Cancer Foundation of Australia (1996) and Breast Cancer Network Australia (1999). CanTeen was developed in 1985, advocating for young people with cancer.

‘Nothing about me without me’,16 – the catch phrase for improving the quality of healthcare by involving patients – exemplifies the approach used in Australia. Early efforts in consumer engagement ensured that Australian cancer care focused on a comprehensive view of care delivery – ‘the whole journey’. The prominence of psychosocial care for cancer patients was driven by consumers and resulted in the world’s first guidelines in this area, released by the National Breast Cancer Centre.17 Cancer consumer groups helped identify crucial issues to be addressed – talking about cancer, breaking bad news, support for partners and children, palliative care and survivorship. Consumers also helped clinicians to consider guidance on subject matter that they were typically not comfortable with – the ‘no treatment’ option and alternative and complementary therapies. Issues for younger cancer patients came to the foreground in consideration of fertility preservation before cancer treatment and treatment during pregnancy. With the increasing successes of treatments for a range of cancers, came the question of how to support people living with the longer term sequelae of those treatments. Personalised, tailored therapies appeared on the market, with evidence of improved survival rates. Consumers mortgaging their homes reminded us that these new therapies often came with a price tag. In areas where services were perceived as lacking, cancer advocacy groups lobbied for increased access to health services (e.g. radiotherapy).

Consumers and cancer research

Aligning research priorities with consumer priorities is another area where Australian consumer groups have shown leadership. The ‘Consumer Involvement in Research Program’, initiated by Cancer Voices NSW in 2002 in partnership with Cancer Council NSW, has supported consumer engagement through training and ‘match making’ consumers with research programs – either as advisors, grant reviewers or investigators. More broadly, cancer consumers have been involved in helping to identify priorities for future research across the patient journey continuum,18 and ensuring that consumer-friendly websites about clinical trials are available.

COSA has also contributed to promoting consumer engagement in clinical cancer research. Through the ‘Enhancing Consumer Engagement in Clinical Cancer Research’ project, funded by Cancer Australia, COSA has focused on developing a comprehensive strategy for increased consumer involvement at all levels of clinical cancer research, through increased training, mentoring and collaboration across the 14 Cancer Cooperative Trial Groups.

Assume nothing

Consumers have taught us the importance of ‘assuming nothing’. Assumptions can lead to “patient preference misdiagnosis”.19 This gap between ‘what patients want’ and ‘what doctors think patients want’ is illustrated by a study of the views of breast cancer patients.20 Although doctors believed that 71% of patients with breast cancer would rate keeping their breasts as a top priority, only 7% of patients rated this as their top priority. Similarly doctors thought that 96% of breast cancer patients considering chemotherapy would rate living as long as possible as a top priority, when in fact only 59% agreed.

This lesson of ‘assuming nothing’ has extended into the cancer consumer groups with the acknowledgement that ‘cancer patients’ are not one amorphous group. Rather, in the broad multicultural community of Australia with different cancer profiles, there has been increasing recognition over recent decades of the need to hear voices from a range of cancer survivors. The challenge to engage ‘hard to reach’ consumers continues, particularly in the Indigenous and culturally and linguistically diverse communities, as evidenced by the work of CanNET Victoria, supported by Cancer Australia.21

The need to support cancer consumers with science and advocacy training was also identified early on in Australia, with a program developed in the late 1990s by the National Breast Cancer Centre in collaboration with Breast Cancer Network Australia. Consumers having attended training were then supported to engage in decision-making forums and committees through the Breast Cancer Network Australia’s ‘Seat at the Table’ program.

As synergies among the cancer consumer groups and their priority issues emerged, Cancer Voices formed in most Australian states, initially in NSW (2000), culminating in the establishment of Cancer Voices Australia in 2005. These organisations work at a range of levels, ensuring that the voices of people affected by cancer continue to be heard and consumers are engaged across the spectrum.

Frameworks and standards

Working in partnership Cancer Voices Australia, and Cancer Australia developed a ‘National Framework for Consumer Involvement in Cancer Control’.23 Released in 2011, this framework identified key elements to help guide organisations to engage consumers. The framework highlighted four essential elements for effective cancer consumer involvement: committed organisations; capable consumers; inclusive groups; and shared focus. The framework’s approach to consumer participation builds on
Popay’s model for community engagement, which is widely used internationally. The framework will be accompanied by resources tailored for a range of professions to further support engagement.

In 2011, the Australian Commission on Safety and Quality in Health Care released a national discussion paper on ‘Patient Centred Care: improving quality and safety through partnerships with patients and consumers.’ This paper summarised international initiatives and research evidence about partnership approaches to improving quality health care.

Moving beyond discussion, the commission’s National Safety and Quality Health Service Standards have devoted an entire standard to ‘Partnering with consumers’, with engagement of consumers of health services being integrated throughout the remaining standards. This new system for accreditation of health services came into effect across Australia on 1 January 2013.

Rising to the challenge

In recognition that an organisation-wide approach is required to transform care for a greater patient focus, the Clinical Excellence Commission released ‘The Patient Based Care Challenge’ in NSW, promoting strategies for engaging patients, families and carers at all levels within health care services. Rising to the challenge of transforming health care sees services undertaking engagement in strategic planning, quality improvement and assurance, staff education and employment selection, utilising patient feedback, through to involvement in bedside handover and activation of medical emergency teams. The Chris O’Brien LifeHouse at Royal Prince Alfred Hospital is the first cancer-specific service to sign up to The Patient Based Care Challenge in NSW.

Striving to deliver patient-based care means that we need to rise above the “disease-based” model of care that we inherited in the 18th Century and move beyond the military model of care delivery that dates back to ancient Rome. Tanya Hall’s 2012 article, entitled ‘More than the sum of parts’, challenged us to see some of the present deficiencies in cancer care too often focused on “pathology at the expense of the person”. While acknowledging receipt of excellent medical care, Hall was “surprised and dismayed by the lack of basic humanity and courtesy from some of the health professionals I encountered.” Her concluding advice to health care professionals is to “try, always, to look beyond the diseased part you are treating to the person underneath. Perhaps then the rhetoric of patient-centred care can begin to approach reality.”

Thinking back over the decades, consumer engagement to improve Australian cancer care has grown to support all aspects of the journey and become a mainstream approach particularly, at a systems and policy level. I recall reflecting on how far things really had come when in more recent years a doctor said to me, “Obviously, we will have a consumer included on this working group. We couldn’t do it without them.” We have come a long way.

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This article is dedicated to Emeritus Professor Tom Reeve – wise mentor and champion of consumer engagement in cancer care.

References

PSYCHOSOCIAL ASPECTS OF DELIVERING CANCER CARE: AN UPDATE

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Abstract

Cancer patients face psychological and physical challenges after diagnosis, and can benefit greatly from appropriate psychosocial care. This paper presents a brief history of psychosocial oncology care and recent developments in Australia. Consumers, doctors, nurses, allied health and psychosocial health professionals have all played an important role in this area. Some highlights include: the Australian psychosocial clinical practice guidelines; the development of key patient reported outcome measures; documentation of stress and burnout in oncology health professionals; the development and evaluation of communication resources; a recent focus on survivorship; and a growing body of intervention research which is aiming to be clinically feasible and implementable. The Clinical Oncological Society of Australia hosted the first psycho-oncology professional group in Australia, supporting the development of psychosocial guidelines for adolescents and young adults and undertaking key work in survivorship and rural issues.

Cancer patients face practical, emotional and psychological demands in addition to the physical effects of their disease and treatment. Challenges include existential fears following diagnosis with a life-threatening disease, treatment decision dilemmas, pain, discomfort and functional impairment associated with the disease and its treatment, and body image changes associated with cancer treatment. A cancer diagnosis can impact on patients’ physical and psychological health, sexuality, finances, relationships and ability to continue in roles at home and work.1 Further, the disease affects not only the patients, but their families and carers, who can experience as much or greater distress as the patient themselves.2

The number of people diagnosed with cancer in Australia is set to increase from just over 100,000 per annum in 2012 to 150,000 by 2020. Efficient, effective and clinically feasible supportive care interventions are required to both reduce morbidity in this growing population, as well as assist in preventing the high rate of burnout reported by front-line oncology staff.3 This article will present a brief history of psychosocial oncology care in Australia and describe recent developments within the field, highlighting Australian achievements, and the important role that the Clinical Oncological Society of Australia (COSA) has played.

Establishing psycho-oncology

Psychosocial care is broadly provided in Australia by specialist psychosocial staff (psychiatrists, psychologists and social workers), as well as front-line medical, allied health and nursing staff in oncology and palliative care. While social work has had a significant and ongoing role in oncology since the beginning of the 20th century,4 psycho-oncology is a relatively young discipline internationally, emerging only 40 years ago in Europe and the US. In Australia, the first psycho-oncology clinical interest group was formed under the auspices of COSA in 1996 by Stewart Dunn, becoming an incorporated society (OzPos) in 2008. Psychosocial research began in 1986 within the state Cancer Councils’ behavioural research units, and has matured with the emergence in 2004 of the Psycho-Oncology Co-operative Research Group (PoCoG), one of the 14 national cancer clinical trial groups funded by Cancer Australia, coming together under the umbrella of COSA.

Consumers have walked hand in hand with Australian cancer researchers to advance the field of psycho-oncology.
since the establishment of the first national breast cancer consumer group in 1996-97, now known as the Breast Cancer Network of Australia. The National Breast Cancer Centre (now auspiced under Cancer Australia) – led the first consumer advocacy training course in Australia, and Cancer Council NSW developed consumer research grant review criteria and training. Both of these initiatives contributed to consumers having a front and centre place at the table at which research funding decisions are made in Australia.

Consumers were heavily involved in advocating for the first Australian (and still the most comprehensive internationally) evidence-based clinical practice guidelines for the psychosocial care of women with breast cancer, and more broadly, adults with cancer. These comprehensive guidelines were initially developed by the National Breast Cancer Centre with endorsement from the National Health and Medical Research Council, and are now being maintained and updated by Cancer Australia. They are complemented by the recent production by COSA of guidelines for health professionals in the psychosocial management of adolescents and young adults (AYA) diagnosed with cancer. These guidelines have provided an important basis for the development of psychosocial services in Australian cancer centres.

Much of the early Australian psychosocial research was focused on achieving a better understanding of the psychosocial, as well as physical impacts of cancer, with Australian researchers at the forefront of developing rigorous measures of ‘unmet needs’ in the early 1990s; and describing the levels and predictors of unmet needs in sizable populations of cancer patients. As increasing evidence of the impact of cancer on other groups came to the fore, Australian researchers responded with development of psychometrically rigorous measures which more specifically targeted other groups, including patients with advanced cancer, cancer survivors who were some time post-treatment, and the partners and caregivers of cancer survivors. These measures have been widely used internationally.

**Patient-centred care**

Understanding the impact of caring for people with cancer and the training needs of the health professional workforce has also been a significant area of advancement in psycho-oncology. In 2007, COSA commissioned a survey of its membership to determine levels and predictors of burnout, with results indicating high levels of emotional exhaustion in 33% of participants with direct patient contact and in 27% of those with no direct patient contact. Importantly, one of the main predictors of burnout was perceived to be the need for communication skills training. National Breast Cancer Centre played a leading role in developing and promoting communication skills training for oncology health professionals in Australia, developing train-the-trainer workshops and teaching modules; and COSA has also strongly supported the delivery of communication skills training workshops associated with its annual meeting.

It is now well recognised that health professional-patient communication is critical to quality patient care and challenging for both health professionals and patients. Australian cancer patients place effective doctor communication high on their list of priorities for care. In an early study assessing the perceptions of 232 ambulatory cancer patients, doctor-patient communication dominated the top 10 aspects of care regarded as important. Over 99% of patients emphasised the importance of receiving quality information about their cancer, having the opportunity to ask their doctor questions and receiving empathy and reassurance from their health care team. The outcomes of patient dissatisfaction with communication have been well documented as including non-compliance with medical advice, doctor shopping, increased uptake of complementary and alternative medicines, poorer mental adjustment and general dissatisfaction.

Australian researchers have played a key role in contributing to the oncology communication literature by developing resources for patients to increase their involvement in care (such as information booklets, decision aids and question prompt lists). Butow and Tattersall are recognised internationally as pioneers in this field, conducting many of the first randomised control trials. Australia also led the way in conducting one of the first communication skills training trials, which was led by the late Jill Cockburn.

With an increasing number of people living with and beyond a cancer diagnosis, one of the most recent international priority areas for the field of psycho-oncology has been the study of ‘cancer survivorship’, the period of time following potentially curative treatments for cancer. The release of the landmark US Institute of Medicine report, ‘From cancer patient to cancer survivor: Lost in transition’, has prompted significant international activity in the survivorship space, including in Australia. The November 2009 issue of Cancer Forum was dedicated to cancer survivorship, and in 2010, COSA hosted the inaugural Survivorship Workshop, bringing together stakeholders in cancer survivorship service delivery and research from across Australia. It was clear that much activity was occurring in this space across Australia and with the continuing interest of COSA members in this area, COSA Council approved the formation of a COSA Survivorship Group in November 2012.

As a community, Australian psycho-oncology researchers have shifted in the last 5 to 10 years from doing largely descriptive research identifying adverse psychosocial outcomes for people with cancer as a problem, and defining the dimensions and characteristics of this problem, to undertaking rigorous randomised control trials of supportive care/psycho-educational interventions which aim to solve the problem. In this way, we are again at the forefront of an international impetus to determine clinically feasible and sustainable ways to improve the psychosocial outcomes for people with cancer. Rob Sanson-Fisher has been largely responsible for this push to convert the focus of research from descriptive to intervention trials.
Quality of Life

A systematic review of the type of research output in psycho-oncology and quality of life, found that only a small proportion of research was intervention work and this had changed little in 10 years.²⁷

Randomised control trials of supportive care/psycho-educational interventions is difficult research. There are stringent methodological requirements, including: recruiting large samples to detect modest effect sizes; loss to follow-up due to patient illness or death; implementing complex interventions which adhere to protocol; variation in usual care across treatment centres; and many others.

Moreover, journals are often reluctant to publish negative trials that are frequent in this field.²⁸ Despite these hardships, Australians have embraced the necessity to conduct randomised control trials in order to improve psychosocial outcomes for patients. There are now key research hubs around Australia whose core business is the conduct of randomised control trials in psycho-oncology, for example: PoCoG, currently conducting a multi-centre study of an intervention to reduce the impact of fear of cancer recurrence; Peter McCallum Cancer Centre, evaluating nurse delivered interventions; Cancer Council Queensland, evaluating nurse, psychologist and peer led interventions; the University of Queensland, evaluating exercise and lifestyle change interventions; and Sydney Children's Hospital, evaluating interventions for paediatric cancer patients.

Prospects

Our next challenge is fostering practice changes - implementing supportive care/psycho-educational interventions that are clinically feasible and have a strong evidence base, demonstrating their positive impact on patient outcomes. Some leading Australian work has been undertaken to evaluate the feasibility and impact of routine screening for distress and communication of these results to the patient and treatment team, such as the early randomised control trial of Dr Sue-Anne McLachlan et al.²⁹ and the later work by Greg Carter and Kerrie Clover et al in Newcastle.³⁰

In summary, psychosocial issues in cancer are now well on the Australian cancer agenda, widely included in cancer plans and a priority area in clinical services. There is a strong and thriving psychosocial research program in Australia. COSA has played a significant role in supporting and acknowledging the growth in this area.

References

MEDICAL AND PSYCHOSOCIAL CHALLENGES IN CARING FOR ADOLESCENT AND YOUNG ADULT PATIENTS WITH CANCER

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Abstract

Over the last five years there have been tremendous changes in the care of adolescent and young adult cancer patients in Australia, generally accepted as 15-25 years old. There has been recognition that the needs of adolescent and young adults with cancer are different from both adults and younger children, and warrant specialised services. A cancer diagnosis during this period of transition has the potential to significantly impact upon many areas of normal development including physical, psychological, social, sexual, educational and financial domains. Relatively little is known about the basic biology, genetic, epidemiologic, therapeutic and economic factors that affect incidence, disease outcomes and cancer related quality of life in this population. This paper explores the medical and psychosocial needs for these patients and summarises the recent progress of the Youth Cancer program in Australia, which has led to the development of this new subspecialty and the creation of youth cancer services.

Young people aged 15-29 years make up 1.7% of all new cancer diagnoses in Australia. This comes from a recent report by the Australian Institute of Health and Welfare, which forms the first comprehensive picture of cancer in adolescent and young adult (AYA) Australians.¹ Five-year relative survival in this population overall is 88%, however greater improvements in survival have been seen in younger children and older adults over the same time period. Importantly, AYA patients living in areas of lowest socioeconomic status have lower rates of five-year survival compared to those living in areas of high socioeconomic status (85% v 90%). AYA patients living outside major cities are 1.3 times more likely to die from cancer compared to those in cities. The biggest concern in the AYA age group however, is the lack of improvement seen in survival figures and the ‘survival gap’ seen between children and AYAs with particular tumour groups such as sarcoma and acute lymphoblastic leukaemia (ALL).²,⁵

A number of reasons have been proposed for this lower survival rate, many of which may have overlapping influences. Delays in diagnosis may contribute towards tumour progression and metastatic spread and therefore worsening prognosis, increasing the need for more intensive treatment and adding to emotional stress.⁶-¹⁰ Causes for delayed diagnosis are multifactorial. Many studies have shown longer duration of symptoms before diagnosis,⁹-¹³ which can be ‘patient related’ due to AYA patients ignoring or minimising symptoms, or due to medical providers having a low suspicion of cancer in this age group and attributing symptoms to other causes such as growing pain, sports injuries or school refusal.

Half of all AYA patients visit a primary care physician three or more times before referral.¹⁷,¹³ Once diagnosed with cancer, the referral pathway for an AYA patient can vary substantially depending on the type of cancer and age at diagnosis. The spread of AYA cancer patients across paediatric and adult facilities can result in the inconsistent application of clinical protocols and limits the enrolment of AYA patients into clinical trials. There is also evidence in some tumours that biological and pharmacological differences exist in AYA patients.⁴,¹⁴,¹⁵

The most common cancers affecting AYA patients in Australia are melanoma, lymphoma, germ cell tumours, leukaemia, brain tumours, sarcomas and thyroid cancers.¹,¹⁶ ¹⁶ AYA patients may also have cancers that are more common in early childhood or those seen in adulthood. This variety of cancer diagnoses represents a unique challenge for clinicians and requires collaboration between paediatric and adult oncologists so that patients can benefit from both tumour specific and age appropriate expertise.

Adherence

Adolescents are consistently less adherent to treatment recommendations than younger or older cancer patients, even when treated on similar protocols for similar diseases.¹⁷-²² Published rates of non-adherence in cancer cohorts that include AYA patients are up to 60%, which may be a contributor to treatment failure. Lack of appropriate psychosocial and parental support during and after treatment is correlated with non-adherence.¹⁷-²² Other factors associated with non-adherence to treatment are the
side-effect profile and likelihood of success with treatment, avoidant coping strategies of AYA patients, undiagnosed mental health problems and the need to attend ‘rite of passage’ events such as school formals.17-22 Age-appropriate cancer information, psychological counselling, being responsible for one’s own healthcare and decision making, and scheduling treatments to fit into AYA lifestyles may help towards increased understanding and adherence to treatment.

Changes in treatment and psychosocial care

Over the last 10 years there have been a number of international ALL clinical trials that have shown AYA patients treated on paediatric rather than adult ALL protocols have improved event free and overall survival.25-28 In Australia, the first AYA ALL trial (ALL6) has started, which uses an accepted paediatric protocol that intensifies treatment based on disease response, cytogenetic and molecular markers.29 In contrast, using the same treatment across paediatric and adult patients has not been as successful for other tumours. For example, AYA patients with Ewing sarcoma and osteosarcoma treated on the same large international clinical trials, still have a significant difference in survival compared to children. There have been concerns that AYA patients will not be able to tolerate intensive chemotherapy programs due to toxicity, however toxicity data for both ALL and sarcoma studies have shown that adverse events remain within normal expected range, although there are some side-effects which increase with age.27,28 Further research on pharmacokinetics in this age group is underway. Supportive care requirements and side-effect monitoring are essential.

AYA patients are particularly vulnerable to distress (a spectrum of clinical conditions from sadness and fear to depression and anxiety),30-32 and this may interfere or change the way in which AYA patients cope with treatment and side-effects.33 In 2009, an AYA specific psychosocial screening tool, care plan proforma and psychosocial assessment measure was developed by CanTeen Australia to guide psychological assessment.34-35 This tool has been implemented successfully in youth cancer services throughout Australia since May 2011, with the aim of ensuring all AYA patients have a comprehensive assessment performed at diagnosis and a support plan implemented that takes into consideration their individual needs as early as possible. Patients who are less distressed are likely to be more adherent to treatment and therefore have better outcomes.36 An international study is planned to validate this tool. Individual factors that promote resilience against psychological distress need to be further examined, as these may also improve outcomes.37

Development of services in Australia

In 2005, an Australian Senate reference committee made two important recommendations that started the development of AYA services in Australia. It was recommended that Cancer Australia consider the development of appropriate AYA referral pathways to take into account particular difficulties confronted by this population, and examine the feasibility of establishing specialised AYA cancer care units in public hospitals.38 In 2007, CanTeen and Cancer Australia formed a reference group that led to the Australian Government recognising the need for specialist care for AYA patients with cancer, with the publication of the National Service Delivery Framework.39 This framework made five key recommendations for development of services:

- lead adolescent and young adult cancer care sites
- access to support services and clinical trials
- comprehensive assessment at diagnosis
- coordinated care to empower adolescent and young adult decision making
- expert multidisciplinary teams skilled in adolescent and young adult cancer care.

In 2010, the Australian Government provided CanTeen with finances to establish and manage the Youth Cancer Networks Program and specialist youth cancer services have now been developed across each mainland state in Australia to provide medical, nursing and allied health care with AYA expertise.35 Although AYA services in Australia have lagged behind the UK and North America, which have successfully introduced teenage cancer centres,40-41 the Australian model of care has had to accommodate a number of differences.42 The geographical spread of AYA patients across Australia means the treatment of these relatively small patient numbers occurs across many locations, in both public and private sectors, and via well-established cancer referral pathways within tumour specific multidisciplinary teams. There is no health legislation, as there is in the UK, about the place of treatment for AYA patients. This has meant referral to youth cancer services has been slow in some areas and further collaboration will be required to increase uptake of AYA services.

With AYA emerging as a subspecialty field in Australia,43 initiatives have been created to support training and provide educational resources. Postgraduate career development is now available through the University of Melbourne, with an oncology specific certificate in Adolescent Health and Welfare created in 2011. Plans for AYA specific topics to be integrated into physician, nursing and allied health training are also underway. A number of AYA career development fellowships were established in 2011, which have allowed both paediatric and adult clinicians with an interest in AYA oncology to gain further medical training. These clinicians will be providing the expertise for youth cancer services in the future and implementing effective programs and practices over the coming years. The Clinical Oncological Society of Australia (COSA) in partnership with CanTeen, have produced guidelines covering fertility preservation, psychosocial assessment and early diagnosis of cancer by general practitioners.44,46 COSA has also developed an active national network of clinicians, which has facilitated the sharing knowledge and fostered national research initiatives.
Research

Implementation research is being undertaken to ensure there is an evidence base to support ongoing funding of youth cancer services and direct referral patterns. National and international collaborative research and clinical trials are underway, with key trials mapping experiences and patterns of care and fertility preservation, as well as medical trials in leukaemia and sarcoma. Despite strong evidence that clinical trials improve cancer survival rates, participation in clinical trials in AYA patients over 15 years of age is still lower than in children, even when clinical trials have appropriate age eligibility criteria. Access to clinical trials will continue to be an issue while there are small numbers of AYA patients treated in a large number of cancer centres across Australia. It is essential that data is collected on medical and psychosocial outcomes for AYA patients, and as such Cancer Australia has developed a national minimum dataset. This has been trialled in a number of youth cancer services in 2012, with outcomes to aid future development of services.

Issues around survivorship and ongoing care are becoming recognised as essential to good cancer management. This is particularly so in the AYA population, who are negotiating all of the usual hurdles associated with transition to adulthood such as completing education, establishing careers and relationships and developing independence. This must be done with the additional burden of possible treatment related effects, both physical and psychosocial, and the potential for long-term or unknown future effects. The high incidence of chronic conditions is well documented in survivors of childhood malignancy, while well established in the paediatric setting, long-term follow-up beyond five years in adult hospitals is not. The developing field of survivorship care has been covered in detail in Cancer Forum, with the need for coordinated care, in particular supportive care, for all patients made clear. Many models exist for delivering this care, although evidence supporting efficacy is sparse. Collaborative research efforts assessing quality of survival in AYA patients and how best to achieve this are required to inform current practice frameworks.

Conclusion

Care for AYA patients in Australia has made a promising leap over a very short period, with adult and paediatric colleagues developing youth cancer services and a strong, dedicated network that has allowed for mentorship, education and career development. Sites in Australia are actively contributing to AYA research and looking at solutions to allow AYA access to clinical trials. Further international research collaborations are essential to improve medical knowledge about AYA cancer treatment and psychosocial care, and share examples of good clinical practice. Work is being done to provide equity in service provision across Australia, with the ultimate aim of improving medical outcomes as well as reducing psychosocial distress during and after treatment.

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ABORIGINAL AND TORRES STRAIT ISLANDER AUSTRALIANS AND CANCER

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Abstract

It is increasingly evident that inequalities exist for Indigenous people with cancer. Incidence for all cancers combined is similar to or lower than that of non-Indigenous people, but incidence of cancers with a poorer prognosis, such as lung cancer, is higher among Indigenous people, largely due to higher rates of smoking. Indigenous Australians with cancer are diagnosed with more advanced disease and are less likely to receive or complete curative treatment than non-Indigenous Australians. Wide disparities exist in cancer survival between Indigenous and non-Indigenous Australians, particularly in the first year after diagnosis. The need to improve cancer-related health services for Indigenous Australians is apparent, however the available evidence is currently inadequate to effectively direct efforts. For example, despite high cancer mortality rates, there is little information about palliative care services, their models of care or their uptake by Indigenous cancer patients. Through an increased understanding of how cancer affects Indigenous Australians and the establishment of collaborations, in particular the recently funded Centre for Research Excellence DISCOVER-TT, and networks such as the Clinical Oncological Society of Australia, an opportunity for targeted efforts in improving cancer outcomes for Indigenous Australians is tangible.

Until recently, little information has been available about the impact of cancer on Aboriginal and Torres Strait Islander (hereafter respectfully referred to as Indigenous) Australians. There were few Indigenous cancer survivors and few Indigenous health professionals specialising in oncology and cancer-related fields. Cancer was not viewed as a high priority issue, obscured by many other health conditions which seemingly had a much greater impact on Indigenous people (relative to other Australians). Now, based on new higher-quality data sources, it is evident that there is an urgent need for our health care system to address the specific needs of Indigenous people and improve its performance across the spectrum of cancer control, from prevention and early diagnosis to effective treatment, palliation and support for cancer patients and their families.

Reliable semi-national cancer incidence statistics that cover 84% of the Indigenous population have recently become available.1 The incidence rate for all cancers combined for Indigenous people is similar to, or slightly lower than, that of other Australians. However, compared with other Australians, Indigenous Australians have much lower incidence of some cancers (breast, prostate, testis, colorectal and brain cancer, melanoma of skin, lymphoma and leukaemia), but much higher incidence of others (lung and other smoking-related cancers, cervix, uterus and liver cancer), many of which are largely preventable.1 In contrast to incidence, cancer mortality is higher for Indigenous than other Australians. The death rate for all cancers combined and for most individual cancers is higher for Indigenous than other Australians; for example, although the incidence of breast cancer is lower for Indigenous than other Australian women, their mortality rate is 30% higher.2

Cancer risk factors: smoking is key

The prevalence of several cancer risk factors is different for Indigenous than other Australians. Some of these are protective against cancer, such as higher melanin levels in skin, earlier age at first pregnancy and longer periods of breastfeeding. Others increase the risk of cancer occurrence, such as lower participation in cancer screening, higher prevalence of Hepatitis B infection and higher prevalence of smoking.

Smoking is the single most damaging risk factor for Indigenous people, for cancer and many other health problems. Most of the cancers that occur more commonly among Indigenous than other Australians are smoking-related, including lung, oesophagus, pancreas and stomach.1 Indigenous smoking prevalence is more than double that of other Australians; 47.7% of Indigenous people aged 18 and over were daily smokers in the most recent reliable national survey.3 However, indigenous smoking prevalence has been falling (except among women living in remote areas), accompanied by reductions in the proportion who smoke more than 20 cigarettes per day and increased proportions who have successfully quit.4,5 The Council of Australian Governments has committed to halving the Indigenous prevalence of daily smoking by 2018, with commitments of nearly $140 million over four years.6 This investment is being used to expand the Indigenous tobacco control workforce, enhance Quitlines, and implement the first national indigenous anti-tobacco marketing campaign, ‘Break the Chain’. This will complement other mainstream Australian tobacco control measures.
Cancer screening

BreastScreen Australia, the National Cervical Screening Program and the National Bowel Cancer Screening Program make up the three cancer screening programs in Australia.

Despite over 15 years of national coverage, the National Cervical Screening Program still cannot provide comparable information on screening participation and outcomes for Indigenous women because pathology request forms and reports, and therefore Pap test registers, do not include information on indigenous status. Although some regional studies have consistently reported lower participation rates in cervical screening among Indigenous than other women, participation rates higher than the national average have been reported from the Tiwi Islands in the Northern Territory, indicating that high participation rates are in fact achievable.7

BreastScreen Australia has recently produced comprehensive information about breast screen participation and outcomes for Indigenous women for the first time. Compared to other Australian women, Indigenous women have lower screening participation rates (although this difference appears to be diminishing), are less likely to attend post-screening assessment, and those diagnosed with breast cancer have larger cancers.8

Indigenous Australians are significantly less likely to accept an invitation to screen in the national program than non-Indigenous Australians (17.0% c/w 38.6%). Indigenous people have higher faecal occult blood test positivity rates (8.6 c/w 7.5%) than non-Indigenous participants (although this is not statistically significant) and a lower proportion of Indigenous people correctly complete the test.9

Diagnosis and treatment

Several studies from South Australia, the Northern Territory and Queensland have reported that Indigenous cancer patients have more advanced disease when diagnosed. In South Australia in 1988-1994, 50% of Indigenous patients were diagnosed with localised disease, compared with 60% of non-Indigenous patients (adjusted for age, sex and cancer site).10 In the Northern Territory in 1991-2000, 30% of Indigenous patients with non-Hodgkins lymphoma, cervical, colorectal and breast cancers had localised disease at diagnosis, compared to 49% of non-Indigenous patients (four cancers combined, adjusted for cancer site and age), although localised disease was more common for Indigenous patients diagnosed with lung cancer (44% c/w 31%).11 In Queensland in 1997-2006, 47% of Indigenous people diagnosed with cancer had localised disease compared to 53% of non-Indigenous people (matched for age, sex, place of residence, cancer site and year of diagnosis).12 These studies highlight the need for identifying and reducing the barriers to early detection of cancer among Indigenous people.

Studies in the Northern Territory and Queensland have found that Indigenous cancer patients are less likely to be recommended for, choose and complete curative treatment than non-Indigenous patients. In the Northern Territory in 1991-2000, Indigenous patients with non-Hodgkins lymphoma, cervical, bowel, breast and lung cancers were less likely to be recommended for curative treatment (Indigenous 59% compared with non-Indigenous 70%); among those offered curative treatment, Indigenous patients were less likely to choose it (90% c/w 96%); and among those who chose it, Indigenous patients were less likely to complete it (85% c/w 94%).13

In Queensland in 1997-2002, Indigenous patients, in general, were also 24% less likely than non-Indigenous patients to receive surgery, 20% less likely to receive chemotherapy and 9% less likely to receive radiotherapy.12 Indigenous patients with head and neck cancers (1998-2004) were significantly less likely to receive any cancer treatment (75% c/w 95%),14 as were Indigenous women with gynaecological cancers (91% c/w 98%).15

In contrast, Indigenous women with breast cancer received comparable treatment to their non-Indigenous counterparts (96% c/w 96%) and treatment completion rates were similar (p<0.05).16

Taken together, these studies indicate the importance of reducing barriers to Indigenous patients accessing high quality specialist care.

Survival

Survival rates for most cancers are lower for Indigenous than other cancer patients. Recently in Queensland, it was found that Indigenous patients had much higher mortality than non-Indigenous patients in the first two years after diagnosis (50% higher in the first year, adjusted Hazard Ratio, 1.50; 95% CI, 1.38–1.63), but similar mortality thereafter (HR 1.03; 95% CI, 0.78–1.35 in the third year after diagnosis).12 Indigenous patients are more likely to have advanced disease when diagnosed and have higher prevalence of chronic diseases than non-Indigenous patients but these factors only partly explain their lower survival.12,13 Other factors related to cancer treatment and the effect of their economic, social and environmental circumstances may also be involved.

Another study in Queensland found that crude cancer survival was 30% worse (HR 1.30, 95%CI 1.15-1.48) and non-cancer deaths were over twice as common among Indigenous than non-Indigenous cancer patients (HR 2.39, 95%CI 1.57-3.63). When stage at diagnosis, socioeconomic status, comorbidities and treatment uptake were taken into account, the risk of cancer death became non-significant.18 These results suggest that treatment, comorbidities and stage at diagnosis explain most of the poorer cancer outcomes among Indigenous patients. This has critical implications for the design and delivery of the full spectrum of health services.

Palliative care

Cancer patients comprise a large part of palliative care services’ caseload. Given the high cancer mortality rates among Indigenous Australians, culturally appropriate palliative care services are warranted. However, to date there is little information available about services on offer, or their uptake by Indigenous Australians with cancer. More broadly, a key finding from a National Indigenous Palliative Care Study reported a lack of comprehensive
Support services

Although prevention, screening, diagnosis and treatment are important determinants of health outcomes for Indigenous people with cancer, many do not access these services. Basic infrastructure and logistical issues such as a lack of transport and having appropriate travel arrangements, and suitable accommodation for both the patient and their support person, may also impede Indigenous people's access to cancer care and treatment services. A recent Queensland study identified that Indigenous adult cancer patients have substantial unmet supportive care needs and that they have most need for additional support with psychological and practical assistance. In Queensland, Indigenous cancer patients have indicated that they most frequently accessed Indigenous health workers (68.8%) for support and use printed cancer information (66.9%) to source information about their cancer rather than access Cancer Council Helpline (12.1%).

Policy, programs, service models

The gaps in diagnosis, treatment and survival indicate that current programs and models of service delivery do not fully meet the needs of Indigenous Australians with cancer. A recent review highlighted the inadequate participation in and ownership of cancer health services by Aboriginal people outside the realm of community-controlled health services, as well as a shortage of Indigenous cancer care workers. Both deficiencies can have a major impact on Indigenous people’s use of cancer services. The National Cancer Control Initiative recommended “… that the needs of special populations, especially Aboriginal peoples, be the focus of special efforts to bridge the current gaps in access to and utilisation of culturally sensitive cancer service.”

Some service initiatives appear to be implemented successfully, but formal evaluations have been rare. For example, telemedicine services have been used to overcome some of the barriers to access and utilisation of medical services by Indigenous cancer patients, especially those living in rural and remote areas. Teleoncology allows the patient to stay in their community for treatment and/or follow-up. The patient and their family, in the presence of a health worker, doctor or nurse, are able to link in at their local health centre via video conference with the specialist located elsewhere. This model of care has received high satisfaction levels when delivered to Indigenous patients located in remote areas of North Queensland.

Recent national initiatives

The first national meeting to focus on cancer as a health issue for Indigenous Australians was convened by Cancer Council Australia in Darwin in 2004, the proceedings of which were published in a dedicated issue of Cancer Forum. From this workshop, Cancer Council Australia established a working party to focus on cancer control for Indigenous Australians. In 2010, Cancer Australia commissioned a report to provide direction for reducing the disparities Indigenous people experience across the cancer control continuum. This report was published in July 2010; Cancer Australia is still considering what actions to take.

In December 2010, the Lowitja Institute hosted a national workshop on priorities for indigenous cancer research in partnership with the Queensland Institute of Medical Research. This workshop was widely supported by leading cancer experts, Indigenous survivors, Indigenous community representatives and advocacy groups. As a direct result of this workshop, a collaboration of Australia’s leading researchers working in the area of cancer in Indigenous Australians, together with collaborators from New Zealand, Canada and the United States, developed a proposal for a Centre for Research Excellence in Indigenous Cancer Control, which was funded by the National Health and Medical Research Council in 2012. This new national centre, DISCOVER-TT (Discovering Indigenous Strategies to improve Cancer Outcomes via Engagement, Research Translation and Training), was established in late 2012. The DISCOVER-TT research program will address some of the key recommendations of the Cancer Australia review, particularly those relating to pathways and outcomes of care and improving models of care and service delivery. An international conference on cancer in Indigenous peoples is planned for 2014. One of DISCOVER-TT’s first initiatives has been to establish the National Indigenous Cancer Network (NICaN), a network devoted to making sure that what is known about cancer in Indigenous Australians is available to people with cancer, their families, practitioners, policy makers and researchers. NICaN has been developed through a partnership involving the Menzies School of Health Research, the Australian Indigenous HealthInfoNet, the Lowitja Institute and Cancer Council Australia. For more information or to join NICaN, visit www.cancerinfonet.org.au.

The Clinical Oncological Society or Australia (COSA) is Australia’s peak national body representing multidisciplinary health professionals whose work encompasses cancer control and care. COSA members are doctors, nurses, scientists and allied health professionals involved in the clinical care of cancer patients, and therefore have the potential to play an important role in addressing poorer survival outcomes for Indigenous Australians. At COSA’s
Annual Scientific Meeting in 2012, inequalities in cancer care were highlighted across a number of poster and oral sessions. COSA embraced this further by including in the program a plenary session on inequalities in cancer care, which included a presentation on ‘Inequality in cancer care for Indigenous Australians’ and a symposium on ‘Translating the evidence to improve cancer care for Indigenous people’.

With the momentum and synergies established through these national partnerships, it is anticipated that inequities that exist for Indigenous Australians with cancer won’t be overlooked, and that prevention and treatment strategies will be enhanced, translating to improved survival and quality of life for Indigenous people.

References
Cancer is the leading cause of illness in Australia and is a national health priority. Primary care in Australia is well positioned to support individuals diagnosed with cancer and their family/caretakers. However, obstacles exist that impact on the quality and continuity of care that primary care providers and community health professionals can provide. A rapid review of the research available revealed that the knowledge, attitudes and beliefs held by health professionals and patients can impact engagement in early detection, treatment and follow-up care. Health professionals have limited knowledge of evidence-based practices, while cancer literacy among minority groups, including Aboriginal Australians, is lower than the population overall. In this paper, we provide a summary of the rapid review of the literature and provide some recommendations based on our research.
An Australian publication on colorectal cancer reported poor strategies are needed to increase awareness. National clinical practice guidelines can impact diagnosis, so bleeding were published in 2012. Lack of knowledge of guidelines for the management of abnormal vaginal bleeding was greater for endometrial cancer, for which there were no clinical practice guidelines at time of publication. The studies included are intended to provide an overview, but are by no means exhaustive.

Knowledge, attitudes and beliefs in primary care for cancer

Continuity of care is a key component of general practice. It begins at referral, through treatment to follow-up care and should be considered within the context of the individual in their community. In this section, knowledge, attitudes and beliefs that impact referral and early diagnosis, treatment and follow-up care are explored. Examples include different types of cancer and draw on research from Australia and other countries. The studies included are intended to provide an overview, but are by no means exhaustive.

Knowledge

Available literature reports that evidence (ie. knowledge) is levels of research evidence.5

Three questions were posed for the rapid review:
- Question one: To identify the knowledge, attitudes and beliefs held by health professionals and patients which can impact on engagement of PCPs and community health professionals with early detection of cancer and following care.
- Question two: What is the evidence that attitudes and beliefs can be modified with measurable impact on primary and community based professionals with cancer care.
- Question three: Which attitudes and beliefs are most likely to be the NSW content drivers.

Levels of evidence were based on the NHMRC six primary levels of research evidence.5

Knowledge, attitudes and beliefs in primary care for cancer

Continuity of care is a key component of general practice. It begins at referral, through treatment to follow-up care and should be considered within the context of the individual in their community. In this section, knowledge, attitudes and beliefs that impact referral and early diagnosis, treatment and follow-up care are explored. Examples include different types of cancer and draw on research from Australia and other countries. The studies included are intended to provide an overview, but are by no means exhaustive.

Knowledge

Available literature reports that evidence (ie. knowledge) is not consistently reflected in practice. Consequently, there may be lost opportunities for early diagnosis. An Australian study found significant variation in PCP referral practices, which was greater for endometrial cancer, for which there were no clinical practice guidelines at time of publication.6

Guidelines for the management of abnormal vaginal bleeding were published in 2012.7 Lack of knowledge of national clinical practice guidelines can impact diagnosis, so strategies are needed to increase awareness.

An Australian publication on colorectal cancer reported poor patient treatment experiences in primary care.8 Several rural participants indicated that high staff turnover in their area hindered continuity of care. A lack of knowledge about local clientele, ineffective clinical networks and referral pathways inappropriate to the locale in which practices operate, may impact adversely on continuity of patient care, particularly in these communities. In urban settings, long wait times to see a PCP cause some people to seek medical care elsewhere, or increasingly self-diagnose using the internet.

Survivorship or shared care plans may facilitate access to knowledge in primary care, thereby improving prognosis. In a US study, PCPs found shared care plans were highly valued; they increased PCP knowledge about survivors’ cancer history and recommended surveillance care and influenced patient care.9 Another US study focused on prostate cancer, further concluded that without shared care plans, practitioners were not confident about their ability to provide appropriate care.10 To improve quality of care, implementing cancer survivorship care plans across specialties, or transferring primary responsibility to PCPs through survivorship guidelines, should be considered.

Integrated systems that use electronic health records are likely to facilitate shared cancer care by improving PCP - oncologist communication.11 Strategies are needed to promote a more active role for PCPs in managing comorbidities, psychological distress and behaviour modification, and to overcome communication challenges between physicians who do not practice within the same integrated system. An example from a study conducted in Western Australia included screening of patients with unmet psychosocial needs in the specialist setting and subsequent referral to their GPs, with recommendations for care plans that could allow Medicare funded access to allied health practitioners.12

Concerns exist about the knowledge base patients expect PCPs to have; some rely on their PCPs to have the appropriate knowledge to ‘fill in the gaps’ with extra information or to clarify specialist advice. Traditionally patients have trusted their PCP to be competent in diagnosis, understanding their problem, advising referral if necessary and giving them appropriate counsel. One small RCT has shown counselling along with treatment as usual can improve depression symptoms and quality of life;13 a larger study is encouraged.

Attitudes

Awareness of the warning signs of cancer was reported to be low across all ethnic groups in a UK interview-based study, with lowest awareness in the African subgroup.14 Women identified relatively more emotional barriers and men, more practical barriers to help seeking, with considerable ethnic variation. These may be related to stigma and misconceptions about cancer. A study of women with gynaecological cancer highlights the problems associated with cancer treatment in a rural community. These women experienced personal and financial upheaval from having to leave home and their communities for treatment. These problems may be ameliorated by receiving care closer to home.15

Attitudes are also important in relation to family history discussions, especially with young people. In a recent US study, the perception that physicians were responsible for initiating family health history discussions was associated with being non-white and less than completely knowledgeable about cancer.16 Having a discussion with a physician was associated with being female, having a regular physician, perceiving genetics as a risk for developing cancer, and having a family member diagnosed with cancer. Attitudes and beliefs of families, both positive and negative, impacted upon the wellbeing of people undergoing treatment. However, literature from the UK suggested the needs and concerns of the partners of cancer survivors in caring for patients were seldom addressed.17 A proactive approach to patients, their partners and other family members at the time of diagnosis, through an offer of
support and their inclusion during treatment reviews, would be useful.

An observational study from Western Australia demonstrated that in 68% of cases, women with breast cancer did not consult their GP about breast cancer-related symptoms in the six months prior to their appointment at a specialist clinic, choosing instead to present to a breast care nurse. Similarly, women in rural Australia have identified limited psychosocial support and resources for breast cancer survivors in their areas.

An Australian study concluded that there was strong support for the development and use of shared care plans for bowel cancer survivors. Patients, PCPs and specialists endorsed the core elements of the shared care plans, including information about diagnosis, diagnostic tests, a summary of treatments received, surveillance plan and information regarding potential late and long-term effects. There was no clear consensus among hospital-based healthcare professionals regarding who should write and deliver the shared care plans.

Although PCPs provide the bulk of care for long-term survivors within the survivorship phase, only some provide multidimensional survivorship care. A US survey of specialists found approximately half thought specialists were more efficient at providing follow-up care than PCPs, but these same physicians recommended significantly longer and more expensive follow-up routines on average than others. PCPs were said to be important allies, especially in managing the psychosocial concerns of patients. Most specialists indicated they should remain involved in follow-up care, but this may result in increased resource use.

Beliefs

Timely diagnosis can be affected by patients’ beliefs about the GP’s role. In Australia, women with breast cancer and their families believed their primary sources of support should be medical practitioners (eg. surgeons, oncologists and GPs), with very few women or family members accessing mental health professionals. Given the importance of adequate support when diagnosed and treated for breast cancer, the authors concluded medical professionals should receive training in providing appropriate support and referrals to their patients.

A US study reported that some healthcare providers were not involved in psychosocial care and that oncologists and PCPs differed in their beliefs regarding who provided specific aspects of care. This underscored the need for better care coordination, informed by the respective skills and desires of physicians to ensure needs were met. Other studies similarly concluded that patients did not believe GPs had the training or skills to monitor the physical or psychological sequelae of cancer. However, many would be willing to have GPs share their follow-up care, with the caveat that they received extra training and were appropriately supported by secondary care specialists. In this study, GPs felt that attending the training seminars and shadowing at clinics enhanced their own skills, benefited their patients and improved communication with secondary care.

Recommendations

These recommendations can, in the opinion of the authors, help to enhance the role of PCPs in the primary care of cancer patients. Gaps in PCPs’ knowledge can be overcome through additional training. Evidence-based guidelines await development and as they develop they will assist PCPs identify patients with ‘red flag’ symptoms and should be in regular use. Research into innovations to create and implement decision support tools in practice would be beneficial.

Communication and advice to patients

- Patients need assurance that PCPs are able to follow specialists’ treatments and strategies.
- Patients need strong reassurance of PCPs’ clinical abilities.
- Specialists should, where possible, engage PCPs in follow-up.
- Specialists should ensure continuity of care and guarantee communication with PCPs.
- Planning shared care to involve the patient, specialists and PCPs before patient discharge could be most useful in appropriate circumstances.

Recommendations for management of special groups

- Acknowledge that diffidence may occur among the young, the elderly, Indigenous patients and culturally and linguistically diverse patients and professionals.
- Develop evidence-based guidelines to facilitate seeking of help, patient referral and follow-up in these groups, and also in more easily managed groups.
- Acknowledge the strong need that exists for help with these groups.

Rural patients

- Ensure maximal use of appropriate facilities that are closer to patients’ homes.
- Support continuance of chemotherapy in local community settings where appropriate abilities, education, skills and inter-medical communication can be mutually achieved.

Wider support

The involvement of significant supportive, capable and empathetic lay and professional people could provide supportively trusted roles to assist patients on their cancer journey.

Conclusion

Cancer is of great concern to Australians, the public and practitioners alike. Continuity of care from referral right through to follow-up care is important, and PCPs have an important role to play. The knowledge, attitudes and beliefs held by patients, their families, PCPs and specialists impact the provision of care. In short, knowledge, attitudes and beliefs are necessary, but not sufficient for clinical engagement. Factors such as age, ethnicity, geography, gender and responsiveness of the patients, their support network and the practitioners all contribute to the need for a continuum of care from referral, through treatment, to follow-up care. Several steps can be taken to enhance
the role of PCPs in the delivery of care for cancer; the recommendations included here are, in the authors’ opinion, a good starting point. Additional research and innovation is also encouraged to assist further development of evidence-based cancer care and the benefit it can bring.

Acknowledgements

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A copy of the rapid review - Jiwa M, McManus A, Dadich A, Hewitt V. The impact of knowledge, attitudes and beliefs on the engagement of primary and community-based healthcare professionals in cancer care: an Evidence Check rapid review brokered by the Sax Institute (www.saxinstitute.org.au) for the Cancer Institute NSW may be obtained from:

Sax Institute
(with permission from the Cancer Institute NSW)
Level 8 Bld 10
235 Jones Street
Ultimo NSW 2007

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Like other health professions, the past 40 years has seen the scope of cancer nursing practice being shaped largely by medical, scientific and technological advances. Indeed, the emergence of a predominantly ambulatory care model of practice, increasingly sophisticated methods for delivering personalised cancer therapies, and the growing demand for highly specialised disease-specific knowledge, has meant the nursing profession has had to demonstrate extraordinary capacity to adapt to change. Importantly, the practice of cancer nursing has also been shaped by social, economic and political factors that present significant opportunities, as well as challenges, in today's health care environment.

Milestones in the development of cancer nursing

Hilkemeyer argues it would have been unthinkable in the early 1950s for a nurse to administer cytotoxic agents to cancer patients. While nurses had long played a role in supporting cancer patients, it was not until the 1970s that the specialty of cancer nursing as we know it today emerged. The late Robert Tiffany, founder and inaugural President of the International Society of Nurses in Cancer Care, described the 1970s as a time of "extension and expansion of the role and function of the nurse in cancer care", alongside the development of educational programs designed to prepare nurses to meet the demands presented by changing cancer treatments. Tiffany's 1987 landmark paper, The Development of Cancer Nursing as a Specialty, described for the first time a role for the specialist cancer nurse as an expert in a specific aspect of oncology nursing. Tiffany argued that the specialist cancer nurse required advanced education preparation to adequately perform their role. At this time in Australia, the only specialist training in cancer nursing was at the Peter MacCallum Cancer Centre, where a largely radiotherapy focused program had been running since the 1950s. The 1970s saw many nurses from Australia and New Zealand travel to the Royal Marsden Hospital in London to undertake specialist courses.

However, the 1970s was a period of time where nursing care was largely functional in its approach and nursing practices were primitive in comparison to today's standards. Cytotoxic drugs were often reconstituted and administered by nurses, a practice unacceptable by today's standards, and the management of chemotherapy side-effects was a trial and error process. For example, Henke-Yarbro noted that "...if one antiemetic did not work, another was tried and that combination of antiemetic regimens were unheard of." She also noted that patient education materials were "uncommon or nonexistent." Specialist nursing courses in the 1970s were largely focused on understanding cancer and its treatment, with nursing responses largely based on clinical protocols (eg. nasogastric feeding), with no substantial evidence base.

As the nursing profession evolved from this functional, task-based approach, to one which was more holistic and patient centred, the core features of contemporary cancer nursing started to emerge. The 1980s in particular, was an historic time for nurses in Australia, as the Commonwealth Government announced its intention to fully transfer preparation of registered nurses to university settings, a process which was not fully complete until 1994.
The transfer, while occurring later than it did in some other countries, distinguished Australia as one of the few countries in the world to have a bachelor’s degree as the single point of entry to practice as a registered nurse. Arguably, this period of time was where Tiffany’s vision for specialist cancer nursing came to be realised, as the paradigm shifted from nurses offering care and comfort to one where nurses based their practice on scientific knowledge.5

By the 1990s, the need for reform in cancer care in Australia was also gaining momentum. Nurses, who now benefitted from much better educational preparation, were increasingly acknowledged for the role they would have in ensuring a quality cancer care system. For example, the 1995 House of Representatives Inquiry into the management and treatment of breast cancer in Australia was replete with examples of the inadequacies of the existing systems of care, and the lack of compassion and sensitivity that was sometimes experienced by women diagnosed with breast cancer. While the multidisciplinary team at that time was narrowly defined in the inquiry report by medical specialties (ie. surgeons working closely with their colleagues in radiation and medical oncology), the key role that nurses were to play in improving the patient experience in the years which followed was also signalled. As the committee report noted: “It is unfortunate that in Australia, the need for the integrated participation of the specially trained nurse or some other professionally trained counsellor in the management and treatment of breast cancer, has received only marginal recognition... The under utilisation of the nurse/counsellor on an integrated pre and post operative basis is the result of the current fragmentation in which rather than referral to a team which includes a specialist nurse or counsellor, referral is made to a broad range of specialists in different physical locations not working as a team” (p. 21-22).

Importantly, nurses’ capacity to contribute to improved patient care was further strengthened during the 1990s by new postgraduate education opportunities in the specialty. In Australia, the first postgraduate diploma in cancer nursing commenced at LaTrobe University in 1990, while the first masters level program, with a specialty in cancer nursing, commenced at Queensland University of Technology in 1995. The year 1991 also saw publication of the first Australian Standards for Oncology Nursing by the Clinical Oncological Society of Australia (COSA) Nurses Group. The second edition of these standards was published in 1996, with a preamble specifically highlighting that nursing practice continued to extend beyond medically related care, requiring the inclusion of new standards in areas including communication, fatigue and hope.7

In the 2000s, the demand for more patient centred approaches to care continued to be a major theme in key reports and policy documents such as Optimising Cancer Care and National Service Improvement Framework for Cancer. These documents emphasised the complex needs of people across the cancer experience and highlighted the importance of supportive care interventions and the need for better coordination of cancer care.

Cancer nursing practice has evolved to play a key role in these areas, with two major developments during this decade worthy of mention. Firstly, under the Australian Government’s Strengthening Cancer Care initiative, funding was provided for the development of education programs for nurses. The resulting program, the National Cancer Nursing Education Project (EdCaN), led to the development of a framework and a set of capabilities outlining the role expectations of nurses working in cancer control, and an associated set of teaching and learning resources to help nurses acquire these capabilities. A key feature of the framework is that the priorities, needs and experiences of people affected by cancer are central to the development of cancer control programs and to the involvement of nurses in such programs. The model presented in figure1 describes nurses’ varying contributions at all phases of the cancer continuum, outlining the competency standards required of nurses working in different roles, in different settings and at different points along this continuum.8 With the continued support of Cancer Australia, the EdCaN framework continues to define the minimum standards expected for cancer nurses today, with the framework and learning resources used extensively in the design, implementation and evaluation of continuing professional development and postgraduate programs across the country and internationally.

![Figure 1: EdCaN Professional Development Model for Nursing in Cancer Control.](image-url)

**Figure 1**: EdCaN Professional Development Model for Nursing in Cancer Control.

### PEOPLE AFFECTED BY CANCER REQUIRE A RANGE OF NURSING SERVICES

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<tr>
<th>ALL NURSES</th>
<th>Demonstrate ANMC competencies applied to cancer control</th>
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<tr>
<td>MANY NURSES</td>
<td>Demonstrate the ability to apply ANMC competencies in cancer control at a more advanced level in specific practice context</td>
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<td>SOME NURSES</td>
<td>Demonstrate the ability to practise according to the competency standards for specialist cancer nurses</td>
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<td>FEW NURSES</td>
<td>In addition to meeting competency standards for specialist practice, these nurses are credentialed to practise at an advanced level or in extended practice roles</td>
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The second major development in cancer nursing during this period has been the strengthening of the evidence base for cancer nursing practice, with nursing research having a greater focus on outcomes from nursing intervention and the processes of care that contribute to better outcomes for patients. For example, one systematic review considered resource-use data and nursing-outcome data collated from 76 case studies of patients referred to 12 specialist cancer and palliative nursing teams (home-based and hospital-based) in the UK. The review concluded that patients who reported better nursing outcomes had a higher proportion of specialist nursing interventions than those reporting poor nursing outcomes (45% v25%). Moreover, the review noted that the overall pattern of health-care use was different for those patients who reported positive nursing outcomes.9

Australian cancer nursing and COSA

The history of cancer nursing in Australia reflects close ties between the profession and COSA. In Australia, a national professional group for cancer nurses did not form until the late 1970s. This first group formed under the banner of COSA, initially as a sub-group of the Medical Oncology Group, beginning a long history of collaboration and partnership between a professionally organised group of cancer nurses and other health professionals working in the field of cancer care. By the mid-1980s, the COSA Nurses Group was formed and gained a seat on COSA Council and the first nurse sat on the Executive Committee in 1991.

The Cancer Nurses Society of Australia (CNSA) evolved from the former COSA Nurses Group and officially commenced operations on 1 January 2000, following several years of debate about the merits of forming a more independent group. The desire for an independent group was very much spurred by members’ experiences of the Oncology Nursing Society in the US, where the development of a professional group for cancer nurses did not form until the late 1970s. This first group formed under the banner of Cancer Nursing Society in the US, where the development of cancer nursing was well advanced. Much of the debate in Australia centred on ensuring that close ties between the new professional group and COSA were enshrined. The following extract from the discussion paper Establishing the Cancer Nurses Society of Australia, distributed to COSA Nurses Group members during 1996, highlights the high value placed on the relationship with COSA at this time: “In 1995, two discussion papers addressing the advantages and disadvantages of forming a national group were circulated amongst cancer nurses in Australia. Written comments from a number of state groups and individual cancer nurses were collated and presented at the COSA Nurses’ Group AGM in 1995. Following discussion of these reports at the 1995 AGM, 75 nurses unanimously agreed to develop a national nursing organisation separate to COSA, while maintaining membership within COSA and a place on the COSA Council…This decision was reached as there appears to be general agreement amongst cancer nurses that there are many advantages for nurses to maintaining such a close affiliation with COSA. This means that membership of CNSA will automatically mean membership of COSA. There also appears to be widespread support for further strengthening our collaborative links with COSA, however, the nature of the relationship between the CNSA and COSA will need to be re-negotiated to accommodate the development of this separate independent group for nurses”.

Table 1 lists the nurses who have participated as Chair/President for the COSA Nurses Group.

Table 1: Nurses who have participated as Chair/President of the COSA Nurses Group.

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<thead>
<tr>
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<th>Name</th>
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</tr>
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</tr>
<tr>
<td>1986 – 1989</td>
<td>Libby White</td>
</tr>
<tr>
<td>1990 - 1994</td>
<td>Sanchia Aranda</td>
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<td>Laurie Grealish</td>
</tr>
<tr>
<td>2003 – 2006</td>
<td>Kate Cameron</td>
</tr>
<tr>
<td>2007 – 2009</td>
<td>Gabrielle Prest</td>
</tr>
<tr>
<td>2010 – 2012</td>
<td>Meinir Krishnasamy</td>
</tr>
<tr>
<td>2013 -</td>
<td>Sandy McKiernan</td>
</tr>
</tbody>
</table>

In 2011, CNSA’s constitution was amended such that it is now no longer a requirement for nurses to hold both membership of CNSA and COSA. This change reflects an increasing sophistication of CNSA’s governance models and a growing diversity in the professional activities of CNSA. This shift aims to encourage nurses who may be new to cancer nursing or whose links with cancer are part of a broader role (e.g. respiratory specialists). However, CNSA’s commitment to a strong relationship with COSA has not changed, with Associate Professor Meinir Krishnasamy the first nurse to be elected as President of COSA commencing from 2014. Indeed, COSA’s commitment to its multidisciplinary model, and the privileged position that nurses have played in the society, is unique internationally. It has enabled cancer nursing in this country to thrive and is recognised by many as being fundamental to a unified and coordinated approach to improving cancer care in Australia.

Australian cancer nurses - international players

In the 1970s, cancer nurses from Australia were travelling internationally and being exposed to developments in the specialisation. From courses at the Royal Marsden in London to attendance at the Oncology Nursing Society (US) annual meetings, these nurses returned with stories of what was happening elsewhere. Our role in such conferences was largely passive, listening but not presenting, often feeling as if Australia was very behind. The substantial contribution of nurse consultants and clinical nurses specialists in the UK and US sparked the imagination of nurses in Australia and helped ignite a passion that did not receive universal support. At a COSA meeting in the early 1980s at the...
University of Melbourne, the first nurse invited speaker was Linda White from the MD Anderson in Texas. White worked as a prevention and early detection specialist at the Anderson and among other roles, performed colposcopies. Her plenary talk at the meeting, sandwiched between talks on oncogenes, sparked heated debate on whether nurses here could aspire to such roles. One gynaecology specialist was adamant that Australian nurses would never be able to perform at this level.

Where then is cancer nursing on the international stage in the year 2013? From a professional perspective, nurses from Australia have played a significant role in shaping the development of the International Society of Nurses in Cancer Care (ISNCC). The previous board of ISNCC had four nurses from Australia out of 14 board members, including the President and Treasurer. From a development perspective, the work of EdCaN and the framework it produced is being used by many nurses around the world as they shape their own developments. In research, our cancer nursing intervention research is among the best in the world and is published in high impact journals, in both nursing and medicine. The early inspiration for improving practice and undertaking research for many nurses was attendance at a COSA meeting. While our development often paralleled what was happening for cancer nursing in other countries, it was always given local context by the important inter-professional dialogue that COSA enabled.

The future for cancer nursing

Today, cancer nursing is facing new pressures to adapt and reform in response the growing demand for cancer services, the recognition of cancer as a chronic disease, the need for accelerated transfer of knowledge into practice, and growing fiscal challenges. Like other health professionals, cancer nurses must respond by developing and adopting new approaches to care. For example, adopting the principles of risk stratification will help to ensure the right care gets to the right person at the right time. Care coordination is also a critical component of cancer care in Australia as an increasing number of patients receive care across different facilities, including across public/private and metro/rural settings. A shift to supported self-management approaches is also required to accommodate the chronic nature of cancer and its effects, and the reality that most people with cancer experience these treatment effects in their homes.

A recent report by Health Workforce Australia highlighted that new advanced nursing roles established in the US and UK have demonstrated potential to increase efficiency and accessibility of cancer care.10 While there are numerous barriers to acceptance and challenges in implementation of such roles,10 the redesign of traditional roles and a greater blurring of practice boundaries will present new opportunities to achieve better patient outcomes.

Ongoing work is required to ensure people affected by cancer receive the best possible care from nurses, no matter what their social, demographic or clinical circumstance. Indeed, a recent report by the Institute of Medicine (IOM) on the future of nursing confirmed that by virtue of its numbers and adaptive capacity, the nursing profession has the potential to effect wide-reaching changes in the health care system.1 The IOM report calls for nurses to be enabled to practice to the full extent of their education and training and for clearer pathways with seamless academic progression and associated credentialing to ensure quality care. Importantly, the IOM report calls for nurses to be full partners with physicians and other health professionals in redesigning health care. COSA and the opportunities such a society presents for multidisciplinary care, mean that cancer nurses in Australia are well placed to respond to this call to action.

References

Evolution of Palliative Care in Australia 1973-2013

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Abstract

In parallel with the rapid development of oncology in Australia, palliative and supportive care has evolved rapidly. The sponsorship for such development was largely generated by oncology services in response to unmet needs that were encountered daily. Development of state, territory and national strategies has mirrored the professional development in service delivery, education (of existing practitioners and tomorrow's clinicians) and research. More recently, national programs are delivering better outcomes for palliative care patients and their families, world-leading clinical research, improved access to essential medications in the community and the ability to access quality evidence to inform practice and policy. These initiatives provide a valuable foundation for continuing to improve access to high quality clinical care wherever people live.

In Australia, the history of the transition from geographically and clinically limited hospice services to palliative care services over the past 40 years has paralleled closely the development of sub-specialist oncology services. Indeed, much of the impetus has come directly from leaders in oncology who recognised and acted to address patients' unmet needs in a better and more responsive way.1,2

By the early 1970s, three major providers accounted for most hospice services in Australia: the Little Company of Mary; Sisters of Charity; and the Deaconess Society. The model of care was built around care for the dying and indeed, as recently as 1982, a neon sign outside one institution read ‘Hospice for the Poor and Dying’. This was care in a tradition that had arisen in the middle ages to ensure that people at the margins (and the dying still face such marginalisation) were provided with care and shelter, often for extended periods of time. At the same time, nursing home bed numbers were expanding and, similar to hospices, tended also to have relatively long lengths of stay. Neither group of institutions had discharge policies, with care provided until death supervened.

The leadership shown internationally by people such as Vittorio Ventafridda (Italy), Cecil Saunders (England) and Balfour Mount (Canada) led to an undeniable shift in care for people with advanced illness. Providing quality health care for the dying that addressed physical, emotional, for the dying that addressed physical, emotional, existential, social and sexual needs became a focus of active needs-based care, rather than simply closeting people away once death became inevitable. Australia, as one can argue often happens in health care, took the best of the international models and philosophies and adapted them to the local health and social systems. No single model could adapt perfectly to the manifest differences in health system design, funding nor geography. This allowed an eclecticism that has served well.

Development of palliative care

A watershed for the early evolution of palliative care in this country was the commissioning of a report by the Anti-Cancer Council of Victoria on care of the dying in 1983. This was a report whose recommendations have echoed through the subsequent three decades – there was a perceived need to have services provided at a geographical level with a team led from, and integrated, with existing health services, given that this was where the population who were facing the end of their life could be identified currently. The report also indicated that building further freestanding hospices would not serve the target population well. The latter was a particularly salient recommendation, given that two of the country's largest freestanding hospices would close within 20 years of this report in order to move to a model that provided much closer integration with existing health services. At least three others have seen fundamental changes, with a decreasing number of beds augmented by hospital liaison and community-based teams. Such evolution has not been without controversy, but it does speak strongly to the vision held by Ross Webster and his committee in 1983 as he looked to the future needs of the population.3

By the mid-1980s several states had palliative care position statements, strategic plans or direction statements.4 Given the time lines, and the paucity of services globally, this showed an extraordinary level of jurisdictional leadership. Every state had its champions, and the diverse backgrounds of these medical and nursing leaders have positioned palliative care well: oncology; primary care; anaesthetics and pain medicine; general medicine; geriatrics and psychiatry.

The late 1980s saw four important steps that have shaped the ensuing quarter of a century:

- Creation of the world's first academic chair in palliative care at Flinders University in 1987 (reflecting similar appointments over the next decade at a number of institutions).
- Formation of the Specialist Advisory Committee in Palliative Medicine by the Royal Australasian College of Physicians in 1988, which was the world's first sub-specialist training program in palliative medicine.
- For the first time, the inclusion of identified funds for states and territories to use to develop palliative care services in the 1988 quinquennial Medicare agreement.
- A meeting convened by the Medical Oncology Group of Australia in 1989 to help map the future direction of palliative care from the viewpoint of oncology services.5

The Chair at Flinders University has evolved into a unit that delivers the largest distance education program in palliative care in the southern hemisphere and one of the biggest in the world, with 400 current post-graduate students, together with a niche program designed to provide affordable post-graduate education to clinicians in resource-poor countries spanning the Middle East to South East Asia. The department is now host to one of several productive research teams across the country, each of which has an international track record of leadership in their areas of expertise.
The Royal Australasian College of Physicians program allowed a direct path to subspecialisation that was gradually taken up. This was augmented in 2000 with the formation of a Chapter of Palliative Medicine within the college to facilitate lateral entry from other learned colleges. This has allowed a group of clinicians from a wide range of clinical backgrounds to undertake palliative medicine sub-specialty training and bring their diversity of skills to care for people at the end of life, reflecting the diversity of early clinical champions of palliative care in Australia and around the world. More recently a clinical diploma has been added to the program.6

Medical oncology

The 1989 meeting convened by Medical Oncology Group of Australia cemented the close relationship between oncology and palliative care, with most palliative care services still providing the majority of their clinical services to people with cancer and their families. This meeting occurred at a time when the philosophical underpinnings of palliative/hospice care were still being hotly debated. The model in the UK was struggling to move beyond cancer, especially with the advent of AIDS, but also with the changing face of dying: chronic, complex, slowly progressive diseases leading inexorably to death.5 Australia’s policies from that time forward have not limited care by perceived prognosis (unlike the US), nor by diagnosis (unlike many charitably funded, freestanding services in the UK).

A national strategy

The 1998 national census (State of the Nation) undertaken by the newly renamed Palliative Care Australia, was an important step in measuring the progress made in ensuring that people, wherever they lived, had access to palliative care. Participants were asked to record their activity over the same 24 hour period and the data collated. This was the first national view of what services were delivering, the patients being seen and the models of service delivery that had evolved over the previous two decades. Much of this local evolution was because of widely varying mechanisms for funding and widely varying commitment at the jurisdictional and local level for the provision of palliative care. The legacy of this is still felt in varying levels of service access, with some tertiary services still only providing nominal support for the vision laid out by Ross Webster in 1983.3

The census demonstrated, as expected, that cancer accounted for approximately 90% of all referrals to services, although again there was wide variation depending on a number of local factors as to the population served. Care was delivered in the community, in hospitals (consultative, direct care or both) or a number of free standing and co-located inpatient palliative care units.

The first national strategy was endorsed by all states and territories and the Commonwealth in 2000, and updated again with jurisdictional support in 2010. This document provided a real basis on which to build, for the first time, truly national initiatives with Commonwealth funds directed nationally, not just for jurisdictional projects. Fundamental principles included equity of access to high quality services underpinned by the best evidence available. There was a specific focus on improving community-based care, to which the Commonwealth has continued to provide resources. As part of this work, a review of research capability in palliative care was commissioned by the Commonwealth, which demonstrated few units with strong competitive track record or the requisite pipeline of researchers coming through.

National programs that arose included improving:

- research capability
- education of the existing and the future workforce
- affordable community availability of key medications for symptom control
- quality of care delivered
- access to the evidence to inform practice and policy.

These programs have put Australia at the forefront of palliative care in the world. This program was conceived and delivered by Rita Evans in the Department of Health and Ageing through the National Palliative Care Program. Without her vision these programs could not have come to fruition.

A variety of models of service delivery evolved. There was however, a key shift with the development of the National Palliative Care Strategy (2000), to which each state, territory and the Commonwealth became a signatory. This set the stage for investment by the Commonwealth directly in initiatives at a national level. This investment has been far-reaching, with each of the subsequent Medicare agreements providing funding in parallel with national initiatives. Much of this initial funding seeded new services, improving geographical coverage.

Research capability

In research, the Commonwealth invested in a specific program which included bursaries for research higher degrees at a masters and doctoral level, together with a number of seed grants that allowed researchers to establish a category 1 track record with a view to improving their access to competitive grants nationally. This program, in conjunction with the National Health and Medical Research Council, was a two way process, as it also encouraged the council to consider reviewers who had research expertise in palliative care. The Commonwealth’s investment has been successful and, within a decade, palliative care has been gaining category 1 grants and completing these studies.8

Health workforce education

In education, the Palliative Care Curriculum program (www.PCC4U.org) has developed and worked to disseminate the key undergraduate competencies for all health professionals irrespective of their discipline. The competencies include: individual attributes (empathy, compassion, caring and a non-judgmental approach); clinical skills (assessment, pathophysiology of dying, pharmacology); communication skills (active listening, reflection); and palliative care
principles (philosophy, multi-disciplinary care). The program has worked with universities to assimilate these handful of essential concepts into curricula. Uptake has been more likely if a curriculum is being rewritten and so the process of uptake will take time. Simultaneously, there have been funded opportunities for existing practitioners to learn or update their skills in palliative care; the Program of Experience in the Palliative Approach (PEPA) has seen a wide range of practitioners take the opportunity for attachments to services often within their referral network.

**Care and medications**

The Palliative Care Clinical Studies Collaborative was a Commonwealth initiative whose genesis lay in the challenges of creating the first patient-defined section of the Pharmaceutical Benefits Scheme (PBS) in Australia. Until 2004, all sections of the PBS had been defined only by the clinician who was entitled to write that prescription. Shifting specific sections to a patient-based focus has since been emulated in both paediatrics and Aboriginal and Torres Strait Islander health. The palliative care section of the PBS started with medications where indications were already registered with the Therapeutic Goods Administration and where there was sufficient evidence to support cost effectiveness for a Pharmaceutical Benefits Advisory Committee application. February 2004 saw this section established and it has grown consistently every year since. However, there were still a number of medications considered ‘essential’ by clinicians for symptom control in the community, for which there was not sufficient evidence for either registration or subsequent subsidy applications. As a result of this, the Palliative Care Clinical Studies Collaborative was established and is conducting nine phase III clinical trials to improve the evidence base. To date, more than 1000 participants have been randomised in these rigorously designed, adequately powered studies to improve the quality of care that is offered. The first of these studies has been reported.

Improving the quality of care has been a focus of the Palliative Care Outcomes Collaborative. The collaborative is built around: point-of-care data collection; aggregated analysis of data nationally, at a jurisdictional level and by model of service delivery; and benchmarking across the country in order to highlight key areas where outcomes can be improved by better models of service delivery. Key success factors for the program include a focused dataset with direct clinical utility, timely feedback of results and trained quality improvement facilitators to work with services in order to improve each service’s own outcomes. To date, more than 15,000 patients are reported in each six monthly report, with clear evidence that the outcomes are improving over the 13 six-monthly periods so far reported (figure 1). More recently, this has been complemented with a National Standards Assessment Program. The program relies on self-report of process measures that are thought likely to influence the quality of care offered. Both of these programs are designed to improve care.

**Access to evidence**

Improving the access to evidence is crucial in palliative care. Given its universal nature, the palliative care literature is spread literally across hundreds of journals. This is a huge challenge for practitioners and researchers in the field. CareSearch was created by the Commonwealth to improve that access and uses a unique system of real time interrogation of PubMed in order to ensure currency, together with unique access to the grey literature (conference abstracts that have not been converted into peer-reviewed publication, government reports, theses and journals before being listed on Index Medicus). It has structured searches for more than 50 topics that are validated for sensitivity, specificity and accuracy. This has improved access both for clinicians and researchers to literature wherever it occurs in the body of knowledge in real time (and is a model now being adapted to Aboriginal health and primary care).

Ultimately, is palliative care living up to the hopes and aspirations of those who championed the needs of people at the end of life? What would Australia’s early palliative care champions, Fred Gunz or Wally Moon say today? Almost every teaching hospital now has a palliative care team, but many still do not have outpatient clinics (especially co-located with the services that are most likely to refer to them), nor the ability to admit patients directly under their care. Some still fail to provide real access to support around the clock for the emergency department. In the community, the models of service delivery vary widely, and clearly some people do not yet have equitable access. But there is now a national approach to many things that until recently have been piecemeal, and quality evidence that the care that is being provided is systematically improving, a claim that can be made by very few specialties at a national level. Access to palliative care has improved where there has been a focused investment in services, but the challenge of poor access persists where health services have failed to make the investment required to strengthen local palliative care. Given the documented level

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**Figure 1: Number of patients, episodes of care, phases (left y axis) and services (right y axis) reported nationally through the Palliative Care Outcomes Collaborative in six monthly time periods 2006-2012.**

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Radiation treatment has evolved over the past 12 decades into a highly sophisticated, cost-effective cornerstone treatment for people with cancer. It adds significantly to the chance of cure for many people with cancer and can be very effective in helping relieve symptoms for those in whom cure is not possible. Since 1956, when linear accelerators (linacs) came into mainstream clinical use in Australia, radiotherapy technology has advanced greatly. This, accompanied by major advances in our understanding of the biology of cancer and radiobiology, and exploitation of the benefits of combined modality treatment with surgery and systemic therapies, has led to significant improvements in treatment outcomes. Although we have described the developments separately, often we see advances in technology, biology and integration occurring simultaneously and scattered across the globe.

The primary goal of radiation treatment delivery for cancer is, always has been and always will be to maximally treat cancer tissue and maximally spare normal tissue. This, always has been and always will be to maximally treat cancer tissue and maximally spare normal tissue. The primary goal of radiation treatment delivery for cancer is, always has been and always will be to maximally treat cancer tissue and maximally spare normal tissue. The primary goal of radiation treatment delivery for cancer is, always has been and always will be to maximally treat cancer tissue and maximally spare normal tissue. The primary goal of radiation treatment delivery for cancer is, always has been and always will be to maximally treat cancer tissue and maximally spare normal tissue. The primary goal of radiation treatment delivery for cancer is, always has been and always will be to maximally treat cancer tissue and maximally spare normal tissue.

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desire to treat our patients’ cancer to the required dose, while reducing collateral damage, drives our modern technology and the delivery of radiotherapy. With advances in technology, we can now shape beams with very steep dose gradients, delivering high doses to cancer tissue while sparing the adjacent healthy organ(s). This requires a deep understanding of anatomical and molecular imaging, tumour and normal tissue biology and treatment related risk factors in order to define the tissues to be treated, the dose to be delivered and the organs to be spared or dose limited. The integration of radiotherapy with other treatment modalities, and the relationship between radiation oncologists and other members of multidisciplinary teams are vital to facilitate access to high quality cancer treatment for our patients. The evidence base for its application is robust, and it incumbent upon all of us involved in radiation oncology to deliver treatment that is of the highest quality and benefit for our patients.

**History**

Modern radiotherapy is built on the shoulders of giants and has a fascinating and rich history. The radiotherapy treatments that we have available today, with brachytherapy (temporary or permanent implants of radioactive material), radionuclides (ingested or injected isotopes with selective organ uptake) and external beam radiation treatment, have been made possible by committed researchers in the fields of biology, physics, chemistry and clinical medicine over 12 decades, since the discovery of X-rays by Rontgen in 1895, radioactivity by Becquerel in 1896 and radium by Marie Curie in 1898.

Less than three months after Rontgen discovered X-rays, a medical student in Chicago, Emil Grubbe, used X-rays to treat a patient with advanced breast cancer in early 1896 thereby commencing the earliest external beam therapy. As early as the 1920s superficial, and deep X-ray treatment was available (100-350 Kilovolts). It was soon appreciated that delivering treatment in a number of smaller doses was highly beneficial and facilitated delivery of much higher doses to the cancer, with equivalent or even better normal tissue tolerance. It was not until megavoltage treatment became available that deep seated organs could be effectively treated using external beams of gamma-rays or X-rays. In 1951, cobalt teletherapy units were brought into therapeutic use. In the same year, Lars Leksell proposed the Gamma Knife®. Linear acceleration of electrons to produce high energy x-rays was proposed in 1924 by both Ising and Wilderoe independently. The war effort played a major role in the development of the modern linear accelerator. The klystron was developed during the Second World War as a source of microwave power for radars, and the combination of the klystron with linear acceleration led to the development of linear accelerators as we know them today. The first linac came into clinical use in 1953 at the Hammersmith in London.

During 1952, Kaplan and Gintzon developed their first linear accelerator at Stanford and the first patient was treated in their hospital in 1956. Interestingly, they had on-board Kv imaging for field verification and image guided radiotherapy (IGRT) was born. During 1956, linear accelerators were commissioned at both Peter MacCallum Cancer Centre and Royal Brisbane and Women’s Hospital by Jake Haimson. Brisbane Hospital’s linac treated the first patient in Australia. By 1962 there were 15 clinical linacs world-wide, three of which were in Australia.

**The technology**

Advances in technology have been amazing and have occurred both in a parallel and sequential fashion. Since 1956, the linac has been the workhorse of modern radiotherapy departments. Linacs deliver megavoltage photons (X-rays) and most are also able to deliver electron beams. While the basic method of linear acceleration to produce a beam of X-rays has remained largely unchanged since the 1950s, the capacity to shape and drive the beams during the delivery of treatment has evolved enormously and is now extraordinarily sophisticated. This has been enabled by three critical developments - the advent of multi-leaf collimators, the invention and evolution of computers and major advances in imaging, particularly CT.

**Shaping the beam**

Since the inception of radiation therapy, shaping the beam to conform more to the treatment shape required has been important. This was initially performed with lead shielding blocks placed between the linac and the patient, and evolved to custom made shielding blocks using low melting point alloys. A revolutionary advance came with the advent
of multi-leaf collimators first developed in the 1960s, built into the head of the linacs - tungsten leaves that can be moved during treatment delivery to alter the shape of the treatment beam. Multi-leaf collimators can now be driven remotely and this has facilitated the delivery of complex beam shapes, arc treatment with fields that can even change shape during delivery, and a much faster delivery time despite increasing the number of treatment fields. These beam shaping developments have culminated in greater conformality of the radiation dose, serving to reduce the amount of adjacent normal tissues that receive an unnecessarily high radiation dose.

**Computers**

The ability to drive the linacs in an increasingly sophisticated manner has been dependent on computers. Computerised planning systems have replaced hand-drawn treatment plans. Furthermore, the ability to incorporate CT images allowed us to map the cancer in three dimensions, thus enabling 3D conformal treatment. More recently, it has become possible through the development of four dimensional (4D) conformal radiation treatment to accommodate the movement that occurs during treatment. The development of inverse planning systems has allowed linacs to not only deliver dose to the target area, but also to modulate the intensity profile of the beam to exclude or restrict dose to organs at risk. Intensity modulated radiation therapy is now considered the standard of care for the radical treatment of cancers in most sites where the limitation of dose to critical organs not requiring treatment is very important for long-term quality of life and survival.5,6

The therapy can be delivered by units with standard linac conformation, or by dedicated helical intensity modulated radiation therapy equipment such as the TomoTherapy machine. The TomoTherapy machine, developed by Mackie, has a compact linac mounted on a rotational gantry and delivers a very large number of beamlets in a rotational fashion, allowing for sophisticated dose sculpting.

*Figure 2: Examples of steep dose gradients from Tomotherapy demonstrating the protection of normal tissues (courtesy Royal Brisbane and Women’s Hospital).*

Advances in computing also underpin a number of other improvements in radiotherapy techniques. A good example of such an improvement is found in the development of stereotactic radiosurgery and stereotactic radiotherapy. Stereotactic radiosurgery and stereotactic radiotherapy can be used to deliver high doses of radiation to small targets, such as brain metastases, and benign but problematic benign lesions, such as acoustic neuromas and arteriovenous malformations. They can be delivered using a specifically precision engineered linac, or with the TomoTherapy or Gamma Knife® machines. Stereotactic radiosurgery may also be delivered using the CyberKnife.

The ability now to sculpt the dose is exquisite and can be tailored to the clinical situation. However, the potential for marginal miss is greater. Determining the volume to be irradiated requires a meticulous approach and quality assurance of the whole process is critical. Computerised systems allow the interlinkage of clinical information, planning simulators, planning CT scanners, the planning systems and the linacs. A number of failsafe mechanisms have been built in, which are an essential part of the quality integration of RT systems. CT scanning is now available on linacs to correct patient positioning and track day to day organ and tumour changes. MRI-guided linacs are under development in Europe, the US and Australia.

**Imaging**

Modern imaging has utterly transformed the delivery of radiotherapy. Planning CT scanners form the basis of acquiring the details of a patient’s anatomy for all but the most straightforward treatment plans. The acquisition of volumetric anatomy allows radiation oncologists to map the volume of tissue to be treated and the organs to be excluded or dose limited. All of this information is reconstructed in either three or four dimensions (incorporating motion). Diagnostic CT scans, MRI and functional PET/CT imaging can be fused on to the planning CT scan, facilitating the best possible radiological identification of tumour. Anatomical data acquired with various imaging modalities must then be combined with all known clinical factors and a deep understanding of the natural history of the specific cancer, to enable the final determination of the volume to be treated, the doses and fractionation required and the organs of exclusion to be mapped. Accordingly, radiation oncologists now need to understand CT, PET/CT and MRI anatomy, as well as surface and surgical anatomy. Often identification of the desired target volumes requires input from surgeons, radiologists and PET physicians.

**Brachytherapy**

By 1900, Danlos had begun brachytherapy treatment at St Louis Hospital in Paris. Brachytherapy using radium was the first curative treatment available for internal tumours, notably cancer of the uterine cervix, with results first published in the 1920s. However, radium is difficult to handle safely and its use results in unwanted whole body patient and operator exposure. Radium has now been replaced by artificial radionuclides such as Caesium137, Iridium192 and Iodine125. The use of these isotopes, with sophisticated afterloading techniques, has eliminated safety concerns and permitted highly conformal dose distributions to be achieved, with major application in the modern day treatment of cervical and prostate cancers. By 1938, artificial radionuclides were used to treat a patient with leukaemia (137P). I131 therapy for differentiated thyroid cancer followed soon after and is now routine.

**Particle therapy**

Charged subatomic particles have the property of a finite,
energy-dependent range in tissues and so offer theoretical dosimetric advantages over X-rays. The most commonly used particles are electrons produced by the same linacs as are used for X-ray therapy. Electrons are most useful in treating relatively superficial tumour volumes because they spare underlying normal tissues.

Heavy particles have also been tested for clinical utility. By 1930, Lawrence developed the first cyclotron at Berkley and by 1945 Wilson had recommended that particles be put to therapeutic use. Initial trials focused on fast neutron therapy based on the anticipated advantage of high LET (densely ionising) radiation in treating hypoxic tumours. However, subsequent radiobiological research showed that the differential sparing of late-reacting normal tissues through dose fractionation of X-ray treatment was lost with high LET beams. Neutron beams (being uncharged) are also much more difficult to shape than X-rays or charged particle beams, resulting in significantly poorer dose distributions. Definitive trials of fast neutron therapy in the 1980s showed no therapeutic advantage with their use.

Attention has since turned to proton therapy, principally based on the precision of dose distribution that can be achieved rather than on any proven radiobiological advantage over ‘standard’ X-rays. The incremental benefit in dose distribution achievable with protons has been significantly narrowed by advances in intensity modulated radiation therapy photon delivery techniques. Accepted indications include some base of skull tumours and paediatric brain tumours because of the reduced risk of late effects on normal tissues. The potential advantage of combining both dosimetric precision and high LET, through the use of heavier charged particles such as carbon ions, is currently being investigated in Japan, Europe and more recently in China.

**Radiobiology**

From the very beginning of radiotherapy there has been a keen interest in the biological factors that influence the response to ionising irradiation. Bergonie and Tribondeau (1906) were the first to note that fractionating doses of radiation in animal models allowed for the same tissue effect at lower toxicity. From there, Regaud, Coutard and Baclesse pioneered the early clinical work in fractionation. In the early days, when only superficial and orthovoltage X-rays were available, skin toxicity was the limiting factor. Coutard’s recognition of the usefulness of fractionation for decreasing mucositis was a revolutionary observation. From there, many radiation oncologists and biologists have looked for ways to exploit fractionation as a way of maximising the therapeutic ratio between the anti-tumour effect of radiation and damage to dose limiting normal tissues. The differential effects of ionising radiation on cancer and normal tissues is predicated on the classic 4 Rs of radiobiology to describe events occurring between radiation dose fractions: repair of sub-lethal damage; reassortment of the cells within the cell cycle; repopulation of surviving clonogenic cells; and reoxygenation of erstwhile radioresistant hypoxic tumour cells. One of the key radiobiological discoveries relevant to optimisation of dose fractionation was that late reacting normal tissues were in general, spared to a greater extent than most cancers by dose fractionation. This difference could be modelled by the $\alpha/\beta$ ratio in an isoeffect equation which enabled safe changes to fractionation schedules to be made. A related pivotal discovery that prolonged overall treatment time increased the risk of recurrence in the treatment of epithelial cancers, notably of the head and neck.

The benefit of altered fractionation schedules to take advantage of these radiobiological considerations has been demonstrated in a number of randomised clinical trials. Their widespread adoption in Australia is largely limited by resource constraints. With the modern trend to use extremely hypofractionated treatment schedules (low number of fractions) in stereotactic whole body radiation therapy, it must be recognised that no differential sparing of normal tissues within the high dose volume is possible and normal tissue tolerance depends entirely on volume effect - all normal tissues in the high dose volume must be considered expendable, and accordingly every effort is made to physically limit the volume of normal tissue that is irradiated.

The next major advance in optimisation of radiation dose fractionation schedules is likely to come from molecular genetic characterisation of individual patients’ tumours and normal tissues. While considerable progress has been made in identifying gene mutations or single nucleotide polymorphisms responsible for modulating radiation responses, no predictive assays have yet been developed to the point of clinical application.

**Integration of radiation treatment**

Radiation oncology is a highly interdisciplinary specialty. Optimum treatment of the majority of cancer patients requires the use of integrated multimodality treatment with various combinations of surgery, radiation and systemic therapies. The Collaboration for Cancer Outcomes Research and Evaluation has developed evidence-based benchmarks for radiotherapy that have provided the basis for the expansion of cancer services in Australia and internationally. The evidence to support the use of radiotherapy has been built on decades of trials and studies, and the methodology to assess this is a disciplined way developed by Delaney and Barton. Radiation treatment in some circumstances may be curative as a sole modality, but is very often combined with surgery and drug treatments to maximise both local and systemic cure. Radiation treatment often will allow for less radical surgery (for example in conservative treatment of limb sarcomas and in breast cancer) or may replace surgery (for many people with oropharyngeal cancer). The integration, sequencing and linking of combined modality treatments is important in offering patients the best possible care. Over 80% of the indications for radiotherapy are for the improvement of cure or the increase of survival.

**Advocacy**

Radiotherapy is a cornerstone of cancer care with deep and historical science and amazing technology supporting it. These attributes are vital, however the overall care of people with cancer drives radiation oncologists first and
foremost and underpins our approach to multidisciplinary care. The Faculty of Radiation Oncology, Royal Australian and New Zealand College of Radiologists (RANZCR), has advocated on behalf of cancer patients since its inception, emphasising the need to close the gap for people with cancer in accessing cancer care in general and radiation treatment in particular. In 2000, together with the Australian Institute of Radiography and the Australasian College of Physicists, Scientist and Engineers in Medicine, the Tripartite Committee was formed. The committee is a shining example of goodwill and multidisciplinary cooperation and its output has had a major influence in Australia and New Zealand in raising awareness of the need for high quality treatment and the shortfalls in physical and staffing infrastructure. The Tripartite committee developed the National Strategic Plan for Australia in 2000, and has recently published a new plan ‘Planning for the best: Tripartite National Strategic Plan for Radiation Oncology 2012-2022’, which makes recommendations for changes required to optimise all aspects of radiation oncology for Australian cancer patients. It also developed the Quality Standards for Radiation Treatment Delivery, which were released in 2011.

The rigour for our radiation oncology trainees is high and the RANZCR was among the first of the professional colleges to be accredited by the Australian Medical Council. The college has since undergone extensive review and taken advice from professional educators in modifying its training and assessment programs.

Quality

The quality standards developed by the Tripartite Committee form the quality base in Australia and New Zealand. Delivering quality treatment is highly complex, and time consuming, but essential. Daily, weekly, monthly and annual quality assurance is an ordinary part of treating departments. The need for participation in clinical trials and to keep accurate recording of short and long-term data cannot be underestimated.

The Trans Tasman Radiation Oncology Group (TROG) and other international trials groups require quality assurance for the majority of trials. This often requires assessment of the entire treatment chain and is a costly part of clinical trial activity. The requirement however, is high. One of, if not the most important trial ever conducted was the TROG 02.02 or HeadSTART Trial. Although the trial was asking a question regarding the addition of an hypoxic cell cytotoxin, quality assurance and real time review of treatment plans was required. The trial demonstrated that inferior quality head and neck radiotherapy resulted in a 24% deficit in locoregional control and a 20% deficit in overall survival at two years. The quality of the radiotherapy dominated the drug question, putting in question all trials where quality assurance of the radiotherapy was not integral.

The future

The possibilities for radiation oncology are extraordinary. By understanding and building on the depth of developments to date, and having a clear understanding of what outcomes we are looking for – be they relief of symptoms, increased cure or a reduction in side-effects, or all three, collaboration will achieve our goals more quickly. Unfettered technology development by our clinicians, radiation physicists and engineers, continuing advances in our understanding of tumour biology and predictive assays, and the interaction of radiation with drugs and other molecules, increasing close to improve local cure, altering the distribution of dose within cancer tissue depending on biological markers of resistance or sensitivity, monitoring change occurring through treatment with functional MRI or PET imaging using novel tracers and altering and adapting the dose accordingly - all of these are tantalising possibilities. Overt cooperation and collaboration from many will be required to see this through.

Currently many factors improve patient outcomes, both in terms of cure and quality of life. Making evidence-based and sensible recommendations upfront as to where and when to have radiation treatment may be of benefit as will having clinicians and patients choose appropriately linked and sequenced care, and when radiation treatment is used, delivering high quality treatment.

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Since the earliest of times, surgery was regarded as the only hope for effective treatment for most cancers. The 18th century English surgeon, John Hunter, suggested that surgery might cure cancer if the tumour was contained. He remarked that "if the tumour is moveable... there is no impropriety in removing it".1 Despite the giant strides made by the modalities of radiation oncology and medical oncology, surgery remains an essential aspect of potentially curative treatment for almost all solid tumours, plays an adjunctive role in other tumours and helps in the management of many patients with advanced cancer.2 Surgery as an effective cancer treatment was made possible by the developments in anaesthesia and in the engineering of precise surgical instruments that occurred in the 19th century. Improvements in anaesthesia, analgesia, intensive care, and the continued improvement of surgical and other technologies has expanded the scope of surgery, rendering previously inoperable tumours resectable, and improving patient safety and comfort during and after surgery.3

Multidisciplinary care

As surgery was the original single discipline used for treatment of many solid tumours, the development of multidisciplinary care and multidisciplinary teams has altered the way that surgery and surgeons are involved in cancer care. This was revolutionary for surgeons who were used to individual decision making and in some cases resisted the intervention of other practitioners. To their credit the flexibility of mind of surgeons shone through and they embraced this new approach.4

In almost all solid tumours, multidisciplinary care offers better outcomes, in terms of better survival and or reduced side-effects. It has allowed for the development of better selection criteria for patients having optimal surgery and made the spectre of incomplete excision a rarity in 2013. The bringing together of committed personnel expert in various modalities of cancer therapy has been the hallmark of the Clinical Oncological Society of Australia (COSA). Breast cancer has been the model for this approach to care, with the early demonstration that patients treated in a multidisciplinary setting overall have better outcomes than those treated in the traditional model of singular or sequential care by various practitioners. As the benefits of adjuvant therapy became apparent in other diseases such as colorectal and oesophageal cancer, that were previously managed predominantly by surgeons, the view that multidisciplinary care is required for effective cancer management has become established across tumour types. This has been accompanied by a major change in the role of the surgeon in cancer care.5

Improved safety and increased expectations

Significant change has occurred in cancer surgery over the last 40 years. Surgical operations are far safer than they ever were, and patient comfort and pain control is now a major feature of care. The accepted operative mortality of major surgery such as pancreatectomy was once at least 10%, and many series with much higher rates of mortality were published by major academic institutions. These institutions are now publishing large series with minimal or even no perioperative mortality.6 Factors behind this improvement include: the introduction of perioperative antibiotics; a much better understanding of perioperative pathophysiology; expert and multifaceted pain control; and the development and widespread availability of supplemental nutrition, either enteral or parenteral.

A further, very important reason for these improved results is the subspecialisation of the team looking after the patient before, during and after surgery. It is clear that selected major procedures are much safer if they occur in institutions with a high case load and if the surgery is performed by surgical teams with specific expertise in that operation and...
its after care. Together, these have resulted in dramatically improved outcomes from surgical interventions. Ensuring that all patients have access to treatment by the appropriate team in the appropriate setting remains a challenge for the clinicians, the colleges and state and federal institutions.

**Surgical intervention**

Early diagnosis of cancer is the best way to improve cancer outcomes and it demands the best of clinicians diagnostic and observational skills. Screening programs for cervical cancer and breast cancer have been established to extend the benefits of early detection to as much of the population as possible. Screening for early colorectal cancer with faecal occult blood testing has also been proven to reduce mortality from the disease, and a national program is being introduced. Prostate-specific antigen testing identified early prostate cancer in many asymptomatic men, and testing for prostate-specific antigen has been shown to reduce the number of cases of advanced prostate cancer in a screened group of men.

In all these cases, some form of surgical intervention to eradicate premalignant or early invasive cancer is the means by which the lesion identified on screening is treated. While it is not really challenged that early treatment of a lesion that is destined to become a clinically significant and potentially metastatic disease is often beneficial, it is also true that screening programs do identify lesions that were not destined to become clinically significant during the person’s natural life. No doubt the balance between appropriate early diagnosis, and so-called ‘over-diagnosis’ will be debated for years to come.

**Tailoring of the extent of cancer surgery**

In the early days of cancer surgery, many decisions seem to have been relatively straight-forward. The patient with a breast cancer underwent at least a total mastectomy, the patient with a kidney cancer underwent a total nephrectomy and the patient with an extremity soft tissue sarcoma underwent an amputation. Massive amputations of cancer were deemed the best treatment during the decade before COSA was established, with extended radical mastectomies, massive head and neck cancer resections and other highly morbid and mutilating operations being performed.

A number of developments have seen this approach carefully re-evaluated, such that function-preserving surgery is increasingly an option. Breast cancer surgery has seen a dramatic evolution, first with the demonstration that breast conserving therapy with local excision of the cancer and adjuvant radiotherapy was equally effective as total mastectomy, followed by demonstration that sentinel node biopsy was as effective as axillary clearance for those with negative nodes, and now the suggestion that many node biopsy was as effective as axillary clearance for those patients with limited disease in the sentinel node may not benefit from further axillary surgery. These changes inevitably caused anxiety, until rigorous trials demonstrated their safety, and future efforts to tailor the extent of cancer surgery by identifying aspects of treatment that can be safely reduced or eliminated will continue to require scientific rigour.

**Neoadjuvant therapy**

The standard multidisciplinary treatment typically involved surgery as the initial modality, with recommendations for adjuvant therapies dependent on the surgical and pathological findings. Over recent decades, a number of situations have been found where altering the sequencing of treatment has resulted in better outcomes, either more effective cancer treatment and/or fewer side-effects. Examples include the approach to T3 or node positive rectal cancer, where pre-operative radiotherapy gives better local control than surgery followed by postoperative radiotherapy, T3 or node positive oesophageal cancer, preoperative systemic therapy for inflammatory and other locally advanced breast cancer, and preoperative radiotherapy for some cases of soft tissue sarcoma. In most of these cases the benefits of altered sequencing of treatment has been demonstrated through randomised trials, with better outcomes or fewer side-effects.

More recently, there has been a paradigm shift in the role of surgery for metastatic disease, with the demonstration that in many cases of metastatic colorectal cancer in the liver, a case that was previously considered incurable, may be rendered potentially curable with the use of systemic therapy prior to surgery. This has produced a new series of challenges to the surgeon, with side-effects specific to the preoperative therapy.

In many diseases where preoperative systemic therapy is used, there is a group of patients who experience a complete pathological response to the systemic treatment alone. In breast cancer, this varies from 5-50% depending on the subtype of cancer and the nature of therapy used. In oesophageal cancer, preoperative chemoradiotherapy is associated with a significant chance of a pathologic complete response. These findings hold promise that some patients will be able to avoid the need for surgery altogether. While at present such a group is not able to be identified, mainly because the achievement of pathologic complete response is only established after surgery, it is one of the hopes for cancer treatment in the future that unnecessary surgery can be avoided to the patient’s ultimate comfort and benefit.

**Cancer genetics and risk-reducing surgery**

The traditional role of cancer surgery in the primary treatment of established malignancy has been extended into the area of cancer prevention. Better understanding of the natural history of cancer and in particular, developments in familial genetics, has allowed much better prediction of individual lifetime risk of cancer. Combined with safer resection surgery and improved options for reconstruction to limit the functional impact of surgery, risk-reducing surgery has become part of the therapeutic armamentarium for many diseases.

Carriers of mutations in the BRCA1 or 2 gene are at substantial lifetime risk of breast and ovarian cancer. Risk-
reducing mastectomy will reduce the risk of developing breast cancer by around 95%, and risk-reducing salpingo-oophorectomy will have a similar impact on the risk of ovarian cancer. While these operations have minimal risk of operative mortality, the physical consequences of premature menopause, and the psychological impact of risk-reducing mastectomy are potentially serious, and the surgeon and other team members involved must address these issues.

People with adenomatous polyposis coli mutations will inevitably develop colorectal cancer, and so risk-reducing colectomy prior to development of the cancer is logical and appropriate. The situation with hereditary non-polyposis colon cancer gene carriers is different, as the risk of cancer is lower. Carriers of a CDH1 mutation will almost certainly develop diffuse gastric cancer. Total gastrectomy is a large operation with a definite risk of mortality and potential long-term side-effects. The surgeon must be closely involved in decision making and must be able to perform the operation with minimal mortality and morbidity. The introduction of minimally invasive techniques for both colectomy and gastrectomy promise to further reduce the morbidity of the surgery, moving the balance of risks and benefits in favour of risk-reducing surgery.

**Technological developments**

Technology and surgery have developed hand in hand. Developments in engineering allowed the production of precise instruments that enabled the pioneering operations of successful gastrectomy and safe thyroidecomy by Theodor Billroth and Theodor Kocher in the late 19th century. Developments in electronics led to the introduction of the diathermy machine, which has contributed to minimisation of blood loss and precise instrumentation, leading to much safer anaesthesia, and developments in imaging have allowed precise pre-operative planning.

The last two decades have seen an explosion of technological developments in minimally invasive surgical technology. From the first laparoscopic cholecystectomy in the late 1980s, a vast range of procedures can now be performed using minimally invasive techniques. Minimally invasive surgery in oncology was initially restricted to staging procedures such as staging laparoscopy in gastric and pancreatic surgery, which allowed incurable cases to be confirmed without the morbidity of open laparotomy. There was concern that minimally invasive procedures may result in port-site recurrences, or less effective oncological surgery, moving the balance of risks and benefits in favour of risk-reducing surgery.

The most recent surgical development is that of robotic surgery. This technology has included a ‘wrist’ that increases dexterity in a confined space, magnification, and removal of tremor to potentially improve surgical accuracy. Many reports show that a variety of procedures are feasible using robotics, and these have been enthusiastically publicised leading to rapid dissemination of the technology. Reports to date have not shown clinical benefits to robotic surgery, and trials demonstrating superiority of this expensive technology are awaited.

**Future developments**

Predicting future developments is always hazardous. What is certain however, is that developments in our understanding of cancer and its various natural histories, development of new and targeted therapeutics and technical developments in surgical instrumentation will continue to modify the role of surgery in cancer care. It is likely that surgery will play a lesser role in many cancers, but also a greater role in others, where improved systemic therapies render a previously incurable situation potentially curable.

Whatever these developments, it is certain that optimal cancer outcomes will be achieved with appropriate teams of practitioners dedicated to the care of the cancer patient and that surgery will continue to play an important role in this.

COSA plays a unique role in bringing all the professionals involved in cancer care together under the one organisation. It has a unique opportunity to continue to promote multidisciplinary care and educate the future generations of cancer practitioners in this manner of cancer care.

“We are what we repeatedly do. Excellence is not an act, it is a habit.” – Aristotle

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CANCER RISK ASSESSMENT AND SCREENING: THE NEED TO TAKE NOTICE

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Abstract

Although efforts to encourage presentation with early signs of cancer has had some impact in down-staging disease at diagnosis, notably in breast cancer and melanoma, assertive, physician-initiated screening for cancer in asymptomatic patients has demonstrably resulted in earlier diagnosis, as well as reduced mortality in some cancers. Although systematic population-wide screening programs optimise the population benefit of cancer screening, there is a long lag time to adoption of public screening programs, during which physician vigilance fills the void. Furthermore, some cancers will never achieve the prevalence threshold for mass screening, and in some common cancers clinical context and physician judgement are essential in screening selection. The potential for early diagnosis through screening is broader than the scope of organised mass public cancer screening. Organised professional groups such as the Clinical Oncological Society of Australia need to develop the evidence base for screening in a range of cancers, and develop guidelines to optimise physician-initiated screening and early detection. Doctors at all levels need to apply risk assessment tools in practice, and be alert to opportunities where screening can benefit their patients.

As early stage cancer generally has a better prognosis, efforts to down-stage disease are important. Although screening programs for bowel, breast and cervical cancer delivered on a mass scale are established, the prospects for detecting most cancers at a pre-invasive or early stage rest with the awareness and actions by clinicians and the community. Mass screening programs may eventuate from these efforts, but the prevalence of many cancers will remain below a threshold for mass screening. Education of the warning signs and symptoms of cancer has been long established and include important efforts in encouraging detection at an early symptomatic stage of cancer. These include specific education in breast cancer and skin cancer detection, as well as the ‘Seven Warning Signs of Cancer’ developed by the American Cancer Society.

From early detection to screening

The Clinical Oncological Society of Australia’s (COSA’s) early years coincided with pioneering efforts to screen for cancer. It was a decade that laid the foundation for more systematic approaches to screening, exemplified by the development, diffusion and evaluation of breast cancer screening in the 1970s and 80s.3

While evidence for the effectiveness of breast cancer screening is solid, the evidence available on cervical cancer screening at the outset of systematic population screening was comparatively weak. Time trends in the relative incidence of carcinoma-in-situ (rising) and invasive cancer (falling) were favourable to the case,4 but it was not until 1978 that research demonstrated at the individual level the protective efficacy of a recent PAP smear.5
In the 1970s, the PAP smear was the poster child for cancer screening, but the program was beset by quality problems, and benefits were unequally distributed. Despite this, the incidence of cervical cancer in women by this time had dropped by over 40% in a few states of the US. Incidence rates continued to rise in the UK, until the advent of systematic screening, even though 40% of potential cervical cancers in women were being prevented by opportunistic screening in general and obstetric practice. Examples of more systematically successful screening rested on commitment and team work between hospital specialists, general practitioners and local authority doctors.

In contrast to cervical screening, by the 70s there was good evidence to support rectal cancer screening – another cancer with a well-defined precursor lesion. Twenty-five year observational cohort data on 92,650 patient years of periodic screening with rigid sigmoidoscopy and polyp removal demonstrated a reduction of 85% in the expected number of rectal cancers, and all cancers detected were localised.

The limitation of the instrument, and the arrival of alternative technologies led to the search for more comprehensive solutions to population-wide colorectal cancer screening. However, given that rigid sigmoidoscopy was a tool within the reach of most primary physicians, at least in the US, and 55% of all cancers of the colon lay within the reach of the instrument, it is hard to avoid the conclusion that considerable benefit to those screened may have flowed from the normalisation of screening for rectal cancer among clinicians. Thirty years later we still await the complete roll-out of a bowel cancer screening program in Australia.

On a more positive note, the development in 1971, and subsequent evaluation of the Danish familial adenomatous polyposis registers, demonstrated the remarkable impact on colorectal cancer mortality from complete documentation, registration and follow-up screening of a very high risk population. This clinician-driven measure demonstrated that, when high risk populations can be identified in clinical practice, their health expectancy is transformed by effective commitment and team work between hospital specialists, general practitioners and local authority doctors.

Another lesson from the early years of screening was the failure of trials for early detection of lung cancer. Clinical enthusiasm for screening with chest X-ray and sputum cytology was dissipated by a European trial which showed no reduced mortality benefit from screening, despite an increase in incidence and survival after diagnosis.

Clinical practice and screening today

Mass screening programs judge their effectiveness by the outcome achieved in populations, such as downstaging, mortality reduction, and interval cancer rates, whereas clinicians focus on individual patient benefit. In mass screening, clinicians are central to screening in cervical cancer, but insufficient emphasis is placed on the impact of their endorsement and promotion of screening for breast and bowel cancers.

Physicians can also realise the possibility of benefit and reducing the risks associated with screening for other cancers.

Screening for melanoma

Organised screening from community clinics increases participation in whole body skin examination. However, Australia remains reliant in melanoma screening on the combined effects of public education and general clinician vigilance, much like the Pap test in the 70s. Only level three evidence exists in support of systematic screening, and the failure to mount support for the Queensland melanoma screening trial suggests that the question of the effectiveness of mass screening in melanoma will remain unanswered.

It is unclear how much Australian success in early detection – either for average risk, or selected higher risk groups – reflects practice level systems for screening, or a high level of community awareness coupled with ready access to general practitioners and skin clinics. The predictable inequity in diagnostic outcome that results from this approach needs to be the focus of greater clinical and educational effort, but organised mass screening programs are best placed to erase these differences.

Screening for prostate cancer

After protracted controversy, consensus may settle on the view that a mortality benefit emerges seven years after prostate-specific antigen screening and increases thereafter. Screening has driven a very large increase in the incidence of prostate cancer, but many men express dissatisfaction with outcomes because of long-term side-effects. The potential to benefit from screening depends not only on age and other comorbidities, but also on individual preferences and acceptance of trade-offs. A customised approach to selection for screening is needed to enhance the likelihood of net benefit among those screened. This can only be accomplished if clinicians are at the centre of any organised screening effort and common protocols are employed.

Lung cancer screening

The National Lung Cancer Screening Trial has confirmed the effectiveness of spiral CT screening in lowering both lung cancer specific mortality (by 20.3%) and all-cause mortality (by 6.7%) in smokers and ex-smokers. However cost-effectiveness is poor, and worsens if the behavioural impact is to discourage quitting. There is also limited capacity in Australia to screen and handle large increases in cases, and false positives. Any debate over screening for lung cancer will be further spiced up by the record of tobacco industry support. However, in the US at least, 22% of primary physicians use spiral CT to screen for lung cancer, and one may sympathise with a physician who initiates screening...
for, say, ex-smokers in their care. While this benefits those patients, it also raises the issue of equity, which can only be solved by an organised program where clinicians are key to risk profiling and assessment.

Less common cancers

Risk profiling and screening for some less common cancers offer potential for benefit from an organised, clinically driven approach, as exemplified by the pioneering work in familial bowel cancer. Early detection in both hepatocellular cancer (HCC) and oesophageal adenocarcinoma (EAC) are discussed, as they have been the focus of research and/or program development in association with Cancer Council.

Hepatocellular Carcinoma (HCC)

Since 1982, the incidence of liver cancer in Australia has risen strikingly, particularly in NSW through the weight of migration from HBV endemic regions of East and Southeast Asia and the Pacific. The incidence of HCC among these immigrants is around 10 times that of Australian born.37

The risk of developing HCC in the REVEAL study,38 of 3613 participants with chronic hepatitis B over an average of 11.3 years, was closely related to the level of HBV-DNA. The risk of HCC rose in a monotonic gradient to 17.7 in those with HBV-DNA copies over a million per ml. with no other markers of liver disease. Effective antiviral treatment for CHB reduces viral load to low levels, and meta-analysis of six treatment studies (of which two were randomised control trials) demonstrated a 70% reduction in long-term liver complications including HCC.29

Robotin et al. have demonstrated that a systematic program to screen people for chronic hepatitis B in general practice, initiating treatment and cancer screening in accordance with guidelines, would be a cost-effective approach to reducing the incidence of and mortality from HCC and associated liver disease.30 A primary care program targeted at-at-risk demographic groups is being tried in South West Sydney,31 and similar efforts are under way in Melbourne.

Effective control of liver cancer should be a priority in multicultural Australia. The current epidemic of chronic hepatitis B acquired overseas cannot be addressed by Australia’s domestic immunisation program, and unless effective measures in screening and treatment are introduced, annual deaths from liver cancer may rival those from breast cancer in NSW. For benefit to be realised, clinicians will need to dispense with the out-dated concept of the healthy HBV carrier, and be mobilised to reach the population at risk.

Oesophageal Adenocarcinoma (EAC)

The incidence of EAC has increased substantially, and continues to rise at a rate of 2.2% per annum (among men).32 EAC is thought to develop through precursor states of intestinal metaplasia in response to oesophageal reflux, with dysplasia developing on the background of Barrett epithelium at a rate of about 1% per year. EAC often presents at an advanced stage with a poor survival rate, so there is a strong prima-facie case to detect and treat precursor lesions or diagnose EAC at a localised stage. However, to date, in only a small proportion of EAC cases has Barrett’s been diagnosed prior.33

Risk factors for EAC are readily identifiable clinically. The Australian Oesophageal Cancer Study identified reflux, elevated body mass index and smoking as independent risk factors.34 The most startling risk elevation resulted from synergy between reflux and obesity, elevating the relative odds of EAC up to 16.5. Ninety-two percent of the population risk of EAC could be attributed to these factors when combined with educational level, acid suppressant medication use and non-steroidal anti-inflammatory drug use.35 This model could conceivably be developed as a clinical tool to assist in identifying patients for further assessment.

Medical and surgical anti-reflux treatments are widely used, but they fail to prevent disease progression,36 and it is unclear how much awareness exists in general practice of the potential future consequences of reflux. Research is also needed to establish how patients should be selected for ongoing surveillance, as the yield from endoscopic surveillance in simple Barrett’s oesophagus is low.37

The economics of screening and surveillance strategy for EAC and its precursors are not yet compelling,38 and reliance on endoscopy limits its wider spread. However, the development of less invasive methods for mucosal sampling,39 better predictive tests and well-targeted case selection may overcome these limitations. The rising burden of illness from this disease provides a strong incentive to accelerate these developments.

Conclusion

Screening generates a remarkable level of controversy, in part because large-scale screening is expensive, and exposes people who don’t directly benefit from screening to unsolicited risk.40 While encouraging symptom awareness for early presentation has a long history, it is not clear that this results in any lower burden of investigation,41 and decades after their launch, community knowledge of the seven warning signs of cancer is low.42

The landscape for screening is expanding, with better understanding of risk factors and precursors for a variety of cancers. Organised medicine needs to be alive to this landscape by supporting and promoting research in risk assessment, early detection and screening. Furthermore, the role of clinicians is crucial in mediating the potential benefits from screening for prostate cancer and melanoma. Organised medicine needs to provide guidelines to motivate and assist doctors to optimise the benefits of screening and early detection for their patients, both within and beyond the three public mass cancer screening programs.

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References


BREAST CANCER

Abstract
Breast cancer and its treatment have changed enormously over the last four decades. Most newly diagnosed patients will not die of breast cancer, and the burdens of treatment are substantially less than formerly. Biological understanding of breast cancer has increased at an exponential rate, and has yielded many new therapeutic options. Clinical trials, to which Australian groups have made major contributions, provide the evidence base to utilise these discoveries to provide more effective, less onerous therapies.

Biology
Many of the changes in breast cancer management stem from understanding of its biology. Jensen’s discovery of the oestrogen receptor explained the previous empirical use of endocrine ablative surgery and additive natural hormones and led to the therapeutic application of tamoxifen, undoubtedly the single most important drug in breast cancer during the last 40 years. Over-expression and/or amplification of the HER2 (erb-B2) oncogene led to a major impact of trastuzumab in advanced disease, and adjuvant therapy. Classification of breast cancers into intrinsic subtypes, based on assays of gene expression and whole genome sequencing, have added to the depth of our understanding, if not always to the clarity of its therapeutic implications.

Early detection
When I commenced practice, breast cancer usually presented as a palpable mass, not infrequently involving adjacent structures such as the skin and chest wall, and in most cases having spread to the draining lymph nodes. Increased awareness and mammographic screening have contributed to a steadily decreasing stage at presentation. In screened populations, many patients present with disease which cannot be palpated, and a minority show nodal metastases. Randomised clinical trials have established that population-based mammographic screening reduces breast cancer mortality. Though debate continues about the optimal target age-group, mammographic screening is now widely adopted in Western countries.

Surgery
As a surgical houseman only a little over 40 years ago, I was taught the Urban super-radical mastectomy. Expertise in this procedure was judged by the completeness of removal of all soft tissue down to the rib cage, and by the transparency of the skin flaps. Not surprisingly, when (and if) such flaps healed, the transparency was all too apparent. Surgical research since that time has demonstrated the safety of breast conservation, and if mastectomy is performed, immediate oncoplastic reconstruction. Similarly, sentinel node biopsy has reduced the indications for axillary dissection, reducing the risk of lymphoedema without compromising efficacy.

Therapy
Local control of disease is enhanced by postoperative irradiation, and recent data shows that this is accompanied by a later reduction in breast cancer mortality. Refinements in radiotherapy technique have reduced late adverse effects due to radiation damage of adjacent vital structures, particularly the heart. Radiation is indicated after breast conservation, while indications for radiation after mastectomy appear to be increasing. Intraoperative radiotherapy delivered using ortho-voltage or electron techniques limits radiation to normal tissues and appears promising.

More than half of all breast cancers contain oestrogen receptor, a marker of sensitivity to endocrine therapy. Oophorectomy, ovarian suppression and tamoxifen remain important tools in premenopausal patients, while more recently the aromatase inhibitors have provided incremental benefit over tamoxifen among postmenopausal patients. Ongoing research is examining the optimal timing and duration of these agents. Forty years ago, the cytotoxic armamentarium consisted of 5-fluorouracil, methotrexate, the alkylating agents and little else. Today,
a wide variety of drugs and combinations offer palliation in advanced disease.25 Studies have shown that such treatment should be continued in the absence of disease progression or unacceptable toxicity.26 Chemotherapy also improves survival in the adjuvant setting.27 No single drug or combination has established itself as superior to others. Meta-analyses suggest overall improvement with the inclusion of anthracyclines and taxanes,27 but the contribution of each of these classes may depend on the subtype of the tumour. The threshold indications for adjuvant cytotoxic therapy undergo recurrent review.26,29

Undoubtedly the most exciting area of developmental therapeutics in breast cancer centres on the evaluation of agents targeting specific molecular changes in the cancer cell. In addition to the archetypal targeted agent, tamoxifen,1 and more recently trastuzumab,30 agents targeting multiple intracellular metabolic aberrations are in various phases of clinical trial.

Clinical trials
Breast cancer was in the forefront of the evaluation of therapy by randomised clinical trials, perhaps the first being the Manchester radiotherapy trial commenced in the first half of last century.31 Successive trials have established the safety and efficacy of lesser surgery,10,32 adjuvant endocrine therapy,33 adjuvant cytotoxic therapy,34,35 and in appropriate patients trastuzumab.2,3 The Early Breast Cancer Trialists Collaborative Group, led by Sir Richard Peto, has since 1994 brought together virtually all the randomised evidence from trials in early breast cancer, providing an invaluable evidence base for treatment selection.21,27,36 Today’s patients owe an enormous debt to their sisters who participated in these clinical trials.

Quality of life
All treatments have adverse effects. In order to assess the net effect of the benefits and harms of treatment, patient self-evaluation of quality of life using scales feasible for use in the clinical trial setting,38 has been used to demonstrate the benefit of chemotherapy in metastatic disease both in terms of survival and quality of life.25 In the adjuvant setting, similar studies demonstrated that the adverse effects of chemotherapy were perceived as modest, transient and fully reversible.30

An important corollary of the high survival rate of breast cancer patients has been the emergence of organised, knowledgeable and vocal groups of breast cancer survivors. These groups contribute to better service delivery, and to the design and conduct of clinical trials.30 Australia can claim to be at the forefront of this movement, with bodies such as the Breast Cancer Network of Australia and the Consumer Advisory Panel of the Australian New Zealand Breast Cancer Trials Group. Importantly, patient advocates can argue to regulatory bodies to reduce bureaucratic impediments to research, to facilitate trial participation and to promote academic independence from the pharmaceutical industry,11 roles in which the professional researcher is often regarded with suspicion.

Conclusion
Both the disease and its management today are radically different from their equivalents of 40 years ago. Most patients now present with early, frequently impalpable disease, receive vastly less mutilating local treatments, increasingly effective systemic adjuvant therapy, and go on to join the increasing number of long-term breast cancer survivors.

References

**PROSTATE CANCER**

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**Abstract**

The field of prostate cancer treatment and research is finally growing up after many years as the orphan child in oncology. It is sobering to reflect that the first Therapeutic Goods Administration approval of a cytotoxic therapy for metastatic castrate-resistant prostate cancer, docetaxel, occurred less than 10 years ago. No further improvements in the treatment of this condition occurred until the last two to three years. Since then, several new treatments targeting various aspects of prostate cancer biology have shown clinical benefit, including improved survival, and are now entering clinical practice. All of these advances have been made on the basis of better understanding of the unique biology of prostate cancer and its interaction with host tissues and systems. For example, the pivotal role of ongoing signaling through the androgen receptor axis, even in the setting of apparent resistance to manipulation of this pathway, has led to rethinking of long-held dogmas and the development of effective new therapies. Significant advances have also been made in surgical and radiation techniques, and in imaging, that are expected to lead to improved outcomes.

Prostate cancer is the most common non-skin malignancy in western populations and is a frequent cause of cancer deaths in men. Most men diagnosed with prostate cancer have localised disease. Ablative treatments such as prostatectomy or radical radiotherapy lead to excellent cancer outcomes, although morbidity of treatment can sometimes be substantial. Relapsed or metastatic prostate cancer is usually treated with some form of androgen deprivation, most commonly medical castration using a gonadotropin releasing hormone agonist with or without an antiandrogen. This treatment is highly effective, but the condition is not curable and over a period of time that
can be highly variable, inevitably develops into metastatic castrate-resistant prostate cancer (mCRPC), the lethal form of the disease.

Docetaxel was the first cytotoxic drug to demonstrate survival benefit in mCRPC and was approved in Australia following two pivotal studies published in 2004. Few other options existed for men with mCRPC until 2010. Since that time, several new agents have demonstrated benefit for men with mCRPC, including improved survival and have subsequently been approved by the United States Food and Drug Administration and other jurisdictions around the world. Many of these agents have been developed specifically in the light of better understanding of the biology of mCRPC.

**New approaches**

**Androgen receptor (AR)**

Signalling through the AR remains critical for many cases of mCRPC, even when conventional methods of androgen deprivation or receptor blockade appear to have failed. Several new agents targeting AR and/or androgen production are now available or under development. Abiraterone acetate (Zytiga®; Janssen) inhibits production of androgens by the testes, adrenals and from within the tumour. Side-effects related to mineralocorticoid excess are mitigated by concomitant prednisone or prednisolone. A pivotal trial showed 36% improvement in the hazard ratio for overall survival and increase in median survival from 11.2 months (placebo plus prednisone) to 15.8 months (abiraterone plus prednisone). Secondary endpoints were also in favour of the experimental arm. A second trial in chemotherapy-naïve mCRPC patients also showed a trend to improvement in overall survival (HR 0.75; p=0.01), although this trial may have been unblinded prematurely. Abiraterone acetate is now approved for both indications in the US and in the post-docetaxel setting in Australia.

Another major advance also targeting the AR is the development of new generation AR antagonists such as enzalutamide (MDV3100, Xtandi®, Medivation/Astellas). Enzalutamide competes for ligand binding, impairs translocation of the AR into the cell nucleus, and inhibits binding of the AR to DNA and the recruitment of coactivators. Enzalutamide improves the hazard ratio for survival by 37% (HR 0.63, P<0.001) and improves median overall survival (18.4 months v 13.6 months), as well as secondary endpoints. A second trial in chemotherapy-naïve men with mCRPC has completed accrual and results are pending. Enzalutamide is generally well tolerated, with a further potential advantage being the lack of requirement for concomitant corticosteroids.

**Cytotoxic chemotherapy**

After docetaxel, this field had been an area of disappointment in prostate cancer until the results of the TROPIC trial comparing cabazitaxel (a semi-synthetic taxane developed for activity against docetaxel-resistant cell lines) to mitoxantrone in the post-docetaxel setting. This trial demonstrated superiority of cabazitaxel in terms of the primary endpoint of overall survival (HR 0.70, p<0.0001; median survival 15.1 months v 12.7 months), although toxicity was higher in the cabazitaxel arm. Cabazitaxel is now approved and reimbursed in Australia for mCRPC post-docetaxel.

**Bone-targeted therapy**

Zoledronic acid has been shown to improve skeletal-related event endpoints in clinical trials, although its use is not universal. Denosumab, a fully human monoclonal antibody specific for RANKL, has been shown to be non-inferior to zoledronic acid in men with bone metastases, and superior to placebo in non-metastatic mCRPC (improved time to first skeletal-related event from 25.2 months to 29.5 months [HR 0.85, p=0.028]). Osteonecrosis of the jaw occurred at similar rates with denosumab and zoledronic acid. An exciting innovation in the field of ‘bone-targeted’ therapy is radium-223 chloride ($^{223}$Ra; Alpharadin®, Bayer). The chemistry of radium is similar to calcium and radium-223 chloride is deposited in bone. Radium-223 is an emitter of alpha particles, providing high energy over a very short path length. It was therefore expected that this intravenously administered radioisotope might provide a useful palliative benefit, together with less marrow toxicity than conventional beta-emitters in current use such as strontium-89 or samarium-153. Radium-223 chloride was shown in a pivotal trial of men with mCRPC after docetaxel to be well tolerated, especially with respect to: marrow toxicity; effectively controlled pain from bone metastasis; and remarkably also improved overall survival compared to placebo (survival HR 0.695, 95% CI 0.552-0.875, p=0.00185; median survival 14.0 months for radium-223 compared to 11.2 months for placebo). The precise mode of action remains unclear, but is probably more than a direct anticancer effect; the short path length of alpha particles implies that effects on other cellular targets in bone such as osteoclasts and osteoblasts are involved.

**Immunotherapy**

Prostate cancer now holds the remarkable distinction of being the first solid malignancy for which adoptive cellular immunotherapy has shown an advantage. Sipuleucel-T (Provenge®, Dendreon) is an active cellular immunotherapy consisting of autologous peripheral blood mononuclear cells activated ex vivo, with a recombinant fusion protein comprising prostatic acid phosphatase and granulocyte-macrophage colony-stimulating factor. A placebo-controlled trial of men with mCRPC demonstrated improved overall survival (HR 0.78; 95% CI 0.61 - 0.98; P = 0.03) and median survival (21.7 months v 25.8 months) compared to placebo, leading to the registration of this therapy in the US. Progression-free survival did not differ between the two arms, however this does not detract from the primary survival endpoint benefit; the discrepancy relates to flawed systems for response evaluation in mCRPC, and the delayed effects of cellular immunotherapy. Other immunotherapeutic approaches are also under development in mCRPC.

**Therapy of localised disease**

New treatments are being tested or adopted in efforts to improve treatment of prostate cancer localised to the gland. These include: surgical techniques such as robotic prostatectomy; advances in delivery of radiation, including intensity-modulated and image-guided adaptive radiotherapy; and other ablative techniques such as cryoablation or high-intensity focused ultrasound. Some of these techniques have been adopted in the absence
of evidence showing their superiority to conventional techniques. It remains to be seen whether these new approaches live up to their promise.

Imaging

The choice of initial therapy for prostate cancer often relates to the confidence of the clinician as to whether the cancer is localised or not. Unrecognised locally advanced or metastatic disease that cannot be resected is currently incurable, and such men might not need to undergo prostatectomy, but perhaps should start other treatment options earlier. Current imaging techniques include CT, ultrasound and MRI, however novel approaches including PET are also being tested. These may allow better selection of men for local therapy and thus improve outcomes.

Supportive care

The adverse effects of androgen deprivation on bone and cardiovascular health, and the increased risk of metabolic syndrome, were long overlooked by medical oncologists, despite the fact that a large proportion of men with mCRPC will not die of prostate cancer. These men are now living longer, commencing treatment earlier, being treated for longer periods of time, and are receiving therapies that produce profound blockade of AR signalling in the tumour and systemically. The increased non-cancer morbidity and mortality that will inevitably ensue will need to be predicted and managed for each individual man.

Conclusions

All aspects of the management of prostate cancer, from diagnosis, initial therapy, therapy of advanced disease and supportive care, have undergone fundamental change, especially within the last 10 years. This has already translated into benefits for mCRPC, the lethal form of prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study. The Lancet Oncol. 2012;13(10):863-92.


Prevention

Strong evidence regarding the role of diet, weight control and exercise, in both primary and secondary prevention, has led to increasing community awareness regarding the nexus between healthy lifestyle and cancer. Agents such as aspirin and COX-2 inhibitors are being investigated for their cancer prevention activity, via action on anti-inflammatory pathways, following demonstration of reduced colorectal cancer (CRC) incidence in the large studies of their use for cardiovascular and stroke prevention.1

Screening

Although covered in a companion article, it would be remiss not to mention the solid evidence for faecal occult blood testing (FOBT) which has led in Australia to the government funded National Bowel Cancer Screening Program, which is still to be fully rolled out.2 Issues of funding for repeat testing at five yearly intervals, and of adequate and timely colonoscopy services to follow-up positive tests, remain on the agenda.

Diagnosis

Technological advances in imaging have seen significant improvements in CRC staging. With CT then MRI, staging of primary and detection of secondaries are now much more accurate. MRI staging is funded and standard of care for rectal cancers, although expertise in interpretation is required. PET scanning in combination with CT has also improved selection of patients with limited liver metastases who are suitable for curative hepatic resection.

Surgery

Many advances have occurred, with the routine implementation now of total mesorectal excision (TME) for rectal cancer and laparoscopic, rather than open procedures, where appropriate. Australian surgeons led a randomised trial demonstrating equivalence of laparoscopic with open resection for colon cancers (ALCCaS study),3 and are currently randomising patients in the AGITG Australasian Laparoscopic Cancer of the rectum Trial (A La CaRT).4 The rigorous assessment in clinical trials of surgical techniques is a tribute to the academic nature of Australian surgeons, and is reflected by the training and accreditation of members belonging to the Colorectal Surgical Society of Australia and New Zealand. Given the repeated demonstration of superior outcomes for patients with CRC managed by specialist surgeons,5 there is an awareness of the importance to patients of receiving care from specialised teams. Other major advances have included surgical stapling techniques to allow ultralow anastomoses, leaving very few patients with a permanent stoma.

Multidisciplinary teams

Perhaps the most important advance over the past 20 years has been the recognition of the multidisciplinary teams, usually including surgeons, medical and radiation oncologists, stomal therapists, nursing and allied health members and radiologists and pathologists among others. Multidisciplinary team meetings, where individual cases are reviewed and optimal management discussed, have facilitated equity for patients in accessing best practice. As a multidisciplinary organisation, COSA has provided the model on which these multidisciplinary teams are based and has laid the foundation for combined education, research, debate, discussion and open disclosure.

Chemotherapy

Advances have been made in adjuvant chemotherapy, with combination chemotherapy now standard for Stage III disease. Ease of administration of chemotherapy has been improved using central venous access devices (CVAD) that can be inserted under local anaesthetic (by interventional radiologists) and facilities for disconnection of infusers by community nursing teams. Trials demonstrating at least equivalence, if not superiority, of the fluoropyrimidine capcitabine, have opened options for patients, as this is an...
oral agent, thereby removing the need for a CVAD if given as a single agent. It is particularly useful for patients from rural and remote settings.

Disappointingly, recent trials (with large Australian participation) of adding the new targeted therapies which are beneficial in the treatment of advanced CRC, to adjuvant therapy have been negative. The AGITG has been a world leader in trials in CRC, both local investigator initiated academic trials and those developed in collaboration with other national trials groups. Current studies include the SCOT, study examining whether a shorter duration (three months) of adjuvant chemotherapy is non-inferior to the standard six months.6

Many chemotherapy options now exist for patients with metastatic CRC, with median survival of patients now more than two years, and 10-15% patients living more than four years, compared to less than six months 40 years ago. The addition of ‘targeted therapy’ to standard chemotherapy agents has incrementally improved survival: the antiangiogenic antibody bevacizumab and the EGFR-inhibiting antibodies, being two classes which have now entered routine practice, with others on the verge. However, the most exciting development is the paradigm shift towards ‘personalised medicine’, aiming to match specific treatments with the tumour and patient genotype. The landmark identification of the KRAS gene as being predictive of response to anti-EGFR agents was led by Christos Karapetis.7 Further translational studies are being undertaken to refine the subgroups that respond to medication to achieve the core of ‘individualised therapy’. It is gratifying to be involved with many COSA investigators in trials such as the current AGITG ICECREAM study, examining the role of cetuximab (EGFR-inhibitor) in patients whose tumour bears a KRAS G13 D mutation.8 AGITG studies have also included the MAX study and the CO20 studies, both establishing standard of care in CRC treatment, involving not only tumour assessment but quality of life and patient preferences.

Radiation therapy

MRI staging of rectal cancers has allowed identification of patients with locally advanced tumours (T4 and/or N1 and/or high risk T3) where trials have clearly shown improved outcome with preoperative chemoradiation. The landmark TROG study established equivalence of short course (five days) of preoperative RT compared to long course (six weeks chemoradiation) for most patients.9 New techniques such as IMRT and incorporating PET/CT imaging into planning have reduced treatment toxicity and are likely to improve outcomes.

Psychosocial care, survivorship and supportive and palliative care

These areas have been addressed in other articles in this edition, but are mentioned here to emphasise their importance as vital parts of the advances in management of patients with CRC.

Translational research

CRC has been at the forefront of the paradigm shift to personalised medicine. Collaboration between basic scientists and clinicians has facilitated better understanding of the pathogenesis and clinical behaviour of CRC at a genetic and cellular level. New therapies are targeting vulnerable pathways within the CRC cell, and biomarkers which predict for prognosis and most importantly, response to therapy, are increasingly aiding selection of patients for the most effective treatments. By correlating banked tissue and blood samples, clinical trials in CRC are the best vehicle for studying the complex behaviour of the cancer cell.

Rural and regional centres and the Asia-Pacific region

The emphasis on provision of care in rural and regional centres has allowed COSA input into government policies and decisions contributing to improved resources, including provision of radiation services, PET scanning etc, so that most patients with CRC can be treated within a reasonable distance of their homes, but still within a centre of sufficient volume and expertise. Supporting rural and regional clinicians to become involved in clinical trials has led to increased recruitment of patients from this demographic.

The improving economic conditions in the very populous countries in our region provide opportunities and challenges for leadership from COSA. Active engagement with China, Singapore and many other countries through COSA’s Developing Nations Program and the interest and engagement of leading clinicians, allows us to play a significant role in enhancing the lives of patients with CRC beyond Australia.

References

In 1973, the Australian lung cancer epidemic was at its peak, yet the only treatments available were surgery for the small proportion of patients with operable early stage cancers, and palliative radiotherapy for more advanced cases. An influential but nihilistic British trial had shown that active treatment was no better than best supportive care. The message was clear: only prevention through reduced tobacco consumption could reduce the number of deaths. As a result of this trial, progress in the treatment of non-small cell lung cancer (NSCLC), in particular, stalled and it would be another two decades before evidence became available that treatment could alter the natural history of inoperable NSCLC. Since 1973, the character of the disease has changed. Squamous cell cancer was replaced by adenocarcinoma as the most common form of NSCLC, and the proportion of small cell lung cancer (SCLC) fell to 15% of all lung cancers. Lung cancer mortality has fallen, partly a result of more effective treatment, but mostly the consequence of successful public health policy in which Australian campaigners have a proud and internationally acclaimed record. Strategies championed by the health lobby which have resulted in reduced tobacco consumption have included media advertising, using confronting images, and punitive taxation.

This review will however, now focus on practice changing treatment developments decade by decade; citations which were either Australian or had a significant Australian contribution are underlined.

**1970s: understanding and mapping the disease**

The importance of stage (disease extent) and performance status as critical prognostic factors came to be recognised in studies by the Veterans Administration Lung Cancer Group in the US. One of the most important developments in this decade was the introduction of computed tomography of the chest for disease staging and radiotherapy planning. The distinct nature of small cell lung cancer, with its more aggressive natural history and propensity for early distant metastasis, came to be appreciated, with a resulting shift away from surgical resection to systemic therapy. Initially, this consisted of single agent alkylating agents, and then combination chemotherapy. It was also at this time that a possible role for prophylactic cranial irradiation was suggested by Hansen, although it would be 15 years before an impact on survival could be demonstrated.

**1980s: the small cell cancer decade**

In the landmark RTOG 7301 trial, 60 Gy was established as the most effective radiotherapy dose for locally advanced NSCLC and it has remained the standard of care to now. But the 1980s really belonged to SCLC. Non-platinum containing regimens gave way to combinations containing cisplatin, and then carboplatin. It was also in this decade that the addition of thoracic radiotherapy to chemotherapy in patients with limited disease was shown to improve survival, later confirmed by meta-analysis.

**1990s: treatment for NSCLC works as well**

Although the activity of platinum based agents had been demonstrated in NSCLC during the 1980s, the effect on survival and quality of life remained contentious. Then, after two decades of negligible progress, the combination of cisplatin and radiotherapy administered either sequentially, or concomitantly, was shown to improve survival compared with radiotherapy alone in patients with inoperable NSCLC. For the most common scenario – metastatic disease – the landscape changed in 1995 when a practice-changing meta-analysis confirmed that cisplatin chemotherapy did indeed increase survival compared with best supportive care in advanced NSCLC, and so the modern era of NSCLC treatment began.

In surgery, lobectomy was shown to be superior to limited resection for stage I NSCLC, and the first references to the use of video-assisted thoracic surgery began to appear. In radiotherapy, shortening the overall treatment time with multiple treatments per day produced a survival benefit in both NSCLC and SCLC, subsequently confirmed in meta-analysis.

In imaging, the first reports of the impact of fluorodeoxyglucose (FDG) PET scanning – which would revolutionise the staging and management of NSCLC in the next decade – were published.

**2000 onwards: the desert blooms.**

Chemotherapy was by now an established standard...
of care for good performance status patients with metastatic NSCLC, and various platinum-based regimens containing two drugs seemed to be similarly effective.\(^27\) If chemotherapy prolonged survival in patients with advanced disease, might it not be even more effective in patients with subclinical metastatic disease, as was the case in patients with breast cancer? The IALT study of adjuvant platinum based chemotherapy in patients with completely resected early stage NSCLC was the first to confirm that adjuvant chemotherapy did improve survival.\(^28\) This was confirmed by a subsequent meta analysis.\(^29\) In patients with unresectable locally advanced NSCLC, concomitant chemotherapy and radiotherapy were shown to be superior to sequential treatment.\(^30\)

Recognition that there are lung cancers arising in non-smokers which are associated with specific mutations - some of which occur with greater frequency in particular ethnic populations – dramatically changed the perception that lung cancer was only a disease of smokers. The demonstration that tyrosine kinase inhibitors could prolong progression free survival in patients with EGFR mutations,\(^31\) and that crizotinib was active against tumours with ALK gene rearrangements,\(^32\) opened up a new range of treatment options, and the era of personalised targeted therapies was demonstrated, the research effort has accelerated with that lung cancer was only a disease of smokers. The demonstration that tyrosine kinase inhibitors could prolong progression free survival in patients with EGFR mutations,\(^31\) and that crizotinib was active against tumours with ALK gene rearrangements,\(^32\) opened up a new range of treatment options, and the era of personalised targeted therapies was undergoing refinement. The TNM staging system was sanguineous and that crizotinib was active against tumours with ALK gene rearrangements,\(^32\) opened up a new range of treatment options, and the era of personalised targeted therapies was undergoing refinement. The TNM staging system was revised in 2009, based on over 100,000 cases, the result of a huge international collaboration.\(^33\) Finally, the ability to detect early stage lung cancer by CT screening and so reduce mortality was confirmed by a large randomised trial.\(^34\)

**Conclusion**

In 2013, survival for lung cancer remains among the worst for any cancer, but as the last four decades have demonstrated, the research effort has accelerated with demonstrable improvements in outcomes. While progress in SCLC treatment has slowed, there is no sign of that in NSCLC, and the challenge now is to identify the most promising of the many strategies available for further research.

**References**

During the past four decades, significant progress has been made in identifying the molecular pathogenesis of lymphomas as a clonal expansion of B cells, in the majority, and of T cells. Similarly, our understanding of leukaemia has increased dramatically with the identification of the genetic abnormalities fundamental to the disease process. Such knowledge has led to major breakthroughs in the classification and treatment of these diseases.

Chemotherapy in the beginning

While Paul Ehrlich first coined the phrase ‘chemotherapy’, modern systemic therapy was ushered in by the serendipitous observation that accidental exposure to mustard gas caused bone marrow failure. The resulting application of alkylating agents and combination chemotherapy to leukaemia and lymphoma in clinical trials had early success, leading to the promise of cures in these diseases and decades of progress in cancer.

In reality, there has been good progress in lymphoma and childhood leukaemia, but many other cancers have quickly surpassed gains in acute myeloid leukaemia (AML) in the modern era. In Australia, five year survival from AML was around 10% in the late 1980s, and remains only 24% currently, although some sub-sets do better. In contrast, Hodgkin’s disease has a five year survival of 88%, non-Hodgkin’s lymphoma (NHL) 71% and all cancer 66%.

Standard induction therapy for AML remains based on anthrapyline and cytarabine, with seminal trials of high dose cytarabine induction conducted in Australia. Major advances in AML have included understanding of the importance of genetic changes for classification and prognosis, use of all-trans-retinoic acid in acute promyelocytic leukaemia, and haematopoietic stem cell transplantation. Targets for future advances could include mutations in FLT3, RAS and other genetic mutations affecting cellular pathways that confer a proliferative or survival advantage for leukaemia cells. Another set of mutations associated with improved differentiation and self renewal could be subject to all-trans-retinoic or histone deacetylase or other inhibitors. Haematopoietic stem cell transplantation offers the possibility of cure to individuals, especially in first complete remission. Use of risk stratification based on initial genetic profile and subsequent post-induction bone marrow examinations has been an important area of progress in haematopoietic stem cell transplantation for AML.

transplantation. It is expected that future whole genomic analysis should take this field forward more quickly, with a more sophisticated approach to risk and therapy than the three levels of risk often used, and with the identification additional druggable targets for treatment.

**Targeted therapy**

Chronic myeloid leukemia (CML) is a haemopoietic stem cell disease. Historically, CML patients progressed to blast crisis and death at a rate of around 5–10% per year in the first two years, increasing to 20-25% per year in subsequent years. The majority of genetic changes in progression occur in the transition from chronic phase CML to accelerated phase. CML is one of the first and best examples of the promise of personalised or precision therapy in oncology. The discovery of the Philadelphia chromosome or translocation t(9:22) in 1960, led to an understanding of the central role of the chimeric gene BCR-ABL in the pathogenesis of CML in the 1980s. The function of BCR-ABL is dependent on its tyrosine kinase activity, making it an ideal target for tyrosine kinase inhibitors (TKI). The TKI imatinib is a selective inhibitor of the BCR-ABL tyrosine kinase above and was a major breakthrough in CML, increasing overall survival to around 89%, with only 7% progressing to blast crisis after five years. New TKIs, dasatinib and nilotinib, have been developed for imatinib resistance or intolerance and dose escalation of imatinib developed for resistance. Newer TKIs include bosutinib and ponatinib for specific BCL-ABL mutations of T315I. This approach has shown the promise of TKIs for use in other malignancies. Despite these successes, allogenic haemopoietic cell transplantation remains the only therapy to durably eradicate this disease, offered after assessment of response to TKI therapy. Future advances may occur by targeting processes downstream from BCL-ABL, including P13-kinase, RAF and MEK. An important ongoing area of work is the best approach to minimal residual disease in CML.

The rapid early progress in lymphoma with combination chemotherapy above was not matched by progress in the 1980s and early 1990s. However, the importance of new classifications, better prognostic tests and a better defined, more limited role for radiation were important improvements. Recent advances in NHL include an understanding that chromosomal translocations are important characteristics of NHL. The presence of proto-oncogenes in proximity to chromosomal translocation sites have changed the expression of the proto-oncogene. Examples include the translocation involving BCL6 in diffuse large B cell NHL and less commonly t(11:18) in mucosa associated lymphoid tissue (MALT) NHL, providing possible new targets for therapy.

**Use of monoclonal antibodies**

The development of therapeutic monoclonal antibodies was pioneered in lymphoma with rituximab directed against CD20, the first such antibody approved by the Food and Drug Administration in the US in 1997. Such antibodies are therapeutic through a range of mechanisms, including cell-mediated cytotoxicity, complement-dependant cytoxicity and immunomodulation. The impact of rituximab in addition to chemotherapy was shown in a number of clinical trials across a range of lymphomas. This novel approach has been followed by other therapeutic anti-bodies in oncology practice, including trastuzumab targeting HER2 in breast cancer (1998), alemtuzumab targeting CD52 in chronic lymphocytic leukaemia (2001), cetuximab targeting EGFR in head and neck cancer (2001) and bevacizumab targeting VEGF in colorectal cancer (2004). Recent developments have also included the approval of immuno-conjugates such as gentuzumab targeting CD33 in AML (2000), and ibritumomab targeting CD20 in NHL (2002). Newer approaches include single agent bendamustine plus rituximab in indolent lymphomas.

**Conclusion**

Major advances in haematological malignancies have occurred following the early adoption of research innovation now relevant more generally in oncology. Intractable obstacles remain, with the opportunity for more rapid progress based on insights from genomics.

**References**

Abstract

Forty years ago the causes, incidence and natural history of melanoma were still poorly understood. Little was known about prognostic factors, and radical surgery was routine for all melanomas. However, dedicated melanoma treatment centres had been established in Sydney and Brisbane and Australians were at the forefront of early epidemiological research into melanoma. Today, the natural history of melanoma is much better understood, and a detailed staging system has been developed. Great prognostic accuracy can now be achieved, based on the histological features of the primary melanoma (particularly Breslow thickness, ulcerative state and mitotic rate), and knowledge of whether or not there is metastatic disease in a ‘sentinel’ lymph node. The extent of surgery is now based on the staging, with 1cm excision margins for ‘thin’ invasive melanomas (≤1mm), and 1-2cm margins for thicker tumours. Sentinel node biopsy is routinely offered for melanomas ≥1mm in thickness, and for thinner melanomas with adverse prognostic features.

In recent times, huge advances have been made in the medical management of systemic melanoma metastases, with the introduction of signal pathway inhibitors (BRAF and MEK inhibitors) and effective immunological agents (anti-CTLA4 and anti-PD1 antibodies). In parallel, the roles of surgery and radiation therapy in the treatment of metastatic melanoma have become much better defined. As a result, the importance of multidisciplinary care for all patients with metastatic melanoma has become apparent.

Staging and prognosis

It is now clear that the outlook for a patient who presents with a primary cutaneous melanoma can be predicted with considerable accuracy on the basis of the pathology of the primary tumour, and the knowledge of whether metastatic spread to regional lymph nodes has occurred. The principal determinant of outcome is the Breslow thickness of the melanoma, but other factors such as ulceration and mitotic rate are also of great importance.4 Tumours ≤1mm in Breslow thickness are classified as ‘thin’, are associated with an excellent prognosis. Tumours 1-4mm in Breslow thickness are classified as ‘intermediate thickness’, have a 15-25% risk of metastatic spread to regional lymph nodes, and in most melanoma treatment centres worldwide are now treated not only by wide excision with 1-2cm clearance margins, but also with sentinel node biopsy.5 The latter is a very accurate staging procedure introduced in the early 1990s, involving lymphatic mapping to identify ‘sentinel’ lymph nodes receiving direct lymphatic drainage from a primary melanoma, which are then removed and sent for detailed histological assessment.6 Primary melanomas >4mm in Breslow thickness are classified as ‘thick’, and have a much more serious prognosis, with five year survival rates of the order of 50%. This is because the risk of systemic metastasis is much higher, and until recently there were no satisfactory systemic treatment options available once spread to internal organs had occurred. These patients are nevertheless treated by wide excision, usually with 2cm minimum clearance margins, and sentinel node biopsy, which is still of important prognostic value even in patients with thick melanomas, and permits much better regional node field control, if immediate complete lymph node dissection is performed in those found to be sentinel node positive.
The other breakthrough in melanoma treatment has been the development of systemic treatments that have dramatically changed the treatment landscape for patients with melanoma. While the major changes in surgical melanoma management occurred 20 years ago, with very wide excision of primary tumours and highly morbid elective regional lymph node dissections being abandoned, it has only been in the last few years that significant changes have occurred in the systemic treatment of metastatic melanoma. Several decades of clinical trials with chemotherapy, immune therapy (interferon), vaccines, and combinations of these did not achieve effective systemic treatment options for most patients with melanoma. Dacarbazine was generally considered to be the best systemic therapy for patients with metastatic melanoma, despite low response rates and no proven overall survival advantage over placebo. Similarly, interferon became the chosen adjuvant (post-operative) therapy for high-risk early melanoma, based upon a relapse-free survival advantage, despite no overall survival advantage over placebo. Many argued that supportive care was the best treatment for all patients with Stage IV disease when surgical resection of metastases was not possible. Over the last decade however, improvements in the understanding of molecular biology and immune regulation have led to the development of systemic treatments that have dramatically changed the treatment landscape for patients with melanoma.

Signal pathway inhibitors

Ten years ago, a driver oncogene (BRAF) was discovered that regulates a critical growth and survival signalling pathway in melanoma cells. Mutations in BRAF result in uncontrolled pathway activation and cell growth, and are found in approximately 50% of melanomas. Drugs designed to inhibit the mutant BRAF kinase (BRAF inhibitors) include vemurafenib and dabrafenib. Patients with BRAF mutant metastatic melanoma have high response rates (approximately 50%), a rapid onset of action, achieve dramatic improvements in symptoms, and have a significant survival benefit compared to patients treated with chemotherapy. They have therefore become the new standard of care. Median duration of benefit is only six months however, and toxicities, although mild and rarely requiring permanent drug cessation, include low grade cutaneous squamous cell carcinomas. Trametinib, an inhibitor of MEK kinase situated downstream of BRAF, also has activity in BRAF mutant metastatic melanoma patients, but is less effective than the BRAF inhibitors. Regimens that combine BRAF and MEK inhibitors are currently being assessed, with the aim of improving benefit while reducing toxicity. The first combination in trials, dabrafenib and trametinib, has early data suggesting a higher response rate (75%), prolonged duration of benefit (9-10 months) and a much improved toxicity profile than either drug given alone. Phase 3 trials are in progress, as are trials of several other combinations of pathway inhibitors, and adjuvant studies in patients with high-risk early melanoma have commenced.

New immunological therapies

The other breakthrough in melanoma treatment has been in the area of immune therapy. Drugs designed to prevent the inhibition of activated T cells in order to promote sustained anti-tumour immunity appear superior to older immunotherapies such as interferon. Two classes currently exist, anti-CTLA4 and Anti-PD-1 antibodies. Ipilimumab, an anti-CTLA4 antibody, is the first immune therapy to improve overall survival in phase 3 randomised control trials in patients with metastatic melanoma. While the majority of patients do not benefit from treatment, and the onset of action is slow, ipilimumab has a sustained effect on tumour control in a subgroup of patients, resulting in a 10% increase in patient survival each year. It has however, become another standard therapeutic option, particularly in patients without mutated BRAF. Dermatologic, gastrointestinal and endocrine immune-related toxicities are common with ipilimumab, and can be severe if not managed appropriately. An adjuvant trial has completed recruitment and results are eagerly anticipated. Several anti-PD-1 antibodies are in early clinical development, with phase 1 data suggesting response rates higher than with ipilimumab (approximately 50%), and also with less frequent and less severe toxicity. Trials using combinations of ipilimumab and anti-PD-1 antibodies, as well as combinations of immunotherapies with kinase inhibitors, are in progress.

Prospects for the next 40 years

Despite the advances in treatment for melanoma in the last 40 years, significant further improvements are clearly required. In 2013, the best treatment option for many patients with melanoma may be participation in a clinical trial. Modern melanoma management requires a multi-disciplinary approach, involving a team of clinicians who understand clinical, pathological and molecular factors. Australian clinicians and researchers continue to play an important role in improving the management of patients with melanoma through basic and applied research and the conduct of clinical trials.

References

Basic scientific and clinical translational progress in oncology has advanced at an exponential rate over the last 40 years. Much of this progress was germinated in the laboratory, where rigorous scientific dissection of the biological milieu that is neoplasia has been undertaken. During this time, we have seen parallel progress in information technology systems and mathematical modelling that facilitate experimentation without in vitro or in vivo tissue experimentation. However, our basic understanding of cancer stems largely from interrogation of this very process, in human tissue samples. In Australia, tumour and tissue banks spawned in the latter half of the last century are now beginning to bear the fruit of scientific and translational discovery, as the critical mass required to definitively crystallise the biological and genetic principles of malignant proliferation has been achieved. This will only continue to be the case if clinicians and scientists alike continue their commitment to development and maintenance of high volume and high quality tissue banks.

**Historical perspectives**

In 1952, Rudolf Klen pioneered one of the first modern day tissue banks at the University Hospital Hradec Královo, Czech Republic. The conceptual framework upon which modern day banks operate still rely on the early principles championed by Klen. He originally characterised tissue banks as institutions that specialise “in the harvesting, processing, preservation, storage and distribution of various kinds of tissue for clinical and experimental practice”. While originally a repository for cadaver tissue, this bank slowly evolved to encompass living donor tissue for a number of purposes. The success of this institution, in both biomedical research and clinically related activities, stimulated interest in replication of this experience the world over. Today, tissue banks in various different forms exist in almost every clinical and/or research setting and have contributed unquestionably to our understanding of pathology and cancer in particular. Locally, for example, the Cancer Research Network of Sydney University now formally recognises nine separate tissue banks encompassing a range of neuroendocrine, head and neck, upper gastrointestinal, hepatopancreatobiliary, gynaecological, breast, melanoma and paediatric malignancy. Similar tissue banks exist all over Australasia and have been responsible for innumerable published works of sufficient quality to attract ongoing support from the National Health and Medical Research Council.

The evolution of these banks has seen great change over the years. A ‘snatch and grab’, ‘good idea at the time’ mentality in the early years has given way to a highly structured and organised process of patient consent, tissue procurement, storage, preservation and access. The boom in our molecular understanding of disease has also forced us to think broadly regarding the ethical and moral responsibilities involved in storage of human tissue, issues that will continue to challenge all those involved in tissue banks and society at large forevermore.

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**Tissue Banking and Its Role in Clinical and Biological Advances in Oncology**

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Abstract

Basic scientific and clinical translational progress in oncology has progressed at an exponential rate over the last 40 years. Much of this progress was germinated in the laboratory, where rigorous scientific dissection of the biological milieu that is neoplasia has been undertaken. Our basic understanding of cancer stems largely from interrogation of this very process, in human tissue samples. In Australia, tumour and tissue banks spawned in the latter half of the last century are now beginning to bear the fruit of scientific and translational discovery, as the critical mass required to definitively crystallise the biological and genetic principles of malignant proliferation has been achieved. This will only continue to be the case if clinicians and scientists alike continue their commitment to development and maintenance of high volume and high quality tissue banks.
Translational relevance

Hansson, in his review of the quality of care and ethical issues involved in tissue banks and medical registries, cites the human papilloma virus vaccine as evidence of the translational impact of such resources.\(^4\) He argues that causality was only achieved in the laboratory setting, as a direct result of banked human tissue and prospectively collated clinical data that definitively proved the significance of human papilloma virus in cases of cervical cancer. Further experimentation ultimately led to the development of a vaccine that will unquestionably have a major impact on this disease for years to come.

There are innumerable examples that demonstrate the value of tissue banks. Within our own neuroendocrine tissue bank at the Kolling Institute of Medical Research, we have collected specimens with clinical data for close to 20 years. These samples have been fundamental in identifying biomarkers of diagnostic, prognostic and therapeutic significance, and have been the primary discovery tool for a number of molecular drivers in a multitude of endocrine malignancies.\(^5,6\) The tumour bank has also been an invaluable resource for stimulating international collaboration, especially within the realm of rare neuroendocrine malignancies that would otherwise suffer from a lack of cancer tissue critical mass. Cancer is an extremely heterogeneous disease,\(^7\) and tumour samples are an invaluable resource for demonstrating and documenting that heterogeneity in a real world setting. This fact alone sets tumour banks apart from cell lines and transgenic mouse models of disease as a key primary research tool.

The Clinical Oncological Society of Australia (COSA) has been fundamental to the development of tissue banks Australia wide. Particularly within the translational context of existing clinical trials conducted by the numerous Australia wide Cooperative Cancer Clinical Trial Groups (CCTGs), COSA has assisted in evolution of the Australasian Biospecimen Network (ABN-Oncology). This body serves as a unique local example of biobank cooperation and continues to attract National Health and Medical Research Council (NHMRC) funding. Under this arrangement, numerous biospecimen banks are linked, and among others, includes the Breast Cancer Biospecimen Resource, National Leukaemia and Lymphoma Tissue Bank, kConFab, Australian Prostate Cancer Collaboration BioResource, Australian Ovarian Cancer Study and Victorian Cancer Biobank. Previously, each of the CCTGs was responsible for collecting clinical samples for biospecimen processing under local policy, but this process was not consistent across banks. In 2008, a COSA initiated, national tissue banking workshop assisted in development of a standardised approach to sample collection, storage and access.\(^8\) This led to the development of consensus criteria relating to minimum clinicopathologic data elements, standardisation of consent/ethics, collection and storage of samples, as well as the distribution and sustainability of samples. The ABN-Oncology now serves as a consortium that seeks to centralise and link biospecimen resources in an effort to consolidate the strengths of each individual bank, thus providing “a conduit for researchers to gain access to ethically consented, high quality clinically-annotated biospecimens and data”\(^9\).

In an age of personalised medicine, tissue banks and the techniques that have developed through the investigation of cancer in associated laboratories are now becoming mainstream methods of diagnostics. In many ways, the bench and bedside are getting closer and closer together, not just physically with the development of translational cancer research hubs, but also metaphorically as scientific advances pave the way for future diagnostics and therapeutics.

The future

The ability to take full advantage of precious tissue bank resources into the future will require foresight. The informal ‘snatch and grab’ nature by which such banks originally evolved, is not appropriate for the 21st century climate where consent, confidentially and justification of research funding are at a premium.

As a means of maximising efficiency and protecting patient rights, tissue banks need a high degree of organisational structure and regulatory oversight. A recent review of the German experience highlights many of these themes and serves as a benchmark example of how tissue banks should be structured and managed with an emphasis on planning of service provision.\(^10\) While the audit cycle in the clinical setting is now a recognised means of quality assurance, uptake of this concept has been slow in tissue banks and repositories; not so in Germany however.

Based in Heidelberg, the National Centre of Tumour Diseases provided a total of 769 services over the six year audit period for 680 different research projects. Of these, 605 projects were successfully completed. The projects were composed of basic scientific research (73%), translational studies (22%) and epidemiological projects (3%). The centre facilitated the provision of formalin fixed, paraffin embedded tissue, fresh frozen tissue, tissue microarray based sections and immunohistochemical services. It was also able to track projects following provision of tissue and demonstrated that over 90% of projects were commenced following receipt of tissue by the primary investigator. Most projects were also pursued to completion with a high degree of investigator satisfaction (97%), reflecting the rigorous nature of tissue procurement, preservation and provision.

A prospective mindset is of the utmost importance in deriving clinically relevant information from tumour banks and clinical registries. Even within the realm of oncology, each malignant disease is a unique biological and clinical phenomenon that demands specific diagnostic and therapeutic strategies. The same could be said of tissue banks when it comes to handling related tissue and clinical data. As in the aforementioned German example, quality control should dictate the development of benchmark standards when it comes to tissue procurement and processing. More is needed however, and the Carmignani et al group eloquently describes a dedicated approach to banking prostate cancer samples.\(^11\) Beyond the collation of clinical data, this Italian group showed how it is possible to collate a complete biobank set of urine, blood, fresh cancer tissue and formalin fixed tissue. More specifically, they articulate how collection of high quality fresh cancer tissue requires an intimate knowledge of, and involvement in the biopsy procedure, with a standardised protocol for
procurement of biobank tissue being undertaken in parallel with a clinical diagnostic procedure. This approach was highly successful in obtaining a complete set of biobank tissue without compromising clinical priorities and suggests that minimum world standards should be developed for each cancer type to ensure uniformity, maximise productivity and to serve as a guide for those developing new tissue banks.

Focused procurement of tissue bank specimens according to predefined standards has also been employed in mesothelioma. This example typifies many of the central themes that are now being promoted in an attempt to deliver consistency between biobanks, and translationally relevant information upon which scientific discovery can be pursued. Mohanty and colleagues describe, using mesothelioma as an example, how the development of a set of "international standards organisation" can be used to simplify and standardise the minimum dataset for each malignant disease based on data that is normally collated during a patient’s episode of care. A generic dataset is collated for each disease under the global headings of demographic, epidemiologic, anatomical pathology, genotype and treatment/outcomes. Specific fields then differentiate each cancer type from one another.

Locally, COSA and the ABN-Oncology have driven such initiatives within the context of clinical trials. This is encouraging, but more can be done to further enhance co-operation between tissue banks with a view to standardising the processes governing tissue handling, storage and provision. This will only be achieved if a sustainable health economic model is implemented and if all aspects and opportunities of cancer tissue processing are considered.

With regard to maximising opportunities, the role of the pathologist should not be forgotten; particularly given their role as the ultimate custodian of preserved human tissue samples. By their very nature, pathologists and pathology departments are uniquely positioned to participate in tissue banking. Tissue may not always be banked following biopsy or resection, but clinical specimens will always be sent to the pathologist for assessment. Until recently, the importance of pathology departments within the process of biospecimen procurement, storage and provision had not always been recognised, but this is changing. It is now acknowledged that pathology departments can only be engaged through appropriate funding, resource provision and scientific recognition. As such, COSA has developed a close alliance with the Royal Australasian College of Pathologists (RCPA) to assist in this regard. As an example, COSA and the RCPA have previously collaborated to lobby government in pursuit of a Medicare item number for preparation of specimens for the purposes of research. It makes sense to harness not only the pathologist’s access to tissue, but also their knowledge and skills within the context of malignant disease. The value of pathology support to tissue banking cannot be overstated.

These initiatives highlight the underrated importance of clinician leadership in successful execution of such an endeavour, from patient consent, to tissue bank derived scientific discovery. All too often, in today’s busy clinical environment, tissue banking is an afterthought that is seen as an obstacle to completion of clinical duties, whereby tissue harvesting is frequently attended to by inexperienced or unaccustomed personnel. It is no surprise that disappointing laboratory results often accompany such an approach. In this day and age, it could be argued that a checkbox for tissue banking should be added to the widely adopted “Time Out surgical safety checklist that is carried out before every procedure. The 2008 COSA workshop on tissue banking for cancer clinical trials also raised the possibility of imposing an opt-out approach to tissue donation at the time of each cancer diagnosis.

**Biological informatics**

The boom in bioinformatic information now accompanying banked tissue specimens is also a concern and requires a specific effort to manage this data. Recent whole genome sequencing studies, based entirely upon tissue specimens, are a prime example of the sheer volume of data that must be handled. Coalescing the molecular and genetic data that are generated from these studies with clinical data to derive translational relevance is a difficult task and requires specific bioinformatic expertise. Several groups are now developing software solutions to meet these evolving challenges.

The whole genome sequencing experience has fast-tracked an issue that has plagued tissue banks since their inception. Linking tissue samples with clinical data has long been a difficult task and one that is now of great translational importance. The development of biomarkers in particular, mandates knowledge regarding patient demographics, diagnostics, the treatment employed and clinical outcome. Traditionally, tissue bank repositories acted as tissue storehouses and linking clinical data was a distinct task in its own right. However, there is now an increasing recognition of the need to link clinical data, a task that significantly increases the organisational and ethical burden upon such organisations. It has also been recognised that hospital based medical records fail to capture the necessary data to best take advantage of potential translational project initiatives. This data is often collated retrospectively and is invariably incomplete. However, with the local advent of translational cancer research hubs throughout Australia, and more specifically, the instigation of specific projects geared toward linking various forms of tissue/cClinical data (eg.the CHeReL initiative), these issues are being managed proactively. The increasing uptake of electronic medical records also assists in this regard and is of particular interest in a country like Australia, where the largely dispersed nature of our population makes the study of rarer diseases particularly challenging. International collaboration is also greatly facilitated with such infrastructure in place.

Such an approach requires a high degree of organisational and cross-institutional co-operation. Success is also dependent on developing the necessary infrastructure, and recruiting personnel with an appropriate skill set to manage all aspects of the bank, from tissue handling, to ethics reviews, database management, clinician engagement and patient consent. Legal, ethical and data protection assurance practices should not be neglected. It should also be borne in mind that none of this is possible without adequate funding.
Conclusion - a call to arms

Our current understanding of tumour biology would not have been possible without the access to human tissue that tumour and tissue banks provide for medical research purposes. In the current age of true translational, bench to bedside scientific and clinical progress, tissue banks need to be promoted in a specific effort to ensure that funding is continued, regulatory oversight is maintained (but not obstructive), ethical principles are upheld and clinicians are engaged. These banks will increasingly take advantage of progress in information technology systems and molecular techniques. Above all else, those at the forefront of clinical care must realise the privileged nature of clinical contact with patients. They must continue promoting tissue bank submissions to ultimately assist in completion of the translational progress cycle, from the bedside, to the bench, and then back to the patient again, where it counts.

References


TARGETED THERAPIES, ASPECTS OF PHARMACEUTICAL AND ONCOLOGICAL MANAGEMENT

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Abstract

A revolution is underway in cancer therapy and care. Now, based on identifying in a patient’s cancer those genetic alterations that drive cancer growth, use of cancer therapy is more targeted and cancer care is more personalised. Many genetic alterations are ‘passenger mutations’ in the oncogenic process, but other ‘driver mutations’ promote cancer growth and survival. These harmful genetic alterations usually result in the production of abnormal proteins such as V600-mutant BRAF in melanoma, or in the overproduction of normal proteins such as HER2 in breast cancer. In drug development, the abnormal or excess proteins are described as ‘druggable targets’, and drugs developed to selectively inhibit the function of these proteins are called ‘targeted therapies’. Since a driver mutation can be found in more than one different type of cancer, an approved and available targeted therapy can make the mutation ‘clinically actionable’. Examples of targeted therapies include the small-molecule drug, vemurafenib (Zelboraf®), for advanced V600-mutant BRAF melanoma, and the monoclonal antibody, trastuzumab (Herceptin®), for HER2-positive breast cancer. Although targeted therapies are generally considered less toxic than conventional cytotoxic chemotherapy, the toxicities may be problematic and dose limiting. However, careful clinical management of these toxicities can allow patients to continue to receive effective therapy.
The established modalities of cancer therapy are surgery, radiotherapy and chemotherapy. Immunotherapy can now be included as the fourth pillar of standard cancer therapy.\textsuperscript{1,2} Chemotherapy includes cytotoxic drugs as well as targeted therapies like small-molecule drugs and biopharmaceutical products. Whereas surgery and radiotherapy are local forms of treatment, chemotherapy and immunotherapy are systemic forms of treatment that may be used alone or with local therapy. Cytotoxic chemotherapy used alone can treat locally advanced or metastatic cancer. Chemotherapy with radiotherapy can augment the effects of radiotherapy and add to the cure of patients with locally advanced, unresectable cancers. Used pre-operatively, chemotherapy can make unresectable lesions operable or, after surgery, chemotherapy can reduce the chances of distant recurrence of a cancer. Targeted therapies for non-haematological malignancies have been approved in first, second, or third-line indications (table 1) on the basis of progression free survival and/or overall survival benefits in which control groups of patients received placebo, best supportive care or standard treatment.\textsuperscript{3-5} Hence, we expect that targeted therapy will be as versatile as cytotoxic chemotherapy in the therapeutic armamentarium against cancer.\textsuperscript{6}

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**Table 1:** List of approved targeted therapies for non-haematological malignancies

Abbreviations: renal cell carcinoma (RCC); colorectal cancer (CRC); glioblastoma multiforme (GBM); squamous cell carcinoma (SCC); non-small cell lung cancer (NSCLC); gastrointestinal stromal tumour (GIST); epidermal growth factor receptor (EGFR); vascular endothelial growth factor receptor (VEGFR); platelet derived growth factor receptor (PDGFR); anaplastic lymphoma kinase (ALK); gonadotropin release hormone (GnRH); colony stimulating factor-1 receptor (CSF1R); mammalian target of rapamycin (mTOR).
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**Small molecule allosteric inhibitors**

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<td>advanced RCC; unresectable pancreatic neuro-endocrine tumours; subependymal giant cell astrocytoma, hormone receptor positive, HER2-negative postmenopausal breast cancer</td>
</tr>
<tr>
<td>Temsirolimus</td>
<td>mTOR</td>
<td>advanced RCC</td>
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</table>

**Small-molecule smoothened antagonists**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target</th>
<th>Indication</th>
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<tr>
<td>Vismodegib</td>
<td>smoothened receptor</td>
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<tr>
<td>Ziv-aflibercept</td>
<td>VEGF-A, VEGF-B, PGF</td>
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**Recombinant decoy receptor**

<table>
<thead>
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<th>Drug</th>
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<th>Indication</th>
</tr>
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<tbody>
<tr>
<td>Ziv-aflibercept</td>
<td>VEGF-A, VEGF-B, PGF</td>
<td>none</td>
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**Antibody drug conjugate**

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<tr>
<th>Drug</th>
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<th>Indication</th>
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<tbody>
<tr>
<td>Ado-trastuzumab emtansine</td>
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**Hormonal Agents**

<table>
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<th>Drug</th>
<th>Target</th>
<th>Indication</th>
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</thead>
<tbody>
<tr>
<td>Abiraterone</td>
<td>androgen synthesis - CYP17A1 inhibition</td>
<td>none</td>
</tr>
<tr>
<td>Anastrozole</td>
<td>aromatase</td>
<td>hormone dependent postmenopausal breast cancer</td>
</tr>
<tr>
<td>Bicalutamide</td>
<td>androgen receptor</td>
<td>metastatic prostate cancer</td>
</tr>
<tr>
<td>Degarelix</td>
<td>GnRH receptor</td>
<td>locally advanced or metastatic prostate cancer</td>
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</tbody>
</table>
How do we define targeted therapies?

We define ‘targeted therapy’ operationally because the term has become so broad in scope and widely used. Targeted therapy for cancer can be defined as rationally designed therapy, which usually has a biological rationale and a predefined mechanism of action. Conversely, conventional cytotoxic chemotherapy, has often been developed empirically, and the targets of drug action, such as molecules involved in DNA synthesis and replication, have been determined retrospectively.

The promise of personalised cancer medicine is to deliver the right drug to the right patient at the right time. However, describing therapy as ‘targeted’ does not necessarily: (i) predict which tumour type will be most responsive; (ii) decide which patient will benefit from its use; nor (iii) determine whether toxicity either depends on tumour response or is less than that associated with cytotoxic drugs.

The scope of targeted therapy is broad and aims to encompass the complex biology intrinsic to most cancers. This complex biology is best described by the hallmarks of cancer (table 2). A cancer behaves as a chaotic organ comprising malignant tissue and supporting non-malignant tissues and exerting local (autocrine and paracrine) and distant (endocrine) effects. These tissues are not organised with the tight interlocking architecture typical of a normal organ. Rather, a tissue such as the tumour blood vessel is poorly and intermittently functional because it is often irregular, tortuous and leaky. Additional pathological features of the cancer ‘organ’ include tissue hypoxia and necrosis. Cancers attract and build a stroma of normal (and later altered) host cells, which contribute to such systemic inflammatory manifestations as cancer cachexia and illness behaviour, and to adverse prognosis and impaired metabolism of anti-cancer drugs.

### Table 2: Hallmarks of cancer and therapeutic targets

<table>
<thead>
<tr>
<th>Hallmarks of cancer</th>
<th>Class of intervention</th>
<th>Exemplar drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>sustaining proliferative signalling</td>
<td>EGFR signalling inhibitors</td>
<td>cetuximab, erlotinib</td>
</tr>
<tr>
<td>evading growth suppressors</td>
<td>cyclin-dependent kinase inhibitors</td>
<td>dinaciclib</td>
</tr>
<tr>
<td>enabling replicative mortality</td>
<td>telomerase inhibitors</td>
<td>imetelstat</td>
</tr>
<tr>
<td>activating invasion and metastasis</td>
<td>hedgehog or MET signalling inhibitors</td>
<td>vismodegib</td>
</tr>
<tr>
<td>inducing angiogenesis</td>
<td>VEGF signalling inhibitors</td>
<td>bevacizumab, pazopanib</td>
</tr>
<tr>
<td>resisting cell death</td>
<td>pro-apoptotic BH3 only or SMAC mimetics and IAP inhibitors</td>
<td>ABT-737</td>
</tr>
</tbody>
</table>
Table 1 shows that targeting approaches are manifold: typical points of intervention include ligand-receptor interactions and catalytic and allosteric sites of enzymes. Classes of drugs include small molecule inhibitors, competitive antagonists, and monoclonal antibodies (mAb) (figure 1). Strikingly, the kinome (the set of protein kinases in the cancer genome) representing mainly tyrosine kinases is the principal source of therapeutic targets.15 Interestingly, these kinase targets are found in malignant cells and in stromal or supporting cell types.

**Finding the target**

In spite of its manifestly complex biology, cancer is widely accepted to be a disease of somatic genetics.16 The presence of frequent genetic mutations in cancer cells and not in normal cells represents one of cancer’s differentiating features.17,18 Some of these mutations contribute to the malignant phenotype of uncontrolled growth, invasion and metastasis via gain of function of growth-promoting oncogenes or loss of function tumour suppressor genes.

<table>
<thead>
<tr>
<th>genome instability and mutation</th>
<th>PARP1 or CHK1 inhibitors</th>
<th>veliparib</th>
</tr>
</thead>
<tbody>
<tr>
<td>tumour-promoting inflammation</td>
<td>NFκB inhibitors, PGF, and COX inhibitors</td>
<td>celecoxib, curcumin</td>
</tr>
<tr>
<td>avoiding immune destruction</td>
<td>immune checkpoint inhibitors</td>
<td>ipilimumab, nivolumab</td>
</tr>
<tr>
<td>reprogramming energy metabolism</td>
<td>multiple</td>
<td>metformin</td>
</tr>
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</table>

**Figure 1**: Pharmacological blockade of signalling pathways reveals redundant signalling networks, which enable tumour adaptation and acquired drug resistance

A. Binding of ligands (indicated as diamonds) such as the growth factors, epidermal growth factor (EGF) or vascular endothelial growth factor (VEGF), to the extracellular domain of cell-surface receptor tyrosine kinases (RTKs) activates the RTKs and initiates an intracellular signalling cascade. The signalling cascade is mediated by adaptor molecules, which are often also kinases. Cross-talk between signalling pathways at critical junctures or nodes (indicated as hexagons) creates a signalling network. The cross-talk may be feed-forward (positive) signalling (indicated as an arrow) or feed-back (negative) signalling (indicated as a stem). Signalling redundancy is illustrated since similar cellular outcomes of growth, differentiation and survival can occur irrespective of which signalling pathway is activated. B. Monoclonal antibodies (mAb) such as (a) bevacizumab neutralise the ligand, VEGF, or (b) cetuximab blocks the epidermal growth factor receptor (EGFR) shutting off the dependent signalling pathway. C. Tyrosine kinase inhibitors (TKIs) such as (c) gefitinib inhibit the intracellular kinase domain of a RTK such as EGFR (point of intervention is asterisked), and may shut-down signalling as extensively as a mAb. D. Allosteric inhibitors such as (d) the mTOR inhibitor, everolimus, may inhibit some signalling pathways while relieving feedback signalling of other pathways (point of intervention is asterisked) to produce, for example, compensatory AKT signalling that would require inhibition with a specific inhibitor.
These mutations have been characterised as ‘driver mutations’, which in many cancer genomes exist among a sea of so-called ‘passenger mutations’. Driver mutations are often the targets of new cancer therapeutics. Stringent international cancer genomic efforts are underway both to understand the diversity of cancer genomes and the means by which driver mutations can be identified and validated.15,18,19

Nevertheless, two examples clearly demonstrate the value of finding the target and show that tumour genotype can trump clinical phenotype. Cetuximab is administered to metastatic colorectal cancer patients irrespective of the level of tumour EGFR expression. In a randomised control trial of cetuximab and best supportive care versus best supportive care alone, the survival benefit accrued only to patients whose tumours did not contain an activating KRAS mutation.20 In another randomised controlled trial of gefitinib versus chemotherapy in East Asian non or light smokers with metastatic pulmonary adenocarcinoma, patients whose tumours were EGFR mutation-positive derived the greatest progression free survival benefit from gefitinib, whereas those patients without a tumour mutation fared very poorly if they received gefitinib, rather than chemotherapy.22

Finding exactly the right target has been a protracted and difficult exercise, despite the indubitably curative effect of trastuzumab and chemotherapy as adjuvant treatment in breast cancer. In the registration study of trastuzumab for treatment of metastatic breast cancer patients, patients were randomised after HER2 positivity was determined by immunohistochemistry. However, a retrospective analysis of breast cancer samples from this study showed that the only patients who obtained a survival benefit had tumours with 3+ HER2 expression by immunohistochemistry or HER2 gene-amplification by fluorescence in situ hybridisation. Subsequently, in a consensus statement, the stringency of HER2 testing guidelines was increased so that better target definition might more accurately determine which patients could benefit.22,23 Moreover, after retrospective analyses of breast cancer samples from adjuvant samples, uncertainty remains as to whether patients with discordant HER2 results by immunohistochemistry and fluorescence in situ hybridisation benefit from adjuvant trastuzumab therapy.23

Neo-angiogenesis or new blood vessel formation is a prerequisite of tumour progression. Tumour cell production of vascular endothelial growth factor (VEGF) was identified as one of the key pro-angiogenic factors. VEGF has been targeted either by neutralising immuno-interactive molecules such as bevacizumab and aflibercept, or signalling blockade downstream of VEGF receptor(s) using a host of small-molecule tyrosine kinase inhibitors (TKIs) (table 1). Although early clinical successes offered universal promise, clinical enthusiasm for anti-angiogenic therapy has been tempered by a series of negative randomised controlled data in certain tumour types. For example, the US Food and Drug Administration (FDA) recently revoked its approval for use of bevacizumab in metastatic breast cancer after concluding that it was not proven to be safe and effective for this indication, a view subsequently supported by a Cochrane review.24 Bevacizumab added to oxaliplatin-based chemotherapy did not offer a survival advantage as adjuvant treatment for colon cancer and may be detrimental.25

In advanced non-small cell lung cancer (NSCLC), single-agent activity of VEGFR TKIs has been modest.26 Drug resistance arising from tumour cell elaboration of other pro-angiogenic factors, such as fibroblast growth factor (FGF) and platelet-derived growth factor (PDGF), indicates that specific inhibition of these signalling pathways should be incorporated in future multi-agent clinical trial designs.27

Chasing clinically actionable targets

The clinical benefits of identifying an actionable target mutation are often evident. For example, the V600 BRAF mutation is the main driver of tumour growth in the ‘oncogene-addicted’ state of advanced melanoma (figure 2).28,29 V600 BRAF mutations occur in up to 50% of metastatic melanoma patients and the BRAF inhibitor, vemurafenib, significantly prolongs overall survival to 13.6 months compared with 9.7 months for chemotherapy.28,29 Conversely, oncogene-addicted states are not so apparent in some cancers. For example, among the substantial tumour heterogeneity of 99 early-stage pancreatic cancer samples, an analysis of 16 putative driver gene mutations, some known and some novel, suggested that many different kinds of drugs may ultimately be needed for disease control.30

Figure 2: How the state of oncogene addiction improves therapeutic index

A. Three normal signalling pathways are depicted in a viable normal cell. Ligand binding of the cell-surface receptor activates the intracellular signalling pathway and transmits the signal to the cell’s nucleus, where genetic programs governing cell growth, survival and differentiation are executed. Malignant conversion is facilitated as a genetic mutation results in constitutive (ligand-independent) activation of signalling pathway ‘a’, and in inactivation of the suppressive signalling pathway ‘c’. B. The addition of a selective kinase inhibitor (drug) blocks the activity of signalling pathway ‘a’, and in the absence of sufficient alternative pro-survival signalling, the tumour cell dies.
These clinical data emphasise the importance of prompt and correct identification of actionable tumour mutations, and are reinforced by recent phase 1 clinical trial data. Non-randomised patients whose tumours had actionable mutations, demonstrated significant improvements in tumour response rates, time-to-treatment failure (TTF) and survival if they received a matched targeted therapy (when available), compared to consecutive patients who were not given a matched targeted therapy. Indeed, in a multivariate analysis of patients with one molecular aberration, matched therapy was an independent factor predicting response and TTF.32

In 2012, the Australian Government agreed for the first time, through the Medical Benefits Schedule, to reimburse the cost of genetic tests for determining use of targeted cancer therapies. The approved items were KRAS mutation testing for use of cetuximab in KRAS wild type cases of colorectal cancer, EGFR mutation testing for use of gefitinib in cases of non-small cell lung cancer with activating mutations of EGFR, and in situ hybridisation of HER2 for cases of HER2 gene amplification in breast cancer. Other approvals are anticipated, including BRAF mutation testing for use of oral inhibitors in cases of unresectable stage 3 or 4 melanoma with V600 mutations of the BRAF gene. This progress strengthens the rationale for tumour genotyping at the time that a routine histopathological diagnosis is made, so-called ‘reflex’ testing. However, considerable technical, drug access and reimbursement challenges remain for the delivery of truly personalised cancer medicine.33

**Hitting the target**

Requirements of of successful targeted therapy include that the target be present in the cancer and that the target limits the ability to cure the cancer.34 Targeted therapy is ineffective unless the tumour contains the target. For example, in the absence of the activating V600 mutation of the BRAF gene, metastatic melanoma patients did not respond at all to vemurafenib and died soon after.35 Hypoxia must be cure limiting for hypoxia targeting drugs combined with radiotherapy to be effective in head and neck cancer. Thus, hypoxia should be present initially and during radiotherapy and if not, then as is suspected with better prognosis human papilloma virus-related head and neck cancer, hypoxia may not be cure limiting.34

Approved targeted therapies (table 1) interdict cellular signalling pathways at different points along the signalling cascade (figure 1). For example, the antigen-binding fragment of a therapeutic mAb may neutralise the ligand (e.g. bevacizumab and VEGF), engage the receptor preventing dimerization associated with signalling (e.g. trastuzumab and HER2), blockade the receptor (e.g. cetuximab and EGFR), or modulate the receptor from the cell surface (e.g. cetuximab and EGFR).35 The opposite or Fc end of a therapeutic mAb may engage elements of the host immune system to induce complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity and cellular immunity, although the contribution of these mechanisms to clinical anti-tumour effects remains uncertain.36 Similarly, small-molecule kinase or other inhibitors act at the receptor itself or at nodes in the signalling pathway where critical adaptor molecules are phosphorylated (figure 1).

Sometimes a drug does not hit the target hard enough. In spite of its specificity for the BRAF kinase, the multi-targeted kinase inhibitor, sorafenib, has low selectivity for V600-mutant BRAF.37 Sorafenib failed to exhibit significant anti-melanoma activity in patients with BRAF-mutant melanoma.38,39 In contrast, dose escalation of the highly selective BRAF inhibitor, vemurafenib, achieved sufficient signalling pathway shutdown to produce marked tumour regressions.29,35

**Target delineation, tumour sampling, and tumour escape**

It is almost inevitable that once a kinase inhibitor drug is applied, tumour adaptation via signalling redundancy will result in therapeutic failure (figure 1). In drug-resistant cells, autocrine, paracrine, or endocrine secretion of ligands for receptor tyrosine kinases, which transduce parallel signalling pathways, circumvents targeted kinase inhibition and enables tumour cell survival.40 Alternatively, other genetic aberrations may constitutively activate the redundant RTK/PI3K/AKT pathway. For example, metastatic colorectal cancer (CRC) patients, who harboured KRAS wild type tumours and who were given anti-EGFR mAb therapy, suffered worse outcomes if their tumours also contained PIK3CA exon 20 mutations,41 or PTEN loss.42 In a metastatic melanoma patient treated for seven months with vemurafenib, a single progressing lesion contained two sub-clones, both V600E BRAF-mutant, but one with an additional activating NRAS mutation.19 The NRAS mutation may in effect override mutant BRAF signalling to promote progression.

Genomic studies of primary and metastatic lesions show that tumours of the same type evolve differently over time between patients, but also between metastases within the same patient.43,44 This tumour heterogeneity is at the root of primary and acquired drug resistance and of the differential responses that a particular tumour type makes to the same treatment. Importantly, acquired drug resistance may derive from mutational or non-mutational mechanisms or both.40,45

Tumour heterogeneity limits the ability of genomic approaches to capture therapeutically relevant information because tumour sampling: (i) is invasive and sometimes not feasible or adequate because of practical, clinical and logistical factors; (ii) may not be contemporaneous to the clinically significant disease process; (iii) may derive from an uninformative part of a tumour deposit, which does not contain clinically significant driver mutations.46 Furthermore, some genomics technologies may not be sufficiently sensitive to detect low frequency primary resistance mutations or secondary mutations arise under the selection pressure of treatment.4

It also clear that the same mutation in a different tumour may produce an unexpected response to treatment. For example, selective targeting of V600E-mutant BRAF with vemurafenib produces responses in most melanoma patients, but not in colorectal cancer patients. BRAF-mutant colorectal carcinoma cells express EGFR unlike BRAF-mutant melanoma cells. Consequently, applying vemurafenib to BRAF-mutant colorectal carcinoma cells immediately results in activation of EGFR and Ras and produces BRAF inhibitor resistance, which can be overcome by concurrent anti-EGFR therapy.47
Keeping on target

Following the paradigm established by combination cancer chemotherapy and highly active anti-retroviral therapy that suppresses HIV escape mutants, the obvious implication of tumour heterogeneity and tumour adaptation to therapy is that targeted therapies should be combined and/or incorporated in multimodality therapy.

As figure 3 shows, single targeting of an oncogenic signalling pathway can result in ‘oncogene bypass’ as a resistance mechanism.48,49 In vitro studies have shown that pharmacological blockade of these alternative pathways can restore drug sensitivity to resistant BRAF-mutant melanoma cells.50 However, this example of parallel pathway targeting risks greater toxicity, as was observed in renal cell carcinoma patients with the multi-targeted tyrosine kinase inhibitor (TKI), sunitinib, versus the more selective pazopanib.51 Another successful strategy is vertical pathway targeting (figure 1).5 When inhibitors of BRAF and MEK were combined in patients with BRAF-mutant metastatic melanoma, progression free survival was extended by approximately 50% compared to BRAF inhibitor alone.52 In an unprecedented example, this combination therapy was less toxic than each individual therapy because BRAF inhibitor-induced paradoxical mitogen activated protein kinase (MAPK) pathway activation was blunted.53

![Figure 3: Resistance to BRAF inhibitor therapy can be MEK-dependent or independent and may be overcome by vertical or parallel pathway targeting strategies](image)

A. In normal cells, cell growth and proliferation is partially controlled through the mitogen activated protein kinase (MAPK) signalling pathway. The MAPK pathway is activated physiologically in response to growth factor binding of a receptor tyrosine kinase (RTK), which transduces the signal in series via kinase molecules labelled as RAF, MEK and ERK. B. In a malignant melanoma cell, the BRAF gene is mutated to produce a BRAF kinase that is always locked in the ‘on’ position, thus constitutively activating the MAPK pathway irrespective of upstream signalling from growth factors. The most common BRAF mutation is V600E and this mutant molecule is selectively blocked by a small-molecule BRAF inhibitor (BRAFi) to shut down distal signalling. C. In time, MEK-dependent signalling mechanisms restore signalling flux through the MAPK pathway. Malignant melanoma cells again grow and proliferate to cause relapse of resistant disease. D. As an example of vertical pathway targeting, the addition of a small-molecule MEK inhibitor (MEKi) to the BRAFi drug further suppresses MAPK signalling and prevents melanoma growth and proliferation more effectively for longer. E. Alternatively, in time, MEK-independent signalling mechanisms mediated through a second RTK molecule may also arise and bypass BRAFi-mediated suppression of oncogenic BRAF signalling to cause relapse of BRAFi-resistant disease. Monoclonal antibodies or small-molecule inhibitors may be used to block signalling emanating from this second RTK molecule as an example of parallel pathway targeting.
On and off-target toxicities

Therapeutic index is important in the evaluation of any new therapy. The relatively narrow therapeutic index of many cytotoxic drugs may encourage the perception that targeted therapies are safer because ‘targeting’ could imply that their anti-cancer activity is more discriminating. However, targeted therapies have been associated with life-threatening, catastrophic and fatal adverse events. A meta-analysis of randomised clinical trials comparing the mTOR inhibitors, everolimus and temsirolimus, to controls, indicated that mTOR inhibitors doubled the risk of death, with infection being identified as a significant cause. Similarly, another meta-analysis of randomised clinical trials of VEGFR TKIs showed twice the risk of death from active therapy. The anti-VEGF mAb, bevacizumab, has been responsible for fatal haemorrhage and gastrointestinal perforation. The mAb, ipilimumab, blocks the T-cell surface molecule, CTLA-4, thus removing the brake on expansion of lymphocytes that subsequently target melanoma as well as normal tissues. In the first phase 3 trial, ipilimumab was associated with a 2% rate of treatment-related deaths. However, after implementation of improved toxicity management in the subsequent phase 3 trial, no ipilimumab-related deaths were reported.

Even though serious toxicities of targeted therapies tend to occur in less than 10% of patients, chronic, low-grade toxicities also hamper quality of life for some patients. For example, although sorafenib extends overall survival among patients with advanced hepatocellular carcinoma, the typical best response of stable disease must be reconciled with frequent drug-related toxicities of fatigue, anorexia, weight loss, diarrhoea and hand-foot syndrome. As the same signalling pathways are inhibited in normal tissues as in tumour tissue, many targeted therapy toxicities are on-target and correlate positively with anti-tumour efficacy. Indeed, hypertension is an on-target or mechanism-related toxicity of the VEGFR-targeted agent, sunitinib, and serves as a biomarker of tumour response in metastatic gastrointestinal stromal tumour and renal cell carcinoma. Acneiform rash is a very common toxicity of EGFR inhibitor therapy, and may be severe enough to warrant treatment discontinuation in up to 10% of patients. Given the evidence that rash may be associated with improved tumour control or survival, dose interruption or reduction, and appropriate supportive measures may be sufficient to manage this EGFR inhibitor-related toxicity while treatment continues. The question of equipoise between toxicity and perceived or actual clinical benefit will be more important as the duration of targeted therapy increases, because of adjuvant therapy or maintenance therapy programs with consequently increased risks of cumulative toxicity.

VEGFR-targeted kinases such as sorafenib, sunitinib, pazopanib and axitinib are particularly effective single agents in advanced cases of the clear cell variant of renal cell carcinoma, because the disease depends on VEGF-driven angiogenesis. In the COMPARZ phase 3 study of non-inferiority design, pazopanib was compared with sunitinib as first-line treatment in metastatic renal cell carcinoma patients. The progression free survival was similar, but pazopanib-treated patients experienced fewer troublesome side-effects and an increased quality of life. Some of the most troublesome side-effects, such as fatigue and hand-foot syndrome, occurred more frequently with sunitinib. As a less selective TKI than pazopanib, sunitinib’s inhibition of the critical haematopoietic growth factor receptors, KIT and FLT3 among others, may contribute to its poorer tolerability. Consequently, this example illustrates that toxicity associated with broader inhibition of redundant pathways is generally greater and thus represents off-target toxicity since the intended target is VEGFR.

The future of targeted therapy is bright

Aside from the evident clinical benefits of disease control, the shrinkage or stabilisation of disease afforded by targeted therapies may provide a ‘therapeutic platform’ for concomitant use of emerging and promising immuno-therapies, which have a slower onset of action but more durable effects than some targeted therapies. Despite application of the same cancer treatment, intra-patient and inter-patient tumour heterogeneity help to explain the wide disparity in patient outcomes. Tumour heterogeneity also highlights the shortcomings of current genomic technologies in identifying the cancer treatment targets that limit cure. Graphically, a biopsy sample taken from a single tumour mass at a single time point is unlikely to represent the diverse tumour genomic landscape and may not reliably guide the choice of therapy. Hence, other emerging clinical investigative modalities such as functional cancer imaging, which can apprehend tumour heterogeneity in the whole patient, may complement cancer genomic information to improve the accuracy of personalised cancer medicine.

Future targeted therapy approaches are likely to include more mAb armed with potent toxins or radionuclides, cell and gene therapeutics, and novel therapeutic molecules such as small interfering RNA and stapled peptides that may make protein-protein interaction targets pharmaceutically tractable.

Although unselected patients seen in routine clinical oncology practice may differ significantly from patients enrolled in the pivotal control clinical trials, prompt and sure-footed management of toxicities continues to be essential to maintaining patients on an effective dose and schedule of a targeted therapy. These toxicities also indicate the ongoing need to identify those biomarkers allied with toxicity and tumour response. As cancer incidence tends to increase as populations age worldwide, targeted therapies will be increasingly used in older people who often receive polypharmacy, with an enhanced risk of drug-drug interactions and drug-related toxicities. Therefore, work on providing electronic point of care services may help to mitigate the risks of polypharmacy. Ultimately, however, the targeted therapies boom will oblige clinical oncology professionals to obtain new skills to control cancer.

Acknowledgements

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References


Clinical trials – advancing national cancer care

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Abstract
Investigator initiated clinical trials are critical to the advancement of cancer care in Australia. Cooperative clinical trials groups in Australia and New Zealand contribute greatly to independent investigator initiated research across a wide spectrum of cancer types and interventions. Achievements of the groups and their contributions to improvement in cancer care over the past 40 years are highlighted. Future challenges in the field of clinical trials are discussed with particular regard to cooperative clinical trials groups.

The advantages of conducting clinical trials are widely recognised.1 The information gained from well conducted trials can be readily incorporated into clinical practice, and used to inform policy.

Investigator-initiated trials, often co-ordinated by a cooperative clinical trials group (CCTG), have played a critical role in establishing the efficacy and safety of a wide range of interventions in the treatment of cancer, including a variety of issues in surgery, chemotherapy agents, and radiation therapy, as well as in establishing the role of psychological, supportive care and palliative interventions. Trials are also critical in establishing the benefit or otherwise of primary or secondary screening and preventative approaches, although the majority of CCTGs tend to be less involved in these approaches. The results of these investigator-initiated trials then inform subsequent clinical practice.

Australia is recognised as a region that conducts clinical trials of both high quality and importance across a range of cancer types and clinical scenarios. Over the last 40 years, the growth of clinical trials groups in Australia has paralleled...
the recognition of the importance of conducting clinical research both locally and internationally. While individual patients may or may not receive a personal benefit from the intervention under investigation (for example when patients are randomised to the control arm of a two-armed phase 3 study), there is evidence that outcomes are in general improved for clinical trial participants, perhaps because of the rigour that trial processes impose on treatment options.1 Leading cancer agencies invariably recommend participation in clinical trials as an important part of care for patients and not just confined to situations in which the optimal course of treatment is not known. Even in the absence of measurable benefits to individual patients, participants in clinical trials also contribute to advancing knowledge and increasing treatment options for the future.2

The desire to improve outcomes for patients and carers is the common goal of all clinicians involved in the management of patients with cancer, but it was the realisation that we could all achieve a lot more by working together that led to the formation of the CCTGs. The majority of groups formed out of informal collaborations and developed more formalised structures with time. The willingness of investigators to share their knowledge and experiences has led to the depth and breadth of experience in clinical trials today. The importance of clinical trials to the health system as a whole has contributed to improvements not just in the survival of patients involved as well as those not involved in these studies, but in many other aspects of care for patients across a variety of tumour types and stages. The cancer CCTGs are listed in table 1.

Forty years of achievement through trials

From the oldest CCTG (Australasian Leukaemia and Lymphoma Group) to the youngest (Primary Care Collaborative Cancer Clinical Trials Group), all the groups formed around a nidus of committed clinicians and researchers, who shared the common goal of improving outcomes for patients with cancer. The results of these years of hard work has been a body of evidence that has contributed to improvements not just in the survival of patients involved as well as those not involved in these studies, but in many other aspects of care for patients across a variety of tumour types and stages. The cancer CCTGs are listed in table 1.

<table>
<thead>
<tr>
<th>Name*</th>
<th>Interest Area</th>
<th>Year Established</th>
<th>Members (number)</th>
<th>Number of trials Undertaken/completed</th>
<th>Major Sources of Funding to date</th>
<th>Location</th>
<th>Collaborating Institutions (e.g. international trials groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australasian Gastro-intestinal Trials Group (AGITG)</td>
<td>All gastrointestinal (gastro-oesophageal, pancreatic-biliary, NET, GIST, colon and rectum, anal)</td>
<td>1991</td>
<td>825</td>
<td>15 completed 13 trials currently in follow-up. 9 trials currently open to recruitment.</td>
<td>Cancer Australia, NHMRC, CINSW, Cancer Council Australia, philanthropic, industry</td>
<td>Group office: NHMRC Clinical Trials Centre. Coordinating centre: NHMRC Clinical Trials Centre.</td>
<td>78 national and international participating sites. International collaborations with: OCTO, Oxford, UK; GERCOR, Paris, France; CaCTUS, Glasgow, Scotland; EORTC, Brussels, Belgium; NCIC CTG, Canada.</td>
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<tr>
<td>Australasian Leukaemia and Lymphoma Group (ALLG)+</td>
<td>Malignant disorders of blood components; lymphoma, leukaemia, myeloma, myelodysplasia</td>
<td>1973</td>
<td>&gt;320</td>
<td>26 active / 42 closed to accrual</td>
<td>Cancer Australia, NHMRC, Victorian Cancer Agency, Leukaemia Foundation, philanthropic, industry</td>
<td>Office located at: Peter MacCallum Cancer Centre, East Melbourne, VIC. Centre for Biostatistics and Clinical Trials (BaCT) at the Peter MacCallum Cancer Centre assists the ALLG with design, conduct, analysis and interpretation of cancer clinical trials.</td>
<td>74 participating sites in ANZ. 18 national collaborating groups. 13 international collaborating groups or sites.</td>
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<tr>
<td>Australasian Lung cancer Trials Group (ALTG)</td>
<td>Lung</td>
<td>2004</td>
<td>344</td>
<td>3 completed, 6 active, 10 in development.</td>
<td>Cancer Australia, NHMRC, CINSW, industry.</td>
<td>Group office: NHMRC Clinical Trials Centre. Coordinating centre: NHMRC Clinical Trials Centre. NHMRC Clinical Trials Centre; COSA; Trans Tasman Radiation Oncology Group (TROG); National Cancer Institute of Canada (NCIC).</td>
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<tr>
<td>Australia and New Zealand Breast Cancer Trials Group (ANZBCTG)</td>
<td>Breast</td>
<td>1978</td>
<td>&gt;600</td>
<td>60/56</td>
<td>Cancer Australia, NHMRC, CINSW, Breast Cancer Institute of Australia, Breast Cancer Research Foundation (US), Hunter Medical Research Institute, National Breast Cancer Foundation, NSW Department of Health, University of Newcastle, industry and philanthropic.</td>
<td>Office: NHMRC Telethon Mather Institute, Newcastle NSW Statistical centre: NHMRC Clinical Trials Centre. 80 participating sites. Breast International Group (BIG); Cancer Research United Kingdom (CRUK); International Breast Cancer Studies Group (IBCSG); National Surgical Adjuvant Breast &amp; Bowel Project (NSABP); Translational Research in Oncology (TRIO).</td>
<td></td>
</tr>
<tr>
<td>Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG)</td>
<td>All tumour types present in the paediatric/adolescent population. The most common childhood cancers are acute lymphoblastic leukaemia, brain cancer and neuroblastoma. 1986 as Australian and New Zealand Children's Cancer Study Group (ANZCCSG); changed name to ANZCHOG in 2003</td>
<td>1986</td>
<td>330</td>
<td>Usually 5-6 ‘home-grown’ trials open concurrently. 150 international trials open concurrently.</td>
<td>Cancer Australia funding through Support for Cancer Clinical Trials Program, NHMRC project funding, industry.</td>
<td>Office: Monash University, Clayton Victoria. Members are from all children’s cancer centres across Australia and NZ.</td>
<td></td>
</tr>
<tr>
<td>Australia New Zealand Gynaecological Oncology Group (ANZOG)</td>
<td>Cancers of the ovary, fallopian tube, vulva, vagina, endometrium, cervix.</td>
<td>2000</td>
<td>450</td>
<td>5 currently open. 6 closed. 4 in follow-up.</td>
<td>Nationally competitive grants (NHMRC, Cancer Australia), support from overseas groups (through GOQ), industry.</td>
<td>Group office: NHMRC Clinical Trials Centre. Coordinating centre: NHMRC Clinical Trials Centre. 51 sites (Australia and New Zealand). &gt;30 participating sites (major melanoma treatment centres in Australia, New Zealand and internationally). Collaborations with: Trans Tasman Radiation Oncology Group (TROG); Psycho-oncology Co-operative Research Group (PoCoG); NHMRC Clinical Trials Centre; COSA; Melanoma Network NZ; OCTO, Oxford, UK; EORTC, Brussels, Belgium.</td>
<td></td>
</tr>
<tr>
<td>Australia and New Zealand Melanoma Trials Group (ANZMTG)</td>
<td>Melanoma</td>
<td>1999</td>
<td>&gt;600</td>
<td>6 currently open. 2 closed. 4 in development.</td>
<td>Nationally competitive grants, Cancer Australia funding through Support for Cancer Clinical Trials Program, NHMRC Project Grants, philanthropic.</td>
<td>Office: Melanoma Institute Australia, The Poche Centre, Sydney</td>
<td></td>
</tr>
<tr>
<td>Group Name and Location</td>
<td>Cancer Sites and Related Tumours</td>
<td>Year</td>
<td>Grants</td>
<td>Details</td>
<td></td>
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<tr>
<td>Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP)</td>
<td>Bladder, kidney, testicular and prostate and related cancers</td>
<td>2008</td>
<td>530</td>
<td>Cancer Council / Prostate Cancer Foundation of Australia; infrastructure; QINSAW, Victorian Cancer Agency, Cancer Australia, industry. Group office: NHMRC Clinical Trials Centre Coordinating centre: NHMRC Clinical Trials Centre</td>
<td></td>
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<tr>
<td>Australasian Sarcoma Study Group (ASSG)</td>
<td>Sarcoma and related tumours</td>
<td>2008</td>
<td>400</td>
<td>Cancer Australia, philanthropic groups. Office housed at Peter MacCallum Cancer Center, Melbourne.</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cooperative Trials Group for Neuro-Oncology (COGNO)</td>
<td>Brain</td>
<td>2007</td>
<td>291</td>
<td>Cancer Australia, Cancer Council, Cancer Institute NSW, industry. Group office: NHMRC Clinical Trials Centre Coordinating Centre: NHMRC Clinical Trials Centre</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Primary Care Collaborative Cancer Clinical Trials Group (PC4)</td>
<td>All aspects of cancer in primary care, prevention, screening and early detection to diagnosis, treatment and follow-up</td>
<td>2009</td>
<td>323</td>
<td>Cancer Australia National virtual organisation, with the grant administered by The University of Western Australia.</td>
<td></td>
<td></td>
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<tr>
<td>Palliative Care Clinical Studies Collaborative (PaCCSC)</td>
<td>Palliative care, end of life care</td>
<td>2007</td>
<td>130</td>
<td>Department of Health and Ageing, NHMRC project grants. Central Coordinating Office is at Flinders University, Adelaide, South Australia. 14^</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psycho-oncology Co-operative Research Group (PoCoG)</td>
<td>Psychosocial aspects of cancer, across all tumour groups</td>
<td>2005</td>
<td>1120 (national and international)</td>
<td>Infrastructure funding from Cancer Australia and Cancer Institute NSW, CCUSA, NHMRC enabling grant, direct research funding from various sources. Office: University of Sydney, Sydney, NSW.</td>
<td></td>
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<td></td>
<td>6 of the 14 clinical trials groups, Sydney Catalyst and COSA. Links with other units conducting psycho-oncology and supportive care research.</td>
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</table>
To list all the achievements of the CCTGs (see Table 1) in advancing cancer care is outside the scope of this article. However, some notable achievements include:

Australasian Gastro-Intestinal Trials Group (AGITG) – has led or collaborated on practice changing trials, furthering understanding of the relationship between treatment and biology in gastrointestinal cancers. Notably, the CO.17 trial, conducted in collaboration with the Canadian NCIC CTG, established the benefit to patients with K-ras wild type metastatic colorectal cancer treated with cetuximab, following failure of other therapies.5

Australasian Leukaemia and Lymphoma Group (ALLG) – has conducted several practice changing trials, including AMLM2 which established the role of etoposide in AML.6 More recently the ALLG has established the National Leukaemia and Lymphoma Tissue Bank, in conjunction with the Leukaemia Foundation which will provide a platform for improved healthcare outcomes through translational research.

Australasian Lung cancer Trials Group (ALTG) – has established highly productive international collaborations resulting in large scale randomised trials of novel targeted agents with the Canadian NCIC Clinical Trials Group (BR-26 and BR-29),7,8 and with the Dutch NVALT group (thalidomide in mesothelioma and nitroglycerin in non-small cell lung cancer).9,10

Australian and New Zealand Breast Cancer Trials Group (ANZBCTG) – has developed or collaborated on many randomised phase III trials, that have led to significant advances in the management of both early and late stage breast cancers. One example is the ANZ 0101/BIG 1-01 HERA trial,11 which investigated adjuvant trastuzumab. This led to the registration and pharmaceutical benefit scheme funding of this therapy for Australian women with early breast cancer in October 2006 and Pharmac funding in New Zealand in 2008, and led to other new international trials for HER2 positive early breast cancer.

Australian and New Zealand Children’s Haematology/Oncology Group (ANZCHOG) – has developed a national paediatric cancer clinical trials registry that is available online,12 for the use of health professionals, as well as patients and their families. This registry lists all trials available in Australia, including international trials and the institutions at which they are available.
ANZGOG/National Health and Medical Research Council (NHMRC) CTC served as statistical centre for this international trial.13

Australia and New Zealand Melanoma Trials Group (ANZMTG) – led the first international randomised phase III trial demonstrating a benefit from adjuvant radiotherapy for patients at high risk of lymph-node field relapse after therapeutic lymphadenectomy for melanoma.14

Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP) – lead ANZ participation in an international trial of adjuvant therapy with targeted therapy (sorafenib) to improve cure rates in renal cell carcinoma,15 and developed a substudy determining patients’ preferences.

Australasian Sarcoma Study Group (ASSG) – creation of a national database of sarcoma patients with several projects planned that will provide valuable information to inform current and future research in sarcomas.

Cooperative Trials Group for Neuro-Oncology (COGNO) – has completed a national multicentre trial of bevacizumab in recurrent glioblastoma, the largest conducted to date in this population.16

Primary Care Collaborative Cancer Clinical Trials Group (PC4) – rapid growth since establishment in 2009 with 16 concepts currently under development and 35 trials supported since inception. Establishment of a joint Community Advisory Group with Psycho-oncology Co-operative Research Group (PoCoG).

Palliative Care Clinical Studies Collaborative (PaCCSC) – successful completion of two phase III randomised control trials examining the role of ketamine in treating cancer related pain,17 and octreotide in malignant bowel obstruction.18

Psycho-oncology Co-operative Research Group (PoCoG) – development and initiation of a phase III trial of an intervention for Fear of Cancer Recurrence funded by NHMRC,19 following three successful pilot studies (2009-2011). Development of a searchable database of measures relevant to psycho-oncology, standard operating procedures for psycho-oncology studies and a range of resources to support researchers in this area. Development of a quality of life office to support all trial groups in incorporating quality of life questions and measures into their studies.

Trans-Tasman Radiation Oncology Group (TROG) – the TROG 96.01 trial showed that the chances of cancer returning in the prostate could be reduced by approximately 60% using a course of hormone therapy prior to radiotherapy.20 The study also showed that the treatment with hormone therapy substantially reduced the chances of cancer appearing in other parts of the body, which could otherwise prove fatal. TROG 96.01 was Australia and New Zealand’s largest cancer trial when it completed recruitment of over 800 men with inoperable prostate cancer in February 2000. Long-term follow-up of these men is continuing.

Role of the Clinical Oncological Society of Australia

The Clinical Oncological Society of Australia (COSA) has provided valuable support for the CCTGs in a number of ways. Establishment of an Executive Officers Network was identified as important for the CCTGs; this network facilitates supportive relationships between groups, and acts a reference group for many common issues arising in the conduct of multi-site investigator initiated research. The opportunity to link to other CCTGs through this network allows groups to share information and knowledge on emerging issues in clinical trials, and learn from the collective experience of other groups in facing common challenges. COSA has also supported other initiatives, including commissioning an independent review of biobanking. ‘Developing a nationally coordinated approach to biobanking for Cancer Trials in Australia 2010’ (by Deloitte), support for essential training in good clinical practice training via ARCS Australia, and access to programs of mutual relevance from the funding secured via COSA’s successful NHMRC enabling grant. COSA has been instrumental to the CCTGs’ ability to confront and resolve many issues the groups face in the ever changing regulatory environment. Examples of this include establishing an umbrella clinical trials insurance policy, single CCTG clinical trial research agreements for sites and representing a substantial reduction in administrative burden at costs to the groups.

Future challenges

While CCTGs have achieved much during the last 40 years, many challenges lie ahead if the groups are to continue to undertake relevant, timely and meaningful trials. As is often the case in research, time, money and other external factors are potential barriers to success, although particular aspects of these are of relevance to CCTGs in Australia.

Trial design and patient selection

The recognition that cancers arising in the same anatomical location are a heterogeneous group of diseases with different biological identities, has implications not just for clinical practice but for trial design. The previous paradigm of large benefits from a single intervention in a disease based on tumour site is no longer feasible in many tumour types. As a result of improvements in outcomes for several tumour types, and with the subdivision of anatomic groups by tumour biology, it is increasingly difficult to demonstrate the smaller benefits seen in the previous generation of trials. Traditional trial designs often require both larger cohorts and longer trials, complicated by the decreasing available pool of patients when groups of cancers are subdivided along biological lines. Novel trial designs have been increasingly championed by some as a solution to these problems.21,22 However, the potential improvement in trial feasibility these designs offer, by decreasing the number of patients required for each trial, is offset by the potential difficulty in interpreting results, such that these may not be accepted by clinicians or regulatory authorities.

A similar challenge lies in the identification and incorporation of appropriate endpoints, including surrogate endpoints and patient reported outcomes. Overall survival has previously been accepted as the gold standard for phase III trials, but its relevance is being increasingly challenged, particularly in trials of first line therapies where multiple subsequent treatments exist. The use of surrogate endpoints has the potential to shorten trial duration and accelerate the pace of resulting clinical decision making. However, the identification and incorporation of surrogate endpoints carries its own challenges, with such endpoints requiring validation that...
they are both significant and meaningful for the disease and setting under investigation.

**Strategies for ensuring appropriate funding of investigator initiated trials**

A substantial amount of resources, including both fiscal and human capital, are required in the months and years from concept to activation of a clinical trial. The current model of funding investigator initiated trials requires significant investment in the development of an idea prior to application to government or philanthropic bodies for funding. At present the majority of the groups support these activities through infrastructure grants awarded by Cancer Australia, Cancer Institute NSW and others bodies for this purpose, often in conjunction with collaborating academic centres specialising in clinical trials (see table 1). These grants are typically cyclical in nature and in several cases are used to fund positions jointly with coordinating centres. The short to medium term nature of these grants (typically from three to five years) makes developing and retaining a skilled workforce without job permanency difficult.

Similar challenges lie in the current model of funding trials. The maximum funding terms for grants from NHMRC and Cancer Australia (and partners) are five and three years respectively. The annual process for grant review means a delay of between seven to nine months between submission and outcome of funding requests. The substantial amount of work required to determine feasibility and develop a well thought out concept, often incorporating translational, health, economic and patient reported outcomes, means that an idea for a clinical trial often takes months, if not years to evolve before a request for funding is even submitted. In order for clinical trials to keep pace with and lead clinical practice, more efficient models of funding are required.

Another weakness of the current model is the requirement for individual trials to compete against each other, as well as against other models of research for a fixed pool of funding. The scale and complexity of trials, while representing real value to the community, means clinical trials of all phases are at risk of not being seen as competitive against basic research questions, which may carry shorter term goals for individual projects. Private or corporate philanthropy cannot be relied upon to make up the shortfall; few philanthropic organisations exist with sufficient resources or willingness to fund large scale trials with outcomes that may take many years to be realised. Strategies for funding clinical trials in addition to current funding models have been proposed: allocation of a proportion of the overall health care budget (0.5-1% phased in over several years); central allocation of funding for projects and infrastructure in a similar model to the National Institute of Health Research model in the UK; and evaluation of new drugs or new indications for existing drugs funded by the Pharmaceutical Benefits Scheme.

**Barriers to trial approval and initiation**

Once funding has been obtained, the process for trial approval and initiation at sites can be long and burdensome with seemingly unnecessary delays. Two cooperative groups in the US recently reported their experiences – Cancer And Leukemia Group-B and Eastern Cooperative Oncology Group – with an average time of 784 days and 808 days respectively from concept to trial initiation. Multi-centre ethics approval has demonstrated reductions in time to overall trial approval for national trials, and the rollout of the HOMER multi-state ethics approval process may reap further rewards as it is more widely adopted. However, not all states or sites have signed on and many, particularly private hospitals, are unlikely to do so. Even with a condensed process for ethics approval, the time required for governance approval in tertiary institutions with large trial units can range from four weeks to over six months in our experience. A recent publication examining regional experiences from the international phase III ALTTO trial described an average time from ethics committee approval to the first patient randomised of 172 days across the Asia Pacific region.

**Integration of clinical and basic research**

Clinical trials and the resulting data sets represent a substantial resource with the potential to yield valuable information for current and future questions. In the era of translational research and personalised medicine however, the clinical data is most valuable when it is able to be linked with biospecimens. Similarly, a biobank that is not linked to high-quality clinical data – often confined to clinical trials – is a (bio) bank that pays no interest. How to best obtain, preserve and utilise the resources entrusted by clinical trial participants remains a challenge for researchers. Obtaining and storing biospecimens in physical or virtual biobanks is an ongoing challenge, as is the prioritisation of subsequent research on a finite amount of specimens. Researchers must also attempt to predict the direction of future research and obtain appropriate types and amounts of biospecimens for as yet unspecifed research, without placing an unnecessary burden on participants.

**Site issues**

As the complexity of trials increases, the need to provide site payments that reflect actual costs of conducting research grows in importance. While actual costs to individual sites are difficult to establish, models for determining workload for clinical trials based on complexity have been developed. Per patient payments for CCTG trials are frequently lower than commercial trials of the same phase; sites must often choose between commercial and investigator initiated trials in the same indication. For sites where only a few eligible patients are likely to be recruited, it may not be feasible to open a CCTG trial. Rural and regional sites are particularly vulnerable, more so since schemes that provided direct support for site staff and infrastructure targeted at the conduct of cooperative group trials have recently been withdrawn by Cancer Australia. Additional complexities are often encountered in attempting to conduct research in the private sector, which represents a growing proportion of cancer care. How to maintain equitable access to clinical trials for patients in the private sector, and in rural and remote areas remains a challenge that the CCTGs cannot address alone.

**Conclusions**

Considerable efforts by CCTGs and collaborating centres in Australia and New Zealand have resulted in significant gains in the understanding and treatment of patients with cancer over the past 40 years. Many challenges still exist if the CCTGs are to continue to successfully undertake the ‘ordinary miracle’ of completed clinical trials. Input is needed from government and policymakers to ensure the
many roadblocks to successful research and improved health outcomes are removed or minimised. However, the collective enthusiasm, skills and experience of the CCTGs and their many members, as well as the collaborating academic institutions (trial centres), ensure that local trials are well placed to continue to deliver world class research and improved outcomes for patients and the health system.

Acknowledgements

The authors would like to thank the chairs and executive officers of the CCTGs who provided information for inclusion in this article.

References


PATIENT REPORTED OUTCOMES ARE IMPORTANT IN ONCOLOGY

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Abstract

Cancer is a major health problem in Australia. As such, improving cancer outcomes is a priority. Traditionally, cancer outcomes such as mortality, survival rates and local recurrence rates have dominated clinical decision making. The past several decades has seen a paradigm shift in that there has been an increased emphasis on patient reported outcomes, both in the research arena as well as clinical practice. However, despite the rapidly expanding volume of outcomes research, uptake into clinical practice has been slow. As treatments in oncology often involve complex tradeoffs between survival and functional sequelae, it is important that the patient is involved in clinical decision making. In order to allow patients to make an informed decision, patient reported outcomes need to accompany and complement traditional objective outcomes such as survival and treatment efficacy.

Measuring the success of any organisation is critical, regardless of the nature of the organisation. Although somewhat over-simplistic, the key index of performance in private companies is usually measured in terms of profits. Unlike the private sector however, measuring outcomes in health care is much more complex and multi-dimensional. Depending on the perspective adopted and the outcomes one is interested in, individual patient outcomes, clinician performance, outcomes for specific diagnostic groups, compliance to system processes or even cost effectiveness of the system can and have all been measured.1, 2 Contributing to the complexity of measuring health outcomes in patients is the fact that health is not a dichotomous state, but a subjective perception that resides on a continuum which is in turn influenced by the individual’s expectations and environment.3, 4

Measuring and understanding outcomes in oncology is important because of the burden of disease that cancer imposes on our society. According to a recent report by the Australian Institute of Health and Welfare, one in two Australian men and one in three Australian women will be diagnosed with cancer by the age of 85, and one in five Australians will succumb because of cancer.5 As a cause of disability, cancer overtook cardiovascular disease in 2003 as the single most important contributor to the total burden of disease in Australia and is a major source of health care expenditure, itself accounting for 9% of Australia’s gross domestic product.6 It is not surprising that cancer was declared a national priority area that is directly reportable to health ministers.7 The problem posed by cancer is not unique to Australia. Most developed countries and even some developing countries are facing similar problems, with an increasing burden of disease from cancer as the population ages and the pool of patients seeking treatment continues to expand. Improving cancer outcomes is therefore important, be it from the point of view of a consumer seeking high quality health care, a health practitioner at the coal face of clinical oncology, or a policy maker trying to ensure a sustainable and equitable health care system.

Traditional outcomes measures in cancer

Traditionally, cancer outcomes have been measured in terms of survival, mortality, treatment efficacy (cure rates) and recurrence rates. These outcomes are concrete and objective, and lend themselves well to conventional methods of measurement. As cancer is a disease that can pose a direct threat to life, survival or mortality as endpoints are logical and are often favoured by policy makers as ‘hard’ endpoints, because they are intuitive in demonstrating performance in health care. While longitudinal trends in survival and mortality are helpful to inform the overall effectiveness of cancer services, a major limitation with these studies is that they are ecological in nature and generally do not demonstrate cause and effect.8 Further, unlike data on cancer incidence, which is generally comprehensive and complete due to mandatory reporting,5 mortality data is generally derived from death certificates where information may be less accurate, particularly in elderly or infirm patients where post-mortems are less likely to be performed and others where co-morbidities exist.5-11 Cancer related mortality in Australia has decreased by 16% over the past 20 years as a result of a combination of increased cancer awareness, uptake of cancer screening and widespread use of effective multi-modal therapy.3 While further reductions in cancer related mortality are expected with ongoing scientific and technological advancement, there may come a time when the ceiling is reached such that further reductions in mortality will be hard earned and slow coming, making mortality a less useful endpoint in clinical trials. With increased survival, the goal of cancer treatment can no longer be restricted to survival alone. Instead, treatment goals need to be expanded to...
include improving the quality of cancer survivorship. This is particularly important in oncology because most cancer treatments can be associated with long-term functional sequelae. This is not to say that the ‘hard’ outcomes are no longer important benchmarks in oncology, it is simply recognising that a good oncological outcome is not merely being alive or free of cancer. As summarised aptly by the World Health Organisation, health is a “state of complete physical, social and mental well-being and not merely absence of disease or infirmity.”

**Patient reported outcomes**

Patient reported outcomes (PROs) is an encompassing term that includes any outcomes measure directly elicited from the patient without interpretation from the treating doctor, carer or other health care professional. Within PROs are measures such as symptoms, functional outcomes, satisfaction and treatment preferences. The drive to develop PROs stems from a number of factors including the spiraling cost of health care, recognition of disparities in quality of care and the appreciation that clinicians and patients often have different opinions and treatment preferences. Further, by their very nature, subjective outcomes such as improved symptoms, reduced anxiety or quality of life are often intangible to everyone else other than the patient themselves, making PROs a logical complement to traditional outcome measures in the assessment of treatment efficacy.

**Measuring health related quality of life**

To accurately quantify health related quality of life (HRQoL) and the impact that illness or treatment has on the patient, novel measures had to be developed. The important attributes of a HRQoL measure are that it needs to be relevant to the condition in question (content validity, construct validity and criterion validity), reliable (test/re-test reliability and internal consistency), sensitive to change, acceptable to patients and easy to administer.

Broadly speaking, there are three types of HRQoL measures – generic, condition specific measures or patient specific measures. Generic measures such as SF 36, EQ-5D (EuroQol) or AQLQ (Assessment of Quality of Life) assess the individual’s global sense of well-being. These measures usually combine symptoms with function in domains that are accepted as being necessary for health, such as physical, social and emotional subscales. Generic measures allow comparison of quality of life across different conditions, however unlike condition specific measures, they are also not sensitive enough to detect clinically meaningful changes in domains relevant to specific conditions to enable treatment related changes.

As such, numerous condition specific measures have been developed over the years. Considering the time and cost associated with the development of each instrument, it is also not surprising that many condition specific instruments are developed by modifying existing generic measures, so as to capture additional condition specific concerns that are not evaluated in the generic measure. Patient specific measures allow individual choice of outcome measures such as the direct questioning of objectives.

Selecting a suitable HRQoL instrument depends on the intended use of the measure and the clinical context. Ease of access to the instrument is also a practical consideration, as the preferred instrument may not be available because of language barriers or maybe culturally inappropriate. Costs associated with the use or scoring of a measure also limits its utility, especially when repeated use is necessary. Finally, the exponential growth in number of instruments over the past two to three decades has made it somewhat difficult for clinicians to stay abreast with instruments that are available. Recognising this problem, the Mapi Research Foundation established an online database to house all known HRQoL instruments on a website known as Patient Reported Outcome Quality Of Life Instrument Database, or PROQOLID for short. The website enables researchers and clinicians to perform multi-field searches of the database so as to facilitate identification of and access to the desired HRQoL instrument.

**Patient preferences and decision making**

Most treatments in oncology, be it chemotherapy, hormonal therapy, radiotherapy or surgery, can be associated with significant short-term side-effects or long-term functional tradeoffs. Some treatments, such as surgery, are obviously irreversible. Quality of life measures in surgery often reflect informed consent and may not reflect true patient preferences made at the time of decision making (ie. cognitive dissonance deduction). Therefore, prospective measures of patient preference and equipoise studies are important. The use of multimodal therapy often increases toxicity for only modest gains in survival. Whether or not the survival benefit outweighs the potential toxicity of treatment to justify a certain treatment option is a decision best judged by the patient. In order to make an informed decision, patients need to be suitably counselled about available treatment options, treatment efficacy, as well as the pros and cons of each option. Notwithstanding this, not all patients will be comfortable with making treatment decisions themselves, even when all options are fully explained. Studies have shown that older patients and those with certain personality traits seem more reluctant to make treatment decisions, preferring instead to defer decision making to their doctor. The positive effects of decision aids are encouraging, their use in clinical practice remains in its infancy. Barriers to facilitate patient participation in clinical decision making, there has been a growing interest in the use of decision aids. These tools come in a variety of formats (pamphlets, decision boards, audio tapes, interactive websites) and can be used either in preparation for a consultation or at the time of consultation with the treating doctor. Although decision aids do provide factual information, they differ from educational pamphlets in that they are also preference sensitive – that is, they help patients clarify their treatment preferences.

In a recent Cochrane review, decision aids were found to improve knowledge, reduce decisional conflict, improve patient participation in shared decision making and reduce the proportion of patients who remain undecided. Although the positive effects of decision aids are encouraging, their use in clinical practice remains in its infancy. Barriers in uptake in clinical practice include time constraints, concerns about the impact decision aids may have on doctor-patient relationship and fear that patients may be overwhelmed by the amount of information provided, or may not comprehend the concept of a decision aid. Whether or not decision aids will benefit all patients equally (low literacy patients, different age groups or different personalities with different decision making styles), and whether they have any beneficial flow on effects on cost or reducing litigation, is
currently unknown and warrants further evaluation. Further, barriers to implementation also need to be addressed before decision aids will be taken up by clinicians.

**Cost-effectiveness of interventions**

An important aspect of the health care system is to ensure that the resources available are used in an equitable and efficient manner. Cancer related expenses have increased over the years because of an increased pool of patients requiring treatment, as well as rising cost of treatment per patient.\(^3\) The rate at which cancer related treatment expenses are increasing is somewhat alarming. In Canada, oncology drug spending is increasing at a disproportionately high rate compared to the incidence of cancer.\(^2\) In the United States, where total health care expenditure represents about 16% of their national gross domestic product (compared to 11% in France, 8.9% in Australia, 8.4% in the United Kingdom and 4.1% in the Netherlands), there is a concern that further increments in cancer treatment costs could outpace inflation, contributing to the rapidly rising total health care expenditure, which has been postulated to approach 20% of their national gross domestic product by 2020.\(^2\) Yet, despite the disparity between different health care expenses, life expectancies and cancer outcomes seem remarkably similar between United States and other countries.\(^2\)

The costs of the new chemotherapeutic agents in particular have attracted the most attention in recent years.\(^3\) Considering the marginal benefits conferred by some of these novel targeted therapies, it is essential that all new interventions are thoroughly evaluated before approved for widespread use. In 1993, Australia was the first country to introduce the requirement for a formal cost effectiveness analysis prior to approving a medication for public use.\(^3\) Today, most major drug approving agencies, including the Food and Drug Administration in the US, National Institute of Clinical Excellence in the UK and European Medicines Agency in the European Union, have all adopted similar policies demanding either evidence of cost effectiveness or improved HRQoL before a drug can be licensed for use.\(^3\)

Developments in adjuvant therapies for colorectal cancer highlight the importance of a comprehensive assessment process prior to approving a medication. Prior to the introduction of new chemotherapy agents, 5-flourouracil and leucovorin were the two most widely utilised agents costing under $100 for a six month course,\(^2\) and have been shown in several trials to result in a 22-33% relative reduction in mortality.\(^2\) In the past 10 years, six new drugs have become available for the treatment of colorectal cancer. In a study from the US, the addition of oxaliplatin to 5-flourouracil and leucovorin increased costs by $30,000 for a six month course for a much more modest increase in overall survival – from 76% to 79% – and disease free survival from 67% to 73%.\(^2\)\(^4\)\(^5\) A more recent Australian study found that the addition of oxaliplatin increased drug costs alone by $12,035 per course of chemotherapy, excluding costs associated with medication preparation and administration, which requires an infusional pump.\(^3\) Notwithstanding this, combinational treatment with 5-flourouracil, leucovorin and oxaliplatin was deemed cost-effective and is now widely available for patients with Stage III colorectal cancer around the world.\(^3\)\(^4\)\(^5\) The same study also found that the addition of novel targeted monoclonal antibodies, such as bevacizumab and cetuximab, further escalated costs by $24,000 and $50,000 respectively, for overall survival and disease free survival benefits measured in months.\(^6\)\(^7\)\(^8\) Cost effectiveness analyses have found both not to be cost-effective and as such, they are only available for use in patients with metastatic colorectal cancer on grounds of terminal cancer treatment and are not offered in all countries.\(^6\)\(^7\)\(^8\)

Due to the large sample sizes required in randomised control trials for oncology studies, several studies in recent years have used surrogate endpoints such as disease free survival or progression free survival, in anticipation that survival benefit will eventuate with longer follow-ups.\(^2\)\(^7\)\(^8\)\(^9\)\(^10\) However, findings of a large randomised trial of tamoxifen in breast cancer and bevacizumab have not found this to be a valid approach.\(^3\)\(^2\)\(^9\)

One major challenge with cost effectiveness analyses is to determine the threshold at which an intervention or a medication is deemed ‘value for money’. Although different countries have different thresholds above which drug approval is unlikely,\(^3\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\) this is also subject to other factors within the assessment, such as the importance of the disease or the availability of other treatment alternatives. More recently, there has been an evolving concept that cost-effectiveness analyses should take into consideration social concerns, such that the cost-effectiveness analysis may account for social inequalities so as to prioritise the disadvantaged.\(^3\)\(^4\)\(^5\)\(^6\) Several approaches have been proposed, but how this can be accomplished in practice remains under investigation.\(^3\)

**Patient reported outcomes in practice**

Although PROs are increasingly used as primary or secondary endpoints in oncology trials,\(^2\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\) a recent review by Maciefeld et al suggests that the uptake of PROs as an endpoint in cancer trials remains slow.\(^1\) Knowledge gleaned from PRO studies has provided invaluable information to guide patient decision making and has enabled clinicians to counsel patients appropriately by providing oncological data alongside HRQoL data. For example, the Dutch TME (total mesorectal excision) trial, comparing surgery alone versus radiotherapy plus surgery for rectal cancer, found that radiotherapy had no impact on overall survival, although it did halve the likelihood of local recurrence at the expense of detrimental effects on post-operative sexual and bowel function.\(^3\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\) The inclusion of some form of PRO outcome measure in randomised control trials is advocated by many cancer agencies, including the Clinical Oncology Society of Australia.

The ultimate goal of PRO research is to translate research knowledge into clinical practice and to collect routine PRO data in daily practice, so as to improve patient care.\(^3\)\(^4\)\(^5\) In a study by Velikova et al, routine PRO data collection immediately prior to a clinic consultation led to a statistically and clinically significant improvement in HRQoL, especially when the HRQoL information was fed back to the clinician during consultation.\(^4\)\(^5\) Pre-consultation PROs also prompted discussion of non-specific chronic symptoms, without prolonging the consultation or altering patient management with more investigations or treatments.\(^4\)\(^5\) Although the study has shown that routine PRO measurements can improve patient outcomes, there remain barriers to implementation, such as the mode of administration (touch screen...
handheld computers or paper questionnaires, concerns for time required for data collection or interpretation and resources necessary to enable routine use of PROs. As a demonstration that routine collection of PRO data was feasible, the US Centres for Medicare and Medicaid Services launched a time limited project whereby medical oncologists were eligible to receive an additional payment of US$130 per patient for collection and submission of data on nausea, vomiting, pain and fatigue. Although unlikely as an ongoing undertaking by the government, the experiment demonstrated that routine PRO data collection was feasible, especially if there was incentive for the clinician to do so.

Conclusions

PROs complement traditional hard oncological outcomes and are important for decision making at all levels. At a macro level, HRQoL outcomes and cost-effectiveness analyses ensure rational use of limited health dollars. For clinicians, PROs can inform while patients are responding to treatment, whereas for patients, their experience and preferences are paramount. Better integration of the conventional hard oncological outcomes and basic science research with patient reported outcomes is needed to not only improve survival, but improve the quality of this survivorship.

References

40. IMPACT Investigators. Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. International Multicentre Focused Analysis of Colon Cancer


2007;57:278-300.


A cancer cluster, defined as a “greater-than-expected number of cancer cases that occurs within a group of people in a geographic area over a defined period of time,”1 usually attracts considerable public and scientific attention.2 Typically, an informed and vocal community concerned about environmental factors influencing health identify and then report the event to health agencies.3-5 The media’s role in shaping public perceptions of cancer clusters has been noted, typically accompanied by observations of misrepresentation, or uneven coverage of events preceding and following scientific investigation of information to ensure profit. Cancer clusters were associated with particular work practices or environments, but concern typically centred on perceived personal relevance. Participants deemed prompt, independent and transparent organisational investigation of cancer clusters as mandatory, nonetheless noting a tension between a responsibility to ensure workplace or public safety and to set appropriate fiscal limits to investigations. Perceived difficulties however, in ‘disproving’ cancer clusters and researching potentially contributory practices or products ultimately sustained enduring doubts about public safety.

Growing public awareness about the effect of the environment on individual health, and the increased capacity to detect, track and analyse patterns of disease via population datasets, may lead to increased reporting of suspected clusters,11 with associated increased public anxiety and costs of investigation. Despite claims, however, that the most important challenge for public health agencies dealing with cancer clusters is to communicate effectively with the public,12 little is known of the perceptions and beliefs regarding cancer clusters within the general public, within which concerns about cancer clusters arise. Such knowledge is vital to public health organisations, informing the development of appropriate evidence-based policy regarding managerial response to public concerns about cancer clusters. This study analyses and describes the perceptions of the general public as they discuss the definition of, cause, effect, significance and appropriate responses to, a cancer cluster.
Method
The University of Adelaide Human Research Ethics Committee (South Australia) approved this research.

Data collection
Six focus groups (total 53 participants) were conducted, providing qualitative data enabling exploration of people’s knowledge and experience.13 Sampling was purposive – four groups following a 2-by-2 design were drawn from the general population, and stratified by: (1) age (25-35; 55-65), because the presence of older persons can hinder young persons from offering opinions, and vice versa;13 and (2) educational level (primary/secondary, tertiary), as this reportedly influences recall of cancer-related materials.14 Two additional groups were drawn from populations previously associated within local media with cancer clusters (namely, nurses and fire-officers), as personal relevance influences perceptions of health-related environmental events (table 1).10 All individuals were fluent English-speakers. Individuals who had previously received a cancer diagnosis, or worked or had previously worked at a location that was or had been the site of a cancer cluster investigation, were excluded because of probable heightened personal relevance.

Table 1: Details and participant numbers for focus groups

<table>
<thead>
<tr>
<th>Group</th>
<th>No. Female</th>
<th>No. Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young (25-35) with tertiary education</td>
<td>6</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Older (55-65) with tertiary education</td>
<td>3</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Young (25-35) without tertiary education</td>
<td>3</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Older (55-65) without tertiary education</td>
<td>5</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Nurses</td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Fire officers</td>
<td>-</td>
<td>10*</td>
<td>10</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>23</strong></td>
<td><strong>30</strong></td>
<td><strong>53</strong></td>
</tr>
</tbody>
</table>

* 11 attended, but one never spoke, despite encouragement from workmates.

A social marketing agency recruited and hosted all groups except fire-officers, and provided a trained moderator. Fire-officers were recruited through the fire-services state office, participating during work-hours at the local headquarters. Informed consent was obtained, and participants provided with a small honorarium, which fire-officers donated to a workplace-organised charity for fire victims.

Sessions were audio and video recorded. Discussion covered knowledge, perceptions and beliefs about cancer clusters. Following focus group methodology,15 participants determined the content of discussions, although prompt questions initiated or extended conversations, particularly regarding perceptions of named instances (eg. “What do you recall/think about what happened in that instance?”). At approximately the session mid-point, four brief videos of local (Australian) news coverage of cancer clusters, covering various locations (a fire-station, a public high school, a government office and a public hospital), were shown to prompt additional discussion.

Analysis
Sessions were transcribed verbatim and individuals de-identified. Transcriptions were entered into the NVIVO software,16 and thematically analysed. Thematic analysis is a qualitative analytic method used in applied healthcare research for identifying, describing, analysing and reporting themes (representing patterns or sets of meanings) in data.17 Our theoretical framework was explicitly essentialist or realist, as we aimed to understand and report the experiences, meanings and the reality of participants with regard to cancer clusters.17 Texts were repeatedly scanned to identify similarities and differences in how cancer clusters, and media coverage of these, were presented or discussed. Themes identified on initial readings were reviewed and refined or collapsed through comparison across the dataset, and relationships between themes clarified. Quotes selected to illustrate a theme were compared, and the most concise and/or representative quotes presented,18 with differences in speakers identified and the group of origin cited in brackets.

Results
Several inter-related and overlapping themes, capturing how participants (struggled to) understand and make sense of cancer clusters, were identified in the data. These were difficulties of definition, explaining the (increased) public interest, the sensationalist media, evil industries, ambivalence about scientific investigation and investigators, and enduring perceptions of (personal) risk. We indicate when themes were evident across all groups, surmising that this may indicate a dominant belief regarding cancer clusters within the general population. We caution however, that qualitative techniques do not justify conclusions drawn based on the comparative presence or absence of themes within particular demographic or vocational populations.

There was remarkable consistency in how groups talked about cancer clusters, particularly in the attempt to arrive at definitive positions. All groups struggled in defining cancer clusters, noting that distinguishing them from ‘normal’ rates of cancer was difficult.

Speaker (SP) 1: What criteria, what incidence of cancer has to be a cluster?

SP2: A higher proportion than cancer in the general public, be it a specific area or a workplace?

SP1: How much higher than the average though? (younger, no tertiary education)

An unusual number of cancer incidents in a particular context. Statistically it’s a significant deviation from the norm that’s related to a location or a context. (older, tertiary education)
All groups stated that, over time, there was a greater awareness of cancer clusters, suggesting various explanations. These included increased coverage of cancer clusters by the media, the naming of cancer clusters as a phenomenon, as well as increased media coverage of cancer and acceptability of disclosing a cancer diagnosis.

SP1: Cancer clusters are more well known now than 10 years ago.

SP2: [It’s] probably just the media as such, taking more notice of it.

SP3: It’s identified now. … Now we’ve got a label for it, like we have become more aware about it … it is easy for us to then draw conclusions [younger, no tertiary education].

Years ago when people got [cancer] they didn’t want to tell anybody they had it, … but as years went on people started discussing it more because of the media, and people got an idea that ‘oh hang on, it’s not just me that’s got it, it’s other people.’ (older, no tertiary education)

All groups raised the possibility that cancer clusters reported within specific populations might be because of regular screening or health checks. Most suggested that awareness of more cases of cancer, because of an aging population or workforce, might be significant.

A lot more people out there have cancer, the awareness is there, and they’re diagnosed earlier. … Particularly people like the fire department, they would have health checks … so they would pick it up a lot earlier. … Why were they all picked up at the same time? It could have been because they screened them all. (nurses)

Now we’re living longer, the cancers are in the foreground now and people are taking notice of it. … You used to retire at 65 and within two years after that, the majority of people who retired had passed away, so you didn’t ever come into the area where cancers are more prevalent for your age. (older, no tertiary education)

Media coverage of cancer clusters was also typically cited as prompting public awareness and discussion, and invariably concern about personal risk. This emerged most when media stories were seen to have personal relevance, either for those in occupations associated with reported cancer clusters, or when practices or places associated with cancer clusters were not occupation-specific.

I think the media plays an important part in the way that’s sort of brought about … just talking about it at work, if someone’s got cancer, you … start to think, well, ‘so and so had that and so and so had this, … maybe we are more prone in our occupation to cancer.’ (fire officers)

SP1: I find it a bit frightening because I work in a building, everyone goes into a building at some time, that seems to be the common ground, so I really want to know what was causing the cancer in each instance so I can stay away from it.

SP2: Those buildings … I wouldn’t go in, I’d be reticent to go in, so I’d bypass it, … it may be a hoax or anything else, but I don’t tempt fate [laughs] if I possibly can avoid it. (older, no tertiary education)

Referring to the ABC [Australian Broadcasting Corporation: see below] situation, we might surmise rightly or wrongly that it was caused by electromagnetic radiation, so those of us who are working in environments where we’ve been sitting in front of a computer for a great part of the day, to what degrees has that exposed us to potential cancer? (older, tertiary education)

However, all groups criticised media accuracy and motives in reporting on cancer clusters, some observing that notification of suspected cancer clusters was not followed by information on subsequent events.

SP1: They [media] contradict, and provide misinformation…. Just sensationalise.

SP2: They just go ‘this is a cancer cluster and it’s a good story’ because how much information did they give you?

Interviewer: Twenty-nine seconds. [laughter]

SP3: Yeah, not much. (nurses)

We haven’t actually received any outcomes from any of those stories. … Nothing seems to have been released since. (fire officers)

All discussed specific workplaces as relevant to cancer clusters, referring to three well-publicised adverse events, arguing that named companies (often motivated by profit) had denied or concealed information; moreover, that the ultimate revelation of potential public risk was because of concerted efforts of concerned individuals or groups. All but one named Erin Brockovich, some mentioning reported significant financial consequences to the relevant company.

SP1: Erin Brockovich, no-one did anything about it until she did. …

SP2: They did that write-up about what happened, how many millions of dollars the company had to pay and how many people were affected. (younger, tertiary education)

Four discussed a reported cancer cluster at the Australian Broadcasting Corporation (ABC) studios in Queensland, Australia, usually voicing concerns that no explanation was forthcoming. Some implied that there was an explanation, but it was not currently available because of limitations in current scientific knowledge.

The ABC situation where it was really unexplained, … it’s the unexplained bit that I get a bit concerned about too. (older, tertiary education)

There’s some cases, we don’t even have the knowledge or the expertise to find out why they happen, like that ABC one, they haven’t actually worked out why. (younger, tertiary education)
In discussing probable industry responses to public concerns about cancer risk and/or cancer clusters, events associated with James Hardie (asbestos manufacturers who denied, then moved to limit liability for compensation to mesothelioma victims), were cited as exemplifying perceived reprehensible corporate behaviour, cover-up and denial of liability. Although this particular instance does not meet scientific criteria for a cancer cluster, participants raised them in this context. Moreover, their knowledge regarding the James Hardie saga and similar corporate behaviour often justified distrust of institutional responses to cancer cluster concerns.

Look at James Hardie, the way they tried to cover up for so long. ... It was only through the individuals bringing it to the forefront of public attention that actually nailed James Hardie ... there's so much against really admitting liability. (older, tertiary education)

A ubiquitous belief, evident across all groups, was that named industries had attempted to conceal information and deny responsibility for any reported problems to avoid litigation or other costs, only reluctantly conceding following concerned individuals' exhaustive efforts prompting public outcry and action. It was also consistently assumed that such behaviours were endemic to all industries (including government).

SP1: With the ABC ... my memory of it, they had been brought kicking and screaming to acknowledge that there was a problem in this building. ... Someone has to go out on a limb and somehow stir up public emotion to actually get public consciousness aroused to bring government and private enterprise to acknowledge there's a problem. ...

SP2: I get the impression that we're not hearing a lot of people's concerns and that information has been dampened down and not given out to the public and you only hear it where people have been trying and trying and trying to get a voice heard and it's only after a long time, if ever, that it gets out. ... big companies would be liable, and if it was proven that there was a cancer cluster.

SP3: And then you wonder, ... is it worth for the government for James Hardie to be sheltered from any sort of litigation because if the business goes down the spout, then presumably the government misses out on revenue and maybe the government is partly liable, maybe it's not good for all the insurance organisations and so on. (older, tertiary education)

There was consensus, nonetheless, that organisations perceived to have increased numbers of cancer diagnoses in the workforce had a duty of care to respond to public concerns and undertake exhaustive investigation into environmental and personal work histories even where concerns and undertake exhaustive investigation into the workforce had a duty of care to respond to public concerns and undertake exhaustive investigation into environmental and personal work histories even where determination was thought unlikely. However, companies were typically perceived as motivated by concern for company image, not employees.

SP1: If enough people have the same thing, they've got to do an investigation. ...

SP2: I expect them to be quite extensive in their investigation, ... [considering] everything ...

SP3: The first thing to do is to look at each individual, ... their histories, where they're working, what type of work they do, what type of machinery they work with, and the environment they were working in. (older, no tertiary education)

SP1: The company obviously has the ultimate duty of care...

SP2: [Employees are] not going to be able to backlash if they [employers] cover their own backside, which seems to be the most common theme with most employers.

SP3: To a certain extent it'd be, you've got to do something, you've got to be seen to be doing something. (fire officers)

Groups held that informing the public of perceived higher incidences of cancer, by announcing an investigation, would always elicit panic, particularly among workers at the relevant site. They nonetheless argued that delays in providing information would additionally provoke anger at being disempowered or denied opportunity to have input. Establishing and using accessible lines of communication to inform those concerned about the progress and outcome of the investigation was viewed as likely to mitigate public concern, panic and spread of misinformation.

SP1: I think yeah, there will be panic, ... [but] if they didn't tell you straight away, then there would be anger and frustration and much more. It would be a lot worse, and still panic. I would rather have the panic and control it. ...

SP2: Investigate us and test, to check if we are ok. ... And put us at ease. ... Ongoing communication, update us, how are things happening, what is happening so we don't have to listen to other people and spread the gossips and innuendos, stop the innuendos, that's false communication, yes? (nurses)

All groups insisted that investigations be conducted by independent and trustworthy sources with perceived expertise and a track record. Only then would reports that cancer clusters were probably products of random events or chance be deemed acceptable.

The Cancer Council ... I would believe them, I would trust them. They're in the business of checking cancer things and testing things. (younger, tertiary education)

However, regardless of probable acceptance of claims from trusted authoritative figures that a cancer cluster was not evident in a particular instance, all groups stated they would have enduring concerns about an ongoing risk. Many noted that they would personally continue to monitor the incidence of cancer that might signal additional evidence of a cancer cluster, some also insisting that management should do likewise.

SP1: I would be prepared to give some weight to a report which cleared the building, but being a careful
person, I’d probably think, ‘well yes, there’s that ok, but there’s sort of this little niggle concern.’

SP2: I agree. … I’d probably be prepared … to go back into that work situation, but I’d be on the lookout to ensure that the incidence of those cancers didn’t seem to be statistically aberrant again. (older, tertiary education)

I would probably stay [working] there, … if it wasn’t obvious that something was causing it. As long as they kept ongoing testing. (younger, no tertiary education)

Widespread scepticism about the scientific investigation of cancer clusters appeared to sustain concern of enduring public risk. Doubt partly reflected participant understanding of the processes constituting relevant scientific testing, with more extensive debate about what this involved occurring within groups with a tertiary education. Participants variously perceived that there were limitations of determining causality, some suggesting that it was, in practice, impossible to follow gold-standard testing procedures in a cancer cluster situation (i.e. to retrospectively and accurately identify the presence of all potentially suspected carcinogens, or the extent or significance of individuals’ exposure to these). Some implied that difficulties in accurately determining the incidence of cancer in the target population (perhaps due to a transient workforce) would undermine assessment of relative risk. Scepticism was additionally supported with the presence of all potentially suspected carcinogens, or the extent or significance of individuals’ exposure to these. Participants variously perceived that there were limitations of determining causality, some suggesting that it was, in practice, impossible to follow gold-standard testing procedures in a cancer cluster situation (i.e. to retrospectively and accurately identify the presence of all potentially suspected carcinogens, or the extent or significance of individuals’ exposure to these). Some implied that difficulties in accurately determining the incidence of cancer in the target population (perhaps due to a transient workforce) would undermine assessment of relative risk. Scepticism was additionally supported with the presence of all potentially suspected carcinogens, or the extent or significance of individuals’ exposure to these.

SP1: Most people in their lives are gonna change jobs a number of times and without having a way of actually tracking where people work, it’s very difficult … Like there’s one workplace where 20 people went through and they developed cancer, but they didn’t develop it until 20 years after they were there. (younger, no tertiary education)

Various factors (including the number of potential products perceived to be possibly implicated, time-lag between exposure and diagnosis, difficulties of establishing cause and effect, public distrust of institutions, and financial costs of reviewing all persons and products potentially involved) were thought insurmountable obstacles to garnering definitive proof of workplace safety and ultimately dispelling concern. Although participants cited these factors as reasons to query reported conclusions, paradoxically, they also served as reasons to limit the scope of investigation.

SP1: Why aren’t tests done every two years on all buildings for example?

SP2: Does that mean you test every single building? … If you’re going to test for that, what else? Where do you draw the line? (older, without tertiary education).

SP1: Testing is expensive, very expensive.

SP2: I doubt that any big companies would go to the extent of paying for check-ups every year.

SP3: It would cripple the business if they played every small chance.

SP2: Yeah totally.

SP4: What would happen to the health system as well? (younger, tertiary education)

Discussion

This qualitative study is the first to elicit and analyse the perceptions of the public (including individuals in professions publicly associated with cancer clusters) regarding cancer clusters and surrounding events. As a qualitative study, it did not aim to determine the prevalence of particular views, or to make claims regarding generalisability of findings. Data collection was limited to six focus groups (53 participants) conducted in one city within a dominant language group. Nonetheless, sampling across demographic and vocational criteria ensured that multiple perspectives were included, allowing identification of factors influencing perceptions of cancer clusters in various settings. Further research regarding the perceptions of individuals with additional demographic (including ethnicity) and vocational criteria is warranted, including those directly affected by cancer clusters.

Even within this small group of participants, there was variation in how cancer clusters were defined, suggesting that there is no single ‘lay definition’ of cancer clusters, and highlighting the challenge in communicating effectively to a diverse public about suspected incidents. Findings confirmed observations that the media, though providing information, could contribute to public confusion and anxiety regarding cancer clusters. Participants typically
interpreted information regarding risks and outcomes of cancer clusters in the light of previous knowledge regarding highly-publicised adverse events (e.g. those associated with Erin Brockovich, the ABC Toowong incident and James Hardie), which effectively functioned as archetypal events. Not all such events met scientific criteria for cancer clusters, indicating a discrepancy between public and scientific definition and assessment of risks, which may increase the probability of social conflict.20 Commonly noted features of archetypal events were perceived inadequacies, even reprehensible corporate responses to public or employee concerns, and such knowledge shaped current responses.2, 21 The role of public trust in public health authorities charged with investigating suspected cancer clusters has been noted previously.9,10 This analysis suggests that public awareness of poor organisational responses to media-reported health scares might undermine public trust in investigations into cancer clusters, and this could be exacerbated by (real or perceived) inadequate media coverage of the processes and outcomes of investigations. Nonetheless, participants’ beliefs about various deficiencies in the extent and accuracy of media coverage also worked to moderate their perceptions of the nature, magnitude, or significance of a reported event, suggesting that the contemporaneous media cannot be held ultimately responsible for shaping public responses to reports of cancer clusters.22

Public concerns appeared most pronounced when media stories provided limited or conflicting information, or were perceived to have personal relevance. In these circumstances, participants’ concerns regarding personal risk were informed by fears of ‘insidious exposure to carcinogens’,19 endured despite lack of evidence of environmental hazard. Such fears also appeared susceptible to extrapolation beyond the named event, particularly where practices or products thought present at the suspected cancer cluster site were deemed common in other, personally-experienced situations. If not appropriately acknowledged and addressed, this may increase public anxiety following reports of cancer clusters, and ultimately increase the frequency with which suspected cancer clusters are reported by a concerned community. Public health responses to reports of cancer clusters in environments with potential perceived relevance to wider sections of the community should therefore elicit, acknowledge and counter public concerns. In particular, while investigations are underway, it would be desirable that media coverage of cancer clusters avoid language that either explicitly or implicitly infers a heightened yet nebulous risk to the general public, rather confining commentary to known facts and noting relevant contextual information.

To some extent, cancer clusters could represent one example of public confusion about how to apply population data to the individual, or the differences between association and causation. Therefore, the dissemination of public educational messages about these factors combined with information about the difficulties in, or low probability of definitively identifying a cause, might defuse speculation involving more sinister or devious explanations for scientific reports that do not reveal cause.

Faced with notification of a suspected cancer cluster within a workplace, participants considered that employers must undertake prompt, transparent, and independent investigation. Further, that panic, though inevitable, might be ameliorated by rapid and ongoing consultation and communication with those concerned. As the perception of risk implicitly includes assessment of consulted experts,23 ensuring and communicating the independence of investigators, and reporting the process and outcomes of investigations, could counter scepticism about the perceived trustworthiness of reported outcomes.12 Such measures are unlikely to reassure all however, in part for the reasons discussed above, but also because of differences in individual assessment of acceptable levels of risk, or awareness of limitations of scientific investigation. Given that some concerns were predicated upon particular misapprehensions regarding the nature of scientific enquiry into cancer clusters, clear communication of the scope and rationale of any scientific investigation may help allay some fears.

These participants actively and collectively worked to make sense of available information, drawing upon their shared accumulated knowledge of events, processes, stakeholders and outcomes perceived to be relevant.24 Although able to identify various possibly relevant contributory factors to notification of a suspected cancer cluster, participants acknowledged the impossibility of exhaustively testing everything and everyone following said notification, citing the prohibitive costs this would entail to businesses and the community, and considering that this constituted acceptable justification for limiting the scope of investigation. Accessing and disseminating varying opinions within the community about cancer clusters (specific instances and general phenomena) might serve to mitigate the impact of concerned citizens who reject specific scientific findings and lobby for costly and ultimately inconclusive further investigation.4 Ultimately, identifying and specifically addressing public concerns may prove the most acceptable, effective and responsible strategy to guide and constrain the scope of subsequent investigation.25

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8. Rothenberg RB, Steinberg KK, Thacker SB. The public health importance of notification and responses to cancer cluster reports.


1 Australian non-government non-profit cancer control organisations.
The Medical Oncology Group of Australia, together with Novartis Oncology, presents the Cancer Achievement Award to recognise an outstanding Australian contribution to cancer research and control. The award formally recognises the contributions made by scientists, clinicians and other health care professionals to the scientific study of cancer in Australia.

Since 1999, this award has been presented to 13 leaders in the field of Australian oncology. The recipient of the 2012 Award was Professor Michael Barton OAM, Research Director of the Collaboration for Cancer Outcomes Research and Evaluation (CCORE) and the Ingham Institute for Applied Medical Research at Liverpool Hospital.

The award was received by Professor Barton at the Medical Oncology Group of Australia Annual Scientific Meeting in Brisbane on 10th August 2012, at which he delivered the following address.

It is an honour to join the ranks of those who have received the Oncology Cancer Achievement Award. It made me wonder what have I done with my life and more to the point, why? The honest answer would be I have no idea why I have done what I have done, but there does seem to be an underlying theme - how can we improve what we practice with the knowledge we already have?

The US General Accounting Office published a report on the progress in Nixon’s war on cancer in 1980. They noted that “…many research advances existed…. and these advances were not being disseminated to the medical community to use on cancer victims and, as a result, were on the shelf.”

As a resident at Westmead in 1982, I was fortunate to encounter Allan Langlands. A wise, generous man, he was happy to talk to me about the decision making process in oncology, one of the few medical specialties to have roles in cure and palliation. It was Allan who interested me in oncology and who found me a training job at Royal Prince Alfred Hospital in Sydney in 1983 with David Green, then the Chief Examiner for Radiation Oncology. Not surprisingly David stressed the need for a combination of clinical skills and knowledge synthesis. The year I started at RPAH, one of the two old Cobalt machines caught fire and was finally replaced by a linear accelerator that had gone out of warranty in the warehouse, waiting a year for the room to be re-fitted to take delivery. The Cobalt machine had been installed the year I was born and the NSW Health Department at the time had tried to obstruct its installation because “the cure for cancer was around the corner”. In 1958 this was hormone therapy. It has been a long corner. One of the persisting myths about radiotherapy is that it is about to be superseded. The other myth is that radiotherapy is expensive. A study of the outcomes of nearly 10,000 patients that I undertook at Westmead showed radiotherapy was more cost-effective than treating mild hypertension.
As a young registrar in radiation oncology, the Friday afternoon referral of a spinal cord compression that had been deteriorating in a hospital ward for a few days seemed an obvious area where practice could be improved. An audit of spinal cord compression was my first research project. It demonstrated that better results were seen in ambulant patients.

In 1987, my wife and I went to England and I was employed in Cheltenham as a Clinical Fellow, analysing the results of what became the pilot for the START breast trial of altered fractionation. Our first child was born in June the following year. Three months later we moved to Toronto where, like so many Australian oncologists, I took a job as a Fellow at the Princess Margaret Hospital. I worked on an analysis of over 1000 cases of larynx cancer to quantify the effects of interruptions to radiotherapy treatment courses. In the past, when a patient complained of a severe reaction, we would give them a week's break to recover. My study showed that every day of unplanned interruption reduced local control of larynx cancer by 1.2%. This paper was part of the accumulating evidence that interruptions to radiotherapy resulted in higher recurrence rates and, in some cases, worse survival. Now we try to get patients through treatment without a break.

I returned to Australia at the end of 1989 to take up a consultant position at the Prince of Wales Hospital in Sydney to work with Rodney Withers, one of the world's leading radiobiologists. It was Rod who first used data routinely collected in radiotherapy departments to show the risks of treatment interruption. There are some questions which cannot ethically be asked in a clinical trial. Rod taught me the value of asking questions, even if they sounded trivial. If one of the smartest radiobiologists in the world could admit there were things he did not know, then there was no shame in lesser mortals doing the same.

While at Prince of Wales I began a long friendship with Dr Denise Lonergan, who ran a weekly clinic in Wollongong until the department there opened in the early 1990s. In 2007, Denise joined our department at Liverpool and together we established the radiation oncology training network in Southern NSW.

In 1992, I went to Westmead to work with Allan Langlands. I took over the radiosurgery service and realised that a brain tumour multidisciplinary clinic was needed. Glioma patients and their carers have such a high burden of disease, but neuro-oncology was in its infancy in Australia with very few dedicated clinics or teams. Over the last 15 years we have seen neuro-oncology expand to every major cancer service. A national trials group, the COSA group and a national biobank have been established. I chaired the Australian Cancer Network Clinical Guidelines for Glioma for health professionals and a separate version for consumers in 2009.

The broad areas of research that I have been interested in since returning to Australia are education, evidence-based benchmarks and cancer services. They have given me the opportunity to form productive relationships with committed and energetic colleagues from other medical specialties and non-medical professions.

In the early nineties, I was concerned about the radiation oncology training syllabus, particularly in the basic sciences. The old physics curriculum included Grenz rays and Beryllium windows, but did not mention electrons! A medical oncology equivalent would be including mustard gas but not Adriamycin. With a lot of help from my friends, we started the Basic Sciences of Oncology Course (BSOC) in Sydney in 1992. It covered anatomy, physics, radiobiology, palliative care, communication skills, systemic therapy and molecular pathology in one day sessions, once a month for eight months. Every oncology trainee and now, those aspiring to join oncology programs, have taken the BSOC over the last 20 years.

There was nothing like the BSOC in the other states and I had been to New Zealand on several occasions to teach radiobiology. We needed to provide the course in a distance learning format. I went to a meeting organised by the International Atomic Energy Agency (IAEA) in Islamabad to discuss training in low and middle income countries in 1997 and convinced them to sponsor the conversion of the course to a CD ROM that would run on the slowest PCs. It took nearly five years to collect the materials, and convert them to an interactive form on CD. The course was piloted in seven countries with 25 students. The final version of 80 one-hour modules is now available for free from the IAEA website (http://www.iaea.org/Publications/Training/Aso/register.html) and has been downloaded over 2500 times. Now we are converting the course to a modern content management system so that people can take the course on-line.

In the 1990s, Australian medical schools all seemed to be reforming their courses, with many adopting the fashion for problem-based learning. This was a great opportunity to improve oncology teaching. Martin Tattersall, Allan Langlands and others had documented the low level of knowledge and experience of oncology in Australian medical graduates. The anatomical site model of teaching meant that oncology was not taught as a coherent subject, but was fragmented with overlaps and gaps. I established the Oncology Education Committee of the then Australian Cancer Society, which sponsored the development of the Ideal Curriculum in Oncology for Medical Students. The aim of the curriculum was to provide a checklist for patient-centred cancer teaching for an ‘undifferentiated stem-cell’ doctor. The curriculum could be taught somewhere in the course and has been used as a template for oncology courses around Australia. A few years ago I received an email with a version of the curriculum that had been translated into Icelandic.

Most recently I have been involved in the IAEA’s new Virtual University for Cancer Care Network, which aims to link African countries to provide training resources for a wide range of oncology professionals. Egypt and South Africa act as mentoring nations for trainees from Ghana, Uganda, Tanzania and Uganda. Teaching materials use e-learning delivery.

In 1999, I moved to Liverpool Hospital to found the Collaboration for Cancer Outcomes, Research and Evaluation in order to develop health services research in oncology. Access to cancer services varies a lot within
and between Australian states; the proportion of cancer patients in NSW who receive radiotherapy ranges from 24% in New England to 47% in the Greater Murray. This nearly two-fold difference begs the question, is New England underserviced or is Greater Murray over serviced? In order to develop an evidence-based benchmark to assess access to radiotherapy and to plan future services, we examined national and international guidelines for all the indications for radiotherapy and searched for population data where possible, on the proportion of cases with each indication. The findings were laid out with decision analysis software that allows sensitivity analysis when data were uncertain or indications were controversial. The final decision tree had over 400 branches.

According to the guidelines, 52% of cancer patients had an indication for at least one course of radiotherapy. This benchmark has been used by state and commonwealth governments to plan cancer services and determine where they would be placed. The benchmark has also been used in Europe and in the developing world by IAEA. A similar study examined chemotherapy and found that 49% of cancer patients needed at least one course of chemotherapy. We have extended these methods to other treatment modalities and to estimate survival benefits for populations.

There is a lot of information in routinely collected data which has larger numbers but fewer details than prospective studies. By pooling records of 60,000 patients from three radiation oncology departments, we were able to analyse the patterns of retreatment by radiotherapy for the first time. Administrative data has been useful in reviews of cancer services that I have conducted in most Australian states, and for some developing countries such as Papua New Guinea and the Seychelles. There is enormous variation in the provision of basic cancer services between Australian states. By combining the evidence-based benchmarks, workforce and activity data, it is apparent that large parts of Australia are under-resourced and that there are major workforce shortages. Our review of access to radiation oncology in the Northern Territory has resulted in the establishment of the Alan Walker Cancer Centre in Darwin in 2010. A similar review in Burnie Tasmania has also prompted funding for the development of a cancer centre.

I developed a strategic plan for research in South West Sydney Area Health Service in 2007 and was appointed Research Director. Over the last five years, we have established the Ingham Institute for Applied Medical Research and received $47 million for research facilities at Liverpool, including a five-story research building, a state-of-the-art Clinical Skills and Simulation Centre and $9 million for a research linear accelerator.

The Ingham Institute for Applied Medical Research was officially opened by the Prime Minister, Julia Gillard, on the 23rd October 2012. It comprises three floors of laboratories, two floors of offices for ‘dry’ research, a clinical trials area and a state-of-the art animal house.

The research accelerator is a collaboration of seven universities to produce a prototype MRI-guided accelerator. It is one of only three in the world. We recently received $5.7 million program funding from the National Health and Medical Research Council. MRI will allow us to image the tumour and normal tissues during radiotherapy for the first time. Magnetic Resonance Spectroscopy can be used for the first time for real-time physiological targeting and to non-invasively investigate biological changes during a course of treatment.

Over the last 30 years, since I began working in oncology, we have seen an enormous increase in the survival after a diagnosis of cancer. In the early 80s, the five-year survival was about 45%. Now it is over 66%. In the 80s you were more likely to die if you were diagnosed with cancer. Now, two out of three people are cured. Those who are not cured live longer and better with fewer side-effects. Our work on benchmarks shows that there have been a large number of improvements for small groups of patients that all together add up to big changes. It has also demonstrated that although Australia has some of the highest survival from cancer in the world, we could do even better if we had greater application of our current knowledge. This work has underpinned the establishment of a series of comprehensive cancer centres. By next century, I hope that people will look at the cancer centres we have built in the same way that we now view tuberculosis sanatoriums; historical monuments to a disease whose threat has faded.
THE TOM Reeve Award For Outstanding Contributions to Cancer Care

The Tom Reeve Award for Outstanding Contributions to Cancer Care, offered annually by the Clinical Oncological Society of Australia, formally recognises a national leader who has made a significant contribution to cancer care.

Since its inception in 2005 where the inaugural award was presented to Professor Tom Reeve himself, there have been seven recipients of this prestigious award. In 2012 the winner of the Tom Reeve Award was Professor David Ball MBBS FRANZCR, a highly respected radiation oncologist and Deputy Director, Division of Radiation Oncology and Cancer, and Imaging Chair, Lung Service, Peter MacCallum Cancer Centre, Victoria.

Professor Ball delivered an oration at the COSA Annual Scientific Meeting in Brisbane on 14 November 2012 paying homage to the individuals whose guidance and leadership influenced his career. His oration can be read below.

I am deeply honoured to have been selected for this award, one of the summits of my professional life. It is a proud moment for me, for my family, for radiation oncology and for all my colleagues at Peter Mac, across the country, and around the world. Without their collaboration and support I would not be standing here tonight. When I read through the list of the previous winners of this award, I am humbled to be considered worthy of it, alongside people for whom I have the greatest respect and admiration, such as Lester Peters and Tom Reeve himself. I once heard leadership defined as the ability to get people to do things that they would not otherwise have done, and I could not think of a better example of this than Tom Reeve. His leadership in the development of clinical guidelines

THE LAYing ON OF HANDS: APOSTOLIC SUCcession IN ONCOLOGY

David Ball
Deputy Chair, Radiation Oncology
Peter MacCallum Cancer Centre, Melbourne, Australia
Email: david.ball@petermac.org

I am deeply honoured to have been selected for this award, one of the summits of my professional life. It is a proud moment for me, for my family, for radiation oncology and for all my colleagues at Peter Mac, across the country, and around the world. Without their collaboration and support I would not be standing here tonight. When I read through the list of the previous winners of this award, I am humbled to be considered worthy of it, alongside people for whom I have the greatest respect and admiration, such as Lester Peters and Tom Reeve himself. I once heard leadership defined as the ability to get people to do things that they would not otherwise have done, and I could not think of a better example of this than Tom Reeve. His leadership in the development of clinical guidelines
AWARDS

has been one of the major achievements in attempting to standardise cancer care in Australia according to the principles of evidence-based practice. His powers of persuasion are legendary, and he is much admired for his broad clinical knowledge, as well as his skill and tact in medical diplomacy. I can also vouch for the fact that he is a wonderful dinner companion with his wide ranging and entertaining conversation on all manner of subjects. The reverence accorded Tom by his peers was evident in the large attendance and wonderful presentations at a festschrift held in his honour at Sydney University in 2010. Figure 1 shows a photograph of Tom, his wife and myself at that memorable event. The fact that this award is named after Tom makes it all the more significant for me.

Figure 1: Tom and Mary Jo Reeve with the author, University of Sydney 2010.

I would like to give thanks to the Clinical Oncological Society of Australia (COSA) and those who nominated me for this award. I have a long association with COSA, having been a member for over 30 years, and having served on Council and the organising committee of the annual meeting among other activities. I first attended COSA in 1974 as a young registrar; I think it was the second ever meeting, held in Melbourne, and it was a revelation for me to hear surgeons and oncologists vigorously debating the merits of various treatments at a time when the evidence for most interventions was either weak or non-existent. It was remarkable because at that time multidisciplinary care did not exist, and for us in radiation oncology, the surgeons and emerging medical oncologists were then often regarded as ‘the opposition’ rather than collaborators. That has always been the great strength of COSA, that it is the only society bringing together in the one room all the craft groups, medical and allied health, involved in the care of cancer patients, and long may the society prosper in this endeavour.

Apostolic succession

The laying on of hands refers to the symbolic ritual in the church of physical connection through hands, indicating the passing on of religious authority. In this way, today’s bishops and priests can trace their lineage back to Christ and his apostle Peter in an unbroken line, the so-called apostolic succession. I am not a spiritual person, but I like to think that similar lines of succession also occur in the scientific world, and although not rich with the physical symbolism of the church, the passing on of influence of great teachers and thinkers also merits the title laying on of hands. I am deeply affected and humbled by this notion, that great men and women have touched on my own life, sometimes closer than one thinks. In this oration, to illustrate my point, I will focus on three of my teachers with connections to major figures in 20th century medicine.

Peter Last OAM and RJ Last

My start in oncology really owes everything to Peter Last, a dynamic general physician and teacher, who first pointed me in the direction of radiation oncology when I sought career advice working as a second year HMO at the Repatriation General Hospital, Daw Park in Adelaide in 1972. Our diagnostic tools were then much more limited than they are today – we had no CT or MRI or PET scanners – so the physical manifestations of disease assumed great importance. The famous Canadian physician, Sir William Osler, is quoted as having said: “One finger in the throat and one in the rectum makes a good diagnostician.” Peter Last was the quintessential bedside diagnostician. More than anyone else he emphasised to me that the laying on of hands was a critical part of the diagnostic process, to learn for example if a lymph node was rubbery or rock hard. Was it fixed or mobile? Was it hot? Was it tender? These are features of a lump that you will not find in a radiologist’s report. Peter Last thus fully opened for me the door to the fascinating and exciting world of physical diagnosis. His teaching rounds were justly famous for unforgettable teaching moments, and I give you one example.

A patient with neurofibromatosis and the associated characteristic pigmented skin changes known as café au lait spots was chosen as a short case. Dr Last’s questions would come quickly: What does it mean – café au lait? (Such a lovely euphonious phrase!) Are the spots ‘coast of Maine’ (irregular margins) or ‘coast of Florida’ (smooth margins)? This short but typical episode thus combined medicine, language and geography, and was only one of many I have never forgotten.

So where does Peter Last fit into the line of succession that I initially referred to? Peter’s father Ray was an Adelaide medical graduate who completed surgical training in the UK, and was for a while physician to Haile Selassie, the emperor of Abyssinia. That in itself is almost enough to make someone famous, but he went on to become the Professor of Anatomy at the Royal College of Surgeons in London. There he gave brilliant and memorable lectures.
which I am told stimulated his audience, even though anatomy is one of the most boring subjects in the medical curriculum.

He also wrote and personally illustrated his legendary textbook Anatomy Regional and Applied, which unlike Gray’s famous textbook, for the first time made anatomy relevant to practice, rather than a dry academic compendium of facts. Last’s Anatomy is now in its 12th edition, has been translated into other languages, and there is no way of measuring the size of the indirect but beneficial effect it has undoubtedly had on human health, but it would have to be large. The skill to impart knowledge is clearly in the Last bloodline, and a marvellous gift. I was reminded recently that doctor is derived from the Latin and means teacher. Last father and son justifiably deserved to be called doctor.

Sir R Douglas Wright AK and Lord Florey

Peter Last was one of my referees for the job as a radiation oncology registrar at Peter Mac. When I began there on the 19th of March 1973, the first person I met was the medical director, R Douglas Wright, known universally as ‘Pansy’. Pansy had recently taken up the role of Medical Director at Peter Mac, after retiring as the Professor of Physiology at the University of Melbourne. As well as being a distinguished physician, he was also a trained surgeon and pathologist, and could have had an outstanding career in any of those specialties. He subsequently became the Chancellor of the University of Melbourne. He was also the last person to become a knight in the Order of Australia. He took it on himself to tutor me in anatomy for my first part exam, and we would meet each week, sometimes going to the anatomy museum at the University for one-on-one tutorials. In the event, we talked about many things, but not a lot about anatomy. He had an unassuageable curiosity, and encouraged thinking outside the box. He was also a formidable medical politician and institution builder – the Howard Florey Institute of Experimental Physiology at the University of Melbourne and the Australian National University in Canberra are largely the result of his lobbying and planning. Pansy was also the most politically incorrect man I have met, with a ribald and sometimes sexist sense of humour. He was once described as half-caveman, half genius.

There are many, many anecdotes about Pansy, and most of them would not be suitable for polite company, so I am restricting myself to one example. During his impenetrable physiology lectures, he was given to asking questions which required the lateral thinking he sought to encourage in his students. An example of one of these questions was: During the act of urination, which muscles does a man use to get rid of the last few drops of urine? So while the students are trying to recall the anatomy of the muscles of the pelvic floor, that is no use at all. Pansy’s answer is, of course, the muscles of the thumb and forefinger! Those interested in Pansy’s life are advised to read Peter McPhee’s excellent biography, which contains many more stories of a similarly ribald nature.

I mentioned the Florey Institute, which was named in honour of Sir Howard, later Lord Florey, with whom Pansy had worked in Oxford during 1937-9. Florey was Pansy’s most important mentor, and they maintained a long and close friendship. Florey was a graduate of the University of Adelaide, my alma mater. Florey’s name is always associated with the development of penicillin for which work he received the Nobel Prize in Medicine in 1945, together with Fleming and Chain. One estimate is that these discoveries have saved over six million lives, an achievement which most medical researchers would aspire to, but about which they can only dream.

H Rodney Withers AO and Harold Gray

The next person I wish to pay tribute to is a Queenslander, Rod Withers, who has had a major influence on the international practice of radiation oncology through his astute observations in clinical radiobiology. For much of his professional life, Rod had been based in the US, but I encountered him regularly on his frequent trips to Australia for scientific meetings such as COSA or the Royal Australian and New Zealand College of Radiologists, and he in fact spent a sabbatical at Peter Mac in 2006. He has been a wonderful supporter of and ambassador for Australian radiation oncology.

One of Rod’s greatest contributions was his discovery of the phenomenon of accelerated repopulation that occurs in some cancers during treatment. This was an astonishing insight at the time, namely that some cancers, while visibly shrinking in size during treatment, are in fact growing at a faster rate. How can something that is getting smaller be growing faster? This paradoxical phenomenon is now scientifically well established and has had major implications for how we treat patients, whether with radiotherapy, surgery or chemotherapy, but at the time it was hard to believe. I would also point out that these findings were not a result of molecular biology or laboratory work, but came from careful clinical observation, and the remarkable ability to see what others could not.

The unit of absorbed radiotherapy dose is of course the gray, and it was named after Hal Gray who first described it. There can be few greater accolades than to have an SI unit of measurement named in your honour. Gray was an eminent physicist, who subsequently branched into studying the effects of radiation on living tissues, so becoming an autodidact, as many of the original radiobiologists were. In addition to the development of ionisation chambers to measure radiation dose, his achievements also included the demonstration of relative biologic effectiveness of neutron irradiation, and early work on the resistance of hypoxic cells to radiotherapy. Although he fostered many careers, Gray only ever had one graduate student - Rod Withers - whose PhD he supervised.

The laying on of hands

In the Hermitage Museum in St Petersburg there hangs a late work by Rembrandt, ‘Return of the prodigal son’, in which the father welcomes home his wastrel son by
laying his hands softly on the shoulders of the young man who kneels before him.\textsuperscript{3}

As with so many of Rembrandt’s works, the human emotions of the moment are powerfully conveyed. It is hard to imagine that human tenderness has been more lovingly captured in art than in this beautiful painting. In many ways, the patients with lung cancer who have been the focus of my professional life for over 30 years are prodigal sons and daughters. Scorned and stigmatised within society because of the association with smoking, and neglected by funding agencies, lung cancer sufferers have carried the greatest brunt and burden of suffering of all cancer diagnoses.

Within the Lung Service at Peter Mac, we have worked hard to improve the outcomes from lung cancer, and there is evidence that we are making some modest gains. When I began in the Lung Service, to consider just one metric, the five year survival for our patients treated for cure with radiotherapy was under 10%.\textsuperscript{4} Now it is 30%.\textsuperscript{5}

Now as far as I know, neither Last senior, Florey nor Gray ever treated or had much to do with patients with lung cancer, but I am an incurable romantic and I would like to think, somewhat fancifully and very presumptuously, that there is a tiny bit of their touch, their influence, however indirectly, in the improvements that my team have achieved with this tough disease in the last 25 years.

I am sorry that I have not mentioned a single woman, but the demographic of the medical workforce was very different in my formative years to what it is now. It is a wonderful thing to see women who represent 50% of our country’s available brainpower – some would say considerably more than 50% – now playing such important roles in medical life, and joining the line of succession, many of them my former registrars who are now consultants and unit heads.

And in my own life the women are there of course because, as they say, behind every successful man there is usually a very surprised woman. I would like to acknowledge the love and support my wife Mary and our family have given and continue to provide. Without them, there would have been a different orator this evening.

References

3. The Hermitage Museum [Internet]. Available from: http://www.hermitagemuseum.org/html_En/08/htm88_0_1_44_0.html
The state and territory Cancer Councils, which comprise the member bodies of Cancer Council Australia, are the major sponsors of cancer research and related activities in Australia. Grants are made following competitive, peer-reviewed assessment of funds derived from donations and bequests.

In 2013, the value of these grants is more than $54 million.

Please note: for research grants spanning more than one year, only funds to be dispersed in 2013 have been included.

### CANCER COUNCIL WA

#### Research Project Grants 1st Year of Funding

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<td>Lawrence Abraham</td>
<td>The University of Western Australia</td>
<td>Mechanism of action of thalidomide</td>
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<td>Georgia Halkett</td>
<td>Curtin Health Innovation Research Institute</td>
<td>Confidence to care: A randomised controlled trial of structured home-based support and education for carers of people with high grade glioma</td>
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<td>Evan Ingley</td>
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<td>Control of nuclear/cytoplasmic shuttling by Liar/AnkRD54</td>
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<td>Targeting FLT3 kinase activity to treat haemopoietic neoplasms</td>
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<td>Peter Leedman</td>
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<td>Using a microRNA to treat cancer</td>
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<td>Robert McLaughlin</td>
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<td>Pre-operative assessment of neoadjuvant therapy for breast cancer using optical coherence tomography</td>
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<td>Fiona Pixley</td>
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<td>Targeting CSF-1-induced macrophage migration to inhibit tumour invasion and metastasis</td>
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<td>Cameron Platell</td>
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<td>Predicting response to neo-adjuvant chemo-radiotherapy in patients with resectable rectal cancer</td>
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<td>George Yeoh</td>
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<td>Elucidating the cellular and molecular mechanisms which link liver progenitor cells, inflammation and hepatocellular carcinoma</td>
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#### Research Project Grants 2nd Year of Funding

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<td>David Joseph</td>
<td>Sir Charles Gairdner Hospital</td>
<td>Verification of long-term outcomes of the randomised TARGIT trial: TARGETed Intraoperative radioTherapy for early breast cancer</td>
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<td>Cleo Robinson</td>
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<td>A high fidelity model of malignant mesothelioma</td>
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**Total Research Project Grants**

$1,026,636

### Early Career Investigator Grants

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<td>Targeted medical imaging: the future of medical diagnostics</td>
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<td>Alison McDonnell</td>
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<td>Malignant pleural effusion: tracking anti-tumour immunity at the effector site</td>
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<td>Robert White</td>
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<td>Engineering tools to repress MYCN in Neuroblastoma</td>
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<td>Novel gene regulation targets for cancer therapy</td>
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<td>Occupational cancer epidemiology</td>
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<td>Improved intra-operative breast cancer imaging with OCT</td>
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<td>Steven Mutsaers</td>
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<td>Anna Johansson</td>
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<td>Targeting of LIGHT to tumour vessels for anti-cancer combination therapy</td>
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<tr>
<td>Claire Johnson</td>
<td>The University of Western Australia</td>
<td>A program of research to optimise quality of care for people with cancer and their families: A peer review framework to promote best practice in multi-disciplinary cancer teams in Australia</td>
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<td>Benjamin Hug</td>
<td>The University of Western Australia</td>
<td>Advanced radiotherapy techniques - development and modelling of advanced radiation guided technologies</td>
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<td>Adam Passman</td>
<td>The University of Western Australia</td>
<td>Establishing the molecular and genetic mechanisms of liver progenitor cell transformation and whether these are linked to hepatocellular carcinoma development in vivo</td>
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<td>Samuel Taylor</td>
<td>The University of Western Australia</td>
<td>Tyrosine kinase inhibitors for treating c-Cbl and Flt3-driven leukaemias</td>
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<td>Philip Hardy</td>
<td>The University of Western Australia</td>
<td>Identifying chromosomal and molecular aberrations that correlate to various stress events in human and mouse liver models</td>
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### Total PhD Top Up Scholarships

**$38,000**

### Honours Scholarships

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<tr>
<td>Ayeesha Arshad</td>
<td>The University of Western Australia</td>
<td>Dysregulated cell signalling in megakaryocytes contributes to thromboses in myeloproliferative neoplasms</td>
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<tr>
<td>Britt Clynick</td>
<td>The University of Western Australia</td>
<td>Molecular characterisation of squamoproliferative lesions arising in the setting of BRAF inhibition</td>
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<td>Sarah Lacey</td>
<td>Murdoch University</td>
<td>The effects of adoptive cell therapy on anti-tumour immunity</td>
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<tr>
<td>Jacques Malherbe</td>
<td>The University of Western Australia</td>
<td>Mutation profiling of megakaryocytes in myeloproliferative neoplasms</td>
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### Total Honours Scholarships

**$30,000**

### Vacation Scholarship

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<tr>
<td>Jennifer Currenti</td>
<td>The University of Western Australia</td>
<td>Molecular mechanism of breast cancer metastases to bone</td>
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<td>Sara-Jane Laurensen</td>
<td>Curtin University of Technology</td>
<td>Paediatric Multislice CT Scanning: Are the scanning protocols optimised for paediatric patients?</td>
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<td>Anna MacTiernan</td>
<td>The University of Western Australia</td>
<td>Western Australian adults’ perceptions of cancer risk factors</td>
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<td>Claire McLaughlin</td>
<td>WA Institute of Medical Research</td>
<td>Establishing a novel role for the metalloprotease ADAM28 in human prostate cancer</td>
<td>$3,000</td>
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<tr>
<td>Kelvin Oo</td>
<td>The University of Western Australia</td>
<td>Analysis of the implementation of multi-disciplinary team decisions in breast cancer</td>
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<tr>
<td>Win Myo Thaw</td>
<td>The University of Western Australia</td>
<td>The role of WFDC1/ps20 in intercellular communication within the basic multicellular units in bone</td>
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<td>Douglas Velho</td>
<td>The University of Western Australia</td>
<td>The preparation of thalidomide analogues for the treatment of liver cancer</td>
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### James Crofts Hope Foundation Vacation Scholarship

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<th>Amount</th>
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<tbody>
<tr>
<td>Arosha Dissanayake</td>
<td>The University of Western Australia</td>
<td>Prognostic factors for survival in high grade glioma - analysis of the Australian Genomics and Clinical Outcomes of Glioma (AGOG) questionnaire</td>
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### Total Vacation Scholarships

**$24,000**

### John Nott Travel Grant

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<thead>
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<tbody>
<tr>
<td>Dr Alan Kumar</td>
<td>Cancer Science Institute of Singapore</td>
<td>Collaboration with researchers at UWA on the project: RNA helicase DDX20 (DP103, Gemin3), a novel prognostic/chemoresponse marker and potential therapeutic target in colorectal cancer (West Australian patients)</td>
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### Total John Nott Travel Grant

**$5,000**

### Professorial Chairs

| Chair of Behavioural Cancer Research | Centre for Behavioural Research & Cancer Control (Curtin) | $160,000  |
| Chair of Clinical Cancer Research  | School of Medicine & Pharmacology (UWA)                  | $331,354  |
| Chair of Palliative and Supportive Care | School of Nursing & Midwifery (ECU)                      | $115,000  |

### Total Professorial Chairs

**$606,354**

### Other Research Grants

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<tr>
<th>Grant Name</th>
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<tr>
<td>Bone Tumour Registry</td>
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<td>$5,000</td>
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<tr>
<td>Cancer Council Crawford Rural Cancer Research Initiative</td>
<td>A partnership intervention trial to redress treatment delay and improve outcomes in rural cancer patients</td>
<td>$90,000</td>
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</table>
### Priority-driven Collaborative Cancer Research Scheme
- **Strategic Research Partnership (STREP)**
  - To improve cancer control for Indigenous Australians
  - **Amount:** $100,000
- **Travel Grants**
  - **Amount:** $15,000

### Total Other Research Grants
**Amount:** $254,280

**TOTAL RESEARCH FUNDED**
**Amount:** $2,881,209

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#### CANCER COUNCIL QLD

**Research Project Grants 2013-2014**

**2013 Funding**

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Project Title</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Maher Gandhi</td>
<td>Queensland Institute of Medical Research</td>
<td>Monocytic myeloid derived suppressor cells and antiCD20-antibody dependent cellular cytotoxicity in diffuse large B-cell lymphoma</td>
<td>$99,891</td>
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<tr>
<td>Stephen Rose</td>
<td>University of Queensland</td>
<td>Understanding radiation insensitivity and temozolomide resistance in Glioblastoma Multiforme</td>
<td>$99,920</td>
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<tr>
<td>Gregory Monteith</td>
<td>University of Queensland</td>
<td>Identification and characterisation of calcium signalling modifying proteins as drug targets for basal breast cancer</td>
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<tr>
<td>Mat Francois</td>
<td>University of Queensland</td>
<td>Inhibitors of SOX18 transcription factor: from developmental biology to pre-clinical trial of novel anti-metastatic compounds</td>
<td>$100,000</td>
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<tr>
<td>Helen Blanchard</td>
<td>Griffith University</td>
<td>Design of specific chemical probes to target and inhibit galectin-3</td>
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<tr>
<td>Kum Kum Khanna</td>
<td>Queensland Institute of Medical Research</td>
<td>Role of FBXO31-mediated protein degradation in mitotic progression</td>
<td>$100,000</td>
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<tr>
<td>Susan Jordan</td>
<td>Queensland Institute of Medical Research</td>
<td>Patterns of care in renal cell carcinoma</td>
<td>$94,127</td>
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<tr>
<td>Thomas Gonda</td>
<td>University of Queensland</td>
<td>Targeting Myb transcriptional elongation in cancer</td>
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<tr>
<td>Graham Leggatt</td>
<td>University of Queensland</td>
<td>Immunotherapy of non-melanoma skin cancer and their precancerous lesions during lymphopenia</td>
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<tr>
<td>Melissa Brown</td>
<td>University of Queensland</td>
<td>The role of BRCA non-coding mutations in breast cancer susceptibility</td>
<td>$94,891</td>
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<tr>
<td>Pamela Pollock</td>
<td>Queensland University of Technology</td>
<td>Mechanisms of resistance to FGFR inhibition in endometrial cancer</td>
<td>$100,000</td>
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<tr>
<td>Judith Clements</td>
<td>Queensland University of Technology</td>
<td>Kallikrein proteases have key roles in tumour cell aggregation in ascites and chemoresistance in epithelial ovarian cancer</td>
<td>$100,000</td>
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<tr>
<td>Jermaine Coward</td>
<td>Mater Medical Research Institute</td>
<td>Targeting inflammatory pathways in epithelial ovarian cancer</td>
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<tr>
<td>Stephen Wood</td>
<td>Griffith University</td>
<td>Dissecting Usp9x’s tumour suppression function in pancreatic ductal adenocarcinoma</td>
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<td>Graeme Walker</td>
<td>Queensland Institute of Medical Research</td>
<td>In vivo functional dissection of the respective roles of the CDKN2A and MTAP loci in naevus susceptibility</td>
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<tr>
<td>Nigel McMillan</td>
<td>Griffith University</td>
<td>Nanoparticle mucosal delivery systems for siRNA-based cancer therapies</td>
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<td>Benjamin Hogan</td>
<td>University of Queensland</td>
<td>A novel mechanism regulating lymphatic vascular precursor cell migration</td>
<td>$99,891</td>
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<tr>
<td>Name</td>
<td>Institution</td>
<td>Title</td>
<td>Funding</td>
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<td>Andreas Moeller</td>
<td>Queensland Institute of Medical Research</td>
<td>Regulation of the pre-metastatic niche by hypoxia</td>
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<tr>
<td>Jiri Neuzil</td>
<td>Griffith University</td>
<td>How to efficiently treat resistant breast cancer</td>
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<tr>
<td>Fiona Simpson</td>
<td>University of Queensland</td>
<td>The role of epidermal growth factor receptor trafficking in tumor</td>
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<tr>
<td>John Hooper</td>
<td>Mater Medical Research Institute</td>
<td>A novel Src regulated protease activated signalling pathway in</td>
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<tr>
<td>Martin Lavin</td>
<td>Queensland Institute of Medical Research</td>
<td>Role of ATM-dependent Mre11 Phosphorylation in the DNA damage</td>
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<tr>
<td>Helen Blanchard</td>
<td>Griffith University</td>
<td>Design of inhibitors targeting the tumour promoting protein Galectin-1</td>
<td>$99,725</td>
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<tr>
<td>Glen Boyle</td>
<td>Queensland Institute of Medical Research</td>
<td>Does &quot;phenotype-switching&quot; control melanoma proliferation, invasion</td>
<td>$99,548</td>
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<tr>
<td>Melissa Brown</td>
<td>The University of Queensland</td>
<td>Transcriptional regulation of non-code RNA genes implicated in breast cancer</td>
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<tr>
<td>Russ Chess-Williams</td>
<td>Bond University</td>
<td>Cytotoxic drugs, urothelial function and the ageing bladder</td>
<td>$89,593</td>
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<tr>
<td>Judith Clements</td>
<td>Queensland University of Technology</td>
<td>Kallikrein proteases are key players in the ovarian tumour-stroma</td>
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<tr>
<td>Margaret Cummings</td>
<td>The University of Queensland</td>
<td>Re-defining the molecular evolution of breast cancer and its precursors</td>
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<tr>
<td>Camile Farah</td>
<td>The University of Queensland</td>
<td>Oral epithelial stem cell markers as a platform for better diagnosis of mouth cancer</td>
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<td>Kwun Fong</td>
<td>The University of Queensland</td>
<td>Detection of treatment-responsive lung cancer mutations</td>
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<td>Brian Gabrielli</td>
<td>The University of Queensland</td>
<td>Defining a response to UV exposure that is defective in melanoma</td>
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<td>Sandi Hayes</td>
<td>Queensland University of Technology</td>
<td>LEGS follow-up: Lymphoedema Evaluation following Gynaecology Cancer Study</td>
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<td>Nick Hayward</td>
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<td>Characterisation of novel melanoma susceptibility genes through whole-genome sequencing</td>
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<td>Tanya Holt</td>
<td>Princess Alexandra Hospital</td>
<td>SCORAD III -- a randomised phase III trial comparing the effect on ambulation rate of single fraction radiotherapy to multifraction radiotherapy in patients with metastatic spinal cord compression</td>
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<td>John Hooper</td>
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<td>A novel molecular pathway in cancer</td>
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<td>Barbara Leggett</td>
<td>Queensland Institute of Medical Research</td>
<td>Molecular and clinical features of serrated adenomas that predict risk of malignant transformation and risk of development of further polyps</td>
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<td>Michael McGuckin</td>
<td>Mater Medical Research Institute</td>
<td>Targeting MUC13 to sensitize colorectal cancer cells to apoptosis</td>
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<td>Peter Mollee</td>
<td>Princess Alexandra Hospital</td>
<td>Catheter-related bloodstream infections in adults with cancer: a prospective randomised controlled trial</td>
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<tr>
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<td>Pamela Pollock</td>
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<td>Genomic analysis of serous endometrial cancer and development of in vitro and in vivo models</td>
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<td>Nicholas Saunders</td>
<td>The University of Queensland</td>
<td>Dysregulated H3K27me3 contributes to differentiation-insensitivity and squamous cell carcinoma development</td>
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<td>Andreas Suhrbier</td>
<td>Queensland Institute of Medical Research</td>
<td>The function of Sin1 isoforms in mTORC2 and Ras signalling</td>
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<td>Graeme Walker</td>
<td>Queensland Institute of Medical Research</td>
<td>An ultraviolet radiation-induced inflammatory response involving infiltrating macrophages drives melanocyte proliferation and triggers melanoma development</td>
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<td>Ingrid Winkler</td>
<td>Mater Medical Research Institute</td>
<td>Characterisation and manipulation of bone marrow niche factors regulating Myeloid Leukaemia Stem Cell fate</td>
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<td>Chengzhong Yu</td>
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<td>Novel photodynamic therapy for targeted skin cancer treatment: an integrated bionanotechnology</td>
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<td>Michael Kimlin</td>
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<td>Nicholas Saunders</td>
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<td>Kelli MacDonald</td>
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<td>Graeme Walker</td>
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<td><strong>John McCaffrey Senior Clinical Research Fellowship</strong></td>
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<td>Maher Gandhi</td>
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<td><strong>2013-2015</strong></td>
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<tr>
<td>Nicholas Ashton</td>
<td>Queensland University of Technology</td>
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<td><strong>Joint Cancer Council Queensland / Griffith University PhD Scholarship 2013-2015</strong></td>
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<tr>
<td>Mary Minhuta</td>
<td>Griffith University</td>
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<td><strong>2012-2014</strong></td>
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<tr>
<td>Marissa Daniels</td>
<td>The University of Queensland</td>
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<td>Mark Bettington</td>
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<td><strong>2011-2013</strong></td>
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<tr>
<td>Donald McLeod</td>
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<td>Bryony Thompson</td>
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<td>Australian paediatric cancer registry</td>
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<td><strong>Other grants total</strong></td>
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## Clinical trial data manager grants

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<th>Department(s)</th>
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<tr>
<td>Brisbane Colorectal Group</td>
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<tr>
<td>Cairns Hospital</td>
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<tr>
<td>Gold Coast Hospital</td>
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<tr>
<td>HOCA Research Centre</td>
<td></td>
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<tr>
<td>Holy Spirit Northside</td>
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<tr>
<td>Mater Health Services</td>
<td>Oncology</td>
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<tr>
<td></td>
<td>Palliative Care</td>
</tr>
<tr>
<td>Nambour Hospital</td>
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<tr>
<td>Premion</td>
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<tr>
<td>Prince Charles Hospital</td>
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<tr>
<td>Princess Alexandra Hospital</td>
<td>Surgery</td>
</tr>
<tr>
<td></td>
<td>Haematology and medical oncology</td>
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<td>Oncology</td>
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<td>Radiation oncology department</td>
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<td>Queensland Children’s Cancer Centre</td>
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<tr>
<td>Radiation Oncology Services</td>
<td>Mater Centre</td>
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<tr>
<td>Royal Brisbane and Women’s Hospital</td>
<td>Gynaecology</td>
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<td></td>
<td>Medical oncology</td>
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<td>Radiation oncology</td>
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<tr>
<td>Toowoomba Regional Cancer Research Centre</td>
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<td>Townsville Hospital</td>
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<tr>
<td>Wesley Research Institute</td>
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**Clinical trial data manager grants total**: $1,228,680

## Epidemiology and psycho-oncology research programs

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<td>Prostate cancer and supportive care outcomes trial</td>
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<tr>
<td>Prostate cancer sexuality intervention</td>
</tr>
<tr>
<td>Trial of mindfulness intervention for men with advanced prostate cancer</td>
</tr>
<tr>
<td>ProsiCan for Life</td>
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<tr>
<td>Breast Cancer Outcomes Study</td>
</tr>
<tr>
<td>Lung Cancer and Stigma Study</td>
</tr>
<tr>
<td>Chemobrain Study</td>
</tr>
<tr>
<td>Descriptive Epidemiology Reports</td>
</tr>
<tr>
<td>Geographical Inequalities in Cancer Survival</td>
</tr>
</tbody>
</table>

**Epidemiology and psycho-oncology research programs total**: $2,681,964

**TOTAL RESEARCH FUNDED**: $9,399,886
### New Research Project Grants (2013)

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Title</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Minoti Apte</td>
<td>University of NSW</td>
<td>Targeting the stroma in pancreatic cancer - a novel therapeutic approach focusing on the hepatocyte growth factor/c-MET pathway</td>
<td>$120,000</td>
</tr>
<tr>
<td>Dr Tao Liu</td>
<td>University of NSW</td>
<td>The critical role of the long intergenic noncoding RNA MALAT1 in neuroblastoma</td>
<td>$118,551</td>
</tr>
<tr>
<td>A/Prof Janette Vardy</td>
<td>University of Sydney</td>
<td>Evaluation of a Web-based Cognitive Rehabilitation Programme in Cancer Survivors with Self-reported Cognitive Impairment</td>
<td>$106,094</td>
</tr>
<tr>
<td>A/Prof Deborah Marsh</td>
<td>University of Sydney</td>
<td>Monoubiquitinated histone H2B – marking key pathways in ovarian cancer</td>
<td>$89,891</td>
</tr>
<tr>
<td>Prof Markus Seibel</td>
<td>University of Sydney</td>
<td>Novel Cytoplasmic Functions of the Vitamin D Receptor in Bone Metastases</td>
<td>$119,891</td>
</tr>
<tr>
<td>Dr Megan Hitchins</td>
<td>University of NSW</td>
<td>Genetic determination of hereditary MLH1 epimutation as a cause for familial cancer</td>
<td>$119,891</td>
</tr>
<tr>
<td>Dr Elena Shklovskaya</td>
<td>University of Sydney</td>
<td>Role of dendritic cell subsets in regulating CD4 T cell memory responses in inflammation and cancer</td>
<td>$119,061</td>
</tr>
<tr>
<td>A/Prof Lisa Horvath</td>
<td>Garvan Institute</td>
<td>Novel strategies to overcome Docetaxel resistance in castration-resistant prostate cancer (CRPC)</td>
<td>$120,000</td>
</tr>
<tr>
<td>Prof Samuel Brent</td>
<td>University of NSW</td>
<td>The role of the TGF-b superfamily cytokine MIC-1/GDF15 in cancer growth and spread</td>
<td>$119,551</td>
</tr>
<tr>
<td>Dr Linda Bendall</td>
<td>University of Sydney</td>
<td>Sphingosine Kinases as Potential Therapeutic Targets for Acute Lymphoblastic Leukemia</td>
<td>$120,000</td>
</tr>
<tr>
<td>A/Prof Xu Dong Zhang</td>
<td>University of Newcastle</td>
<td>Functional consequences of epigenetic repression of PIBSPA in melanoma</td>
<td>$119,750</td>
</tr>
<tr>
<td>Prof Christine Clarke</td>
<td>University of Sydney</td>
<td>Determinants of genomic binding of the progesterone receptor in endocrine target cells</td>
<td>$120,000</td>
</tr>
<tr>
<td>Dr Nickolas Haass</td>
<td>University of Sydney</td>
<td>Effect of three-dimensional tumour organisation on the sensitivity of individual melanoma cells to endoplasmic reticulum stress</td>
<td>$119,891</td>
</tr>
<tr>
<td>Dr Kerrie McDonald</td>
<td>University of NSW</td>
<td>The biological basis of success or failure to the anti-VEGF agent, bevacizumab in patients with recurrent glioblastoma</td>
<td>$117,422</td>
</tr>
<tr>
<td>Prof Edna Hardeman</td>
<td>University of NSW</td>
<td>The role of epigenetic modifications in longterm memory of irradiation in cancer survivors</td>
<td>$120,000</td>
</tr>
<tr>
<td>A/Prof Xu Dong Zhang</td>
<td>University of Newcastle</td>
<td>Targeting PP2A to improve the therapeutic efficacy of mutant BRAF inhibitors in melanoma</td>
<td>$119,750</td>
</tr>
<tr>
<td>A/Prof Tim Price</td>
<td>University of Sydney</td>
<td>PETACC-6: Preoperative chemoradiotherapy and postoperative chemotherapy with capecitabine and oxaliplatin vs. capecitabine alone in locally advanced rectal cancer</td>
<td>$19,624</td>
</tr>
</tbody>
</table>

**Total new research Project Grants** $1,889,367

### 2013 Priority-driven Collaborative Cancer Research Scheme

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Title</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Lorraine O'Reilly</td>
<td>Walter &amp; Eliza Hall Institute of Med. Res</td>
<td>Understanding the role of NF-κB in the progression of gastric adenocarcinomas and assessment of new therapies.</td>
<td>$200,000</td>
</tr>
</tbody>
</table>

**Total new Priority-driven Collaborative Cancer Research** $200,000

### Continuing Priority-driven Collaborative Cancer Research Scheme
<table>
<thead>
<tr>
<th>Researcher</th>
<th>Project Title</th>
<th>Grant Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Kerrie McDonald University NSW</td>
<td>RG 12-09 PdCCRS Mechanisms underpinning how brain cancer cells respond to drugs</td>
<td>$160,000</td>
</tr>
<tr>
<td>A/Prof Gianluca Severi Cancer Council Victoria</td>
<td>RG 12-10 PdCCRS Risk and Prognostic Factors for Glioma in Australia</td>
<td>$40,000</td>
</tr>
<tr>
<td>Prof Anna Nowak University of WA</td>
<td>RG 12-11 PdCCRS Phase III trial of Concurrent &amp; Adjuvant Temozolomide chemotherapy in non-1p/19q deleted anaplastic glioma</td>
<td>$20,736</td>
</tr>
<tr>
<td>Prof Robyn Ward University of NSW</td>
<td>RG 11-17 Role of dietary compounds on PGC 1alpha methylation in colorectal cancer</td>
<td>$97,352</td>
</tr>
</tbody>
</table>

**Total continuing Priority-driven Collaborative Cancer Research** $318,088

### Continuing Research Project Grants

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Project Title</th>
<th>Grant Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Karen Mackenzie University of NSW</td>
<td>RG 11-01 The prognostic and therapeutic significance of dyskerin and telomerase enzyme activity in neuroblastoma</td>
<td>$117,508</td>
</tr>
<tr>
<td>Dr Tao Liu University of NSW</td>
<td>RG 11-02 The critical role of the histone demethylase JMJD1A in cancer</td>
<td>$110,250</td>
</tr>
<tr>
<td>Dr Megan Chircop University of Sydney</td>
<td>RG 11-03 Dyanin as a new drug target for the treatment of glioblastoma</td>
<td>$120,000</td>
</tr>
<tr>
<td>Dr Beric Henderson University of Sydney</td>
<td>RG 11-04 Regulation of APC intracellular dynamics and function</td>
<td>$120,000</td>
</tr>
<tr>
<td>Dr Peter Greer University of Newcastle</td>
<td>RG 11-05 Does the initial treatment plan predict doses delivered to normal tissues during prostate radiation therapy</td>
<td>$116,598</td>
</tr>
<tr>
<td>Dr Philip Vial University of Sydney</td>
<td>RG 11-06 A next generation detector for radiotherapy treatment verification with dual capability for simultaneous imaging and dosimetry</td>
<td>$110,375</td>
</tr>
<tr>
<td>A/Prof Tracy Bryan University of Sydney</td>
<td>RG 11-07 G-quadruplex stabilisers as cancer therapeutics</td>
<td>$97,508</td>
</tr>
<tr>
<td>Prof Finlay Macrae (multi-state Vic) Melbourne Health</td>
<td>RG 11-08 The effects of butyrylated high amylose maize starch on polyposis in FAP volunteers</td>
<td>$111,639</td>
</tr>
<tr>
<td>Prof Rob Baxter University of Sydney</td>
<td>RG 11-09 Targetting IGFBP-3 signalling pathways as a novel therapeutic approach in triple-negative breast cancer</td>
<td>$119,681</td>
</tr>
<tr>
<td>A/Prof Xu Zhang University of Newcastle</td>
<td>RG 11-10 Targeting Pro-Survival Mechanisms to Sensitize Human Melanoma to Immunotherapy</td>
<td>$119,750</td>
</tr>
<tr>
<td>Prof John Rasko University of Sydney</td>
<td>RG 11-11 The role of small non-coding RNAs in alternative splicing</td>
<td>$120,000</td>
</tr>
<tr>
<td>Prof John Rasko University of Sydney</td>
<td>RG 11-12 Dissecting the multi-component machine that controls chromatin architecture</td>
<td>$119,858</td>
</tr>
<tr>
<td>A/Prof Richard Lock University of NSW</td>
<td>RG 11-13 Predicting the in vivo sensitivity of paediatric acute lymphoblastic leukaemia to BH3-mimetic drugs</td>
<td>$109,750</td>
</tr>
<tr>
<td>Dr Viive Howell University of Sydney</td>
<td>RG 11-14 New opportunities for the study of ovarian cancer through characterisation of mouse models</td>
<td>$103,000</td>
</tr>
<tr>
<td>Prof Robyn Ward University of NSW</td>
<td>RG 11-15 Laterally spreading tumours of the colorectum: an alternative pathway of colorectal cancer development in the Western world</td>
<td>$120,000</td>
</tr>
<tr>
<td>Prof Robyn Ward University of NSW</td>
<td>RG 11-16 PdCCRS Role of dietary compounds on PGC 1alpha methylation in colorectal cancer</td>
<td>$107,087</td>
</tr>
<tr>
<td>A/Prof Tracy Bryan University of Sydney</td>
<td>RG 12-01 Involvement of helicase DHX36 in human telomere maintenance</td>
<td>$97,508</td>
</tr>
<tr>
<td>Dr Scott Cohen University of Sydney</td>
<td>RG 12-02 Structure and Inhibition of the Human Telomerase Enzyme complex</td>
<td>$120,000</td>
</tr>
<tr>
<td>Name</td>
<td>University/Institute</td>
<td>Project Title</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Dr Sue Firth</td>
<td>University of Sydney</td>
<td>RG 12-03 IGFBP-3 enhances autophagy to promote breast cancer cell survival during stress</td>
</tr>
<tr>
<td>Dr Beric Henderson</td>
<td>University of Sydney</td>
<td>RG 12-04 Novel regulation of beta-catenin intracellular transport and its role in cell polarity and migration</td>
</tr>
<tr>
<td>Dr Megan Hitchins</td>
<td>University of NSW</td>
<td>RG 12-05 The mechanistic basis for prediction of response to alkylating chemotherapy in high grade glioma patients by molecular markers of MGMT activity</td>
</tr>
<tr>
<td>A/Prof Geraldine O’Neill</td>
<td>University of Sydney</td>
<td>RG 12-06 A Sting in the Tail: Focal Adhesion Targeting and Mechanotransduction</td>
</tr>
<tr>
<td>Dr Nicole Verrills</td>
<td>University of Newcastle</td>
<td>RG 12-07 Activating a tumour suppressor for leukaemia therapy</td>
</tr>
<tr>
<td>Dr Stuart Tangye</td>
<td>Garvan Institute of Medical Research</td>
<td>RG 12-08 Mechanisms underlying impaired anti-EBV and anti-tumour immune responses in the absence of SAP</td>
</tr>
</tbody>
</table>

**Total continuing research Project Grants** $2,726,530

**Continuing Research Program Grants**

<table>
<thead>
<tr>
<th>Name</th>
<th>University/Institute</th>
<th>Project Title</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Roger Reddel</td>
<td>Children’s Medical Research Institute</td>
<td>PG 11-08 Alternative Lengthening of Telomeres: from basic biology to drug discovery</td>
<td>$450,000</td>
</tr>
<tr>
<td>Prof Murray Norris</td>
<td>University of NSW</td>
<td>PG 11-06 Toward cure of childhood ALL: improved diagnostics, therapeutics and prevention strategies</td>
<td>$450,000</td>
</tr>
<tr>
<td>Prof Christopher Ormandy</td>
<td>Garvan Institute of Medical Research</td>
<td>PG 11-07 Personalising breast cancer management by discovering the transcriptional basis for tumour phenotype</td>
<td>$449,992</td>
</tr>
<tr>
<td>Prof Philip Hogg</td>
<td>University of NSW</td>
<td>PG 11-03 Metabolism inhibitors for the treatment of brain and pancreatic cancer</td>
<td>$450,000</td>
</tr>
</tbody>
</table>

**Total continuing research Program Grants** $1,799,992

**New (2013) Strategic Research Partnership Grants**

<table>
<thead>
<tr>
<th>Name</th>
<th>University/Institute</th>
<th>Project Title</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/Prof Gail</td>
<td>Garvey Menzies School of Health Research</td>
<td>Strategic Research Partnership to improve cancer control for Indigenous Australians (STREP Ca-CINDA)</td>
<td>$398,081</td>
</tr>
<tr>
<td>Prof Andrew Grulich</td>
<td>Kirby Institute UNSW</td>
<td>Preventing morbidity and mortality from anal cancer</td>
<td>$403,950</td>
</tr>
<tr>
<td>Dr Gillian Mitchell</td>
<td>Peter MacCallum Cancer Centre</td>
<td>The Inherited Cancer Connect (Icon) Partnership</td>
<td>$391,953</td>
</tr>
</tbody>
</table>

**Total continuing Strategic Research Partnership Grants** $1,193,984

**Continuing Strategic Research Partnership Grants**

<table>
<thead>
<tr>
<th>Name</th>
<th>University/Institute</th>
<th>Project Title</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Andrew Blankin</td>
<td>Garvan Institute of Medical Research</td>
<td>Genotype Guided Cancer Therapy (Genomic Theranostics)</td>
<td>$300,000</td>
</tr>
<tr>
<td>Prof Sanson-Fisher</td>
<td>University of Newcastle</td>
<td>New 3C</td>
<td>$400,000</td>
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</tbody>
</table>

**Total continuing Strategic Research Partnership Grants** $700,000
### International Cancer Genome Consortium (ICGC)

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Andrew Biankin</td>
<td>Garvan Institute of Medical Research</td>
<td>$500,000</td>
</tr>
<tr>
<td></td>
<td>International Cancer Genome Consortium (ICGC)</td>
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</tr>
</tbody>
</table>

### Pharmacogenomics

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/Prof Susan Henshall/ Horvath</td>
<td>Garvan Institute of Med Res</td>
<td>$299,724</td>
</tr>
<tr>
<td></td>
<td>Building capacity in Pharmacogenomics across NSW: PRIMe (Pharmacogenomic Research for Individualised Medicine)</td>
<td></td>
</tr>
</tbody>
</table>

### Other Research Programs

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Research Division - (internal + external but excluding NHMRC funding)</td>
<td></td>
<td>$3,277,030</td>
</tr>
<tr>
<td>Test the acceptability and feasibility of chronic hepatitis B (CHB) screening, ongoing CHB management and liver cancer prevention in South West Sydney</td>
<td></td>
<td>$300,000</td>
</tr>
<tr>
<td>45 &amp; Up Cohort Study</td>
<td></td>
<td>$300,000</td>
</tr>
<tr>
<td>A randomised controlled trial of online versus telephone-based information and support: Can electronic platforms deliver effective care for lung cancer patients?</td>
<td></td>
<td>$100,000</td>
</tr>
<tr>
<td>Caring at end of life: Understanding the nature and effect of informal community care networks for people dying at home</td>
<td></td>
<td>$64,000</td>
</tr>
<tr>
<td>Fertility research project</td>
<td></td>
<td>$55,000</td>
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</tbody>
</table>

### CCNSW Commissioned research

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Funding Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Youth skin cancer prevention research and evaluation (University of Western Sydney)</td>
<td></td>
<td>$50,000</td>
</tr>
<tr>
<td>Tobacco Retail Literature Review</td>
<td></td>
<td>$20,000</td>
</tr>
<tr>
<td>Tackling Tobacco Evaluation</td>
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<td>$40,000</td>
</tr>
<tr>
<td>Smoking cessation in drug and alcohol treatment settings (University of Newcastle)</td>
<td></td>
<td>$25,000</td>
</tr>
<tr>
<td>Eat It To Beat It Evaluation</td>
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<td>$50,000</td>
</tr>
</tbody>
</table>

**Total CCNSW Commissioned and other research** **Total RESEARCH FUNDED**

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Funding Amount</th>
</tr>
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<tbody>
<tr>
<td>Total CCNSW Commissioned and other research</td>
<td></td>
<td>$4,281,030</td>
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<tr>
<td>TOTAL RESEARCH FUNDED</td>
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<td>$13,908,715</td>
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### CANCER COUNCIL VICTORIA

**BUDGETED EXPENDITURE FOR 2013**

#### Fellowships

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Total $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carden fellowship</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D Metcalf</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>$243,000</td>
</tr>
<tr>
<td></td>
<td>Regulatory control of normal and leukaemic cells</td>
<td></td>
</tr>
<tr>
<td>Lions fellowship</td>
<td></td>
<td></td>
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<tr>
<td>A Ng</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>$16,000 (approx)</td>
</tr>
<tr>
<td></td>
<td>Identification of genetic factors involved in haematopoiesis and the development of blood cancers</td>
<td></td>
</tr>
<tr>
<td>Dunlop fellowship</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C Scott</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>299,989</td>
</tr>
<tr>
<td></td>
<td>The generation of improved mouse models of high-grade serous ovarian cancer for preclinical development of therapeutics for women with ovarian cancer</td>
<td></td>
</tr>
</tbody>
</table>

**Total fellowship funded** **$558,989**
# Research grants-in-aid

<table>
<thead>
<tr>
<th>Researcher(s)</th>
<th>Institution(s)</th>
<th>Project Title</th>
<th>Funding (AUD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Cutts, P Pigram, G Pietersz, C Cullinane</td>
<td>La Trobe University</td>
<td>Tumour-targeted nanoparticles as sensitisers for cancer chemotherapy</td>
<td>$100,000</td>
</tr>
<tr>
<td>N Haynes</td>
<td>The University of Melbourne</td>
<td>Characterisation of the immunological factors that influence the local and abscopal anti-tumour effects of radiotherapy in preclinical models of solid and metastatic cancer</td>
<td>$99,633</td>
</tr>
<tr>
<td>K Kinross</td>
<td>The University of Melbourne</td>
<td>Mechanisms of resistance to P13K pathway inhibitors in ovarian cancer</td>
<td>$100,000</td>
</tr>
<tr>
<td>G Lieschke, C Keightley, Z Gong</td>
<td>Australian Regenerative Medicine Institute</td>
<td>The role of ZBTB11, a novel transcriptional regulator in liver development and the pathogenesis of hepatocellular carcinoma</td>
<td>$100,000</td>
</tr>
<tr>
<td>H Richardson, A Veraksa</td>
<td>The University of Melbourne</td>
<td>Regulation of signalling pathways and protein trafficking by Lgl/aPKC</td>
<td>$100,000</td>
</tr>
<tr>
<td>A Roberts, D Huang</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>Targeting pro-survival Bcl-2 family proteins for cancer therapy: exploring and defining new applications</td>
<td>$99,736</td>
</tr>
<tr>
<td>P Rogers, J Crosbie, Y Yang, P Paiva</td>
<td>Royal Women’s Hospital</td>
<td>Investigator of dose equivalence and therapeutic index for synchrotron microbeam radiation therapy</td>
<td>$100,000</td>
</tr>
<tr>
<td>J Rossjohn, D Godfrey</td>
<td>Monash University</td>
<td>A structural and functional investigator into tumour recognition by NKT cells</td>
<td>$99,891</td>
</tr>
<tr>
<td>A Shulkes, G Baldwin</td>
<td>Austin Health</td>
<td>Targeting proGRP as a therapeutic strategy for gastrointestinal cancers</td>
<td>$98,551</td>
</tr>
<tr>
<td>A Strasser, J Silke</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>The role of necroptosis in tumour suppression and the response of malignant tumour cells to anti-cancer therapy</td>
<td>$99,730</td>
</tr>
<tr>
<td>D Vaux, W Cook</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>Regulation and function of RIP kinase 1 and RIP kinase 3</td>
<td>$100,000</td>
</tr>
<tr>
<td>C Walkley, E Baker, M Robinson</td>
<td>St Vincent’s Institute of Medical Research</td>
<td>Novel approaches to understanding osteosarcoma</td>
<td>$100,000</td>
</tr>
</tbody>
</table>

**Total new research grants-in-aid**: $1,197,541

# Continuing research grants-in-aid

<table>
<thead>
<tr>
<th>Researcher(s)</th>
<th>Institution(s)</th>
<th>Project Title</th>
<th>Funding (AUD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M Buchert, M Ernst</td>
<td>Ludwig Institute for Cancer Research</td>
<td>Molecular elucidation of PI-3K/mTor pathway as a therapeutic target in inflammation-associated (gastrointestinal) cancers</td>
<td>$97,184</td>
</tr>
<tr>
<td>I Campbell, A Trainer, L Lipton, P James, M Doyle</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Identification of novel genes predisposing to familial colorectal cancer by full exome sequencing</td>
<td>$100,000</td>
</tr>
<tr>
<td>A Dobrovic, T Mikeska</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Constitutional DNA methylation: a new paradigm for predisposition to lung cancer</td>
<td>$100,000</td>
</tr>
<tr>
<td>C Hawkins, D Curtis, E Algar</td>
<td>La Trobe University</td>
<td>Are direct apoptosis inducers less mutagenic than chemotherapy drugs?</td>
<td>$98,725</td>
</tr>
<tr>
<td>J Hopper, J Stone, C Apicella, E Makalic, D Schmidt, R MacInnis</td>
<td>The University of Melbourne</td>
<td>Mammographic density of young women and their relatives</td>
<td>$98,120</td>
</tr>
<tr>
<td>P Humbert</td>
<td>Peter MacCallum Cancer Centre</td>
<td>The role of cell polarity regulators in mammary gland development and breast cancer</td>
<td>$100,000</td>
</tr>
<tr>
<td>R Johnstone</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Defining the apoptotic and therapeutic activities of histone deacetylase inhibitors</td>
<td>$98,723</td>
</tr>
<tr>
<td>P Lobachevsky, R Martin, O Martin</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Radioprotection by combination of DNA binding antioxidants and aminothiol radical scavengers</td>
<td>$100,000</td>
</tr>
<tr>
<td>Name</td>
<td>Institution</td>
<td>Title</td>
<td>Funding</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>M McCormack, W Shi</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>Identifying commonality amongst T cell oncogenes</td>
<td>$100,000</td>
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<tr>
<td>A Scott, V Pillay, J Mariadason, N Tebbutt</td>
<td>Ludwig Institute for Cancer Research</td>
<td>siRNA therapies for colorectal cancer</td>
<td>$100,000</td>
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<tr>
<td>E Vincan, N Barker, T Phesse, H Clevers</td>
<td>The University of Melbourne</td>
<td>Frizzled function in the intestinal crypt and adenoma formation</td>
<td>$95,699</td>
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<tr>
<td>R Anderson</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Regulation of breast cancer metastasis by bone morphogenetic protein 4</td>
<td>$100,000</td>
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<tr>
<td>L Bach, G Rice</td>
<td>Monash University</td>
<td>Insulin-like factor binding protein-6 and ovarian cancer</td>
<td>$97,508</td>
</tr>
<tr>
<td>P Ekert, A Lopez</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>Transcriptional and post-translational mechanisms regulating apoptosis in cytokine receptor signalling</td>
<td>$100,000</td>
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<tr>
<td>K Harvey</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Phosphorylation-mediated regulation of the Hippo tumour suppressor pathway</td>
<td>$100,000</td>
</tr>
<tr>
<td>B Jenkins</td>
<td>Monash Institute of Medical Research</td>
<td>Novel regulation of microRNAs by cytokine signalling pathways in gastric inflammation and cancer</td>
<td>$97,236</td>
</tr>
<tr>
<td>M Kershaw, P Darcy</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Investigations into differential responses to immunotherapy of orthotopic tumours compared to subcutaneous tumours</td>
<td>$74,644</td>
</tr>
<tr>
<td>F Macrae, A Boussioutas, J Clarke, D Topping, S Toden, P Lynch, A Spigelman, M Appleyard, P Hollington, H Ee, D Cameron</td>
<td>Melbourne Health</td>
<td>The effects of butyrylated high amylose maize starch on polyposis in FAP volunteers</td>
<td>$100,000</td>
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<tr>
<td>B Mann, A Skandarajah, A Rose, B Chua, J Forbes</td>
<td>Melbourne Health</td>
<td>PROSPECT -- Post-operative Radiotherapy Omission in Selected Patients with Early breast Cancer Trial</td>
<td>$98,189</td>
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<tr>
<td>M Smyth, M Teng</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Immunoregulation of the tumor microenvironment</td>
<td>$99,736</td>
</tr>
<tr>
<td>Total continuing research grants-in-aid</td>
<td></td>
<td>$1,955,764</td>
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</tbody>
</table>

**Postdoctoral research fellowships**

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Title</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Grabow</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>The role of the pro-survival Bcl-2 family member Mcl-1 in the development and sustained growth of lymphoma and leukaemia</td>
<td>$34,363</td>
</tr>
<tr>
<td>SL Khaw</td>
<td>Walter and Eliza Hall Institute of Medical Research</td>
<td>Translational and mechanistic studies with BH3-mimetics</td>
<td>$34,363</td>
</tr>
<tr>
<td>S Jurado</td>
<td>St Vincent’s Institute of Medical Research</td>
<td>Role of ASCIZ in B cell lymphoma pathogenesis</td>
<td>$34,946</td>
</tr>
<tr>
<td>A West</td>
<td>Peter MacCallum Cancer Centre</td>
<td>Investigating the immunomodulatory properties of histone deacetylase inhibitors to develop better anti-cancer combinatorial therapeutic regimes</td>
<td>$69,891</td>
</tr>
<tr>
<td>Two fellowships to be appointed mid-year</td>
<td></td>
<td>$69,892</td>
<td></td>
</tr>
<tr>
<td>Total postdoctoral research fellowships</td>
<td></td>
<td>$243,455</td>
<td></td>
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</table>

**Postgraduate research scholarships**
S Boyle  Understanding melanoma progression and therapy resistance using in vivo modelling  $32,340

F Chang  Telomere maintenance mechanism (TMM) in human cancers  $32,422

S Davis  Integrated analysis and functional characterisation of gene aplicons ovarian cancer  $13,475

H Duivenvoorden  The role of myoepithelial proteins in blocking breast cancer invasion  $27,978

D Flanagan  The role of frizzled 7 in colorectal cancer  $32,340

KS Lee  Evaluating novel targeted therapies for prevention and treatment of squamous cell carcinoma  $32,340

SH Kim  Breast Cancer Metastasis to Brain: Mechanisms and New Therapies  $27,978

A Lim  Defining the molecular landscape of oral tongue squamous cell carcinomas and its impact on patient outcome  $42,579

E Nolan  Identification of Novel Breast Cancer Genes using a Transposon-Based Mutagenesis Screen in Mice  $27,978

A Policheni  Discovery of cancer genes in lymphomas  $27,978

G Ryan  Designing dendrimer-based lymphatic drug vectors as improved treatment for metastatic cancer  $32,422

N Sapre  Use of discrete gene expression signatures in diagnosis and risk stratification of bladder cancer  $42,030

S Sawyer  Translational studies of the genomic variation associated with breast cancer in clinic-based breast and ovarian cancer families  $27,978

H To  A genetic study of Barrett’s oesophagus and oesophageal adenocarcinoma using next-generation sequencing  $3,053

AK Win  Development of a comprehensive model for colorectal cancer risk prediction  $42,305

Total postgraduate research scholarships  $445,196

Other

21 summer Vacation Studentships were awarded  $31,000

Support for medical and scientific activities  $292,000

Total other  $323,000

Clinical research

The Cancer Council supports clinical research via the Cancer Trials Management Scheme, which aims to increase clinical trial recruitment by funding on-site trial coordinators. In 2013, CCV will contribute $600,000 to more than 40 research departments across the State. This amount is increased with aid from the Victorian government of $100,000 and a research grant provided by the Victorian Cancer Agency of $1 million. $1,700,000

Victorian Cancer Biobank

The Victorian Cancer Biobank (Biobank) is an infrastructure platform that supports cancer researchers in academia and industry. The Biobank is funded by the Victorian government through the Victorian Cancer Agency to supply biospecimens for clinical and translational research studies as well as processing samples for clinical trials according to study specific protocols. $2,300,000

Cancer control research

Cancer Epidemiology Centre  $5,530,000

Victorian Cancer Registry  $3,401,000

Centre for Behavioural Research in Cancer  $4,790,000

Nigel Gray Fellowship Group  $867,000

Total cancer control research programs  $14,588,000

TOTAL RESEARCH  $23,311,945
## Cancer Council South Australia

### BEAT CANCER PROJECT - A joint initiative of Cancer Council SA, South Australian Health and Medical Research Institute, SA Health and University of Adelaide, University of South Australia and Flinders University

### 2013 Research Project Grants *

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Project Title</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Lisa Ebert, SA Pathology</td>
<td>A new molecule involved in melanoma vascular development</td>
<td>$94,891</td>
</tr>
<tr>
<td>Dr Claudine Bonder, The University of Adelaide</td>
<td>A new target to combat breast cancer</td>
<td>$99,891</td>
</tr>
<tr>
<td>Dr Natasha Harvey, The University of Adelaide</td>
<td>Defining the role of GATA2 in lymphatic vascular development as a means to understanding how GATA2 mutations predispose to human lymphoedema</td>
<td>$100,000</td>
</tr>
<tr>
<td>Dr Michele Grimbaldeston, The University of Adelaide</td>
<td>Mast cells regulate skin neoplasia</td>
<td>$100,000</td>
</tr>
<tr>
<td>Dr Michael Samuel, The University of Adelaide</td>
<td>Skin tumourigenesis and tumour progression: A new function for 14-3-3zeta?</td>
<td>$100,000</td>
</tr>
<tr>
<td>Dr Carmela Ricciardelli, The University of Adelaide</td>
<td>Hyaluronan: a marker and therapeutic target to overcome ovarian cancer chemoresistance</td>
<td>$93,891</td>
</tr>
<tr>
<td>Dr Michael Michael, Finders University</td>
<td>Diet and microRNA-mediated control of apoptosis: A Role in colorectal cancer prevention</td>
<td>$99,551</td>
</tr>
</tbody>
</table>

**Total Research Project Grants** $688,224

### Blue Sky Funding**

<table>
<thead>
<tr>
<th>Researcher</th>
<th>Project Title</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Carmela Ricciardelli, University of Adelaide</td>
<td>Novel markers and drug targets for ovarian cancer</td>
<td>$25,000</td>
</tr>
<tr>
<td>Dr Olga Sukocheva, Finders University</td>
<td>Role of estrogen receptor signalling in oesophageal adenocarcinoma</td>
<td>$29,250</td>
</tr>
<tr>
<td>Professor Shudong Wang, University of South Australia</td>
<td>A new anti-cancer drug</td>
<td>$50,000</td>
</tr>
<tr>
<td>Dr Roger Yazbek, University of South Australia</td>
<td>A new breath test for the early detection of oesophageal cancer</td>
<td>$36,000</td>
</tr>
<tr>
<td>Professor Brendon Coventry, University of Adelaide</td>
<td>Timed therapy for cancer</td>
<td>$80,000</td>
</tr>
<tr>
<td>Professor Carlene Wilson, Finders University</td>
<td>Web-based decision support for colorectal cancer prevention</td>
<td>$40,000</td>
</tr>
<tr>
<td>A/Professor Deb White, SA Pathology</td>
<td>Assessing the cause and drug susceptibility of High Risk Adult ALL</td>
<td>$80,000</td>
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</table>

**Total Blue Sky Funding** $340,250

**Total Research Projects** $1,028,474

### Workforce

### Chairs in Cancer Research**

<table>
<thead>
<tr>
<th>Institution</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Adelaide</td>
<td>$250,000</td>
</tr>
<tr>
<td>Professor Ross McKinnon</td>
<td>$250,000</td>
</tr>
<tr>
<td>Professor David Roder</td>
<td>$250,000</td>
</tr>
</tbody>
</table>

### Total Research Chairs

**Principal Cancer Research Fellowships**

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Project Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Daniel Worthley</td>
<td>University of Adelaide</td>
<td>Identifying and targeting the important supportive cells in cancer</td>
<td>$210,000</td>
</tr>
<tr>
<td>Professor Shudong Wang</td>
<td>University of South Australia</td>
<td>New therapeutics for cancer treatment</td>
<td>$210,000</td>
</tr>
<tr>
<td>Dr Caroline Miller</td>
<td>SAHMRI</td>
<td>Packaging and labeling of tobacco products, food and alcohol</td>
<td>$210,000</td>
</tr>
</tbody>
</table>

**Total Principal Research Fellowships**  

$750,000

### Research Fellowships and Senior Research Fellowships

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Project Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor Ross Butler</td>
<td>University of South Australia</td>
<td>Novel non-invasive detection of early oesophageal and gastric dysplasia and neoplasia</td>
<td>$105,000</td>
</tr>
<tr>
<td>Dr Loretta Dorstyn</td>
<td>University of Adelaide</td>
<td>Characterisation of the role and mechanisms of caspase-2 in tumour suppression</td>
<td>$100,000</td>
</tr>
<tr>
<td>Professor Gordon Howarth</td>
<td>The University of Adelaide/Women’s &amp; Children’s Hospital</td>
<td>Strategically developed bioactive nutraceutical formulations will prevent, or reduce the severity of, experimentally-induced intestinal mucositis</td>
<td>$100,000</td>
</tr>
<tr>
<td>Dr Carmela Ricciardelli</td>
<td>Women’s &amp; Children’s Hospital</td>
<td>The tumour microenvironment: Identification of novel cancer biomarkers and therapeutic targets</td>
<td>$105,000</td>
</tr>
<tr>
<td>Dr Philip Gregory</td>
<td>The University of Adelaide</td>
<td>Discovery and functional characterisation of novel microRNAs and other non-coding RNAs that regulate epithelial-mesenchymal transition and breast cancer metastasis</td>
<td>$95,000</td>
</tr>
<tr>
<td>Dr Spomenka Simovic</td>
<td>University of South Australia</td>
<td>Advanced therapeutic strategies for oral administration of anticancer drugs</td>
<td>$95,000</td>
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</tbody>
</table>

**Total Research Fellowships**  

$630,000

### Travel Grants, PhD Top-ups

To be awarded  

$50,000

### Total Workforce

$2,030,000

### Infrastructure

#### One Year Infrastructure Grants

<table>
<thead>
<tr>
<th>Name</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor Pamela Sykes</td>
<td>$143,882</td>
</tr>
<tr>
<td>One year grants to be awarded (currently under review)</td>
<td>$556,118</td>
</tr>
</tbody>
</table>

**Total One Year Infrastructure Grants**  

$700,000

### Data managers program

- Prostate Cancer  
  $29,750
- Familial Cancer Unit  
  $56,000
- Royal Adelaide Hospital  
  $42,900
- Flinders Medical Centre  
  $22,000
- The Queen Elizabeth Hospital  
  $15,000
- Lyell McEwin Hospital  
  $8,600
- Ashford Cancer Centre  
  $15,000
- Women’s & Children’s Hospital  
  $6,600
Total Data Managers $195,850
Micro-array facility** $45,000
SANT Data Link** $100,000
Total Infrastructure $1,040,850

TOTAL RESEARCH FUNDED $4,099,324

Research administered and funded solely by Cancer Council SA

Peter Nelson Leukaemia Research Fellowship
H Ramshaw IMVS Hanson Institute $100,000

Other research grants

Chair in Cancer Prevention (Behavioural Science) $150,000
SA Cancer Genome Facility $105,000

TOTAL RESEARCH FUNDED SOLELY BY CANCER COUNCIL SA $355,000

* Based on calendar year 2013
** Based on financial year to end 30 June 2013

All figures are based on budgeted figures.

CANCER COUNCIL AUSTRALIA

Priority Driven Grants

Meiser
University of NSW The impact of treatment focused genetic testing in patients newly diagnosed with breast cancer $20,175

Grimison
University of Sydney Accelerating First-Line Chemotherapy to Improve Cure Rates for Advanced Germ Cell Tumours: An Australian-Led, International Randomised Trial $111,000

Friedlander
Prince of Wales Hospital An international multi-stage randomised phase III trial of dose-fractionated chemotherapy compared to standard three-weekly chemotherapy for women with newly diagnosed epithelial ovarian cancer $84,000

Nowak
University of Western Australia Phase III trial of Concurrent and Adjuvant Temozolomide chemotherapy in non-1p/19q non deleted anaplastic glioma. The CATNON Intergroup Trial. $64,000

Severi
Cancer Council Victoria Risk and Prognostic Factors for Glioma in Australia $160,000

Total research funded $439,175

IARC Fellowships

Muller
International Agency for Research on Cancer IARC Research Fellowship $50,000

International Agency for Research on Cancer for the institution to be named IARC Research Fellowship $50,000

Total research funded $100,000

TOTAL RESEARCH FUNDED $539,175
### CANCER COUNCIL TASMANIA

**Current research grants allocated for 2013**

<table>
<thead>
<tr>
<th>Research Grants</th>
<th>Amount</th>
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<tr>
<td>CCTAS NHMRC Grant</td>
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<table>
<thead>
<tr>
<th>Small Grants Program</th>
<th>Amount</th>
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<tbody>
<tr>
<td>To be announced May 2013</td>
<td>$40,000</td>
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**Funded by David Collins Leukaemia Foundation**

<table>
<thead>
<tr>
<th>Cancer Council Tasmania Fellowship</th>
<th>Amount</th>
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</thead>
<tbody>
<tr>
<td>Dr Stuart Ferguson</td>
<td>$92,465</td>
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**Other**

<table>
<thead>
<tr>
<th>Royal Hobart Hospital</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Data Management Clinical Trials</td>
<td>$32,500</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Launceston General Hospital</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Management Clinical Trials</td>
<td>$37,500</td>
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**Scholarships**

<table>
<thead>
<tr>
<th>Jeanne Foster Scholarships</th>
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<tr>
<td></td>
<td>$5,000</td>
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<table>
<thead>
<tr>
<th>Athena Karydis Foniadakis Scholarship</th>
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<tr>
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<table>
<thead>
<tr>
<th>Cancer Council Tasmania Honours UTAS Honours Student</th>
<th>Amount</th>
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<tbody>
<tr>
<td></td>
<td>$10,000</td>
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</table>

**Total research funded**

$222,465

**Continuing research grants**

<table>
<thead>
<tr>
<th>Dr S Ferguson</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promoting cessation &amp; reduction in smokers who are not interested in quitting</td>
<td>$3,250</td>
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</table>

<table>
<thead>
<tr>
<th>Dr A L Cook, A/Prof E T Snow, Dr A F Holloway</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epigenetic regulation of tumour suppressors in skin cancer</td>
<td>$11,150</td>
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$14,400

**TOTAL RESEARCH FUNDED**

$236,865

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### CANCER COUNCIL ACT

**Research grants**

<table>
<thead>
<tr>
<th>S Rao University of Canberra</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Novel histone demethylase inhibitors: potential treatment against cancer metastasis and relapse by targeting cancer stem cells&quot;</td>
<td>$45,164</td>
</tr>
</tbody>
</table>

**TOTAL RESEARCH FUNDED**

$45,164
AUSTRALIAN BEHAVIOURAL RESEARCH IN CANCER

Behavioural Research and Evaluation (BREU), South Australia

11th Behavioural Research in Cancer Control (BRCC) Conference

Cancer Council SA will host the 11th Behavioural Research in Cancer Control Conference to be held from 8-10 May 2013 at the Crowne Plaza, Adelaide.

Supported by Cancer Council Australia through its Public Health Committee, the conference will bring both international and interstate keynote speakers on a breadth of topics and is recommended for those working in behavioural research, program delivery, evaluation and management working on cancer control issues in Australia.

In addition to our keynote speakers, the program will include parallel sessions on topics such as: tobacco control; nutrition and physical activity; alcohol; skin cancer prevention; cancer screening; supportive care; media research and other cancer control issues.

For further information or to register for the conference and pre-conference workshops, head to: www.themeetingpeople.com.au/brcc13.

National Primary School Survey of Sun Protection

The National Primary School Survey of Sun Protection is the principle tool of state and territory Cancer Councils for: (i) benchmarking sun protection policies and practices in primary schools around Australia; and (ii) evaluating the effectiveness of the National SunSmart Schools Program, on a periodic basis. The 2011 survey, the fourth since 1998, was conducted by Cancer Council SA.

For the first time in the history of the survey, data collection was conducted via an online survey tool between September 2011 and March 2012.

In total, 859 schools with primary school years participated in the survey. The majority of schools displayed sound sun protection practices, especially in key areas such as hat wearing, sunscreen and school uniform. In addition, the majority of schools had a written sun protection policy that frequently addressed key sun protection areas.

Of note, schools that participated in the National SunSmart Schools Program demonstrated improved sun protection policies and practices compared with non-participatory schools. Hence, a future focus of Cancer Council is to continue to increase participation rates in the National SunSmart Schools Program for the benefit of students in the area of sound sun protection practices.

National Early Childhood Survey of Sun Protection Policies and Practices

In 2013, Cancer Council SA will conduct the second National Early Childhood Survey of Sun Protection Policies and Practices in online format. The survey was first conducted in 2008, yielding information on sun protection practices such as hat wearing, sun protective clothing, sunscreen use and shade in early childhood services.

The survey will provide a current snapshot of sun protection policies and practices across early childhood services in Australia, assess the uptake of sun protection policies and practices since 2008 and measure adherence with Cancer Council sun protection recommendations.

The survey also aims to examine services’ use of SunSmart resources in the educational curriculum and membership into the SunSmart Early Childhood Program. Overall, the survey will provide insight into the progress towards creating sustainable change for sun protective environments in early childhood services. Data collection is scheduled to begin in March, with results expected to be available later in the year.

Centre for Behavioural Research in Cancer (CBRC), Victoria

What types of nutrition menu labelling lead consumers to select less energy-dense fast food?

Increased consumption of foods prepared away from home is an important contributing factor to rising rates of obesity, with consumers largely unaware of their high energy density. Three Australian states recently introduced mandatory provision of kilojoules on restaurant chain menus. The few evaluations of the effectiveness of menu labelling on the energy content of purchases have shown mixed findings, suggesting that including additional nutrition information may enhance the existing policy initiative. This study aimed to test the influence of models of point-of-sale nutrition menu labelling on the energy content of adults’ fast food meal selections. Using a between-subjects experimental design, 1294 Victorian adults were randomly assigned to one of five online menu labelling conditions: none (control); kilojoule (kJ); kJ + percent daily intake; kJ + traffic light; and all three. Respondents shown no labelling selected meals with the highest mean energy content and those viewing kJ and kJ + traffic lights selected meals with a mean energy content that was significantly reduced by around 500 kJ. Respondents also most commonly reported using the traffic light labels in making their selections. These findings support mandatory disclosure of energy content on menus at restaurant chains, and given the prevalence of fast food consumption and the magnitude of the reduction in energy density, nationwide implementation has the potential to yield substantial health benefits at the population level.

Maximising students’ use of purpose-built shade in secondary schools: quantitative and qualitative results of a built-environment intervention

Adolescent’s poor compliance with sun protection hampers secondary schools implementation of sun protection strategies for students. Provision of high-quality shade for students’ outdoor activities offers an alternative to regulating hat-wearing. A cluster-randomised trial installing shade sails at secondary schools in Melbourne.
found increased student use of newly shaded areas compared with unshaded areas at control schools, but overall usage was low. Our study aimed to further examine the trial observations and qualitative research to identify shade site features, weather conditions, and student factors related to students use of the shaded areas. Post-test lunch-time observations of students using the primary study areas at 22 schools receiving shade sails and complying with trial protocols were analysed. A thematic analysis of discussions from 14 focus groups at eight intervention schools was also conducted. Results indicated tables with seats and temperatures ≥27°C increased student use of shaded areas on average by 6.67 and 2.06 more students respectively. Presence of grass decreased student use of areas. Students reported their main lunchtime activities were sitting, talking, eating lunch and enjoying friends’ company. Their opinions suggested they were unaware that the shade sails changed their patterns of use of favoured school ground locations. These findings suggest careful area selection and addition of tables with seats are needed to maximise investments in shade sails. This is important given shaded areas is increasingly recognised as a useful strategy for skin cancer prevention.

Centre for Behavioural Research in Cancer Control (CBRCC) Western Australia (Curtin University and Cancer Council WA)  

A home-based intervention improved physical activity and nutrition behaviours of seniors  

This National Health and Medical Research Council (NHMRC) funded study aimed to confirm if a low-cost, home-based physical activity and nutrition program could improve physical activity and nutrition behaviours of insufficiently active 60-70 year-olds. A six month randomised control trial targeted sedentary and overweight adults from low to medium socio-economic suburbs within metropolitan Perth. Intervention participants (n = 248) received mailed materials and telephone/email support to improve nutrition and physical activity behaviours. Controls (n = 230) only received small incentives to complete baseline and post-intervention questionnaires. A questionnaire measured nutritional behaviours, and physical activity was measured using the International Physical Activity Questionnaire. Generalised estimating equation models were used to assess the repeated outcomes over both time points. A total of 176 intervention and 199 control group participants (response rate 78.5%) with complete data were available for analysis. After controlling for demographic and other confounding factors, the intervention group demonstrated increased participation in strength exercise (p < 0.001), walking (p = 0.029) and vigorous activity (p = 0.015), together with a significant reduction in mean sitting time (p < 0.001) and waist to hip ratio measurements (p = 0.03) relative to controls. Improvements in nutritional behaviours for the intervention group were also measured in terms of fat avoidance (p < 0.001), fat intake (p = 0.021) and fruit intake (p = 0.008). The results demonstrated that a home based program can positively influence changes to seniors’ physical activity and nutrition behaviours.

The project provides guidelines for the development, implementation and evaluation of a minimal, home-based tailored physical activity and nutrition intervention program.

For further information contact Peter Howat (p.howat@curtin.edu.au)  

Improvement in physical activity and nutrition behaviours of young women in a playgroup setting  

This NHMRC funded study aimed to evaluate the effect of a six-month physical activity and nutrition randomised control trial for mothers with young children in Perth, Western Australia. Women were recruited via playgroups and randomly assigned to either a control group (n=394) or an intervention group (n=322). The intervention group received a six-month theory based, behaviour change program which was delivered via playgroups. The multi-strategy intervention included physical activity and nutrition resources tailored to the target group, face-to-face workshops and a home-based component. Physical activity data was collected using the International Physical Activity Questionnaire. A validated Fat and Fibre Barometer recorded food intake at baseline and post-intervention. The intervention had a significant effect on the time for vigorous (p=0.008), moderate (p=0.023) and total physical activity (p=0.001), when compared to the control group. The intervention group increased their vigorous activity by a mean of 24 minutes/week, moderate activity by 23 minutes/week and total physical activity by 72 minutes/week. The intervention had a significant effect on lower fat (p=0.005) and higher fibre diets (p=0.000), when compared to the control group. There was a 5.03% greater fruit and vegetable intake (p=0.000), 4.69% wholegrain food intake (p=0.002) and 5.21% lower-fat dairy foods (p=0.006) intake, as well as a 22.5% lower sugar (p=0.003) intake at post-test for the intervention group compared to the control group. A relatively minimal intervention program with a home-based component was able to demonstrate modest, but statistically significant improvements to physical activity and diet in a hard to reach target group. These changes, if maintained over a longer period, are likely to reduce the impact of several cancer risk factors. Improved health behaviours of mothers are likely to also have a positive impact on their partners and children.

Funding body: National Health and Medical Research Council; in collaboration with Playgroup WA Inc.

For further information contact Peter Howat (p.howat@curtin.edu.au)  

Newcastle Cancer Control Collaborative (New-3C) NSW  

Haematological cancer patients’ perceptions of patient-centred care  

The Institute of Medicine has endorsed six objectives for achieving patient-centred care. These dimensions propose that care must be: 1) respectful to patients’ values, preferences and expressed needs; 2) coordinated and integrated; 3) provide information, communication and education; 4) ensure physical comfort; 5) provide
emotional support; and 6) involve family and friends. A cross-sectional study that examines haematological cancer survivors’ perceptions of quality across the six IOM patient-centred dimensions is underway. A random sample of 600 adult patients diagnosed with ICD-10 and ICD-0-3 M defined haematological cancers including leukaemias, lymphomas (Hodgkin and Non-Hodgkin) and myeloma in the previous three years is being recruited from two cancer registries. Patients who agree to be contacted by the researchers are mailed a package containing an invitation letter, the questionnaire and a postage-paid envelope for return of the questionnaire. One mailed reminder and one telephone reminder staggered at three week intervals are sent to non-respondents. To date, 477 haematological cancer survivors have completed the questionnaire. Preliminary results indicate that more than one-quarter of survivors perceived that care could be improved by helping patients and their families find others in a similar situation they could talk to, explaining to patients that they could get a second medical opinion and how each treatment option might affect their length of life. These results will inform quality improvement efforts and provide opportunities for translation into benefits for cancer patients and their families.

**Faecal Occult Blood Test (FOBT) screening history among those recently diagnosed with colorectal cancer**

National Health and Medical Research Council guidelines recommend a biennial Faecal Occult Blood Test (FOBT) for people aged 50 and over. FOBT screening can be accessed through general practitioners, some pharmacies and through the National Bowel Cancer Screening Program. The national program, however, currently targets only those aged 50, 55 and 65. Given the limited use of proactive strategies to engage the community in colorectal cancer (CRC) screening in Australia, we sought to examine screening participation among people recently diagnosed with CRC who were recruited to participate in a randomised control trial. People with CRC who were registered with the Victorian Cancer Registry within nine months of diagnosis were invited to participate in the study. Consenting participants completed a telephone interview, which included questions on family history of CRC and participation in CRC screening tests. Of the 2928 cases identified as potentially eligible, 1084 (37%) consented to their contact details being passed on to the research team and 763 (26%) consented to the study. Of these, 36% reported ever having undertaken a FOBT to screen for CRC. The low rate of FOBT participation among those recently diagnosed with CRC suggests that there is considerable scope to improve participation in FOBT screening. The 36% FOBT participation rate reported may be an overestimate due to consent bias. Efforts to improve FOBT participation are needed. Given previous evidence of the benefits of CRC screening, this will have implications for improving detection of early stage disease, leading to reductions in CRC mortality.

**Flinders Centre for Innovation in Cancer Survivorship Conference 2013**

The inaugural Australian Cancer Survivorship Conference was hosted by the Flinders Centre for Innovation in Cancer in Adelaide in February. This event was a unique collaboration between clinicians, researchers and cancer survivors.

The conference focus was on:

- understanding and addressing the issues faced by cancer survivors and those affected by cancer, and
- the priorities for survivorship care and research.

Patti Ganz, Director of Cancer Prevention and Control Research at the Jonsson Comprehensive Cancer Centre in Los Angeles, was unable to attend in person, instead delivering her insights to the conference via Skype. Her key messages included the importance of treating every patient as a survivor – the survivorship clock starts at the point of diagnosis. While acute cancer care occurs in specialist settings, survivorship care frequently occurs in the primary care setting, suggesting the cancer conversation needs to engage primary care providers of all types, along with community-based organisations. Current follow-up care plans focus on surveillance for cancer recurrence, not survivor wellness. We learned Patti’s three Ps of survivorship care: palliation (of symptoms), prevention and (health) promotion. Bogda Koczwarra added a fourth P: psychosocial.

Patti presented her five potential strategies for healthcare professionals working in the cancer survivorship sphere:

i. Developing trans-disciplinary teams focusing on common symptoms or chronic conditions.

ii. Engaging social and behavioural scientists.

iii. Working closely with researchers who work with the ageing population.

iv. Working with your health system and examining new models of care delivery.

v. Studying diseases other than breast cancer.

Patti set the scene with these themes and insights replicated throughout the conference in specific contexts and projects.

Lee Jones, Scientific Director of the Duke Centre for Cancer Survivorship North Carolina, discussed the role of exercise as an anti-cancer treatment and a contributor to improved survivorship care. Lee’s comprehensive
translational research program is evaluating the cardiovascular and functional impact of cancer therapy, the efficacy of defined exercise training to prevent and/or treat dysfunction, and underlying systemic and molecular mechanisms of defined aerobic training on tumour progression and metastatic dissemination. The theme of exercise and physical activity was repeated throughout the conference. The possibility of using exercise as an anti-cancer treatment is attractive, raising a future of minimising other anti-cancer treatment modalities to reduce late effects of these treatments for survivors. Everyone – survivors, caregivers, and healthcare providers – should be doing zonal training to keep fit and maximise physical wellness.

Australia has a strong track record of high-quality psychosocial research and we learnt that there is a substantial amount of research in the survivorship sphere happening now in Australia. Clinicians, researchers, consumers, community organisations and government were encouraged to identify relevant research and to share and connect with one another to conduct this research more efficiently and disseminate the results widely within the community.

Bogda Koczwara, Conference Convenor, drew together the meeting presentations and discussion into key points:

- Cancer survivors as ‘warriors without a war’ highlighting the language of cancer survivorship and how we need to examine the meaning of words, of time and of life.
- The major ‘known unknown’, how can the cancer community engage with general practice and who is responsible for the care of survivors?
- Perhaps it is survivors who are responsible for their care; they are the experts in their own care, so let’s place them at the centre of care.
- Prescriptions for ‘wellness’ are likely to meet survivors needs more effectively, but this is a challenge to those of us working in a system focused on illness; changing our framework is complex.
- If exercise could be an anti-cancer drug, what other adjuncts may be considered and studied as anti-cancer treatments?
- This work is continuing and will continue to deliver incremental improvements for people living with cancer and their caregivers and the health system.

The Flinders Charter of Cancer Survivorship was developed as a tangible outcome of the conference, affirming the importance and value of collaboration between survivors, clinicians and researchers in advancing the field of cancer survivorship, and is available at: http://www.fcic.org.au/survivorship/charter/default.aspx.

COSA (Gold Sponsor at the conference) has already started to take the next steps on some of these issues. Its Survivorship Group members have committed to developing a statement of quality survivorship care, engaging all stakeholders to develop an Australian minimum standard of cancer survivorship care, and establishing research priorities in this arena.

There is much work to be done to achieve these aims and we will be keeping the community updated about progress in this field.

Marie Malica and Haryana Dhillon

CANCER COUNCIL AUSTRALIA

South Australia solarium ban to reduce skin cancer deaths

Cancer Council Australia CEO, Professor Ian Olver, has congratulated the South Australian Government on its decision to ban solariums from January 2015.

Research has shown that solarium use under the age of 35 increased an individual’s risk of melanoma by 87 per cent, while a study released in October confirmed it also caused basal and squamous cell carcinomas, the two most common non-melanoma skin cancers.

“Cancer Council Australia supports any measure to protect people from the potential harms of solariums,” Professor Olver said.

“We commend the South Australian Government for putting the health of South Australians before the commercial interests of solarium operators and moving to enforce a ban.”

Cancer Council Australia

SPF50+ sunscreens set to hit shelves this summer

A new standard allowing manufacturers to increase the sun protection factor in sunscreens from SPF30+ to SPF50+ was announced in November.

The new SPF50+ sunscreen offers marginally better protection from UVB radiation, which is the major cause of sunburn and increased skin cancer risk. SPF50+ filters out 98% of UVB radiation compared to 96.7% blocked by SPF30.

The new standard also improves UVA protection. UVA contributes to ageing of the skin, as well as skin cancer risk.

SPF50+ needs to be applied just as generously as SPF30+, reapplied every two hours, and used in conjunction with protective clothing, a broad-brimmed hat, sunglasses and shade.

Any new SPF30 sunscreens will have the same UVB protection as previous SPF30 sunscreens, but are
required to have a higher UVA protection in order to be labelled ‘broad-spectrum’.

There is no need to throw away previous formulas as long as they are SPF30+, not passed their expiry dates and broad spectrum. Manufacturers will continue producing and selling previous formulas. The new standard applies to new products only and is simply a little better, and offers more choice.

More information at bit.ly/WvynfK

**Non-melanoma skin cancers cost health system $500 million a year**

New research published in November shows that non-melanoma skin cancers cost the Australian health system more than $500m in 2010 and are expected to cost $700m by 2015.

Using Medicare data, the researchers, whose findings are published in the *Medical Journal of Australia*, based the cost blowout on an 86 per cent increase in treatments from 1997 to 2010.

Co-author, Professor Rodney Sinclair, Director of Dermatology at the Epworth Hospital Melbourne, said cases rose from 412,000 to 767,000 annually and were set to increase further before they decline.

“That rate in over 65s increased at a significantly higher rate than under 45s,” Professor Sinclair said. “So it’s not all doom and gloom. If this trend continues, as our under 45 ‘SunSmart generation’ gets older, the net effect in coming decades could be billions of dollars in savings.”

Professor Olver said the savings were conservative as the research only counted patients treated by GPs and specialists in the community and did not include those treated in public hospitals. “What’s more, the analysis didn’t consider the costs to the individual such as out of pocket medical costs, travel and time away from work,” he said.

**Men urged to watch their backs**

In their summer campaign, Cancer Council Australia and the Australasian College of Dermatologists urged men to watch their backs.

Men aged 45 and over have more than double the risk of dying of melanoma than women the same age, with two men in this age group dying of melanoma every day.

Although melanoma can develop anywhere on the body, around one in three cases in men occurs on the back.

It seems men are failing to protect themselves properly in the sun, with Cancer Council research from the National Sun Protection Survey indicating only 24 per cent of men aged 45-69 years wear sunscreen and 12 per cent - the equivalent of almost 400,000 men - still believe a tanned person is healthier.

Tennis legends John Newcombe and Tony Roche, who have both had skin cancers, took centre court at the campaign launch in November, urging men to ‘watch their back’ in two ways: 1) always protect yourself in the sun and check your entire body for skin changes and 2) ask your wife, partner or a mate to check your back, and anywhere else you can’t see yourself.

**Tobacco in plain packs ‘tastes worse’**

Since the nation’s world-leading tobacco plain packaging laws took effect in December, young Australians will no longer be attracted to smoke by the lure of glossy branded tobacco packaging.

Professor Olver said that although more than 20 years of research showed branded packaging was a powerful marketing tool for recruiting new smokers, early observations suggested plain packs might exceed expectations and also help established smokers to quit.

Early anecdotal reports indicated that smokers suspected the flavour of the tobacco in the plain packs tasted worse and had been changed, when it hadn’t.

Professor Olver said smoking caused 14 types of cancer and anyone deterred from smoking because of plain packaging would have dramatically reduced their risk of developing one of these cancers.

Dr Lyn Roberts, CEO of the National Heart Foundation of Australia, said nine out of 10 smokers wished they could quit, and most were addicted at a young age. “The next generation of Australians will not be conned into a deadly addiction by identifying with the heavily-marketed look of a particular pack,” Dr Roberts said.

Professor Olver and Dr Roberts congratulated federal MPs from all parties who supported the plain packaging laws last year.

**HRT safest with short-term unopposed oestrogens**

Most women for whom hormone replacement therapy (HRT) is indicated can safely be prescribed short-term unopposed oestrogens, according to the latest review of HRT.

Published in the November issue of *Cancer Forum*, the review found the use of unopposed oestrogens was preferable to other forms of HRT and a “highly desirable” population health goal for the vast majority of women where HRT was indicated.

Author Professor Ian Olver, of the Department of Medicine at the University of Sydney and CEO of Cancer Council Australia, said he reached the conclusion after analysing a wide range of studies, including the Million Women Study and Women’s Health Initiative.

The study is available online at www.cancerforum.org.au

**New clinical guidelines for lung cancer treatment**

New clinical practice guidelines for the treatment of lung cancer have been published in an electronic ‘wiki’ format to assist doctors and their patients to make informed treatment choices based on the most current research available.
The Clinical Practice Guidelines for the Treatment of Lung Cancer, commissioned and co-funded by Cancer Australia and developed by Cancer Council Australia, revise the treatment section of the 2004 Clinical practice guidelines for the prevention, diagnosis and management of lung cancer.

Professor David Ball, from the Peter MacCallum Cancer Centre, and Chair of the Lung Cancer Guidelines Working Party, said the web-based electronic format allowed editing and updating by expert committees as new evidence became available.

The guidelines are available online on Cancer Council Australia’s Cancer Guidelines Wiki (wiki.cancer.org.au).

Time to rethink sugary drinks

Cancer Council, Diabetes Australia and the National Heart Foundation of Australia have called for immediate action by governments, schools and non-government organisations such as sport centres to tackle one of the key contributors to obesity in Australia – sugary drinks.

Consumption of sugar sweetened beverages, which include all non-alcoholic water based beverages with added sugar such as soft drinks, energy drinks, fruit drinks and sports drinks, is associated with a range of serious health issues including weight gain and obesity, which in turn are risk factors for diabetes, cardiovascular disease and cancer.

Craig Sinclair, Chair of Cancer Council Australia’s Public Health Committee, said that many people would be surprised to know that a regular 600ml soft drink contained about 16 packs of sugar.

He said comprehensive action needed to be taken to highlight the amount of sugar and empty kilojoules in these drinks and the potential health impacts of high levels of consumption.

Sugary drinks are widely consumed by Australian adults and children. In the 12 months to October 2012, Australians bought 1.28 billion litres of carbonated/still drinks with sugar, with regular cola drinks being the most popular (447 million litres).

The 2007 Australian National Children’s Nutrition and Physical Activity Survey found that almost half (47%) of children (2 to 16 years of age) consumed sugar-sweetened beverages (including energy drinks) daily, with a quarter (25%) consuming sugary soft drinks daily.

The health organisations have together launched a new TV Community Service Announcement designed to highlight the amount of sugar in these types of drinks and encourage Australians to switch to water or reduced-fat milk. The TV ad has been licensed from the New York City Department of Health and tailored for an Australian audience.

Cancer Council busts internet cancer myths

A snapshot of cancer causation inquiries to Cancer Council Australia’s iheard website (www.iheard.com.au) largely reflects concerns about unfounded risk factors promoted on websites, email and via social media.

Professor Olver said that while the internet was a phenomenal information resource, it was also a vehicle for unproven claims and misinformation.

Concerns about plastic bottles, deodorants and artificial sweeteners are among the many inquiries to the iheard website, along with questions about so-called cancer treatments which are either ineffective, harmful or both. Cancer Council experts assess the inquiries and provide evidence-based answers.

Cancer Council Australia launched a mobile friendly version of iheard on World Cancer Day (4 Feb) to help Australians separate the evidence from the misinformation. An iheard app will also be available soon.

New network to push indigenous cancer into the spotlight

A new national cancer research network aimed at improving quality of life and survival rates among Aboriginal and Torres Strait Islander cancer patients in Australia was launched at Cancer Council Australia on World Cancer Day (4 Feb).

Cancer is the second leading cause of death among Aboriginal and Torres Strait Islander people.

The National Indigenous Cancer Network (NICaN) will encourage and support collaboration in indigenous cancer research and the delivery of services to Indigenous people with cancer, including carers and families.

Senior cancer researcher, Associate Professor Gail Garvey of the Menzies School of Health Research, said the launch represented a huge step forward towards closing the gap on indigenous cancer mortality rates.

“NICaN is about making sure that what’s known about cancer in Indigenous Australians is available for use by people with cancer, their families, practitioners, policy makers and researchers,” Professor Garvey said.

Research shows sunbakers burning out

New Cancer Council research released in February shows Australian adults are less interested in getting a suntan and fewer are being sunburnt.

The research, published in the Australian and New Zealand Journal of Public Health, compares the results of the National Sun Protection Survey conducted in summer 2010-11 with the surveys in 2003-4 and 2006-7.

The proportion of adults desiring a tan fell from 39% in 2003-4 and 32% in 2006-7, to 27% in 2010-11. Fewer reported getting sunburnt at the weekend – 18% in 2003-4 compared with 13% in 2010-11.

Similar changes were reported for adolescents. The proportion of adolescents desiring a tan fell from 60% in 2003-4 and 51% in 2006-7, to 45% in 2010-11, while 25% were sunburnt in 2003-4 and 24% in 2006-7, falling to 21% in 2010-11.

The seven-year research period coincided with the first national skin cancer awareness campaign, broadcast...
from 2006 to 2010, with a number of state governments also investing in TV campaigns during this time.

**Cancer research grants announced**

Federal Health Minister, Tanya Plibersek, announced $10.6 million in new grants for cancer research in February through the Priority-driven Collaborative Cancer Research Scheme.

The 38 new cancer research projects include two projects jointly funded by Cancer Australia and Cancer Council Australia.

“It is important that there continues to be targeted investment in cancer research aimed at reducing the impact of the disease and improving the quality of life and outcomes for patients,” Minister Plibersek said.

The two projects with Cancer Council Australia co-funding include:

- **Michael Friedlander – ICON8:** An international multi-stage randomised phase III trial of dose-fractionated chemotherapy compared to standard three-weekly chemotherapy for women with newly diagnosed epithelial ovarian cancer.
- **Peter Grimison - Accelerating first-line chemotherapy to improve cure rates for advanced germ cell tumours:** an Australian-led, international randomised trial.

**Boys join national HPV vaccination program**

Health Minister, Tanya Plibersek, has launched the world’s first National Human Papilloma Virus (HPV) Immunisation Program for boys.

From February 2013, males aged 12-13 years will receive the HPV vaccine at school. Males aged 14-15 years will also receive the vaccine as part of a catch-up program until the end of the 2014 school year.

Females ages 12-13 years will continue to receive the vaccine at school.

Gardasil, the vaccine used in the national program, protects against four types of HPV that are pre-cursers to some cancers, in particular cervical cancer, as well as genital warts in men and women.

Since the HPV vaccination program started in 2007, there has been a reduction in HPV-related infections in young women and a reduced incidence of genital warts in males and females. There has also been a reduction in pre-cancerous lesions in young women.

For more information on HPV, the vaccine and the national program visit www.hpvvaccine.org.au

**CLINICAL GUIDELINES NETWORK**

Cancer Council Australia’s Clinical Guidelines Network is continuing to develop and revise clinical practice guidelines on its wiki platform wiki.cancer.org.au

Cancer Council Australia CEO, Professor Ian Olver, has been invited as a guest speaker at the Guidelines International Network conference to be held in August in San Francisco. Professor Olver will speak about ‘the wiki approach to keeping guidelines up to date’.

As well as developing new guidelines, existing guidelines are being translated online in preparation for their revision phase on the Cancer Guidelines Wiki.

**Clinical practice guidelines for the Prevention, Diagnosis and Management of lung cancer**

These guidelines were the pilot development on the Cancer Guidelines Wiki. Focusing on the revision of the treatment section of the 2004 guidelines and comprising management of non-small cell lung cancer and small cell lung cancer, they were launched in December 2012.

Revision of the prevention and diagnosis sections of the 2004 guidelines is now underway. A multidisciplinary working party, chaired by Professor Kwun Fong, met in November 2012 to decide the key clinical questions and develop literature search strategies for the guidelines.

**Clinical Practice Guidelines for PSA testing and management of test-detected prostate cancer**

These guidelines are being developed in collaboration with the Prostate Cancer Foundation of Australia. An expert advisory panel met in November 2012 to develop clinical questions that will undergo systematic review. National Health and Medical Research Council approval will be sought for these guidelines.

**Clinical practice guidelines for the management of sarcoma**

Working party authors are currently assessing the relevant literature and developing their topic content and evidence-based recommendations. The draft guidelines are planned to be released on the Cancer Guidelines Wiki for public consultation by mid-year. Relevant organisations, experts and interested parties will be consulted during the public commenting phase.

**Clinical practice guidelines for the diagnosis and management of Barrett's oesophagus and mucosal neoplasia**
COSA’s Annual Scientific Meeting was held in November, in Brisbane, and was attended by nearly 1300 delegates. The partnership between COSA and the International Psycho-Oncology Society was appreciated by members of both societies, in particular COSA’s psycho-oncology and other allied health members.

Planning for the 2013 Annual Scientific Meeting in Adelaide is well underway. The theme – ‘Cancer Care Coming of Age’ – will cover geriatric oncology. Disease themes will feature all gastro-intestinal cancer, encompassing gastric, oesophagus and hepatobiliary tumours, often neglected at major meetings.

The 2013 ASM marks the 40th conference for COSA, as does this issue of Cancer Forum.

Leadership in improving cancer research

In 2011, COSA was funded by Cancer Australia for a project to enhance consumer engagement in clinical cancer research. The aims were to develop a strategy for increased consumer involvement at all levels of clinical cancer research through increased training, mentoring and collaboration across the 14 cancer cooperative trial groups, in order to enhance knowledge, skills and confidence of consumers involved in clinical trial development and oversight.

The end result and most tangible outcome is the Consumer Learning website, which contains short online learning modules and video presentations to guide consumers who are seeking to participate in clinical trials and research. The website was launched by Cancer Australia on World Cancer Day (4 Feb) and can be accessed at consumerlearning.canceraustralia.gov.au

Geriatric oncology

COSA activities in geriatric oncology continue to expand to meet the membership’s interests. Last year, our Geriatric Oncology Interest Group had just over 100 members, which was anecdotally the largest interest group within a cancer society worldwide. By December 2012, membership of the group had grown to 135. The group will host a concept development workshop in March 2013, while the 2013 ASM in Adelaide will feature a geriatric theme under the guidance of convenor Nimit Singhal. Cancer Forum will also feature a geriatric oncology theme in its November issue.

Cancer survivorship

Cancer survivorship re-emerged as a growing area of interest for COSA members in late 2012. At their November 2012 meeting, Council approved the formation of a COSA Survivorship Group. Members met at the ASM in Brisbane to commence discussions about activities for the group, which will include:

- collating the available systematic reviews related to cancer survivorship
- considering the need for specialist referrals to allied health outside the public hospital system
- exploration of what cancer survivorship is and how this differs from life
- integration of community-based organisations, particularly Cancer Councils, into the delivery of post-treatment cancer care
- models of care and survivorship planning.

The inaugural Australian Cancer Survivorship Conference in February, hosted by the Flinders Centre for Innovation in Cancer, was supported by COSA as gold sponsor. The conference is reported on separately in this issue of Cancer Forum.

Marie Malica, Executive Officer
In 2012 the Faculty Board (now to be known as Council, due to the College’s recent governance restructure) set the direction for the College’s work in radiation oncology for the next few years by identifying seven key strategic priorities. The unifying theme across all the areas is to ensure the provision of timely, appropriate and high quality radiation oncology services for cancer patients, including patient access, access to new techniques and technologies, research and quality.

Those strategic directions are resonant with issues and recommendations listed in the Tripartite National Strategic Plan for Radiation Oncology 2012-2022 (radiationoncology.com.au). The biggest challenge ahead for the Faculty is to translate the strategic directions into actions, and to implement the recommendations in conjunction with other professions in the sector, stakeholders and governments.

Radiotherapy techniques and technologies

The Radiation Oncology Horizon Scan is an annual initiative of the Faculty of Radiation Oncology. The aim is to highlight new and evolving techniques and technologies in the radiotherapy sector and support their timely and appropriate implementation in Australia and New Zealand.

The 2012 Horizon Scan Industry Roundtable was held in November, and provided an opportunity for the Faculty to discuss with industry representatives our position regarding new techniques and technologies. Subsequently, the Radiotherapy Innovation Summit, held the following week in Canberra, was well attended by representatives from the Department of Health and Ageing, peak cancer organisations, advocacy groups and individuals, as well as research and academic bodies. Introductory addresses were made by Prof Chris Baggoley, the Chief Medical Officer of Australia, discussing quality in the healthcare system and A/Prof Rosemary Knight, Principal Advisor Chronic Disease and Cancer, contextualising the issues faced by Radiation Oncology within the cancer care system of Australia.

The Roundtable and Summit in 2012 were highly successful, with increased attention being focused on the place of radiotherapy and the positive outcomes that it can achieve for cancer patients. An updated Faculty position paper: ‘Techniques and Technologies in Radiation Oncology, 2012 Horizon Scan Australia’ is available at ranzcr.edu.au/advocacy/consumers/764-radiotherapy-technologies

Funding for radiation oncology services

In January 2012, the Commonwealth Department of Health and Ageing announced a review of the radiation oncology section of the Medicare Benefits Schedule (MBS) from July 2012. The Faculty has expressed our willingness to partner with DoHA in the MBS review. We anticipate the final scoping document for the review will be available early this year and the review completed in the next 18 months.

In the meantime, the Independent Hospital Pricing Authority is charged with determining the national efficient price for health care services provided by public hospitals, and the national introduction of activity based funding. The Faculty recognises the complexities of the implementation of activity based funding and their potential effects on radiation oncology funding arrangements. The Faculty considers that the key imperative for any proposed changes must be ongoing support for the provision of a high quality, effective and cost-effective service to Australian cancer patients.

As the key professional organisation in the sector, the Faculty is committed to fully and effectively engage with Department of Health and Ageing and Independent Hospital Pricing Authority, in order to achieve the best possible outcomes for our patients.

RANZCR Annual Scientific Meeting

The RANZCR 64th Annual Scientific Meeting will be held 17 – 20th October in Auckland, New Zealand. The Scientific Program Committee has worked hard to create an intellectually stimulating program that combines education with discussion of the latest advances in radiology and radiation oncology.

The radiology scientific program is planned around a theme of ‘Clinical collaboration – radiology at the core of clinical practice’. The scientific program continues on the theme of clinical collaboration, with a focus on collaboration with our multi-disciplinary colleagues. Our outstanding list of international speakers will cover a selection of topics such as image guided radiotherapy, and deformable and multi-modality imaging associated with a number of site specific malignancies.

RANZCR-ESTRO collaboration for radiation oncology trainees and the radiobiology course

RANZCR has signed a memorandum of understanding with the European Society for Therapeutic Radiology and Oncology (ESTRO), which takes effect from January 2013. This is the first concrete step in a collaborative program in which we will harness the resources available through ESTRO for our trainees and in turn, share our extensive experience with our training curriculum.

Part of this agreement is the ESTRO radiobiology course, which will be held in Sydney from 23 – 26 November 2013. The course represents a unique and valuable opportunity for radiation oncology professionals, both qualified and in training, to access radiobiology education from an international faculty of expert radiobiologists and clinicians, and addresses an unmet need in oncology education in Australia.
REPORTS

International Conference on the Use of Computers in Radiation Therapy

The 17th International Conference on the use of Computers in Radiation Therapy will be held 6 – 9 May 2013 in Melbourne. The meeting will have a clinical focus and will highlight how increasing computer sophistication has enhanced the capability of radiotherapy to benefit cancer patients. For more information, visit iccr2013.org.

Prof Gillian Duchesne, Dean, Faculty of Radiation Oncology

MEDICAL ONCOLOGY GROUP OF AUSTRALIA

The Medical Oncology Group of Australia (MOGA) has a strong commitment to the training and professional development of medical oncologists.

The Sciences of Oncology Program for Australian trainees in late May will provide in-depth training in core oncology science topics. Up to five communications skills training sessions on ‘transition to palliation’ have also been scheduled throughout the year. Communication skills training is a mandatory requirement of the three year medical oncology training program through the Royal Australasian College of Physicians. Effective and skilled communication is a core capability for members of our profession and is the distinguisher of not only a good, but a great clinician.

Applications for the 2014 Australia and Asia Pacific Clinical Oncology Research (ACORD) Workshop, 7-13 September in Queensland, will open online in November. This program plays an important role in building regional expertise, networks and a body of skilled professionals in clinical oncology trials design and practice. Over the next six to nine months junior oncology clinicians in our region will be encouraged to work with their supervisors and colleagues on the development of concept outlines for clinical research protocols that can be submitted for development at the next workshop.

Potential applicants are invited to attend ‘Getting started in clinical research: writing a concept outline to start the clinical trials process’, a palliative care clinical studies collaborative/ACORD concept development workshop on 2 September in Canberra. This workshop aims to help early career researchers turn their new ideas for cancer-related clinical research studies into persuasive one page concept outlines. Concept outlines are an ideal starting point for writing study protocols, letters of intent to industry, or grant applications to funding bodies. Concept outlines prepared at the workshop will be ideally suited for applications to attend the 2014 ACORD Workshop in 2014 www.acord.org.au.

The theme of the 2013 MOGA Annual Scientific Meeting is ‘Blood, Biomarkers and Beyond’ (Melbourne Convention Centre, 1-2 August). The meeting will consider: biomarkers as tools for screening, diagnosis and treatment; translational biomarker issues; practical aspects of biomarker development; future approaches and applications in translational research; drug development; research; and clinical practice. The meeting will feature international guest speakers Caroline Robert (melanoma) and Professor Amit Oza (gynaecological cancer). Australian experts will complete the line up. Other topics that will be examined include: circulating tumour and stem cells; proteomics; next gen sequencing; plasma DNA; and genomics. The Asia Pacific perspectives session will feature Kazuo Tamura, President of the Japanese Society for Medical Oncology, and Allen Chan from the Chinese University of Hong Kong, discussing clinical practice and research developments in their countries and opportunities for future collaboration.

An industry symposium will focus on the newly established Oncology Industry Taskforce, which is examining barriers to patient access to oncology medicines in Australia with speakers from the government and regulatory sectors, MOGA, industry and Medicines Australia. While in the viewpoint session a panel of experts will consider the question, “Who pays for high costs drugs?”
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## Australia and New Zealand

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<td>14-16</td>
<td>Australian &amp; New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group Annual Scientific Meeting</td>
<td>Gold Coast, Queensland</td>
<td>Australian &amp; New Zealand Urogenital and Prostate (ANZUP)</td>
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<td>Phone: +61 2 9562 5033</td>
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<td>25-27</td>
<td>Cancer Nurses Society of Australia 16th Winter Congress</td>
<td>Brisbane, Queensland</td>
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<td>Phone: +61 2 8005 1867</td>
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<td>1-2</td>
<td>Medical Oncology Group of Australia (MOGA) Annual Scientific Meeting</td>
<td>Melbourne, Victoria</td>
<td>Medical Oncology Group of Australia Secretariat</td>
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<td>26-28</td>
<td>Familiar Aspects of Cancer 2013</td>
<td>Cairns, Queensland</td>
<td>Meeting Makers</td>
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<td>Phone: +61 3 8344 1831</td>
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<td>InSiGHT 2013 Conference</td>
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<td>Getting started in clinical research: writing a concept outline to start the clinical trials process, a Palliative Care Clinical Studies Collaborative/ACORD Concept Development Workshop</td>
<td>Canberra, Australian Capital Territory</td>
<td>Palliative Care Clinical Studies Collaborative &amp; ACORD</td>
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<td>Email: <a href="mailto:paccsc@flinders.edu.au">paccsc@flinders.edu.au</a></td>
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<td>Phone: +61 8 8275 1926</td>
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<td>3-6</td>
<td>12th Australian Palliative Care Conference</td>
<td>Canberra, Australian Capital Territory</td>
<td>DC Conferences Pty Ltd</td>
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<tr>
<td>12-14</td>
<td>Clinical Oncological Society of Australia’s (COSA)’s 40th Annual Scientific Meeting</td>
<td>Adelaide, South Australia</td>
<td>Clinical Oncological Society of Australia (COSA)</td>
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<td>Phone: +61 2 8063 4100</td>
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<td>21-24</td>
<td>Global Controversies and Advances in Skin Cancer Conference</td>
<td>Brisbane, Queensland</td>
<td>Cancer Council Queensland</td>
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<td>30-2 June</td>
<td>13th World Congress of the European Association for</td>
<td>Prague, Czech Republic</td>
<td>European Association for Palliative Care</td>
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<td>31-4 June</td>
<td>2013 American Society Clinical Oncology (ASCO)</td>
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<td>June</td>
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<tr>
<td>19-22</td>
<td>12th International Conference on Malignant Lymphoma</td>
<td>Lugano, Switzerland</td>
<td>American Society of Clinical Oncology (ASCO)</td>
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<td>The 6th International Nasopharyngeal Carcinoma</td>
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<td>27-29</td>
<td>Multinational Association of Supportive Care in</td>
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<td>Congress Organizer: Kenes International</td>
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<td>Cancer (MASCC) International Symposium on Supportive</td>
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<td>Worldwide Innovative Networking (WIN) 2013</td>
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<td>19-22</td>
<td>12th International Conference on Malignant Lymphoma</td>
<td>Lugano, Switzerland</td>
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<td>Multidisciplinary Cancer Management Course (MCMC)</td>
<td>La Paz, Bolivia</td>
<td>American Society of Clinical Oncology (ASCO)</td>
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## CALENDAR OF MEETINGS

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<tr>
<td>29-31</td>
<td>11th Annual Meeting of Japanese Society of Medical Oncology (JSMO2013)</td>
<td>Sendai, Japan</td>
<td>Congress Corporation&lt;br&gt;Website: <a href="http://www.congre.co.jp/jsmo2013/english/index.html">www.congre.co.jp/jsmo2013/english/index.html</a>&lt;br&gt;Email: <a href="mailto:jsmo2013@congre.co.jp">jsmo2013@congre.co.jp</a>&lt;br&gt;Phone: +81 22 723 3211</td>
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<tr>
<td>September</td>
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<tr>
<td>7-9</td>
<td>2013 Breast Cancer Symposium</td>
<td>San Francisco, United States</td>
<td>American Society of Clinical Oncology (ASCO)&lt;br&gt;Website: <a href="http://www.breastcasym.org">www.breastcasym.org</a>&lt;br&gt;Email: <a href="mailto:membermail@asco.org">membermail@asco.org</a>&lt;br&gt;Phone: +1 571 483 1300</td>
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<td>2nd International Conference on UV and Skin Cancer Prevention</td>
<td>Berlin, Germany</td>
<td>Porstmann Kongresse GmbH (PCO)&lt;br&gt;Website: <a href="http://www.uv-and-skin-cancer2013.org/">www.uv-and-skin-cancer2013.org/</a>&lt;br&gt;Email: <a href="mailto:ESCF2013@porstmann-kongresse.de">ESCF2013@porstmann-kongresse.de</a>&lt;br&gt;Phone: +49 302 844 9919</td>
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<tr>
<td>22-24</td>
<td>5th International Symposium – Primary Systemic Treatment in the Management of Operable Breast Cancer</td>
<td>Cremona, Italy</td>
<td>American Society of Clinical Oncology (ASCO)&lt;br&gt;Website: <a href="http://www.asco.org.au">www.asco.org.au</a>&lt;br&gt;Email: <a href="mailto:membermail@asco.org">membermail@asco.org</a>&lt;br&gt;Phone: +1 571 483 1300</td>
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<tr>
<td>26-1 Oct</td>
<td>17th European Cancer Organisation (ECCO) - 38th European Society of Medical Oncology (ESMO) - 32nd European Society for Therapeutic Radiology and Oncology (ESTRO) European Cancer Congress</td>
<td>Amsterdam, The Netherlands</td>
<td>European Cancer Organisation (ECCO)&lt;br&gt;Website: <a href="http://www.ecco-org.eu">www.ecco-org.eu</a>&lt;br&gt;Email: <a href="mailto:info@ecco-org.eu">info@ecco-org.eu</a>&lt;br&gt;Phone: +32 2 775 0201</td>
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<tr>
<td>27-28</td>
<td>Cancer Survivorship Conference</td>
<td>Houston, United States of America</td>
<td>MD Anderson Cancer Centre&lt;br&gt;Website: <a href="http://www.mdanderson.org">www.mdanderson.org</a>&lt;br&gt;Email: <a href="mailto:dschultz@mdanderson.org">dschultz@mdanderson.org</a>&lt;br&gt;Phone: +1 713 745 9208</td>
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<td>4-5</td>
<td>Symposia on Cancer Research, Genomic Medicine</td>
<td>Houston, United States</td>
<td>MD Anderson Cancer Centre&lt;br&gt;Website: <a href="http://www.mdanderson.org">www.mdanderson.org</a>&lt;br&gt;Email: <a href="mailto:register@mdanderson.org">register@mdanderson.org</a>&lt;br&gt;Phone: +1 713 792 2223</td>
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<tr>
<td>10-11</td>
<td>5th InterAmerican Oncology Conference: ‘Current Status and Future of Anti-Cancer Targeted Therapies’</td>
<td>Buenos Aires, Argentina</td>
<td>InterAmerican Oncology Conferences&lt;br&gt;Website: <a href="http://www.oncologyconferences.com.ar/index.html">www.oncologyconferences.com.ar/index.html</a>&lt;br&gt;Email: <a href="mailto:secretariat@oncologyconferences.com.ar">secretariat@oncologyconferences.com.ar</a></td>
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<td>10-11</td>
<td>Management in Radiology (MIR) Annual Scientific Meeting</td>
<td>Nice, France</td>
<td>Management in Radiology (MIR)&lt;br&gt;Website: <a href="http://www.mir-online.org/cms/website.php">www.mir-online.org/cms/website.php</a>&lt;br&gt;Email: <a href="mailto:office@mir-online.org">office@mir-online.org</a>&lt;br&gt;Phone: +43 153 340 64</td>
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<td>European Society in Breast Imaging (EUSOBI) Annual Scientific Meeting</td>
<td>Rome, Italy</td>
<td>European Society in Breast Imaging (EUSOBI)&lt;br&gt;Website: <a href="http://www.eusobi.org/">www.eusobi.org/</a>&lt;br&gt;Email: <a href="mailto:office@eusobi.org">office@eusobi.org</a>&lt;br&gt;Phone: +43 1 535 89 25</td>
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<td>Global Breast Cancer Conference</td>
<td>Seoul, Korea</td>
<td>INTERCOM Convention Services Inc.&lt;br&gt;Website: <a href="http://www.gbcc.kr">www.gbcc.kr</a>&lt;br&gt;Email: <a href="mailto:gbcc@intercom.co.kr">gbcc@intercom.co.kr</a>&lt;br&gt;Phone: +82 2 501 7065</td>
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<td>17-18</td>
<td>International Clinical Trials Workshop</td>
<td>Santiago, Chile</td>
<td>MD Anderson Cancer Centre&lt;br&gt;Website: <a href="http://www.mdanderson.org">www.mdanderson.org</a>&lt;br&gt;Email: <a href="mailto:register@mdanderson.org">register@mdanderson.org</a>&lt;br&gt;Phone: +1 713 792 2223</td>
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<tr>
<td>24-26</td>
<td>European Society Cardiac Radiology (ESCR) Annual Scientific Meeting</td>
<td>London, United Kingdom</td>
<td>European Society of Cardiac Radiology (ESCR) Website: <a href="http://www.escr.org/cms/website.php?tid=-/en/meetings/escr_2013.htm">www.escr.org/cms/website.php?tid=-/en/meetings/escr_2013.htm</a> Email: <a href="mailto:office@escr.org">office@escr.org</a> Phone: +43 1 535 50 93</td>
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<tr>
<td>31-Nov</td>
<td>Advances in Cancer Survivorship Practice: A Conference for Health Care Professionals</td>
<td>Houston, United States of America</td>
<td>MD Anderson Cancer Centre Website: <a href="http://www.mdanderson.org">www.mdanderson.org</a> Email: <a href="mailto:register@mdanderson.org">register@mdanderson.org</a> Phone: +1 713 792 2223</td>
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<td><strong>November</strong></td>
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<td>6-8</td>
<td>Chemotherapy Foundation Symposium XXXI</td>
<td>New York, United States of America</td>
<td>The Chemotherapy Foundation Website: <a href="http://www.chemotherapyfoundationsymposium.org">www.chemotherapyfoundationsymposium.org</a> Email: <a href="mailto:jaclyn.silverman@mssm.edu">jaclyn.silverman@mssm.edu</a> Phone: +1 212 866 2813</td>
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<td>7-8</td>
<td>2013 American Institute for Cancer Research (AICR) Annual Research Conference on Food, Nutrition, Physical Activity and Cancer</td>
<td>Bethesda, Maryland</td>
<td>American Institute for Cancer Research Website: <a href="http://www.aicr.org/cancer-research/conference/">www.aicr.org/cancer-research/conference/</a> Email: <a href="mailto:aicrweb@aicr.org">aicrweb@aicr.org</a> Phone: +1 800 843 8114</td>
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<td>21-24</td>
<td>African Organisation for Research and Training in Cancer (AORTIC)</td>
<td>Durban, South Africa</td>
<td>African Organisation for Research and Training in Cancer (AORTIC) Website: <a href="http://www.aortic-africa.org">www.aortic-africa.org</a> Email: <a href="mailto:info@aortic2013.org">info@aortic2013.org</a> Phone: +27 21 689 5359</td>
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<td><strong>December</strong></td>
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<td>10-14</td>
<td>36th Annual San Antonio Breast Cancer Symposium</td>
<td>San Antonio, United States of America</td>
<td>Cancer Therapy Website: <a href="http://www.sabcs.org/">www.sabcs.org/</a> Email: <a href="mailto:sabcs@sabcs.org">sabcs@sabcs.org</a> Phone: +1 210 450 1550</td>
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CANCER COUNCIL AUSTRALIA
Cancer Council Australia is the nation’s peak cancer control organisation. Its members are the leading state and territory Cancer Councils, working together to undertake and fund cancer research, prevent and control cancer and provide information and support for people affected by cancer.

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Cancer Council ACT
Cancer Council New South Wales
Cancer Council Northern Territory
Cancer Council Queensland
Cancer Council South Australia
Cancer Council Tasmania
Cancer Council Victoria
Cancer Council Western Australia

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Clinical Oncological Society of Australia

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CLINICAL ONCOLOGICAL SOCIETY OF AUSTRALIA
The Clinical Oncological Society of Australia (COSA) is a multidisciplinary society for health professionals working in cancer research or the treatment, rehabilitation or palliation of cancer patients.

It conducts an annual scientific meeting, seminars and educational activities related to current cancer issues. COSA is affiliated with Cancer Council Australia.

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Survivorship
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MEMBERSHIP
Further information about COSA and membership applications are available from: www.cosa.org.au or cosa@cancer.org.au
Membership fees for 2013
Medical Members: $170
Non Medical Members: $110 (includes GST)
Information for contributors

*Cancer Forum* provides an avenue for communication between all those involved in the fight against cancer and especially seeks to promote contact across disciplinary barriers.

To this end articles need to be comprehensible to as wide a section of the readership as possible. Authors should provide sufficient introductory material to place their articles in context for those outside their field of specialisation.

Format

*Cancer Forum* welcomes original articles about medical, scientific, political, social, educational and administrative aspects of cancer control. All manuscripts should be submitted by email to info@cancerforum.org.au as MS Word documents.

Length: 2000-2500 words.

Font: Arial - 20pt for title, 12pt for headings and 10pt for text.

Following the title, include your full name, organisation and email address.

Include an introductory heading and sub-headings that describe the content.

Number pages in the footer.

Abstract

All manuscripts must include an abstract of approximately 200 words, providing a summary of the key findings or statements.

Illustrations

Photographs and line drawings can be submitted via email or on disk, preferably in tiff or jpeg format, or as transparencies or high quality prints.

If images are not owned by the author, written permission to reproduce the images should be provided with the submission.

Referencing

Reference numbers within the text should be superscripted and placed after punctuation.

The list of references at the end of the paper should be numbered consecutively in the order in which they are first mentioned and be consistent with the National Library of Medicine’s International Committee of Medical Journal Editors’ *Uniform Requirements for Manuscripts Submitted to Biomedical Journals.*


A full guide is available at www.nlm.nih.gov/bsd/uniform_requirements.html

The Editorial Board will make the final decision on publication of articles and may request clarifications or additional information.

Manuscripts should be emailed to:

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