



Geriatric oncology

OVERVIEW

GERIATRIC ONCOLOGY: A MEDICAL SUB-SPECIALTY WHOSE TIME HAS COME

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It is a truism that cancer is a disease of older people and that as the population ages the incidence and prevalence of cancer increases. Fifty per cent of cancers occur in those over 65 years of age and the number of people over the age of 65 is increasing steadily.¹ Cancers such as those of the colon and lung increase dramatically with age.¹

In 1981, only 9.2% of the population was aged over 65, but in 2004 that had risen to 13% and is projected to be 26-28% in 2051.² As we prevent more deaths from other diseases such as heart disease and infection, the number of cancers will continue to rise and the number of older people with cancer will also continue to increase. Mortality from cancer in the over 65s is also increasing, while it is decreasing in the under 65s.^{1,3}

Over the past 20 years, the upper age limit for many medical procedures and treatments has increased. This is partly due to the increase in life-expectancy that occurred throughout the 20th Century, the fact that older people are also fitter and healthier as they reach old age than they have ever been before and because techniques in anaesthesia and surgery have improved to allow safer operations and less morbid recovery. As with all treatments, performance status is a better predictor of outcome than is age.

However, not everything is completely straightforward in older people. Older people are not just "adults but older" just as children are not "adults but smaller". There are physiological changes that occur with ageing, as well as multiple co-morbidities which can complicate management of elderly cancer patients. Some tumours, such as breast cancer and non-small cell lung cancer, are more indolent in the elderly, while others such as lymphoma and ovarian cancer may be worse.⁴ Under-treatment may cause poor outcomes in elderly (>60 years) patients. With aggressive lymphoma for example, older patients are less likely to be treated for cure, and are less likely to survive for five years.⁵ Older women with breast cancer are less likely to be offered

enrolment in clinical trials and older patients tend to receive less aggressive diagnosis and treatment for lung cancer.^{6,8}

Onco-geriatrics: do we need it?

Over the past 15 years, cancer in the older person, or onco-geriatrics, has increasingly been talked about as a coming thing, within both geriatric and oncology circles. Meetings have been held, societies formed and positions taken. Both the Clinical Oncological Society of Australia and the Medical Oncology Group of Australia have held sessions on 'cancer in the older person' at their annual meetings; the International Society of Geriatric Oncology held its 8th meeting in Madrid in November 2007 and there are regular sessions at the American Society of Clinical Oncology about treating elderly cancer patients. This edition of *Cancer Forum* is the first one dedicated to this area and covers several of the most important issues. However, in Australia we still do not have routine, protocol-based care for our older cancer patients.

Oncologists feel every patient with cancer deserves to have a consultation with an oncologist. Geriatricians judge many of their patients to be inappropriate for oncological treatment. Neither point is fully objective and onco-geriatrics has a major potential benefit in informing both specialties. Does every elderly cancer patient need to see a geriatrician? Could we reduce the 'burden of care' by supporting our elderly cancer patients better? A proactive approach to the management of the elderly patient with cancer reduces toxicity. We should look at general clinical measures and manage underlying health problems, treat toxicities and use prophylaxis where possible. We should also make dose adjustments for renal function and ensure that older people are adequately represented in trials of new cancer treatments.⁹

In this issue of *Cancer Forum*, Khasraw and Marx discuss the use of chemotherapy in the elderly.¹⁰ We are

aware that clinical trials of new agents need to include elderly patients, as they are most likely to be major users of all new drugs. In the last five years, the upper age limit for most clinical trials has been removed. It was a first when Mabthera was introduced in the older patient before the general adult lymphoma population,¹¹ although it is now available in all adults with appropriate CD20+ tumours. Giving chemotherapy to older patients is not exactly the same as giving it to younger patients. Older patients are more prone to certain toxicities and may take longer to recover from them, but the evidence for this is not the most rigorous. Among toxicities thought to be more common are myelosuppression,¹² mucositis¹³ (although the evidence for this is particularly weak), cardio-depression, peripheral neuropathy and central neurotoxicity (cognitive decline, delirium, cerebellar dysfunction). Toxicity of adjuvant chemotherapy for breast cancer increases with age while the likelihood of receiving full dose chemotherapy decreases with age, decreasing the chances of cure.¹⁴

Both pharmacokinetic and pharmacodynamic changes occur with ageing. Pharmacokinetic changes include changes in drug distribution, metabolic and renal clearance. Steer's paper shows how misleading serum creatinine can be as a measure of renal function in the older patient.¹⁵ Unfortunately, a single answer regarding the best way to measure renal function is not yet available, but progress is being made.

Pharmacodynamic changes are harder to measure and include effects of concurrent therapies and multiple disease processes, making it hard to ascribe exactly the correct amount of responsibility to ageing per se. Older patients particularly have increased sensitivity to psychoactive drugs such as opiates and benzodiazepines, drugs commonly used by oncologists. In relation to chemotherapy, the geriatrician's mantra of 'start low, go slow' may be particularly inappropriate; it may be dangerous to begin at a lower than usual dose as the patient may suffer side-effects while not deriving any benefit from the treatment.

Rights to therapy are the same for older as for younger individuals. However, that doesn't mean that decision making is the same in an 80 year-old as it is in a 20 year-old. At 80, many people may feel that they have lived long enough and do not want their life to be prolonged, even where that is possible. That sort of feeling would be most unusual in a 20 year-old with his/her whole life ahead. Questions of competence to make a decision often arise in the elderly, particularly because of the prevalence of dementia. When the patient is competent, he or she is able to make decisions about treatment. But when competence is impaired, decision making tends to revert to families, unless other arrangements such as enduring power of guardianship, advanced directives or the appointment of a medical attorney have been made. Chemotherapy also has the potential to 'unmask' dementia. A patient may be managing to hide early signs of dementia by using all his/her coping skills. Once the chemotherapy is administered however, energy reverts to maintaining physical health and dealing with side-effects, so the ability to hide the cognitive problems is reduced. This will increasingly be an issue as the population ages and the prevalence of dementia increases.

Effectiveness is an important concept in healthcare. Time to response may have important implications. If a drug is going to take six months to work and the patient's life expectancy is short, that may be too long. Cost-effectiveness is often talked about and interestingly enough many drugs turn out to be more cost-effective in the elderly than in young/middle aged adults. Although anti-toxicity treatments are expensive, sick, elderly patients are more expensive¹⁶⁻¹⁷ and recent studies suggest older patients may derive more benefit from anti-toxicity treatments than younger people.¹⁸

Lung cancer is one of the most common cancers in the elderly population and it brings particular problems with dyspnoea, malnutrition and fatigue. Cheong's paper reviews what is known about lung cancer in the older patient, reiterating the reluctance in some clinicians to treat elderly patients with lung cancer.¹⁹ Again, renal function is critical; platinum agents are hard to use in renal impairment, but single agents with less toxicity do provide some benefit, as do non-platinum doublets.

Kichenadassa reports an audit of the treatment of rectal cancer in older people at Queen Elizabeth Hospital in South Australia and a review of Australian literature on the subject.²⁰ He shows that patients are not as involved in decision-making as they probably should be and that decisions are not always evidence-based.

Alam looked at decision making in elderly cancer patients and reports that physician bias, rather than patient opinion or disease characteristics, plays a large part in treatment plans for older patients.²¹ These two papers demonstrate that this is an area of increasing importance and it is to be hoped that they will become a catalyst to many other studies in this area.

Rationale for investigating cancer in older people

Why investigate an older person with possible cancer? If treatment is possible for cure, prolongation of life or palliation of symptoms, then investigations to determine this are appropriate. Likewise, just knowing the prognosis may be important. It may influence the treatment of other diseases, it may help with lifestyle decisions such as placement, and it may help to advise families about their own plans.

Many factors guide cancer management in the elderly and can be divided into those relating to the disease, such as cellular type and staging, and those relating to the patient such as overall fitness, comorbidities, functional status, mental status and family/social support.⁹

A comprehensive geriatric assessment addresses the physiological, functional and psychosocial factors, as discussed by Singhal,²² but one of the vexed questions in geriatric oncology is exactly which scale to use to make an assessment of the fitness of a patient for chemotherapy. Domains that need to be considered are mental and emotional status, activities of daily living (ADL) and instrumental activities of daily living (IADL), home environment, social support, comorbidity, nutrition and polypharmacy. There is merit in a self-administered screening tool that could define a group for more intensive investigation.

Frail elderly patients are a distinct patient population, occurring especially in the over 80s, with other factors such as dependence in ADLs, comorbidities and geriatric syndromes. The treatment algorithm proposed by Balducci states that independent elderly patients with no comorbidities and in whom full treatment would lead to a greater life-expectancy than no treatment, should have full treatment. Patients with comorbidities or dependent in IADLs should have precautions taken with treatment, by using a dose reduction for cycle one to assess toxicity, increasing in cycle two if well tolerated. Frail elderly patients should receive supportive care.

Future Plans

In 2007, a group of interested clinicians from both oncology and geriatrics met to develop a plan for onco-geriatrics; they will hold their first national workshop in Sydney in April this year. Issues for discussion will include models of care for older cancer patients, the need for specialist geriatric assessment of older cancer patients and the utility of the various tools available. As we move nationally towards care in cancer networks, it is important that the rights of older cancer patients are considered and that we have a unique opportunity to build appropriate geriatric assessment into our cancer plans.

Given all the above, it is time to propose the introduction of screening for geriatric patients with cancer. The Royal Adelaide Hospital Cancer Centre, in partnership with the hospital's Department of Geriatric and Rehabilitation Medicine, and as a pilot project for the South Australian Cancer Network, is setting up such a service. At referral to (initially) medical oncology, patients over the age of 70 will be sent a questionnaire to fill in as a screening assessment. This will be reviewed by the geriatric nurse attached to the program and assessed as high, medium or low risk. High and medium risk cases will then be discussed in an onco-geriatrics multidisciplinary meeting, while low risk patients will be treated as usual through the medical oncology clinic. Any low risk patients can be referred subsequently to the geriatric team if required. At the onco-geriatric multi-disciplinary team meeting, patients will be assessed for suitability for normal treatment with increased supports, pre-emptive geriatric management to optimise status prior to normal treatment, or supportive/palliative care only. A database is being constructed so that all cases can be reviewed and outcomes reported. It is expected that this pilot will be refined and then expanded across the health region, and inform practice elsewhere.

In conclusion, we believe that there is a role for onco-geriatrics to assist oncologists to optimise treatment recommendations for patients and to help elderly cancer patients, both to make informed treatment decisions and to cope with the rigours of treatment. Perhaps one of the most important roles for onco-geriatrics will be to ensure that decisions about treatment of elderly cancer patients in the future are made by the patient whenever possible, with expert advice being based on evidence rather than on bias.

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TOOLS FOR ASSESSING ELDERLY CANCER PATIENTS

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Abstract

The population segment that is seeing the most growth is the geriatric population. Oncologists are increasingly facing the problem of how best to treat an elderly patient with cancer. Treatment decisions are mostly empirically based on past experiences. There is an increasing need for geriatric assessment tools that can help a clinician to ascertain whom to offer treatments that have potential for toxicities. Comprehensive Geriatric Assessment is a useful tool but unsuitable for daily clinical practice because of the time constraints. Screening tools that are mostly self-administered have shown early promise in fulfilling the gap.

The Australian population is ageing. It is estimated that between the years 2002-2011, the population aged 65 and over is projected to increase by 30%. Cancer is predominantly a disease of elderly, with more than 60% of new cancer diagnosis and 70% of cancer deaths occurring in the elderly, ie. ≥ 65 years. The largest increase is seen in the most elderly ie. those persons ≥ 85 years of age. Medical oncologists will be faced with making treatment decisions for these patients and often the decision to initiate life sustaining but toxic treatment is empirical, based on the physician's personal judgment and past experiences. It is now well documented that the elderly are less likely to receive chemotherapy and when they do receive chemotherapy it is often dose-reduced, leading to poorer outcomes.¹ The majority of studies evaluating the role of chemotherapy in the elderly have found significant and equivalent benefit when compared to their younger counterparts, so chronological age should not be the only factor in treatment decisions.

Oncologists possess a limited set of assessment tools to evaluate functional status of the elderly which assist in making treatment decisions. The most commonly utilised tools include the Karnofsky Performance Score and Eastern Cooperative Oncology Group performance status. Both are brief and easy to perform, but do not provide information beyond physical functionality. They are insensitive to functional decline and do not take mental status or co-morbid conditions into account.

Geriatricians commonly use Comprehensive Geriatric Assessment (CGA), which has been defined as a "multidisciplinary evaluation in which the problems of the elderly are catalogued, need for services assessed and a coordinated care plan developed to focus interventions on the person's problems".² The International Society of Geriatric Oncology has come up with recommendations regarding the use of CGA in older cancer patients.² The use of CGA has been shown

to reduce early re-hospitalisations and mortality in older patients, particularly if linked to geriatric interventions. For example, CGA can be used to identify patients who will tolerate treatment well and those who will require geriatric interventions during treatment. In a study of 363 elderly cancer patients with a median age of 72 years, it has been demonstrated that CGA adds substantial information on the functional assessment of elderly cancer patients, including patients with a good performance status.³

Over the years, there have been several different tools to conduct CGA. Most of them evaluate functional status, co-morbid conditions, cognition, nutritional status, social support, psychological state and concomitant medications.⁴ These domains of CGA have been briefly described below (Figure 1):

1. Functional status

Functional status predicts survival, chemotherapy toxicity, post-operative morbidity and mortality. Functional status has been traditionally evaluated using activities of daily living (ADL) and instrumental activities of daily living (IADL). ADL takes into account the activities for self care, while IADL assess ability to use tools to remain independent in the society. Functional status can be judged by questionnaire and objective, performance-based measures like "Timed Up and Go".

2. Comorbidity

Presence of comorbid illness influences tolerance to treatment, as well as increasing morbidity and mortality associated with malignancy. For example, diabetes mellitus is associated with decreased disease specific survival in breast, colon and prostate cancer.⁴

3. Cognition

Cognition has been shown to influence diagnosis, treatment and survival of malignancy. Folstein's Mini

Mental status examination is commonly used to assess cognitive impairment.⁴

4. Nutritional status

Unintentional weight loss is an important prognostic factor and adversely impacts outcome after treatment with chemotherapy or radiotherapy. Similarly, obesity is associated with increased mortality in cancer patients.⁴

5. Social support and psychological state

Social isolation has been shown to increase mortality and depression and is a common finding in elderly patients with cancer. The Hospital Anxiety and Depression scale and Geriatric Depression Scale are commonly used to assess psychological state.⁴

6. Concomitant medications

Polypharmacy increases the risk of drug interactions and can increase the risk of adverse effects and decrease efficacy of chemotherapy drugs. On average, elderly patients take six concomitant medications, significantly increasing the risk of drug interactions. In a study it was shown that pharmacist consultation could lead to decreased use of concomitant medications with the additional benefit of lower drug expenditure.⁵

The most important aspect of CGA is identification of a specific problem that leads to an intervention and then regular follow-up. The only drawback of CGA is time constraints. On average it can take between 45 minutes to two hours to conduct CGA for a single patient. This is not always feasible in a busy oncology clinic, hindering adaptation of CGA in routine practice.

There is a growing need for a brief, yet concise screening questionnaire which would not be so time consuming, or which could be self-administered. Hurria et al in a pilot trial evaluated a comprehensive, self-administered questionnaire in elderly cancer patients.¹ The mean time to complete this questionnaire was 27 minutes, with 78% of patients completing it without assistance and 90% being satisfied with the questionnaire length. It is now being studied in a larger group of elderly cancer patients in the form of an ongoing prospective trial. The interim results have revealed 250 patients completed the questionnaire and 78% required no assistance. The mean time to completion was 15 minutes and more than 90% of participants were satisfied with the questionnaire.⁶ There are other screening questionnaires in development and we eagerly await their publication and validation for general use.

Figure 1: *The essential domains of Comprehensive Geriatric Assessment*



Conclusions

There is a growing need for a standardised, validated and brief screening tool to assess elderly patients with cancer. An ideal tool will not only triage patients for treatment, but will prompt geriatric intervention to optimise care for senior adults.

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CHEMOTHERAPY IN THE ELDERLY

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Abstract

The number of elderly patients with malignancy is growing and is likely to have a major impact on resources, quality of care, health economics and treatment options. Decisions regarding treatment options with chemotherapy are limited by the scarcity of data specifically addressing the issues regarding chemotherapy in the elderly. The problem is further confounded by issues such as co-morbidity, poly-pharmacy, cognitive impairments, emotional problems, functional limitations, sensory impairment and a lack of social support. Ageing is associated with specific physiologic changes in functional status, organ function and drug pharmacokinetics. Optimising cancer care and chemotherapy delivery in the elderly requires a better understanding of the specific pharmacokinetic and pharmacodynamic issues and administration of chemotherapy in this age group. Elderly participation in clinical trials and specific research is essential to guide treatment decisions and further research is required to provide evidence-based models to guide treatment decisions. In an Australian setting, the development of a geriatric oncology specific group as a means of facilitating collaboration with geriatricians, development of specific elderly research programs and clinical trials, education and development of treatment guidelines would further improve outcomes of our elderly patients undergoing cancer treatment.

Magnitude of the problem

Cancer is a disease that mostly affects older individuals, with approximately 60% of cancer morbidity and 70% of cancer mortality occurring in patients over 65 years of age.^{1,2} This age group is growing rapidly: in Australia in 2003, there were 3.35 million people aged 60 years and over (17% of the population), compared to three million people (16%) in 1998. It is expected these numbers will increase steadily. In 2002, median life expectancy at age 65 years was 17.3 years for males and 20.8 years for females. Since 1982, at 65 years of age males have gained 3.7 years of life expectancy and females three years. In 2003, just over half had a reported disability (51%) and 19% had a profound or severe core-activity limitation.³ People aged 85 years and over reported a much higher need for assistance than those aged 60-69 years (84% compared with 26%).⁴

Ageing is an important part of human development and it is influenced by the biological changes that occur, but also reflects cultural and societal conventions. Specific strategies to address these problems need to be developed as a priority. Elderly cancer patients often present with medical and physiologic problems that make the selection of their optimal treatment challenging. The problem is further confounded by issues such as co-morbidity, poly-pharmacy, cognitive impairments, emotional problems, functional limitations, sensory impairment and a lack of social support.

Until recently, almost all clinical cancer research under represented elderly patients.⁵⁻⁸ Most of the published trials in oncology have used chronological age limits to define cancer patients as elderly; 65 or 70 and less often 80 years of age are commonly used limits for patients with solid tumours. Data from these trials have been extrapolated to guide treatment decisions in the elderly population. Despite these limitations, physicians attempt to tailor chemotherapeutic treatments for this

population of patients that limit exposure to potentially futile or unjustifiably toxic treatments, while not denying them beneficial treatments which may impact on survival, symptoms and quality of life. This is further complicated by the diversity and heterogeneity of this population. At present, there are few evidence-based guidelines or trials to assist in this regard.

Under-treatment of elderly cancer patients with dose reduction of adjuvant chemotherapy or total therapeutic abstinence is not unusual in practice. Under-utilisation of resources might also include access to palliative care, treatment of pain, surgical reconstruction and rehabilitation. Common justification for under-treatment includes co-existing medical problems, chronological age, lack or scarcity of data for that age group, lack of relevant clinical trials and increased risk of adverse events.

In current practice, the elderly are often excluded from participation in clinical trials and receive untested or inadequate treatment based on unvalidated criteria. Elderly specific clinical trials are an essential requirement to guide clinicians more appropriately to optimise chemotherapy delivery to this specific population. Studies incorporating the pharmacodynamic and the pharmacokinetic effects on ageing are necessary. This paper will address issues related to chemotherapy delivery in the elderly.

Impact on the pharmacokinetics and pharmacodynamics

Ageing is associated with physiologic changes in functional status, organ function and drug pharmacokinetics. Physiologic reserve decreases progressively with ageing.^{9,10} Organ specific age related physiologic decline begins in the third decade of life. It is not evident at times of rest but becomes most apparent when the body is stressed.¹¹ Both cancer and its treatment can be considered as physiologic stressors

and the age related decrease in physiologic reserve can affect tolerance to cancer treatment.

Ageing is associated with decreases in marrow reserve, drug clearance and lean body mass. Furthermore, concomitant co-morbidities that affect functional status, general health and tumour symptoms are frequently present in this patient population. Co-morbidities in older patients can strongly affect the risk and behaviour of cancer and their related treatment. This effect is associated with syndromes with common patho-physiologic mechanisms, such as diabetes mellitus, the metabolic disorders and inflammatory diseases.¹²⁻¹⁵

The levels of a number of inflammatory cytokines have been found to be elevated in common cognitive disorders of ageing.¹⁶ The circulating level of Interleukin-6 is elevated in most geriatric syndromes and often reflects compromised muscular function.¹⁷ The circulating level of C-reactive protein, another inflammatory marker, predicts increased risk of cardiovascular mortality.¹⁸ Non-specific markers of autoimmunity, such as antinuclear antibodies, also tend to increase with age.

A number of age related changes in drug absorption, distribution, metabolism and excretion with ageing can contribute to differences in treatment tolerance between older and younger patients. An increased toxicity in elderly patients with cancer may be due to increased exposure to a drug either by prolonged half-life, due to decreased elimination, or by impaired renal function and also changes in pharmacodynamics caused by increased vulnerability of organs with age. The volume of distribution changes; total body water is reduced to about 50% (instead of 60%), whereas total body fat increases. Other factors associated with a change of distribution are binding of drugs to erythrocytes (eg. anthracyclines, epipodophyllotoxins and oxaliplatin) and proteins (especially albumin). Thus, hypoproteinemia and anaemia can alter drug distribution. The absorption of drugs can be affected by decreased gastrointestinal motility, decreased splanchnic blood flow, decreased secretion of digestive enzymes and mucosal atrophy.¹⁹⁻²⁰ However, to date no unfavourable data for orally applied cytotoxic drugs due to a decreased absorption have been reported in elderly patients.

With the increased use of oral therapy, drug compliance is an important issue.²¹ The increase in body fat leads to a rise in the volume of distribution for lipid soluble drugs and a diminution in the volume of distribution for hydrophilic drugs. In the cancer population, malnutrition and hypoalbuminaemia can result in an increased unbound concentration of drugs that are albumin-bound.²² Hepatic mass and blood flow decrease with age.^{9,23} The impact of the decline in hepatic mass and blood flow on hepatic enzyme function is controversial.²⁴⁻²⁶

Changes in renal function are less controversial. The decline in Glomerular Filtration Rate (GFR) with age is estimated at 0.75 mL/min per year after age 40; however, approximately one third of patients have no change in creatinine clearance with age.²⁷ This reduced renal function does not usually result in increased serum creatinine levels because of the simultaneous loss of muscle mass.²⁸ Therefore, serum creatinine is not an

adequate indicator of renal function in the older patient. All formulas used to calculate renal function have been primarily validated in a younger group of patients without renal disease and are not as accurate in older patients.^{29,30} The accuracy of the Cockcroft-Gault, Jelliffe and Wright formulas in a population of older patients with cancer has been evaluated and the Wright formula was the most accurate formula to calculate GFR; however, the majority of patients in this study had a GFR >50 mL/min.³¹

The decline in GFR with age translates into pharmacokinetic alterations of drugs or their active metabolites which are excreted by the kidneys. Prudence with adjusting doses of renally excreted drugs to prevent toxicity cannot be overemphasised.

Polypharmacy, which is common in the elderly, increases the risk of adverse events.³²⁻³⁴ The older patient with cancer is particularly at risk for adverse drug events due to issues relating to polypharmacy. Agents such as supportive care medications (anticholinergics, benzodiazepines, dexamethasone) may have exaggerated effects in an older person.^{33,34} In addition, clearance of chemotherapeutic agents may be affected by concomitant drugs, which can lead to decreased clearance of the chemotherapy (placing the patient at increased risk of toxicity) or increased clearance (placing the patient at risk of ineffective therapy).

Many older patients are on common drugs causing cytochrome P450 related interactions, including selective serotonin reuptake inhibitors, phenytoin, steroids, ketoconazole and macrolide antibiotics. These patients may experience important drug interactions which involve antineoplastic agents such as ifosfamide, vinca alkaloids, etoposide, taxanes and aromatase inhibitors.²⁴

Strategies to minimise the risk for drug-to-drug interactions involve: a thorough medication history including prescribed medications, over-the-counter medications and herbal medicines at each visit, becoming familiar with the lists of drugs that should be avoided in older patients; eliminating any unnecessary medications; and paying attention to patient adherence to prescribed medications.^{33,35} Moreover, it is essential to realise that elderly patients often have more than one clinician prescribing different medications without adequate communication among them.

Older patients are at increased risk of myelosuppression and toxicity resulting from age-related decline in organ function.³⁶ Haematological toxicity is more common in elderly patients. Chemotherapy is associated with a higher rate of infection, more hospitalisations and a higher mortality in older age groups.³⁶ Furthermore, the increased use of haematopoietic growth factors has led to a shift in the toxicity profile. The dose-limiting toxicity of many regimens has shifted to non-haematological toxicity, particularly neuropathy and gastrointestinal toxicity, which remain significant problems for older patients.

It is important to appreciate the limitations of the data on chemotherapy in the elderly available at present. Few studies have looked specifically at the older patient

group, with most analysing a subpopulation of older participants within larger studies, limiting the numbers, validity and reliability. Additional studies of pharmacokinetics of cancer therapies in the older patient are needed, based on the data to date, it is likely that more factors in addition to pharmacokinetics and chronologic age may be significant predictors of tolerance to chemotherapy. Future pharmacokinetic studies in older patients should include a thorough evaluation of physiologic factors, such as baseline renal function, hepatic function, haemoglobin and albumin levels. In addition, studies should include an assessment of factors apart from chronologic age that independently predict morbidity and mortality in the geriatric population, including all aspects of functional status, cognitive state, comorbid illnesses, nutritional state and psychological status.³⁷⁻³⁸ Studies that include these parameters may provide insights into the factors contributing to tolerability of chemotherapy and lead to interventions to improve treatment tolerance.

Chemotherapy agents and the data

Although it is beyond the scope of this article, we will briefly discuss a few aspects of specific chemotherapeutic agents commonly used in clinical practice. In elderly breast cancer patients treated with doxorubicin and cyclophosphamide there is evidence of an age-related decrease in absolute neutrophil nadir count. However, Dees et al concluded that healthy older patients should not be denied adjuvant chemotherapy on the basis of age alone.³⁹ There is no reproducible evidence for systematic dose reduction of cyclophosphamide based on age alone, particularly in the adjuvant setting.

Cisplatin is utilised in the treatment of numerous malignancies. The clearance is primarily dependent on renal function. The potential nephrotoxicity of cisplatin is a concern, but toxicity in the elderly can be minimised with appropriate safety measures, particularly with intravenous hydration.⁴⁰⁻⁴¹ Carboplatin, which has a mechanism of action similar to cisplatin, is primarily excreted renally while the remainder binds to tissue proteins and is inactivated.⁴² Dosing using creatinine clearances derived from formulae have limitations, particularly in elderly patients. Retrospective studies have attempted to quantify the reliability and the accuracy of these methods in a particular elderly cancer patient group.³¹

Fluoropyrimidines such as fluorouracil and capecitabine are widely used agents in solid malignancies in the geriatric population. They are often arbitrarily reduced in dosage.⁴³⁻⁴⁵ The pharmacokinetics of capecitabine for instance is not affected by age in patients with normal renal function.⁴⁶ There is no pharmacokinetic basis for dose modification based on age alone.⁴⁷ However, there may be significant age-related toxicities. An overview of seven phase III trials involving fluorouracil with either leucovorin or levamisole showed that no interaction between age and outcome could be identified. However, age older than 70 years correlated with a higher occurrence of treatment-related leucopaenia of borderline significance.⁴⁸ A retrospective analysis of European trials has showed that fit elderly patients

experience equivalent benefits and toxicities as younger patients.⁴⁹

With regard to taxanes, several phase II trials have concluded that the pharmacokinetic analysis of differences in age related clearance of this agent were negligible compared with the interpatient variability in drug metabolism.⁵⁰

Conclusions

Optimising cancer care and chemotherapy delivery in the elderly requires a better understanding of the specific pharmacokinetic and pharmacodynamic issues and administration of chemotherapy in this age group. Utilising a comprehensive geriatric assessment that incorporates aspects such as polypharmacy, comorbidities and social issues will be of great assistance. Outcomes of such an assessment tool may influence chemotherapy delivery, toxicity and prognosis. Further research is required to provide evidence-based models to guide treatment decisions.

There are great opportunities for research and development of scientific, evidence-based guidelines for geriatric oncology practice. There is an increasing demand for elderly specific cancer research. In an Australian setting, the development of a geriatric oncology specific group as a means of facilitating collaboration with geriatricians, development of specific elderly research programs and clinical trials, education and development of treatment guidelines, would further improve outcomes of our elderly patients undergoing cancer treatment.

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RENAL FUNCTION IN THE ELDERLY

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Abstract

Although it is generally accepted that renal function declines with increasing age, this should not be assumed in all cases. The estimation of renal function on an individual patient basis is therefore required. This is especially important in patients who are prescribed potentially nephrotoxic agents or chemotherapy which is renally excreted. The measurement of serum creatinine alone is inadequate for this task. The various ways in which more accurate measures of renal function can be estimated are discussed. The most common method in clinical practice is the estimation of creatinine clearance using the Cockcroft and Gault formula. The International Society of Geriatric Oncology has produced clinical practice recommendations on the estimation of renal function in the elderly and on chemotherapy dosing in patients with impaired renal function. These practical recommendations can be easily adapted into everyday clinical practice.

It is generally accepted that renal function declines in the elderly patient population. This is due to the presence of co-morbidity and a decline in renal reserve. Care must be taken not to assume that a reduced Glomerular Filtration Rate (GFR) is a normal part of ageing. Studies such as the Baltimore Longitudinal Study on Ageing suggest that the principle cause of the decline seen in the general elderly population is hypertension.^{1,2} This debate aside, most studies show a decline in GFR with increasing age (Figure 1).

Assessment of patients' renal function is therefore vital prior to the use of renally excreted or potentially nephrotoxic drugs. Reliance on the serum creatinine concentration is inappropriate in the elderly patient population and may lead to dosing errors and avoidable toxicity. More accurate methods of assessment of renal function are readily available.

Population ageing – global scope of the problem

A recent United Nations report on the global phenomenon of the ageing population produced four major findings; population ageing is unprecedented, global, enduring and profound, having implications for all facets of human life.³ As long as old age mortality continues to decline and fertility remains low, the proportion of older people will continue to increase.

Globally, the population of older people is itself ageing. Among those aged 60 years or over, the fastest growing population is that of the oldest-old, that is, those aged 80 years or over. Today, people aged 80 years or over account for about one in every eight older people (60 or over). By 2050, this ratio is expected to increase to approximately two in every 10 older people.

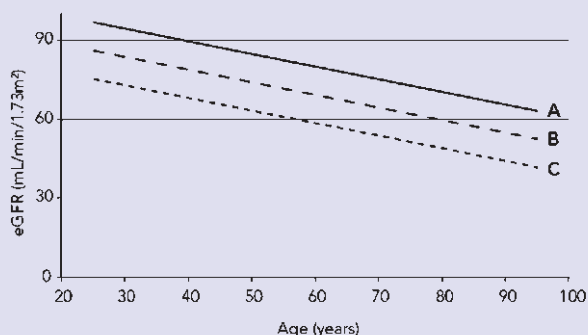
In 2000, the population aged 60 years or over numbered 600 million, triple the number in 1950. In 2006, the number had surpassed 700 million. By 2050, two billion older people are projected to be alive, implying that their number will once again triple over a span of 50 years.

The median age of patients in Australia at the first diagnosis of cancer is 67 years.⁴ As the population ages we expect the burden of cancer to be more common, especially in the elderly patient population.

Terminology

Definition of renal failure and stages of chronic kidney disease – American National Kidney Foundation Guidelines.⁵

Figure 1: Relationship of estimated glomerular filtration rate (eGFR) as derived by the MDRD formula to age*



* A: median (50% of subjects have eGFR above this line); B: 80% of subjects have eGFR above this line; C: 97.5% of subjects have eGFR above this line. These reference lines are derived from over 300 000 presentations to a large private pathology service, with exclusion of creatinine results lying outside a Gaussian distribution for each age decade (personal communication, Ken Sikans, Chemical Pathologist, Melbourne Pathology Service, VIC). ◆

Source: Matthew TH et al. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: revised recommendations. *MJA* 2007; 187: 459-46319. ©Copyright 2007. *The Medical Journal of Australia* – reproduced with permission.

The impact of physiological changes associated with age on the pharmacokinetic and pharmacodynamic properties of drugs can be considerable, particularly for the renal elimination of drugs and metabolites. This is especially so for those drugs that are principally renally excreted and/or are nephrotoxic. These drugs typically have a narrow therapeutic range and dose adjustment may be required to avoid drug accumulation and toxicity.

Stage	Description	GFR (ml/min/1.73m ²)
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR < 60 ml/min/1.73² for more than three months.

Serum creatinine concentration

Serum creatinine concentration is the most commonly used marker of renal function. It is an easily measured parameter, but when used alone does not provide an accurate measure of renal function. Serum creatinine concentration varies with sex, age, muscle mass, drugs and diet. Ingestion of a meal containing cooked meat has been shown to raise serum creatinine concentration by a median value of 20 μmol/L.⁶

Serum creatinine is expressed in different units in different countries. In Australia and New Zealand, the use of SI units (μmol/L) is now recommended.⁷ In the United States serum creatinine is reported in mg/100ml (mg/dL). The following formula is used to convert from mg/100ml to μmol/L:

$$SCr(\mu\text{mol/L}) = SCr(\text{mg}/100\text{ml}) \times 88.4$$

Whereas renal function as defined by GFR decreases with age, serum creatinine concentration may not rise accordingly. Elderly patients with normal serum creatinine concentrations may have significant impairment of renal function. Swadko and colleagues investigated the specificity and sensitivity of serum creatinine concentration in the diagnosis of renal failure (GFR ≤ 50 ml/min).⁸ If a serum creatinine concentration of 150 μmol/L was used as a definition of renal failure in a population of 854 patients over the age of 65 years, the sensitivity was 12.6% and specificity 99.1%. The sensitivity of detecting severe renal failure (GFR ≤ 30 ml/min) was 45.1%. For this reason it is vital to estimate GFR in elderly patients rather than rely on serum markers alone.

Serum Cystatin C is a serum marker which has the potential to be more accurate in the estimation of GFR than serum creatinine. Despite studies demonstrating increased accuracy, this marker has not been widely accepted, largely due to increased cost.⁹

Glomerular Filtration Rate

The best estimate of renal function is the GFR. True GFR is measured in ml/min. Standardised GFR is routinely used by clinicians such as nephrologists as a marker of patients' renal function. This is an adjusted figure that assumes an average body surface area of 1.73m². Standardised GFR is reported in ml/min/1.73m².

It is important to note that the standardised GFR should not be used to calculate the dose of renally excreted drugs. An estimate of actual GFR should be used. Conversion from ml/min/1.73² to ml/min requires knowledge of the patients height and weight. After calculation of body surface area (BSA) the following formula can then be used:

$$GFR(\text{ml}/\text{min}) = GFR(\text{ml}/\text{min}/1.73\text{m}^2) \times BSA/1.73$$

Estimating GFR

The estimation of GFR requires sophisticated testing techniques which are widely available but impractical for routine use. Nuclear medicine isotopic methods are the "gold standard" against which other techniques are measured. The two commonly used methods in clinical practice involve the use of:

- ⁵¹Cr – EDTA ([⁵¹Cr]-ethylenediamine tetraacetic acid)
- ^{99m}Tc – DTPA (technetium-^{99m} diethyl triamine penta-acetic acid)

Timed blood samples are taken after delivery of a dose of radioisotope. The concentration of isotope in the sample is then used to determine "true" GFR.

Creatinine clearance (CrCl)

The creatinine clearance is an estimate of GFR. CrCl can be either measured or calculated.

CrCl can be measured using a 24-hour urine collection however this method is unreliable, labour intensive and is not recommended for routine use.¹⁰

Alternative techniques to estimate CrCl have been developed based on the serum creatinine concentration. Over 40 formulae have been devised to estimate CrCl. All formulae are based on the patient's serum creatinine concentration and age. Some also require knowledge of the patient's height and weight.

Commonly used formulae

1. Cockcroft and Gault

$$CrCl(\text{ml}/\text{min}) = \frac{(140 - \text{Age}) \times \text{wt}(\text{kg})}{72 \times SCr(\text{mg}/100\text{ml})}$$

The formula published by Cockcroft and Gault¹¹⁻¹³ was derived from a population of 249 men in a veterans' hospital. As no women took part in the study the formula employs an arbitrary correction factor of 0.85 when calculating the CrCl of female patients. The mean age of patients in the dataset was 57 years (range 18-92 years). Twenty nine per cent of the study population were over the age of 70 years. The formula was derived using measured 24 hour creatinine clearance as the "gold standard".

The Cockcroft and Gault formula is reported in ml/min and does not require conversion when used to calculate doses of renally excreted drugs such as carboplatin. The published formula uses a SCr value expressed in

mg/100ml. To convert from $\mu\text{mol/L}$ to mg/100ml, multiply by 0.0113.

2. Jelliffe

$$\text{CrCl (ml/min/1.73m}^2\text{)} = \frac{98-16((\text{Age}-20)/20)}{\text{SCr(mg/100ml)}}$$

The formula originally described by Roger Jelliffe in 1973 was derived from 128 observations in 15 patients following renal transplantation.¹⁴ Intended as a quick bedside estimate, it asks that the patient's age be rounded to the nearest 10 years. The figure derived from the equation is reduced by 10% in females. A feature of this formula is that the patient's height and weight are not required, however it yields an estimate of "standardised" CrCl in ml/min/1.73m² and technically should be "uncorrected" to give a result in ml/min.

3. Wright

$$\text{GFR (ml/min)} = \frac{[(6550 - (38.8 \times \text{Age})) \times [1 - (0.168 \times \text{Sex})] \times \text{BSA}]}{\text{SCr } (\mu\text{mol/L)}}$$

SCr – $\mu\text{mol/L}$ (Jaffe method), Sex - male = 0, female = 1, Age – years,

BSA – m² Dubois¹⁵ formula ($0.007184 \times \text{weight}^{0.425} \times \text{height}^{0.725}$)

This formula was derived in a population of 62 cancer patients.¹⁶ The median age of the population was 58 years (range 23-81). As the "gold standard" used in this study was the ⁵¹Cr-EDTA estimation of GFR, this formula is designed to yield an estimate of GFR in ml/min. No conversion is required to calculate doses of renally excreted drugs. The formula was derived using population pharmacokinetic methods. Different formulae were devised depending upon the type of serum creatinine assay used (enzymatic or Jaffe) and if the serum CK was known.

4. eGFR – The revised Modification of Diet in Renal Disease (MDRD) formula (the "175" formula)

$$\text{eGFR (ml/min/1.73m}^2\text{)} = 175 \times (\text{SCr} \times 0.0113)^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ [if female]})$$

eGFR = estimated glomerular filtration rate, age = years,

SCr = serum creatinine concentration ($\mu\text{mol/L}$),

The original MDRD formula was derived from 1704 patients with renal disease.¹⁷ A modified MDRD formula has been recently published.¹⁸ This formula yields a result in ml/min/1.73² and requires the patient's age and sex in addition to serum creatinine concentration. To initially derive the formula, glomerular filtration rate measured by the urinary clearance of ¹²⁵I-iothalamate was used as the "gold standard". The mean age of patients was 50 years. In the updated publication only 2% of participants had a GFR of >90ml/min/1.73m².

The eGFR is now reported routinely by pathology

laboratories in Australia. As outlined in the position statement from the Australasian Creatinine Consensus Working Group the upper reporting limit has been extended to <90ml/min/1.73m².¹⁹ Although the eGFR has been shown to decline with advancing age (Figure 1), age related reference intervals have not been recommended.

The eGFR is intended as a screening tool for patients with renal disease. As it is reported in ml/min/1.73² it requires "correction" for BSA if the result is to be used for dosing of renally excreted drugs (see above). The eGFR has not been validated in certain ethnic groups such as the Aboriginal and Torres Strait Islander population. Although it has been recommended to be reported in non-caucasian Australian populations, validation studies are needed to ensure accuracy and precision.

Limitations of formulae to estimate creatinine clearance

All formulae used to estimate creatinine clearance rely on the serum creatinine concentration. All formulae are imprecise in their estimation of GFR. The formulae lack precision and are particularly unreliable in the following circumstances:

1. At the extremes of serum creatinine. In patients with high serum creatinine and with low measured GFR or patients with very low serum creatinine and high GFR.
2. In patients at the extreme of body size (ie. in cachexia, severe malnutrition and obesity).
3. If the serum creatinine is changing rapidly (eg. in intensive care).
4. Formulae may not be validated in specific patient populations (eg. the elderly and different ethnic groups) eg. the MDRD equation was devised in patients with renal disease and care needs to be taken if it's going to be applied in patients with GFR>90ml/min/1.73m².

As all formulae are inaccurate at the extremes of GFR, it remains appropriate to perform isotopic estimation of GFR in some cases.

How do the formulae compare?

A number of studies have been published in which the various formulae have been compared. Most studies compare the formulae against a "gold standard", which is usually an isotopic method of estimating GFR. The formulae then are assessed as to their bias and precision in estimating GFR.

The formulae mentioned above have been compared by a number of authors.^{15, 20-28} The literature does not enable us to detect a clear "winner", however some formulae are more practical and seem to be better in certain situations.

The Cockcroft and Gault formula is the most widely known and the simplest test to perform; it is truly a bedside test of renal function. The Wright formula is slightly more complex, and was devised in patients with

malignancy rather than renal disease. The MDRD cannot be assessed without the aid of a computer due to the need to calculate exponentials. In addition, most online calculators of the MDRD formula do not report a GFR figure $>90\text{ml/min}/1.73^2$. Despite this, there has been at least one call for the MDRD to be utilised more widely by cancer physicians.²⁹

Despite the bias and imprecision of the various formulae, it is much better to use one of them than rely on measurement of the serum creatinine concentration alone. Use of the formulae will require acceptance of some degree of inaccuracy. In some clinical situations, small errors may be acceptable and not lead to clinically relevant adverse outcomes.

Use of formulae in the elderly patient population

In medical oncology practice, formulae to estimate creatinine clearance are used principally to estimate GFR (ml/min), to insert into the Calvert equation to then calculate the dose of carboplatin.³⁰ Currently this is the only chemotherapeutic drug that is dosed in this fashion. Other drugs (eg. capecitabine) require calculation of patients' renal function and subsequent dose reduction in the event of renal impairment. Due to the decline in GFR seen with increasing age, often seen despite a serum creatinine concentration in the normal range, the estimation of creatinine clearance is essential.³¹

The Cockcroft and Gault, Wright and Jelliffe formulae have been compared in a population of 225 elderly patients with cancer.²¹ In a retrospective analysis, the Wright formula was found to be the least biased and most precise in patients over the age of 70 years. This advantage was seen in the patients with "normal" renal function (GFR between 50-120 ml/min). The Wright formula appeared to perform no better than the other equations in patients with some degree of renal impairment (GFR $<50\text{ml/min}$).

The use of equations in elderly patients has been explored in other studies,^{28,32-33} one of which studied only patients aged over 100 years, but a reliable equation was unable to be found in these populations.

The International Society of Geriatric Oncology has produced clinical practice recommendations on the assessment of renal function in the elderly.³¹ Summary points of these recommendations include:

1. Before drug therapy in elderly patients with cancer, assessment and optimisation of hydration status and evaluation of renal function to establish any need for dose adjustment is required.
2. These recommendations, for the evaluation of renal function, apply for patients with any type of cancer (decreased renal function occurs in $>50\%$ of patients with solid tumors).
3. Serum creatinine concentration alone is insufficient as a means of evaluating renal function.
4. More accurate tools, including CrCl methods such as Cockcroft and Gault, are available and are generally good indices of the renal function status of the

patient. In elderly patients however, the Cockcroft and Gault and other similar formulae are not as accurate as in the younger population.

5. More recently developed tools, such as the MDRD, may be the estimation of choice in elderly patients with chronic kidney disease, whereas the Cockcroft and Gault estimate can be used in subjects younger than 65 years.
6. For drug dosing calculations the Cockcroft and Gault formula may be more practical. However, in extremes of obesity and cachexia and at very high and low creatinine values, no single tool is really accurate. The best estimate of GFR is provided by direct methods such as $^{51}\text{Cr-EDTA}$.
7. Coadministration of known nephrotoxic drugs such as non-steroidal anti-inflammatory agents or Cox-2 inhibitors should be avoided or minimised.

Dose modification of chemotherapy in the elderly – focus on renal function

Appropriate dosing of chemotherapy in elderly patients is often difficult. Chemotherapy dosing is an individualised process which requires assessment of the patients' functional status and comorbidities. The most important rule to remember is that treatment should not be withheld or attenuated on the basis of advanced chronological age alone. Complete assessment includes estimation of creatinine clearance as outlined above.

If renal impairment is demonstrated, dose reduction of some drugs may be indicated. Truly evidence-based guidelines on such dose reduction are lacking. The National Cancer Institute Organ Dysfunction Working Group conducts rigorous studies of chemotherapeutics in patients with renal and hepatic dysfunction,³⁴ however not all drugs have been studied to date. To further complicate decision-making, dose reduction recommendations are varied depending upon the source of the information. Product information leaflets produced by pharmaceutical companies are often inadequate in dictating the need for dose reduction in patients with renal impairment. A study of four sources of drug information regarding adjustment of dose for renal function revealed variable definitions and a significant proportion of the drugs studied had contradictory information between the different references.³⁵

Work performed by a taskforce of the International Society of Geriatric Oncology has attempted to clarify this situation specifically for the elderly patient population. This group has produced a summary of the recommendations for dose adjustment of most chemotherapy drugs in patients with renal impairment.³⁶

The introduction of the eGFR into routine practice in Australian pathology laboratories has raised awareness of the need to consider CrCl as a measure of renal function rather than spot serum creatinine concentration. This is of utmost importance in the elderly. The current formulae used to estimate CrCl all have failings and their imprecision is exaggerated in patients with low or high GFRs. Although considerable

efforts have been made to help clinicians treating elderly patients,^{31,36-37} standardised evidence-based guidelines regarding dose reduction in renal impairment are lacking.

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NON-SMALL CELL LUNG CANCER IN THE ELDERLY – SYSTEMIC THERAPY

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Abstract

Elderly patients represent a significant and rising proportion of patients with Non-Small Cell Lung Cancer and historically they have been under-treated and under-represented in clinical trials. Increasing elderly specific research into the management of this disease has been performed in the last decade and has demonstrated both quality of life and survival benefits for patients with advanced non-small cell lung cancer managed with modern chemotherapy. This paper will discuss the evidence for systemic therapy (chemotherapy and targeted therapy) in advanced non-small cell lung cancer and adjuvant therapy.

Lung cancer is the most lethal of the common solid malignancies. The median survival for advanced disease, despite modern oncological techniques, remains less than 12 months. Long-term cure is largely limited to early stage disease and unfortunately this remains the exception rather than the norm. The most common sub-type is Non-Small Cell Lung Cancer (NSCLC), now representing three quarters of lung cancer presentations in the western world.¹ Histological patterns in NSCLC are also changing with time, with the frequency of adenocarcinoma presentation now much more frequent. This is believed to reflect both the rising incidence of NSCLC in non-smokers and the change in cigarette composition.² The median age at presentation of lung cancer is 68 years, with one third of patients aged over 75 years. Patterns of care studies from both Europe and the US have demonstrated that elderly patients receive non-standard treatment and often receive no active treatment at all.^{3,5} Patients aged over 65 years have largely, until the last decade, been excluded from clinical trials based predominantly on the premise of age rather than inadequate organ function.⁶

Ageing is associated with reductions in physiological reserve and also the increasing prevalence of co-morbidity, all having distinct implications for the delivery of chemotherapy and the ability to withstand its toxicity. Arbitrary definitions for 'elderly' have often been used largely based on the availability of population and census data eg. 65 years. However, 70 years of age is a more appropriate physiological definition for when changes in organ reserve are more common.^{4,7} More recent studies concentrate on patients aged 75 years or older. This age group has a much higher likelihood of frailty, implying limited minimal physiological reserve. Prospective data on this group, with regards to outcome or toxicity with treatment, is sadly lacking.

Comprehensive geriatric assessment has been a concept widely encouraged in geriatric oncology, although it has largely been limited to the research setting due to its multidisciplinary nature. Its benefit is that it formally assesses multiple areas which may

influence an older patient's ability to tolerate therapy. These include functional status, nutrition, psychological state and social support, in addition to the more routinely assessed co-morbidity and medication.⁸ Importantly, these additional parameters can also provide prognostic information separate to what is gained from performance status assessment, which is by far the most common tool employed by oncologists to stratify treatment paradigms based on fitness for therapy.

Functional state has been shown to be a more useful prognostic indicator than performance status in many studies of elderly patients receiving cancer therapy, including one specific for NSCLC. In this study, impairment of instrumental activities of daily living (IADL) was a stronger predictor of prognosis than impaired activities of daily living (ADL) regarding survival.⁹ Functional status is also often impaired despite preservation of a good performance status. In one study of elderly patients, 20% of patients were assessed as ECOG 2 or greater, however over half had impairment of IADLs.¹⁰ Application of co-morbidity indices such as a Charlson score, can also provide prognostic information independent of performance status. A French group has employed both the Charlson score and performance status to stratify patients to treatment and demonstrate that good performance status patients with a low Charlson score tolerate combination chemotherapy with similar results to those aged <65 years.¹¹

Advanced NSCLC

The current standard of care for advanced NSCLC is a platinum-based doublet using a third generation agent such as gemcitabine, vinorelbine or a taxane.¹² It is also generally accepted that a modern non-platinum doublet is also as effective as a platinum-based doublet, but significantly more expensive.¹³ Currently there are four published elderly-specific phase III studies, the largest performed by Gridelli and colleagues. The landmark study was the Elderly Lung Cancer Vinorelbine Italian Study (ELVIS), which demonstrated that vinorelbine provided both a survival advantage and quality of life

improvement for patients aged over 70 in comparison to best supportive care. Median survival, as expected for a single agent, was 6.4 months in comparison to 4.8 months for best supportive care.¹⁴ Surprisingly then, their second phase III trial, the Multicenter Italian Lung Cancer in the Elderly Study, found that a vinorelbine-gemcitabine doublet did not demonstrate any significant advantage over either vinorelbine or gemcitabine as single agents. This is the largest of the elderly-specific studies with over 700 patients enrolled. Median survival for vinorelbine in this study was nine months and for the doublet 7.5 months.¹⁵

The most recently published study was by a Japanese group which compared docetaxel at 60mg/m² three weekly, lower than the more standard 75mg/m² used in Western populations, to vinorelbine at 25mg/m² d1, 8 q21 and found that there was no significant survival difference between the groups, however there was an improvement in progression free survival. Median survival was 14.3 months for the docetaxel group and 9.9 months for the vinorelbine group. The negative conclusion could be attributed to several reasons. Firstly, the study was powered for 60% improvement in median survival for the docetaxel group, with the control arm presumed to have a median survival of six months. Secondly, 37% of the docetaxel patients received gefitinib as a second-line treatment compared to 20.9% of the vinorelbine group. The prevalence of the EGFR mutation, which is associated with improved activity and survival with gefitinib, is higher in Japanese populations. Interestingly, there was also a significant difference in the severe neutropenia rates between the Japanese vinorelbine group and the Italian vinorelbine group, with rates of 67% and 25% respectively.¹⁶ This may reflect pharmacogenomic differences, which are increasingly being recognised as an explanation for discordance in international study outcomes.

Subset analyses of large phase III studies are the other main source of information regarding chemotherapy management of elderly patients. Langer et al performed a subset analysis of the ECOG 5594, which used cisplatin-based chemotherapy and demonstrated that full dose platinum-based doublets are possible to administer in elderly patients with outcomes consistent with their younger counterparts. However, these were associated with higher rates of neuropsychological toxicity and leucopenia.¹⁷ Subset analysis of ECOG 1594 demonstrated no difference in outcome for fit, elderly patients.¹⁸ There are concerns however, regarding selection bias of fitter elderly patients into these studies. The role of combination chemotherapy in consensus statements is that it should be a consideration, but single agent chemotherapy based on phase III evidence remains the recommendation.¹⁹

Many elderly-specific NSCLC studies, for the purpose of more rapid recruitment, have also allowed entry of ECOG 2 patients of any age into the study, believing them to be similar in terms of capacity to tolerate therapy and outcome. ECOG 2 patients are by definition bedbound <50% of the day, but unable to perform

general activities. Median survival for this group however, is only two months untreated, reflecting how much more frail they are in comparison to a fit elderly patient with advanced NSCLC.²⁰ The median survival in the ELVIS study for the best supportive care arm was 21 weeks.¹⁴ Gridelli's phase II study of fit elderly patients ECOG 0-1 with cisplatin-based doublets and their outcomes were typical of that found in non-age specific first line NSCLC study. This study is important in that cisplatin has been felt to be toxic for elderly patients given its renal clearance, with subsequent for high volume fluid loading pre and post administration and cumulative neuro and oto-toxicity, in addition to its high emetogenicity.²¹ It is the platinum of choice though for efficacy in the management of NSCLC, although substantial debate exists within the oncological community regarding its positions on platinum of choice when quality of life considerations are taken into account in the advanced setting.²²

Data for second line chemotherapy again is limited to subset analysis. Weiss et al demonstrated in their analysis of the pemetrexed versus docetaxel study that elderly patients (aged >70 years) had no significant difference in outcome and toxicity was similar to their younger counterparts. However, elderly patients only represented 15% of patients enrolled. Pemetrexed was associated with a significant reduction in the rate of febrile neutropenia in comparison to docetaxel (2.5% vs 18.9%). Pharmacokinetic substudy studies were also performed in this study, which did not demonstrate any difference for pemetrexed or docetaxel between patients aged >65 years or younger. There were however, higher rates of severe neutropenia and febrile neutropenia in the docetaxel arm for older patients (61% and 16% respectively compared to 30% and 0%), but this did not reach statistical significance.²³ Again the choice of second line agent will be largely influenced by co-morbidity, particularly the presence of neuropathy.

Evidence-based management for patients aged over 80 is particularly sparse. They represented <1% of patients enrolled in ECOG 1594, the landmark study demonstrating relative equivalence for platinum-based doublets in advanced NSCLC.¹² A French group performed a retrospective analysis over 10 years in their department and only found 79 patients aged over 80 with biopsy proven NSCLC. One quarter was early stage, while only 40% were stage IV. Co-morbidity was common, with nearly half having a Charlson Co-morbidity Index of six or more – this appeared to trend with poorer outcome.²⁴

More recently, targeted agents have been incorporated into the management of NSCLC. The oral EGFR tyrosine kinase inhibitors have now been demonstrated to have efficacy in the second and third line setting, and erlotinib has also shown both a survival advantage and quality of life advantage in comparison to placebo.²⁵ They have attracted great interest in the management of the elderly patient with lung cancer given their lesser toxicity in comparison to the chemotherapy. They are not associated with any haematological toxicity and in

general are well tolerated with the main toxicity being that of rash, diarrhoea, ocular irritation and in a small subset, interstitial fibrosis. Response appears related to particular EGFR mutations, which appear to be particularly prevalent in Asian, female non-smoking populations, whereby response rates of 50% or more can be achieved in this cohort.²⁴ First line studies of these agents in chemo-naïve patients aged over 70, not selected for EGFR mutations, revealed the expected 10% objective response rate and a median survival of 10.9 months, with over 40% of patients receiving chemotherapy on progression. Those patients who did have the mutation had a median survival of >15 months.²⁶ Phase III studies are awaited against chemotherapy. Their use in combination with first line chemotherapy did not demonstrate any significant advantage.²⁷⁻³⁰

Bevacizumab is a monoclonal antibody directed against VEGF and its administration with carboplatin and paclitaxel has demonstrated a survival advantage over chemotherapy alone. The magnitude is similar to that achieved with chemotherapy over best supportive care. Its use has been limited to non-squamous varieties due to the increased risk of catastrophic pulmonary haemorrhage with this agent in the squamous sub-type. Enrolment was limited to patients with good performance status ECOG 0-1. Forty four per cent of patients enrolled in this study were aged over 65 years.³¹ Formal subgroup analysis has not been published as yet. These findings have been confirmed in a second study presented in abstract form only in 2007.³²

Adjuvant chemotherapy

The application of adjuvant chemotherapy in resected NSCLC is now considered a standard of care for fit patients, however its routine use in elderly patients on current evidence is not. Evidence only exists for cisplatin-based treatment, which in elderly patients may have considerable long-term consequences regarding peripheral neuropathy and its impact on mobility and independence. Ototoxicity also has significant functional costs for elderly patients, with high-pitched hearing loss the main consequence.

Pepe et al performed a retrospective subset analysis of the Canadian study BR10.³³ This study was restricted to patients with completely resected stage 1B or 2 disease. It compared four cycles of cisplatin and vinorelbine to observation post surgery and demonstrated a 31% reduction in death for the chemotherapy arm.³⁴ Patients aged over 65 represented a significant proportion of patients enrolled in this study (n=155, 32%). Less than half of these patients were aged over 70 years and only 23 patients were aged 75 or older. They found that this sub-group did significantly worse in comparison to those aged between 65 and 74 years. Their survival was found to be half that of those aged 65-74 years, albeit with substantially smaller numbers of patients recruited. There was no difference between the sub-groups for disease free survival.

This suggests that the excess of deaths in the 75 or older age group was due to co-morbid conditions. They also noted a difference in histological subtype for patients aged over 65 in comparison to their younger counterparts with a predilection for squamous carcinoma (49% vs 32%). The survival benefit for adjuvant chemotherapy though remained significant in the elderly as a whole HR 0.61 p=0.04. Interestingly this was achieved with lower dose intensity than in their younger counterparts.³³ This is the most likely explanation for why the severe toxicity profiles were not different in contrast to most subset analyses which in general, demonstrates higher levels of haematological and neuro-psychiatric toxicity for similar doses of drugs to their younger cohorts. Adjuvant chemotherapy should only be recommended with caution to patients aged over 75 years.

Conclusion

Outcomes for patients with NSCLC have significantly improved over the past decade largely due to the availability of effective systemic therapy, with improved patient toxicity profiles. Treatments have demonstrated improvement in both survival and quality of life. Application of chemotherapy to elderly patients has often been low due to perceived difficulties with tolerability and benefit. However, a substantial evidence base now exists demonstrating the benefits. Careful evaluation of the patient with regard to co-morbidity and functional status can minimise potential toxicity and allow the safe administration of treatment. Consideration of therapy remains critical to the optimal management of elderly patients with NSCLC, enabling them with therapeutic options rather than therapeutic nihilism.

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RECTAL CANCERS IN THE ELDERLY – LESSONS LEARNED

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Abstract

Current cancer care, especially rectal cancer, requires the use of a multidisciplinary team approach, including a surgeon, medical oncologist, radiation oncologist and several other allied health specialities. Elderly patients with rectal cancer add another dimension to this complex picture due to the higher frequency of co-existing medical problems. Several studies indicate that carefully selected elderly patients derive equal benefit from appropriate anti-cancer treatment as younger cancer patients. However, this review of the published literature from Australia suggests that the care of rectal cancer, especially in the elderly, requires considerable attention in order to improve their outcomes.

Elderly and rectal cancers

Ever-improving life expectancy and better cancer related outcomes are not uniformly seen in all Australians diagnosed with cancer. There is a disparity in cancer outcomes in some select populations including adolescents, young adults, the elderly, those from rural areas and the Indigenous population. In line with the focus of this issue of *Cancer Forum* we discuss the management of rectal cancers in the elderly with an Australian perspective.

Colorectal cancer is the second most common cancer in Australia and the second leading cause of cancer death.¹ With a rapidly increasing older population and an increasing total number of diagnosed cases of colorectal cancer, elderly cancer patients will become the majority of patients we will see in the future. The approach to the management of elderly patients is more complex, given the high frequency of co-existing medical illnesses and frailty, which are perceived to be a deterrent for administering appropriate anti-cancer therapy.

The management of rectal cancer requires a multidisciplinary approach in all patient groups, using the expertise of all oncology specialties including surgical, medical and radiation oncology. Elderly patients with rectal cancer require further input from a geriatrician and several other supportive allied health units. In this article, we highlight the complexities involved in the care of the elderly with rectal cancer, discussing data recently presented at the Clinical Oncological Society of Australia's Annual Scientific Meeting, based on our experience at a single institute in South Australia with reference to previously published literature.

Octogenarians and nonagenarians constitute a very special population among the elderly who require extra attention for their care. They are more often fragile with multiple co-morbidities than those who are younger. This population is one of the under-served in all spheres of their cancer care. Previously published patterns of care studies indicate that the elderly are less likely to receive the recommended standard of care.^{2,4} This is well documented, despite evidence that radical surgery,

radiotherapy and chemotherapy can be safely administered in carefully selected older individuals. There may be an argument that the elderly have a shorter life expectancy and are unlikely to benefit from adjuvant therapy. However, most rectal cancer recurrences occur within the first three to five years and death related to systemic recurrence is seen in a significant proportion of patients. Men and women who reach 80 years may expect a further five and seven years of life respectively, the majority being disability free. So, appropriate adjuvant therapy can potentially improve cancer related outcomes even those who are older than 80 years of age.

Audit at the Queen Elizabeth Hospital

We performed an audit of newly diagnosed patients of rectal adenocarcinoma aged 80 years and older between the years 1998 and 2006 at the Queen Elizabeth Hospital, South Australia. This audit was conducted with the aim of establishing the pattern of care of the elderly with rectal cancer at our centre. All such patients were discussed in a fortnightly, multidisciplinary team meeting involving colorectal surgeons, medical oncologists, radiation oncologists, radiologists, pathologist and a stoma therapist nurse to decide upon the best recommended plan of treatment. Of note, there was no geriatrician involved at any stage of the treatment decision. As one would expect, the attending primary physician/surgeon then discussed with the patients the recommended treatment and proceeded accordingly.

We identified 55 eligible patients who were over 80 years of age with a new diagnosis of rectal adenocarcinoma. The median age was 84 years (range: 80-93 years) with 60% males. Most were less than 90 years with only seven (12.7%) being nonagenarians. Staging results were Astler-Coller's⁵ Dukes A 16.3%, Dukes B 36.3%, Dukes C 30.9% and Dukes D 14.5%. We were able to obtain pathological staging in 45 who had curative surgical resection. The majority were T3 (52.8%) and T4 in 24.5%. Pathological tumour grading indicated that 80% had average differentiation while 15% had poor differentiation. The median number of

nodes removed was only eight (range 0-25), which was important given the evidence of an association between node harvest number and outcome.⁶

Curative or palliative surgery was performed in 48 (87.2%) patients, while the remaining patients had a diagnostic biopsy alone. Curative surgery, including anterior resection or abdomino-perineal resection, was performed in 26 (47.2%) and 12 (21.8%) patients respectively. Defunctioning colostomy was the most common palliative surgery (10.9%) and local excision alone was done in 5.4%. The median hospital stay for those patients in our group who had surgery was 18.5 days (range: 6-42 days). Post-operative mortality (death within 12 weeks of surgery) was 16.6%; and a number of patients were noted to have major medical events, such as acute myocardial infarction, pneumonia, sepsis, stroke, pulmonary embolism and acute renal failure, complicating their post-operative course in the hospital and highlighting the need to assess older patients carefully before proceeding to surgical intervention.

There are accepted gains in outlook for patients with Dukes B and C pathology who receive pre-operative or post-operative radiotherapy, with or without chemotherapy.⁷ In our patient group, there were 37 (20 Dukes B and 17 Dukes C) patients who were potential candidates for some form of adjuvant therapy. Among the Dukes B patients, 40% had either pre-operative or post-operative radiotherapy +/- chemotherapy (4 each). Of note, only one of the Dukes C received post-operative radiotherapy while 23.5% had post-operative radiotherapy/chemotherapy.

Where pre-operative therapy was given, long-course radiotherapy with concurrent chemotherapy was given in the majority in keeping with current practice. Two patients did receive high dose five-day pre-operative radiotherapy alone. Chemotherapy consisted of continuous infusion of 5-Fluorouracil (5FU) at 200 mg/m²/day during radiotherapy, again consistent with recommended dosing. This combined radiotherapy/chemotherapy appeared well tolerated in those patients selected for pre-operative therapy, although there was one recorded death due to complications from radiotherapy/chemotherapy. Those younger than 86 years of age were more likely to receive radiotherapy/chemotherapy irrespective of their stage.

We explored the decisions for the 37 patients who were eligible for adjuvant therapy. The multi-disciplinary team meeting recommended adjuvant therapy for only 20 patients, with the remaining perceived either to be unfit for adjuvant therapy or the benefit too small. Among those who were recommended to have further therapy, 12 proceeded with the recommended therapy and five died in the post-operative period. Only three refused to have further treatment.

Discussion

In the previously published study from South Australia, patients not treated surgically tended to be aged 80 years or more.⁸ This trend seems to have changed in more recent years (1980-1986 v/s 1995-2002). The National Colorectal Cancer Care Survey reported that nearly 82% of the newly diagnosed colorectal cancers in

all age groups underwent curative resections nationwide in Australia.⁹ In this study, which included patients from the last decade, it appears that the majority (70%) of the elderly do undergo curative surgical therapy for their rectal cancers. This is most likely related to the improvement in the supportive care available for the care of these patients. It appears that elderly patients can undergo surgery relatively safely with an acceptable post-operative complication rate. Surgery for rectal cancer should not be restricted based on age.¹⁰

The use of adjuvant therapy for colorectal cancer varies substantially by age, race, marital status, hospital volume and individual hospital, indicating opportunities to improve care.³ Previously published studies from Australia indicate that the elderly do not receive the recommended adjuvant therapy more often than their younger counterparts.^{11,12} In a review from New South Wales, only 60% received the recommended radiotherapy and older patients were less likely to receive any adjuvant therapy.¹¹ The utilisation rates of radiotherapy remain low, especially among the elderly, and those not seen by a surgeon with a higher caseload.¹² In the current report, 60% of Duke B and 30% of Duke C received adjuvant therapy. The proportion who received the recommended radiotherapy/chemotherapy seems to decrease with increasing age.

There appears to be several physician and patient factors involved in the decisions regarding adjuvant therapy for the elderly with rectal cancers. Lack of referral to the oncologist and patient refusal appear to be important reasons for patients not receiving the standard adjuvant therapy.¹³ As seen in our audit, contrary to popular belief patient refusal is an uncommon reason for not having adjuvant therapy.

Using the Surveillance, Epidemiology and End Results (SEER) data, Luo et al reported that only half of patients older than 85 years with Dukes C colon cancer saw a medical oncologist, and those who met a medical oncologist were 10 times more likely to get adjuvant therapy, highlighting the need for a complex interdisciplinary approach in treating such patients.¹⁴ In the current study, although patients were discussed in the multi-disciplinary team meetings, they were not directly involved in the decisions. If the team decided against recommending adjuvant therapy due to perceived lack of benefit or severe co-morbidities, they were not referred to a medical oncologist. These decisions were made ad hoc rather than using evidence-based approach of comprehensive geriatric assessment. It may be useful to involve a geriatrician for all multi-disciplinary team discussions involving elderly patients. Individualised treatment decisions will be of critical importance in this group of patients.

Conclusions

We conclude that all patients should receive the most intensive treatment thought to be effective and safe according to their age and co-morbidities, as data on survival and the toxicity profile of treatment is not different from the younger age group.¹⁵ Increasing the

use of appropriate adjuvant therapy should be a priority, especially among older people, as mortality appears to decrease among those who receive therapy based on current guidelines. With appropriate patient selection, rectal cancers appear to be cured even in those who are older than 80 years of age.

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DISCRIMINATING FACTORS IN TREATMENT DECISIONS FOR CHEMOTHERAPY IN ELDERLY PATIENTS WITH COLORECTAL CANCER

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Abstract

Chemotherapy is underutilised in patients over the age of 70 and good arguments exist to support active treatment in this group. We examined patient and disease factors in colorectal cancer patients aged <70 years and 75 years or older that might influence treatment choices independently of age. The data were obtained from LANTIS, the electronic medical record system used at Liverpool and Campbelltown Hospitals. Variables collected included patient demographics and treatment-related factors. It was hypothesised that the difference in utilisation between older and younger patients could be ascribed to confounding factors being more common in the older population. There were 445 patients with colorectal cancer in the years 2005 and 2006. Of these, 267 (60%) were under 70 years of age, 278 (63%) were males and 308 (69%) were married. Two-hundred and ninety-four patients (66%) had colon cancer, 137 (31%) had rectal cancer and 14 (3%) had rectosigmoid cancer. Three-hundred patients received chemotherapy, whereas out of the 137 (31%) who did not, 83 (61%) were in the older age group (75 years or older). Data were missing for eight patients. There was a trend for elderly patients to receive less chemotherapy as compared to the younger cohort. Multivariate regression analyses showed no statistically significant differences for gender, ECOG performance status, socioeconomic status or site of disease. Age was the strongest discriminating factor in chemotherapy decisions of older patients with colorectal cancer.

Advanced age should no longer be considered a reason for not treating older cancer patients.¹ There is both anecdotal and clinical evidence to suggest that treating physicians are reluctant to offer chemotherapy to eligible elderly patients as compared to younger patients.² Older patients are also under-represented in clinical trials.³ Evidence has started to emerge that older people tolerate cancer therapies (both molecular and cytotoxic) as well as younger patients.⁴ Are we thus discriminating among our patients, based on their age alone, or are there other factors, such as the presence of comorbidities, that lead to a lower uptake of chemotherapy in this group?

In Liverpool and Campbelltown Hospitals, under-utilisation of chemotherapy for patients with colorectal cancer has been documented,⁵ and age has been identified as an important predictive factor.⁶ The current study was undertaken to explore patient and disease-related factors to determine the differences between younger and older patients. We hypothesised that the difference in utilisation of chemotherapy could be ascribed to confounding factors being more common in the elderly.

Patients and therapy

This was a retrospective study conducted at the Liverpool and Campbelltown Hospitals, Sydney. The data was retrieved from LANTIS, the electronic

database used at both hospitals, for the period between January 2005 and December 2006. All new referrals with a diagnosis of colorectal cancer, seen at the two oncology departments were considered for the study, excluding those patients who were already on treatment on or before 1st January 2005.

Approval from Sydney South West Area Health Service Human Research Ethics Committee was obtained. De-identified patient data was grouped into two cohorts, on age criteria (below 70 years of age and 70 years or older). The information collected included patient demographics: age; gender; language spoken; marital status; co-morbidities; ECOG performance status; and disease related factors such as site of disease, TNM stage, treatment received and outcomes. The treatment-related factors were individually extracted from patient medical files recorded electronically at time of consultation and from correspondence. The socioeconomic index was inferred from the postal code of patient residence in line with the guidelines of the Australian Bureau of Statistics. Patients were then grouped into four categories, indicating the increasing degree of social disadvantage using the Index of Relative Socioeconomic Disadvantage (IRSD).

Co-morbidities were recorded as nil, mild, moderate or severe. Mild co-morbidity meant age related co-morbidities only, which were unlikely to affect survival over the next five years. Severe co-morbidity included organ failure or a condition which may reduce five year

survival. ECOG performance status was available for most patients and was inferred for others. ECOG was recorded as unavailable only where no reference was available from the clinical notes or documents.

The decision to treat or not was at the discretion of the treating oncologist. Treatment received was defined as at least one cycle of proposed chemotherapy. In nearly all patients, treatment was accepted by the patient if it was offered. Type of treatment, whether neo-adjuvant, adjuvant or palliative, was also documented and the outcomes were recorded as treatment completed or not.

SPSS (version 15) was used for analyses, Chi square (χ^2) tests to examine the relationships between the two cohorts. Univariate and multivariate regression analyses were also performed.

Clinical outcomes

Data from 445 patients with colorectal cancer were collected for the study. Of these, 267 (60%) were under 70 years of age, 278 (63%) were males and 308 (69%) were married (Table 1). ECOG performance status was available for 370 (83%) patients – 78% of patients had good performance status (ECOG 0 or 1). Two hundred and ninety-four (66%) had colon cancer, 137 (31%) had rectal cancer and 14 (3%) had rectosigmoid cancer. At time of first consultation, TNM staging was recorded for 430 (93%) with Stage I (10), Stage II (117), Stage III (172) and Stage IV (131). Data on co-morbidity was available for 442 patients; 142 (32%) had no co-morbidities, 112 (25%) had mild, 132 (30%) had moderate and 56 (13%) had severe co-morbidities.

A total of 300 (67%) patients received at least one cycle of chemotherapy, whereas 137 (31%) did not. Data were not available for eight patients. Two-hundred and eight patients (70%) of those treated were younger than 70 years of age and 83 (61%) of those not treated were

70 years or older ($p=0.07$).

Patients 70 years or older received significantly less chemotherapy for any stage of disease, any degree of co-morbidity or performance status. It was interesting to note that for a drop in ECOG performance status from 0 to 1, or a mild co-morbidity compared to none, was significantly associated with a much greater decrease in delivered chemotherapy in 70 years or older age group (Table 2).

Forty-five patients received neo-adjuvant treatment, 181 received adjuvant and 142 received palliative treatment. Some patients were given more than one type of chemotherapy. There was no significant difference between patients' age groups for neo-adjuvant, adjuvant or palliative treatment (Figure 1). There was a clear trend for more adjuvant treatments being given to the younger group and more palliative treatments given to the older (Figure 1).

Figure 1: Types of chemotherapy given to patients by age groups

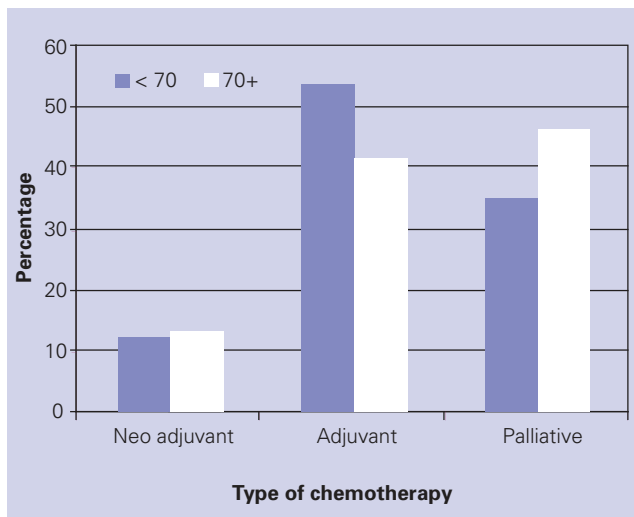


Table 1: Patient and disease characteristics

Characteristics		<70 years (n=267)		70+ years (n=178)	
		%	(n)	%	(n)
Status	Alive on 31/12/2006	87	(232)	71	(127)
Gender	Male	64	(170)	61	(108)
	Female	36	(97)	39	(70)
Marital status	Currently married	73	(194)	64	(114)
	Currently not married	27	(73)	36	(64)
Site	Colon	66	(177)	66	(117)
	Rectum	31	(82)	31	(55)
	Rectosigmoid	3	(8)	2	(6)
Stage	Stage I	2	(5)	3	(5)
	Stage II	27	(71)	26	(46)
	Stage III	42	(112)	34	(60)
	Stage IV	27	(73)	33	(58)
	Unknown	2	(6)	5	(9)

Table 2: *Univariate analysis of those receiving chemotherapy*

		<70 %	70+ %	P value
Gender	Male	79	54	0.50
	Female	75	49	
Currently Married	Yes	79	59	0.01
	No	75	39	
IRSD	1	75	51	<0.001
	2	80	58	0.02
	3	85	44	<0.0001
	4	77	56	0.3
ECOG	0	82	87	0.5
	1	81	59	0.02
	2	78	26	0.02
	3	56	28	0.3
Co-morbidity	Mild	80	68	0.1
	Moderate	85	56	<0.001
	Severe	57	27	0.02
	Any	78	52	<0.0001
Stage	I	60	40	1
	II	54	37	0.8
	III	93	65	<0.0001
	IV	85	59	<0.001
	U	17	0	–

A subgroup analysis was conducted on only stage III and IV patients because the indications for chemotherapy are more clear-cut, however the results were very similar to earlier analysis on the two groups which included all stages (Tables 3 and 4).

In the multivariate regression analysis, a significant association between the likelihood of receiving chemotherapy was observed for Stage III and IV (3.4 times, $p < 0.001$), no co-morbidity (1.7 times, $p = 0.028$), currently married (1.7 times $p < 0.007$) and for age <70 years (3.3 times, $p < 0.0001$). Gender, Index of Relative Socioeconomic Disadvantage (IRSD/SES) and anatomical site of disease did not show significant difference.

Implications

Bowel cancer is second only to lung cancer as the most common cause of cancer related deaths in males and females combined. It is estimated that one in 17 males and one in 26 females will develop bowel cancer by age 75.⁷ Age is unmodifiable and is perhaps the most important risk factor associated with bowel cancer.⁸ In New South Wales the median age at diagnosis for bowel cancer in 2004 was 69 years for males and 72 years for females. The 70 years or older age group is a large proportion of bowel cancer patients. The current study is unique, as it looks particularly at this cohort and explores the utilisation of chemotherapy (for all stages) in relation to patient age and co-morbidities. The authors were unable to apply more stringent criteria to document co-morbidities, due to the retrospective nature of the study and limitation of how these were indexed at the time of initial consultation.

Australian guidelines recommend offering chemotherapy to Stage III and IV patients, but controversy exists about treating Stage II. A consensus is now emerging among the treating oncologists on identifying a higher risk group who would benefit from treatment. The proportion of Stage II cases in the current study was similar in the two age groups.

The low proportion of older (70 years or older) patients receiving chemotherapy was not due to older patients being more likely to refuse chemotherapy if it was offered. In fact very few patients refused chemotherapy if it was offered to them. Our study showed that even after accounting for differences in performance status and co-morbidities, patients over 70 years of age were less likely to be offered chemotherapy. A similar pattern was reported in US.⁹

There could be a selection bias with those patients who are unlikely to undergo surgery being referred for chemotherapy. To examine this we compared the proportions for each stage in our study with data from the Sydney South-west Area Health Service Cancer Registry. The percentage of cases identified were Stage I, 15%; II, 33%, III, 32% and IV 19% respectively. Apart from a lower number of Stage I patients in our study, a high proportion of Stage II and nearly all Stage III and IV were referred for a chemotherapy opinion.

The study was not designed to show a survival advantage of those receiving chemotherapy, as follow-up was not long enough.

Table 3: Proportion of patients with stage III and stage IV disease, who received chemotherapy (by age groups)

Patient Characteristics	Received Chemo		Age groups		Total	P	
			Below 70 yrs	70+ yrs			
Sex	Male	Yes	Count	104	44	148	
			%	70	29	100	
	Female		Count	62	29	91	
			%	68	32	100	
	Total		Count	166	73	239	
			%	69	31	100	
Sex	Male	No	Count	9	27	36	p<0.0001
			%	25	75	100	
	Female		Count	10	18	28	P=0.03
			%	36	64	100	
	Total		Count	19	45	64	p<0.0001
			%	30	70	100	
Marital status	Currently married	Yes	Count	126	53	179	
			%	70	30	100	
	Currently not married		Count	40	20	60	
			%	67	33	100	
	Currently married	No	Count	8	21	29	p<0.001
			%	28	72	100	
Currently not married		Count	11	24	35	P=0.002	
		%	31	69	100		
Co-morbidity	No	Yes	Count	63	14	77	
			%	82	18	100	
	Yes		Count	103	59	162	
			%	64	36	100	
	No	No	Count	8	18	26	P=0.006
			%	31	69	100	
Yes		Count	11	27	38	p<0.001	
		%	29	71	100		

Conclusions

Younger patients (<70yrs) with Stage III or IV disease, no co-morbidities and married patients were more likely to receive chemotherapy than older patients. We could not show that confounding factors significantly predicted the treatment making decisions for older patients and age was the strongest discriminating factor. It also seems that the 70 years or older age group may be missing out on more curative treatments as compared to patients

<70 years. We strongly recommend that a more stringent approach be taken in this particular group and a proper geriatric assessment be done to determine the physical status of those patients who may benefit from potentially curable treatments before ruling them out on basis of age alone. We also recommend more participation of this age group in randomised control trials to determine the impact on survival benefit in those undertaking chemotherapy.

Table 4: Proportion of patients with stage III and stage IV disease, who received chemotherapy (by ECOG status)

Patient performance status	ECOG	Received chemo		Age groups		Total	P
				Below 70 yrs	70+ yrs		
0	Yes	Count	95	20	115		
		%	83	17	100		
1		Count	33	28	61		
		%	54	46	100		
2		Count	6	7	13		
		%	46	54	100		
3		Count	3	6	9		
		%	33	67	100		
Total		Count	137	61	198		
		%	69	31	100		
0	No	Count	5	1	6	P=0.08	
		%	83	17	100		
1		Count	3	8	11	P=0.03	
		%	27	73	100		
2		Count	2	11	13	P<0.001	
		%	15	85	100		
3		Count	3	14	17	P<0.001	
		%	18	82	100		
4		Count	1	3	4	P=0.5	
		%	25	75	100		
Total		Count	14	37	51	P<0.0001	
		%	27	73	100		

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MEDICAL ONCOLOGY GROUP OF AUSTRALIA (MOGA)/NOVARTIS CANCER ACHIEVEMENT AWARD



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This oration was presented at MOGA's Annual Scientific Meeting in August 2007 and the Clinical Oncological Society of Australia (COSA) Annual Scientific Meeting in November 2007.

Members of COSA, dear colleagues and friends,

It is a great privilege and honour to receive the prestigious MOGA/Novartis cancer achievement award for 2007.

It was totally unexpected as I don't feel that I have done anything particularly special, but it is very gratifying to receive such recognition from one's peers and to be included among the previous awardees who have all contributed so much to medical oncology and cancer control in Australia.

My broad brief today was general – I was given free reign and asked to talk about my career.

I'm not the sort of person who spends time contemplating perceived past achievements or basking in self-congratulation. Like most of us, I tend to be more concerned about the problems of the present and the challenges ahead.

But, preparing this talk has given me the opportunity to look back and consider how my career has unfolded, and it provided the impetus for me to reflect on the many people who have influenced me and helped me along the way. I have found this to be gratifying and quite revealing. I expect that much of what I say will resonate with many of you in the audience who would have shared similar experiences in your own careers.

Any achievements that I may have had, have come about as the result of a complex interplay of many factors that include the support and encouragement of

mentors, rewarding personal relationships, productive team work, the influence of individual patients, and at times just good luck.

I'll try to give you a selective history of my career from my own perspective and, in the process, take the opportunity of giving credit and thanks to the friends and colleagues who have encouraged and challenged me over the years. I hope I'll be able to demonstrate how important mentorship and good role models are in supporting and inspiring students and young doctors. This is the real message that I would like to convey today.

Zimbabwe years

I was born and educated in Harare in Zimbabwe. I attended the Godfrey Huggins School of Medicine run by the University of Birmingham and graduated in 1975. It was a very good medical school and we were fortunate to have talented and committed teachers. I think that working in Africa in an underserved and disadvantaged setting had a profound effect on me and most of my classmates. Very early on in our training, we learned about the importance of social responsibility and the fact that as individuals we can make a difference. My interest in clinical research was directly related to the encouragement of our Professor of Medicine, Michael Gelfand. He was an excellent clinician, a committed researcher and prolific writer - a giant of a man both intellectually and morally.

He was convinced that all good physicians had to be continuously and actively involved in research and that training in research was as important as clinical training. I started working with him on a number of projects as a medical student and continued to do so until the completion of my internship when I left the country. His views, value system and work ethic resonated deeply with me then and still do today.

Almost 35 years have passed since I was a medical student, and I am embarrassed to admit that it was only while preparing this talk, that I realised how crucial Michael Gelfand was in shaping my own career values

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and those of many of my colleagues. It also brought home to me just how important the so called “hidden curriculum” is in medical education. This alludes to teaching through role modeling and transmission of professional values through example. It is quite different from formal training and teaching, but is just as important.

When you think about it, I am sure most of you will agree that role modeling is an integral component of medical education and an important factor in shaping students’ values and attitudes, as well as influencing their career choices.

I arrived in Australia from London in 1978 on a working holiday. The plan was to work for a year or so prior to going to the US, where I was going to settle and pursue a career in neurology. My good friend Maurice Slevin, who is now a highly regarded and prominent medical oncologist in London, had just commenced his medical oncology training at Bart’s and he strongly encouraged me to apply for a job in medical oncology.

The special unit

Medical oncology was not a big ticket item in the 1970’s and I don’t recall that there was any competition for the registrar position that, coincidentally and quite fortuitously, had just become available at the Prince of Wales in what was then euphemistically called, the Special Unit for Investigation and Treatment. The term cancer was only used in hushed tones or not at all. In those days doctors spoke of “growths” and neoplasms and the public did not know what oncology was.

Alan Coates had just been appointed as a staff specialist in the Special Unit at the same time that I started working as a registrar. He had just returned from Wisconsin and was filled with energy and enthusiasm. I was, and still am today, in awe of his encyclopedic knowledge and photographic memory, as well as his ability to raise his eyebrows higher than anyone else I have ever known! He was a good teacher and a positive role model. He encouraged me to continue training in medical oncology and transfer to the Ludwig Institute at Royal Prince Alfred Hospital when he moved there a year later.

By this time, I had become enthusiastic about pursuing a career in medical oncology. I had also just met Annie, who was to become my wife. Strangely, my thoughts of leaving for the US dissipated. “Good day mate” and “crook” were fast becoming part of my daily vernacular.

Sydney Ludwig

At the Ludwig, I was fortunate to train with the leaders of medical oncology in Australia at the time, including Martin Tattersall and Dick Fox. Stan Kaye, who now is the head of medical oncology at the Royal Marsden, was also working there for a year. Not long after we were joined by David Hedley and Derek Raghavan. It was an exciting time to be a registrar in oncology and we were all encouraged to be involved in clinical research and to publish our findings. The field was wide open and full of opportunity and I think it’s still much the same today.

I had become very interested in gynaecological oncology, largely as a result of the relationships I had established with a number of individual patients with ovarian cancer and trophoblastic tumours. In addition, I was fortunate to receive a lot of encouragement and support from the gynaecologic oncologists at King George V – Peter Elliott, John Solomon and Malcolm Coppleson. They probably did not realise it at the time, but the personal interest they showed in me and their encouragement nourished my enthusiasm for the field of gynaecological oncology. I expect that many of you can also look back and identify individuals and role models who changed the course of your own careers and primed your own specialty interests.

Among others, Martin Tattersall encouraged me to write a number of chemotherapy protocols for cervical cancer. It turned out that we were among the first to document the benefit of chemotherapy in metastatic cervical cancer and to investigate neo-adjuvant chemotherapy in patients with locally advanced cervical cancer. I spent many hours with Peter Elliott in particular, discussing various projects we were involved in and he organised for me to present the results of our research in meetings in Australia and Asia while I was still a registrar. This undoubtedly strengthened my interest and commitment to gynaecologic oncology.

In hindsight, one of the best decisions I made was to do a PhD, although at the time I was not sure if it would be time well spent. I would strongly recommend all trainees to take time out and devote a period of time to research before they embark on their clinical careers. The skills that I learned and the experience in writing papers and grants was invaluable.

I started off full of enthusiasm, but soon discovered, like many others, that the transition from the clinic to the laboratory could be immensely frustrating. After some time, I began to see that my initial research project was not going to be feasible. This led me to change direction and investigate aspects of the biology of ovarian cancer which had always, and still does fascinate me. I was fortunate to be able to work with Peter Russell, one of the greats in gynaecologic pathology, another mentor and role model who was very generous with his time and eager to share his knowledge with anyone who was interested.

Laboratory research

Like most clinicians who go into the lab. I was initially completely out of my depth and this was quite difficult to deal with. I was very lucky to have found space in Ian Taylor’s laboratory at the Ludwig. I received enormous support from Ian as well as David Hedley and Liz Musgrove, who patiently put up with my inept ways and lack of experience. Ian was a leader and pioneer in flow cytometry and, while in his lab, I planned, among other things, to prospectively investigate the prognostic significance of ploidy in ovarian cancer. I went to theater whenever possible to collect fresh tumours and began to build up a large tumour bank.

It was during one of our regular group therapy or drinking sessions at the university bar with David Hedley and Ian Taylor, as we were bemoaning the time it would take to complete the project, that David Hedley in what I think was a flash of genius said: "why don't we use paraffin embedded blocks for ploidy studies and then we can get tumour tissue from patients whose outcome was known." So simple, yet no-one had thought of, or attempted this before.

Work started the next day to see if we could extract DNA from paraffin embedded tissue and whether this would be suitable for flow cytometry. It turned out that this was indeed possible. In fact, this simple technique subsequently opened the way for others to extract DNA from tumour blocks for Southern Blots and later PCR. It is old hat now but was very novel then. David, Ian and I were then able to embark on a number of retrospective studies which led to many papers. I was able to access the blocks from a large number of ovarian cancer patients who had been enrolled in the one and only ovarian cancer study, carried out in Australia by the gynaecology group of COSA - I guess this is one of the early examples of translational research which we now take for granted.

Toronto

In 1984 I started a post doctoral fellowship at the Princess Margaret Hospital in Toronto, as there were a number of people I wanted to work with. I particularly wanted to meet and work with Alon Dembo in the Gynecological Oncology Unit and to also have the experience of working at a major cancer centre. In hindsight, this proved to be an invaluable move. The experience I gained and the people I worked with had a major influence on my future career. I would strongly urge all trainees to organise an overseas working experience early in their careers and in particular, try and identify the right people to work with. I met John Zalberg in Toronto. We became close friends and remain so today, and we speak with each other often. He is a valued colleague and has contributed greatly to cancer control and clinical trials in Australia.

While in Toronto, I had the opportunity to work with such luminaries as Alon Dembo, Gillian Thomas and Ian Tannock and to later become good friends with them. They were all exceptionally talented and generous with their time. They are all good examples of how important mentors can be to the career of young investigators and junior faculty.

Alon was arguably one of the most original and clear thinkers that I have ever met. He was one of the greats in the field of gynaecologic oncology. Sadly, he died of acute leukaemia in 1988. He invited me to speak at the first International Gynecologic Cancer Society (IGCS) meeting in Amsterdam in 1987 and both he and Gillian encouraged me to join the IGCS – an organisation which was later to become such an important part of my life.

At the time, I never imagined that I would later become President of the IGCS. Coincidentally, I was to follow Gillian Thomas in the presidency. It was an enormous

honour to have been elected and it gave me the opportunity to meet people working in gynaecological oncology from all over the world. It broadened my perspective and understanding of the challenges to health care delivery in different countries and regions throughout the world, including the third world. I was President from 2004 – 2006 and continue to be a member of the executive and chair the development committee and nominations committee.

Prince of Wales

Back in Australia in 1986, I worked at Royal Prince Alfred and later Royal North Shore Hospital and was recruited to the Prince of Wales Hospital by Rod Withers in 1990. This turned out, again, to have been a fortuitous move. I am very proud of the way the medical oncology unit at the Prince of Wales has developed and grown during the last 17 years. I have been fortunate to work with my very good colleagues Craig Lewis and David Goldstein and a strong and committed group of nurses, research and support staff.

One of the main reasons for my moving to Prince of Wales was that I would have the opportunity to also have an appointment at the Royal Hospital for Women. Neville Hacker had only recently returned from Los Angeles to set up the unit and I would like to take this opportunity to acknowledge the immense support and encouragement I have had from him. He is one of the leaders in the field of gynaecologic oncology nationally and internationally.

At this point, I would also like to take the opportunity of acknowledging the nursing and support staff at the Royal Hospital for Women, but particularly my good friend and respected colleague, Mary Ryan, who I have worked with side by side for the last 17 years. She started in the clinic as a relatively junior nurse and now has a PhD for her research into the experiences of women with recurrent ovarian cancer.

I think that working closely with a supportive team of talented people who complement one and other is one of the most satisfying aspects of my working life.

ANZCOG

It was in 2000 that I became closely involved with the formation of Australian and New Zealand Gynaecological Oncology Group (ANZGOG), which I have chaired since its inception. It has been particularly gratifying to see the degree of interest and growth of gynaecologic cancer clinical trials in Australia and New Zealand. This has been, and continues to be, very time consuming, but personally very rewarding. It's hard to believe that in 2000 we had very little - no money, no infrastructure and no members. There were no collaborative gynaecological cancer trials being carried out in the country and we lagged behind the rest of the world.

Now, seven years on, things are very different. We now have an active trials group and a strong infrastructure and have become integral members of the

ARTICLES

Gynaecological Cancer Intergroup, working with clinical trials groups from all over the world. I must acknowledge the support of the many people who have made ANZGOG a success, particularly the initial work done by Haryana Dhillon and the staff at the NHMRC Clinical Trials Centre, as well as all the help and hard work done by Michael Quinn and Danny Rischin and the entire executive and many of our members. We have a very strong team now headed by Julie Martyn. The group is now well established and I expect will grow from strength to strength, providing sufficient funds remain available to support clinical trials groups in Australia.

Moving away from gynaecological cancer, one of my other main interests has been hereditary cancer and the management of families at increased genetic risk. This interest came about once again quite by chance and was a result of the late Michael Donnellan referring a young man with testis cancer to me in 1992. He turned out to have a very strong family history with four affected first cousins with testicular cancer. This greatly interested me as I had not come across this before.

Cancer genetics

In my naïve enthusiasm, I thought that it would be possible to identify the gene through linkage analysis in this one family and the family was very keen to be involved in a research study. So I made contact with Felicity Collins who was a geneticist at the Prince of Wales (POW) Children's Hospital and her registrar Kathy Tucker. We decided to try and collect as many Australian families with testis cancer as possible to identify the gene. I would remind you that this was 1992, before BRCA1 or 2 had been identified and cancer genetics was still in its infancy. We made contact with a group in the UK and Canada who were also collecting families and were closely involved in establishing the International Testis Cancer Consortium. Liz Rapley, who was a PhD student at POW working on the project, subsequently moved to Mike Stratton's lab at the Institute for Cancer Research in London. Before long she headed the project, which continues today and has been very successful. As it turned out, there is not a single gene responsible for testis cancer and it is far more complicated than we initially envisioned.

In the course of dealing with the families with testis cancer, we recognised that we needed to establish a more formal approach to counselling and management of individuals at increased genetic risk. Kathy Tucker was about to complete her training in genetics at the end of 1993 and, by this time, we had become good friends and colleagues. We were very keen to set up a familial cancer clinic together. There were no such clinics anywhere in Australia and very few elsewhere in the world. The first and best established genetics clinic was run by Henry Lynch in Omaha and a clinic had recently also been established by Fred Li of Li Fraumeni syndrome fame, at the Dana Faber Cancer Centre in Boston. I visited both these clinics and spent most of my time in Omaha. Dr Lynch and his team were very

welcoming and generous. They were happy to share their experience and expertise and give advice on how to establish and run a cancer genetics service. I returned full of enthusiasm and fortunately the administration at POW were supportive, but it was a different era and I doubt we would have the same support today given the severe financial constraints common to all hospitals. We had a number of successful fundraising events by the Castellorizian Club, as well as a generous donation of \$300,000 and so were able to establish the Hereditary Cancer Clinic at POW with Kathy Tucker as head in 1994.

Shortly after BRCA1 was identified, the field as well as the clinic expanded rapidly. Soon Lesley Andrews joined us. She and Kathy Tucker have built a very strong unit together. We were closely involved in KConFab, which was set up by Joe Sambrook, together with the emerging cancer genetics clinics around the country at the time. This has now developed a life of its own and has been an enormous success thanks to the work of Joe and so many people throughout Australia. I have been very fortunate to have been able to continue my interest in cancer genetics and to have had the opportunity to collaborate with many people including Kelly Phillips, who has set up a very successful research program using many of the KCONFAB families. She is an outstanding researcher and has rapidly become a leader in the field both nationally and internationally.

Our involvement in KConFab and with genetic testing gave us the impetus to start addressing the psychosocial implications of genetic testing, as well as the impact on families. Bettina Meiser joined us to do her PhD and, over time, our interest and involvement in the psychological aspects of hereditary cancer expanded. Bettina is an outstanding researcher and now heads the Psycho-oncology Research Group at POW, which has over 12 staff and has been very successful.

As you can see one thing leads to another and the influx of psycho-oncologists and students led to us becoming involved in survivorship issues faced by young women with early breast cancer, which has also been one of my other longstanding interests and relates to what our patients had been telling us in the clinic for many years. We had set up a support group for young women with early breast cancer well over 10 years ago and the issues raised by these young women has shaped our research agenda. Belinda Thewes was our first PhD student in this area. She was very successful and has established an enviable reputation for herself as a research psychologist. Amongst others things, she identified the unmet needs of these young women and then carried out original research on the trade-offs and decision making in young women receiving adjuvant endocrine therapy. This led to a whole lot of additional questions and new students.

Kerrie Tiller worked with young women at increased genetic risk of ovarian cancer and developed a decision aid that is widely used in cancer family clinics. Kelly Mok is currently doing a PhD on the psycho-sexual impact of treatment in women with breast cancer, as well looking

at interventions to reduce its impact. The intervention we are investigating interestingly came about as a result of feedback about what worked well for one of my patients. Michelle Peate is doing her PhD on fertility as this was another major concern that emerged from the support groups.

Reflections

I mentioned right at the beginning of my talk, how important individual patients have been in stimulating subsequent research and I have already discussed how the family of the young men with testicular cancer and the support groups for young women with breast cancer, have changed the direction of my research interests and set the future clinical and research agenda for our unit.

There have been a number of other examples, but because of time I will only mention one other. I do so, not only because I think you might find it interesting, but also because I regret that I have not had the time to pursue it in the way I think it should have been and there is probably a message in this as well.

A patient with metastatic colon cancer was referred to me for consideration for chemotherapy. She had a family history consistent with HNPCC and subsequently was shown to have a mutation in HMLH1. What was particularly interesting however, was that in the six weeks between her being referred to me and being seen in the clinic, her metastases had dramatically reduced in size. Her CT scans demonstrated significant improvement and the question was why and what had she done. It turned out that she also had primary pulmonary hypertension and, shortly after being diagnosed with metastases, she became more short of breath. She had been started on high doses of calcium channel blockers as treatment for pulmonary hypertension by her respiratory physician. This had been the only change in her medication and the response of her tumour had coincided with this. Incidentally, her disease regressed completely and she died about two years later as a result of her respiratory disease, with no evidence of recurrence of her cancer.

I found this outcome very interesting and worth investigating. Working with my colleague Lin Yang, we were able to demonstrate that colon cancer cell lines derived from patients with HNPCC and were particularly sensitive to calcium channel blockers. More recently, we have shown that CA1, an oral calcium channel blocker that is well suited for clinical use, is cytotoxic to colon and endometrial cancer cell lines with either germ line or sporadic mismatch repair defects.

I have regrets that we have not capitalised on this serendipitous clinical observation and our laboratory findings. Part of the reason was the difficulty in obtaining research funding for this project, which remains a perennial problem, and partly because there is a limit to how many studies one can do. The message here is to try and remain focused and not take on more than you can reasonably do – a principle that I have not always heeded.

I am predominantly a clinician and have a busy and full-time clinical practice, as well as being the Director of Medial Oncology at Prince of Wales Hospital. Unlike our counterparts in other countries, most of us who work as staff specialists in Australia have no protected time for research and there are few incentives in a system that does not reward or indeed particularly value clinical research. Clinical research funding is hard to come by and most of the work must be carried out outside normal working hours.

So, why do so many of us get involved in clinical research? I can only speak for myself but I expect many will agree, when I say that clinical research helps to give balance to a working life which can be emotionally draining and demanding. The intellectual stimulation and the opportunity to interact and collaborate with so many talented people is particularly rewarding, as is watching younger colleagues move on to develop very successful careers. I am still very excited about clinical research, am involved in many different research studies and am constantly thinking about what other studies to do. I collaborate with a number of people in the audience, as well as many others here in Australia and overseas and the interaction sustains me.

I have been very privileged to work in medical oncology which is an exciting and rewarding specialty. I hope that what I have said will encourage my junior colleagues to pursue careers in clinical research.

I hope that I have been able to convey in this address how important mentoring can be and how influential positive role models are in directing career decisions. I have also taken the opportunity to acknowledge many of the people who I have worked with and who I am currently working with. Because of time I have not been able to mention everyone by name and I apologise to all of my colleagues who I have not acknowledged.

I think that one of the key ingredients in all successful endeavors is the ability to work together, to respect the talent and contributions of all in the team and to collaborate with like minded colleagues.

It's true that chance does play a part in one's eventual career path, but what is important is to see opportunities and take advantage of them.

I have been fortunate to have found myself in Australia quite by chance and to have had the opportunity to work in an area of medicine which is demanding, challenging, but also very rewarding.

Finally, I would like to thank my wife Annie and my sons David and Simon. They have always been supportive of my work and travel commitments. Without their enthusiastic encouragement and a stable home life, it would not have been possible to be involved, as I have been, in clinical research.

I would like to thank the Medical Oncology Group of Australia and Novartis once again for honouring me with the award and to you all for your attention.

CLINICAL ONCOLOGY SOCIETY OF AUSTRALIA 34TH ANNUAL SCIENTIFIC MEETING

Adelaide was the host city for the 34th Annual Scientific Meeting of the Clinical Oncology Society of Australia (COSA). The meeting took place between 14th – 16th November 2007 at the Adelaide Convention Centre in the heart of the city. A record attendance with over 800 registrations emphasised the success of COSA as the premier cancer professionals association. The meeting is the largest oncology specific forum in the nation.

The meeting was opened by Professor Ian Frazer, former Australian of the Year and a prominent cancer researcher, particularly in the field of cancer vaccine development. The opening plenary session was a review of the cervical cancer vaccine. This proved to be an exhilarating session that set the tone for the rest of the meeting. Professor Barrie Cassileth from the US gave an excellent plenary lecture on the first day exploring and analysing the role of complimentary medicine in cancer therapy. The following morning a special breakfast session, chaired by the ABC Health reporter Norman Swan, was held to examine this topic in the Australian context.

The organising committee helped put together a broad and stimulating program which offered something for everyone. The slogan for this year's meeting was "Progress through Prevention, Palliation and Cure – Progress through clinical trials". Clinical trials were an important focus of the meeting with special symposia that examined the organisation and impact of clinical trials in Australia. There were special sessions with significant contributions made by our invited international and national speakers. Professor Nils Wilking from Sweden led a plenary session that addressed the Karolinska report, a report that examined inefficiencies and challenges in translating the latest clinical trial results into clinical practice, with particular emphasis on access to some of the latest medical treatments. The history and the organisation of clinical trials across Australia were reviewed in a special symposium with contributions from the chairs of the major Australian tumour clinical trials groups and Professor David Currow from Cancer Australia.

One of the other key themes covered at the conference was cancer survivorship and cancer in adolescents and young adults. We were fortunate to have Professor Archie Bleyer, an expert in the field, participating in two symposia on these topics. In a special session that examined clinical trials, Professor Bleyer presented recent data from the US that demonstrated a relative lack of participation in clinical trials in the adolescent and young age demographic groups. He correlated this with a lack of improvement in cancer treatment outcomes for this age group.

Urological oncology was a major tumour focus at the meeting. This was largely thanks to the efforts of Dr Ian Davis who organised an excellent program. We were

fortunate to have the involvement of two urological oncology international speakers (Professor Ron De Wit from the Netherlands and Professor Stephen Jones from the US). Their input and that of a large group of national experts helped make the COSA ASM 2007 arguably the best multidisciplinary uro-oncology series of lectures and research presentations in Australia.

The Epidemiology Group ran a series of sessions featuring April Fritz, the former head of SEER American database. Professor Bruce Armstrong presented a review of the recent cancer cluster affecting the ABC and other work places. Lidia Schapira from the US presented and also contributed to cancer communication workshops that followed COSA. Martin Gore from the Royal Marsden Hospital in the UK presented on ovarian cancer and melanoma.

At this year's meeting we attempted to run a series of "general" or overlapping presentations that took place in the main lecture hall. We successfully integrated cancer research, service delivery and the various cancer special interest groups in many of the sessions. There was, for the first time, a major input of familial cancer topics, and we endeavoured to bring epidemiology, palliative care and other specialties into a broad focus. Special interest sessions still took place in separate rooms. The cooperative study groups also used the COSA meeting as a platform for their specific meetings, including the Australian Lung Trials Group, Neuro-oncology Group and for the first time the ANZ Melanoma Trials group.

There were over 200 submitted research papers and this year a select committee, including input from the international invited speakers, awarded six research awards. These comprised four awards for cancer research, one for a presentation relating to cancer service delivery and one for the best poster. The Novartis/MOGA cancer achievement award was presented to Professor Michael Friedlander, and the Thomas Reeve Oration was given by Professor Martin Tattersall.

I would like to take this opportunity to thank the organising committee for their hard work in putting together an excellent program. This helped make the Adelaide COSA meeting a success. The relevance of the program, the quality of the research, the enthusiasm of the presenters and the registrants all contributed to the meeting exceeding expectations. COSA 07 has set the bench mark for future COSA conferences, which should only strengthen with further multidisciplinary cancer service and cancer research collaboration.

Chris Karapetis
Convenor

AUSTRALIAN BEHAVIOURAL RESEARCH IN CANCER

Centre for Health Research and Psycho-oncology (CHeRP), NSW

Telemarketing Smoking Cessation Trial

The Telemarketing Smoking Cessation Trial, a collaborative project between CHeRP, Hunter New England Population Health and the University of Newcastle, commenced in September 2005. This research used a telemarketing approach to recruit adult daily smokers, selected at random from the New South Wales electronic white pages, into smoking cessation support. Participants were allocated at random to receive either proactive telephone counselling delivered by the NSW Quitline, or mailed one-off written self-help materials. Computer assisted telephone interviews were completed during baseline, 4-, 7- and 13-months post-recruitment. Non-participants who declined to participate in the randomised control trial were invited to complete a cross-sectional interview at baseline.

In April 2007, 48,014 households were contacted in order to recruit 1,562 daily smokers into the smoking cessation trial. Of the eligible daily smokers identified, about half (52%) agreed to participate. When compared to research that suggests that less than 5% of adult smokers call the Quitline per year in countries such as the US, UK and Australia, the current trial illustrates the potential of using a proactive recruitment approach to link a smoking cessation service with its target population. Comparisons between the demographic and smoking related characteristics of study participants and non-participants who completed a baseline cross-sectional interview revealed statistically significant differences in quitting-related behaviours and the perceived effectiveness of a number of cessation strategies. The data illustrate the potential of proactive recruitment approaches in increasing smokers' use of cessation strategies. The 13 month follow-up data collection will be completed by mid-2008.

Prevalence and predictors of burnout in COSA members

Care workers with direct patient contact can experience significant psychiatric morbidity and professional burnout, with a potentially negative impact on their professional and personal lives. Clinically important outcomes of burnout, which are documented in the literature, include increased medical errors, increased turnover and absenteeism and decreased quality of patient care. Previous research has clearly established that specific demands are placed on oncology personnel due to the emotionally intense nature of the care provided to suffering or dying patients. This is evidenced through high levels of burnout and psychological distress in this occupational group.

The Clinical Oncological Society of Australia (COSA) is an organisation representing the various multi-disciplinary professional groups providing or

contributing to cancer care and research in Australia. In order to assess the extent to which professional burnout presents within the Australian context, COSA commissioned CHeRP to ascertain the prevalence and predictors of burnout and psychiatric morbidity among its members, with funding from Cancer Australia. To assess the prevalence and predictors of burnout and psychological distress, COSA members were invited to complete a 10-minute online survey. Measures included the Maslach Burnout Inventory [MBI], the Kessler-10 [K-10] and the General Health Questionnaire [GHQ-12]). The survey also explored demographic and occupational factors that may contribute to burnout, the perceived causes of professional burnout, recommended strategies for preventing or reducing burnout and the consultation-specific tasks which oncologists and palliative care physicians perceive as difficult or stressful. Analysis is currently underway and findings from the study are expected to be published in 2008.

Centre for Behavioural Research in Cancer (CBRC) Victoria

Weekend Sun Protection and Sunburn in Australia Trends (1987–2002) and Association with SunSmart Television Advertising

This study examined trends over time in sun-protective behaviours and the effect of SunSmart paid television media on skin cancer prevention attitudes in the context of a long-term health promotion program. In nine cross-sectional surveys from 1987 to 2002, 11,589 Melbourne adults were interviewed by telephone about their sun-exposure and sun-protection during outdoor activities on summer weekends. Sun-protection and sunburn show substantial improvement over time, but have stalled in recent years. Hat and sunscreen use has significantly increased, peaking during the mid to late 1990s, compared to pre-SunSmart. The amount of unprotected skin was reduced and was lowest in summer 1997/1998. Summer sunburn incidence declined over time and was 9.1% in 2002—almost half baseline. Higher exposure to SunSmart advertising in the four weeks before interview increased preference for no tan, hat and sunscreen use, and proportion of body surface protected from the sun. These data highlight that a population's sun-protective behaviours are amenable to change.

[Suzanne Dobbinson, Melanie Wakefield, Kris Jansen, Natalie Herd, Matthew Spittal, John Lipscomb, David J. Hill. *American Journal of Preventive Medicine* (In press)]

Assessing the unmet supportive care needs of newly diagnosed patients with cancer

Adequate monitoring in cancer control needs to include measures of psychosocial outcomes so as to take

account of the totality of cancer experiences. This study investigated the utility of using a telephone-administered survey to identify unmet needs. Participants were identified from a state-wide population-based cancer registry following an episode of hospitalised care in Victoria. Participants completed an adaptation of the Supportive Care Needs Survey. Results indicated that perceived needs for newly diagnosed patients were mostly in the area of information provision. Socio-demographic and disease-specific variables also affected the level of perceived unmet needs. Overall, this study indicated registry-based sampling was practical and timely and the telephone adaptation of this survey provided a reliable method to explore the unmet needs of newly diagnosed patients with cancer.

[Hill D, Sutherland G, Morand M, Pruden M, McLachlan S-A. *European Journal of Cancer Care* (In press)]

Impact of tobacco control policies and mass media campaigns on monthly adult smoking prevalence: time series analysis

To assess the impact on smoking prevalence of tobacco control policies and televised anti-smoking advertising, we used a monthly Australian population smoking prevalence survey from July 1995 to December 2006. Time series analysis assessed the effect on smoking prevalence of televised anti-smoking advertising, cigarette costliness, monthly sales of nicotine replacement therapy (NRT) and bupropion, and restaurant smoke-free laws. Exposing the population to televised anti-smoking ads an average of almost four times per month led to a 0.3% reduction in smoking prevalence, as did increasing the costliness of a pack of cigarettes by 0.03% of gross average weekly earnings. Both effects occurred relatively rapidly and were eroded over time if the interventions were not sustained. Monthly sales of NRT and bupropion, exposure to NRT advertising and smoke-free restaurant laws had no detectable impact on smoking prevalence. Increases in the real price of cigarettes and public health-sponsored mass media campaigns broadcast at sufficient levels at regular intervals are critical for reducing population smoking prevalence.

[Wakefield M, Durkin S, Spittal M, Siahpush M, Scollo M, Simpson J, Chapman S, White V, Hill D. *American Journal of Public Health* (In press)].

Centre for Cancer Control Research (CCCR) and Behavioural Research and Evaluation Unit (BREU), South Australia

Hospitality Venue Smoke-free Laws Compliance Survey

In March 2008, a third survey of hospitality venue compliance with smoke-free laws (SA) will be conducted with 500 randomly chosen licensed venues in South Australia to determine if venues are completely smoke-free following the latest laws implemented (November 2007). This study succeeds two previous surveys of bar and club managers of randomly chosen licensed venues in SA. The first (baseline) survey was conducted in November 2004 by telephone just after

the smoke-free laws were passed through Parliament. The second survey was conducted in May 2005 and included site inspections about six months after the implementation of phase-in laws. At baseline awareness of the laws was high and just over half of venue managers approved of their venues eventually becoming completely smoke-free. At phase 1 awareness and support for the legislation both increased. Inspections showed that most venues appropriately followed laws when designating no-smoking areas. It is expected that awareness, support and compliance among venue managers will continue to be high in 2008, given previous outcomes.

Quitline SMS Trial Evaluation

An evaluation of the Quitline SMS Trial was conducted in November 2007. The SMS trial offered consumers an alternative method to calling the Quitline following one television campaign. A total of 424 consumers responded via text message to receive Quit Kits. A small proportion (7.4%) further requested a callback to speak to a Quitline advisor. The SMS group was aged between 8 and 61 years, with a median age of 26 years. This group was significantly younger than those who called the Quitline during the same period and those who called the Quitline during a campaign period that was run without the SMS option. Results suggested utilising SMS technology successfully motivated a large, young group of smokers to contact a Quitline - an audience with which it is difficult to initiate a professional smoking cessation intervention. This method is now ongoing in three Australian states.

Solaria Compliance Study

The Solaria Compliance Study was conducted to examine solarium industry compliance with voluntary standards. This was the third Australian survey that showed low compliance as found in other states (NSW and VIC). Findings show that regulation and/or education are needed in order to minimise the risks involved in solarium use.

National Survey of Sun Protection Policies and Practices of Early Childhood Services

The first National Survey of Sun Protection Policies and Practices of Early Childhood Services will be conducted mid-2008. The primary aim of the survey is to determine common sun protection policies and practices in early childhood services across Australia, and to examine variation in practices and policies by a range of factors such as management type, level of disadvantage, SunSmart status and location.

Centre for Behavioural Research in Cancer Control (CBRCC)

Increasing fruit and vegetable consumption

Consumption of fruit and vegetables is a known protective factor against many cancers. For five years the "Go for 2 & 5" campaign in Western Australia has encouraged people to consume two serves of fruit and five of vegetables per day. Since the beginning of the campaign there has been an appreciable increase in average fruit and vegetable consumption, with daily fruit

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intake increasing from 0.8 to 1.9 serves per day and vegetable intake increasing from 2.1 to 3.1 serves per day. The aimed level of fruit consumption has been largely achieved, however vegetable consumption remains stubbornly below the goal of the campaign. Quantitative campaign evaluations suggest that minor barriers to increased vegetable consumption include price, (in)convenience and perishability, but by far the biggest barrier is that most people believe they are already eating sufficient vegetables to maintain good health.

The next advertisement in the "Go for 2 & 5" campaign is currently being planned. CBRCC was asked to explore the underpinnings of this belief and conducted a series of focus groups with Perth residents to explore the issue. The results suggested that participants were very familiar with the campaign message and clearly understood what constituted a 'serve' of fruit, and regarded eating such as achievable and realistic. In contrast, participants were largely confused as to what constituted a 'serve' of vegetables. Five serves of vegetables per day was regarded as unrealistic and unachievable and rejected as necessary to maintain good health. The conclusion was that in order to further increase vegetable consumption among West Australians, future public health messages would have to inform people why they should consume five vegetables per day, as opposed to only three and further education would be required about what constitutes a 'serve' of vegetables. Advertising concepts emphasising these messages are currently being developed for ad-testing before the next wave of the campaign is launched in August this year.

Positive portrayals of alcohol in comic strips

Alcohol abuse increases the risk of a variety of health problems, including cancers. A number of studies have looked at the incidence of alcohol in various media, primarily in movies, on television and in magazines, that depict excessive alcohol use in a manner reinforcing of existing attitudes and social norms that trivialise alcohol consumption and negate attempts to question such norms. Newspaper comics remain an area not yet investigated, but they are read by adults and especially young people and children. CBRCC audited 1290 comic strips appearing in *The West Australian* newspaper over a one year period and found that 4% (n=54) depicted alcohol, with over half of these encouraging excessive alcohol consumption. Particularly worrisome was that many of these consisted entirely of animal cartoon characters, which are known to have particular appeal to young children. Newspaper publishers should consider excluding comics that trivialise the abuse of alcohol.

Cancer Prevention Research Centre

Reducing cancer risk through physical activity and weight control

Physical inactivity and adult weight gain are major modifiable risk factors for colon and breast cancer. Recent increases in rates of overweight and obesity and type 2 diabetes have become a public health concern.

Population-based approaches that facilitate the maintenance of physical activity and healthy weight control are now on the cancer prevention agenda. The 'Living Well with Diabetes Program' is a five-year NHMRC-funded collaborative study to evaluate the ability of a telephone counselling intervention to assist initiation and maintenance of physical activity and moderate weight loss in adults with type 2 diabetes. Participants (350 adults with type 2 diabetes) will be recruited from 10 general practices. Participants will be randomly allocated to one of two programs:

- 1) Enhanced Usual Care: Participants will be mailed standard diabetes management brochures every six months over an 18 month period.
- 2) Living Well Telephone Counselling: Participants will receive a detailed workbook plus ongoing telephone support from health educators, to assist them to increase their physical activity and improve their diet (26 calls over 18 months tapered from weekly to fortnightly to monthly).

A motivational interviewing approach will be used to help participants set collaborative behaviour change goals, develop a personalised action plan and draw upon family and community resources to support their health behaviour change and weight loss goals. Following each assessment, participants' GPs will receive brief mailed feedback. All participants will be assessed upon entry into the study, and at 6, 18 and 24 months, on physical activity, weight loss and blood-glucose control. The study will run from April 2008 through April 2013. Cost-effectiveness analysis will be conducted at the end of the trial.

Research by PhD student Geneviève Healy, recently published in *Diabetes Care*, points to physical activity strategies that go beyond the usual focus on moderate to vigorous intensity activity in leisure time. Light intensity activity (which includes such activities as general domestic chores and gentle walking) was shown to be beneficially associated with waist circumference in Australian adults.¹ This builds on previous work that demonstrated that light intensity activity was beneficially associated with blood glucose levels.² In contrast, increased time spent sitting and inactive was detrimentally associated with these metabolic risk factors. Both of these findings were independent of how much moderate to vigorous intensity activity was done. Although moderate to vigorous intensity activity (such as brisk walking) is still a very important component of the healthy lifestyle message - sitting less and standing more can also have beneficial health consequences. This work was done in collaboration with the International Diabetes Institute, Melbourne.

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The Viertel Centre for Research in Cancer Control (VCRCC)

Lung cancer incidence

In 2007, the Descriptive Epidemiology Program used data from the Queensland Cancer Registry and other population-based sources to examine the incidence, mortality, survival and geographical differences of lung cancer. Overall incidence rates among men have declined, but there has been a steady increase among women. Research continues to examine patterns of cancer care in Queensland which will assist in identifying potential areas for improvement in the delivery of cancer care.

Survivorship and quality of life research program

Underway is the Colorectal Cancer and Quality of Life Study, a long-term study examining the quality of life, long-term health outcomes and adjustment of people after treatment for colorectal cancer. The cognitive and emotional functioning and supportive care needs of cancer patients are being explored in a qualitative study of 40 individuals and their partners. The results are informing the development of an intervention program to address the supportive care and lifestyle needs of colorectal cancer survivors that will be trialled during 2008.

Prostate cancer research program

The ProsCan Program, involving over 1000 men, is investigating the attitudes and behaviours relating to the early detection and supportive care needs of prostate cancer patients, with the aim of developing and evaluating a supportive care intervention program which will provide a model for the effective delivery of prostate cancer support services across Queensland. With funding from the NHMRC and Andrology Australia, ProsCan for Couples is also examining an intervention program targeting the challenges couples experience after a radical prostatectomy.

Skin cancer research program

During 2007, results of a study involving over 4000 patients with melanoma highlighted the important role that GPs play in diagnosing this disease and identified the difficulty faced by patients in rural and remote areas in accessing services. A study involving general practitioners and doctors within skin cancer clinics also found that levels of accuracy for diagnosing skin cancer was high in both groups of doctors. Further work in 2008 will examine how skin cancer is managed within primary care. In 2008 the Melanoma Survivors Study will investigate levels of physical and emotional well-being, quality of life and the health behaviours of 3000 melanoma survivors.

CARE COORDINATION WORKSHOP REPORT

Commissioned by the Clinical Oncological Society of Australia

Alison Evans ■ Alison Evans Consulting, Leichhardt, NSW

Care of people with cancer is complex and multifaceted, involving a range of services and health professionals, often in different settings. In the absence of appropriate coordination of the different elements of care, patients and their families report becoming 'lost' in the system, often experiencing unnecessary morbidity and distress.¹ Lack of coordination between services can result in fragmented care, sub-optimal management and high health care costs.^{2,3} Such fragmentation of care is exacerbated by the absence of clear referral pathways and suboptimal communication between health care providers and between providers and patients.

The need to improve continuity of care has been highlighted in a number of national reports.^{1,4} The *National Service Improvement Framework for Cancer*⁴ identifies an optimal cancer service as one in which people with cancer 'will experience the cancer journey as seamless and continuous care provided by one integrated service'. It notes that achieving such continuity of care requires linkages and coordination:

- among different treatment modalities
- among various health professionals and care providers
- among different individuals within the same discipline (eg medical or nursing staff on rosters)
- within any single service, over time
- across the spectrum of cancer care (from detection through treatment to palliative care), and
- across different services types and settings (public and private, inpatient and ambulant, general and specialist hospitals).⁴

Delivery of integrated and coordinated care is likely not only to enhance the patient's experience and minimise the likelihood of further distress, but may also contribute to improved clinical outcomes and efficiency in delivering health care services.

At a jurisdictional level, a range of approaches have been taken to the implementation of care coordination, including appointment of designated Care Coordinator roles and a broader system-based approach. Neither approach has yet been evaluated.

The Clinical Oncological Society of Australia (COSA) has identified cancer care coordination as a priority issue of concern to its members. In 2006, COSA convened a one-day workshop to:

- define the problem of care coordination
- provide some context for exploring a range of strategies for achieving cancer care coordination at the system, organisational, team and individual levels

- review the evidence and experiences of using care coordinators as a means of achieving care coordination, from the perspective of consumers, care coordinators, health care teams and policy makers.

The workshop identified a range of issues relevant to cancer care coordination, with the importance of achieving a patient-centred rather than disease-centred focus the central theme. A set of principles was developed to underpin care coordination in Australia at the patient, team and system level (see Appendix I). A report on the outcomes from the workshop has recently been published.⁵

Workshop overview

A second workshop was convened by COSA prior to the 2007 Annual Scientific Meeting in Adelaide. The aim of the workshop was to define expected outcomes from cancer care coordination and methods for evaluating those outcomes and potential benefits, including health outcomes and economic outcomes. The ultimate goal of the workshop was for participants to achieve a shared understanding of what could be achieved through coordination of cancer care, rather than to identify strategies for the implementation of care coordination.

The workshop was attended by around 50 participants from a range of backgrounds with an interest in cancer care coordination. Attendees included health professionals (including cancer care coordinators), health service administrators, consumers and representatives from cancer and government organisations. Their roles included cancer care coordination, funding, evaluation and those experiencing care coordination.

Workshop introduction

Chief Executive Officer of Cancer Australia, Professor David Currow, opened the workshop by emphasising the importance of care coordination in the management of patients with cancer in Australia and highlighting the complexities of Australia's unique geography and mix of public and private health service delivery. He stressed the importance of ensuring that the delivery of patient care is appropriate, timely, efficient and effective and that the process of navigation through the patient journey respects the challenge faced by those diagnosed.

Professor Patsy Yates presented an overview of outcomes from the 2006 workshop and described the principles for care coordination developed as a result of the workshop. She outlined the objectives for the 2007 workshop, acknowledging that achieving coordination of care was a multilevel issue and that a range of other

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strategies might also be relevant to its implementation, including development of role descriptions and education of health professionals.

In providing their opening comments, Professor Currow and Professor Yates made reference to other relevant initiatives, such as the Cancer Australia CanNETs project, which aims to map the pathway from suspicion of cancer to the development of a definitive treatment plan, and the Continuing Professional Development project for cancer professionals, funded by Cancer Australia and conducted by a consortium led by the Centre for Innovation in Professional Health Education and Research at the University of Sydney.

Panel discussion

In outlining their views on care coordination, a panel discussion agreed that the patient experience should be the focal point. Given that outcomes for many cancers in Australia were good by international standards, it was important to tease out what could or could not be improved by better care coordination.

The panel, comprising Professor Currow, Professor Yates and Professor Bruce Barraclough (Medical Director, Australian Cancer Network), discussed the importance of demonstrating both clinical and non-clinical outcomes from care coordination. There was recognition that there might be a number of intermediate points at which outcomes could be measured between the traditional 'checkpoints' of diagnosis and death. They concluded that improved patient satisfaction alone would not be sufficient to justify significant investment in improvements in coordination of care. However, it was argued that other non-clinical outcomes that were important to patients might influence a patient's response to treatment and improve health service utilisation, for example improvements in the patient experience may in turn increase patient engagement, improve compliance and reduce downtime in health service utilisation. The importance of considering longer term impacts of care coordination, as well as immediate effects, was emphasised, as was the need to clearly identify outcomes in order to engage the community about benefits beyond mortality. It was suggested that better care coordination might result in improvements in patient survival and morbidity by ensuring that patients were referred for the right care and treatments in a timely fashion.

While the aim of the workshop was not to discuss strategies for care coordination, the panel emphasised the importance of care coordination being seen as a shared responsibility across the entire health care team, rather than being the role of one or two individuals. It was emphasised that care coordination was a system-based approach that relies on linkages across the health care system, including both public and private and tertiary and primary care.

Background to evaluation and outcomes

To provide some context for discussion of evaluation and outcomes, Dr Marian Haas, from the Centre for Health

Economics and Research Evaluation at the University of Technology Sydney, gave a brief presentation outlining key issues for consideration.

In the context of health service delivery, Dr Haas described evaluation as being more than an audit – because it measured associated and causative factors – and less than research, which was about achieving knowledge for its own sake. However, she explained that the subject matter was the same in that evaluation measured the extent to which the delivery of health services met pre-determined objectives.

Dr Haas highlighted four key features of evaluation:

- structure (the organisational framework)
- inputs (the resources used)
- process (the activities undertaken)
- outcomes (the impact and cost of activities).

Participants were encouraged when thinking about outcomes of care coordination to consider how they would know that care was coordinated at the patient, health service and system level. Examples were given to demonstrate what should be considered at each of these levels.

Workshop outcomes

Workshop outcomes were achieved through small multidisciplinary group discussion, followed by facilitated feedback and refinement at a plenary level. Time limitations precluded a full consensus approach and the outcomes reported summarise areas of convergence within the group.

Participants were asked to consider issues at a national level using three main frames of reference:

1. people who make investment decisions – funders/system level
2. people who provide care – health services/teams/networks
3. people who receive care – cancer patients/consumers.

Outcomes from coordinated care

Participants identified the outcomes they would expect to see at a patient, service network and investor level within 12–18 months of implementation of a coordinated approach to cancer care. There was some overlap in proposed outcomes for the three levels.

In considering outcomes, two essential components of care coordination were identified, namely the need for:

- clearly defined patient care pathways
- management of care through effective multidisciplinary teams.

Participants agreed that these components should be in place across the whole system, regardless of geography, social or cultural differences and whether care was

delivered in the public or private sector. While the workshop did not consider individual strategies for achieving care coordination, in defining these outcomes,

participants recognised the need to consider potential workforce and resource implications of the approaches listed.

Patient level outcomes

Outcome	Detail
1. Every patient is aware of their pathway of care.	<p>Every patient, irrespective of demographics and health service delivery setting:</p> <ul style="list-style-type: none"> ■ knows what will happen to him/her from the point at which symptoms are reported/detected ■ can identify a key point of contact at each stage in the journey ■ is provided with consistent information throughout their journey. <p>As a result, patients will have increased confidence in the system.</p>
2. The time from diagnosis to treatment is appropriate.	The timing of treatment is efficient, appropriate and takes account of patient preferences.
3. The patient experience is positive.	Every patient feels valued, in control and respected.

Service network outcomes

Outcome	Detail
4. A clear pathway is defined for each patient, and information moves with the patient through the system.	<p>Key elements in the pathway include:</p> <ul style="list-style-type: none"> ■ structured interdisciplinary communication ■ an evidence-based approach.
5. There is an effective multidisciplinary team relevant for each cancer.	<p>An effective multidisciplinary team is one in which team members have the necessary expertise for managing the patient's cancer, and in which team roles are clearly defined and interactions are effective and of a high quality.</p> <p>Team membership may vary according to the stage in the patient journey.</p> <p>It was noted that membership of an effective team may lead to improved satisfaction for participating health professionals.</p>
6. Transfer points are well managed across networks and sectors.	<p>The process for transfer of care at each stage of the patient journey is clear and well managed. Key elements include:</p> <ul style="list-style-type: none"> ■ knowledge by health professionals of relevant contacts at primary and tertiary levels ■ provision of relevant information at the point of transfer ■ clear definition of entry and exit points to the pathway.

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Funder outcomes

Outcome	Detail
7. More patients are cared for by an effective multidisciplinary team.	Includes increases in referrals to multidisciplinary teams, as well as increased numbers of effective multidisciplinary teams.
8. Patients receive appropriate treatment.	Improvements in treatment will include: <ul style="list-style-type: none"> ■ improvements in time to treatment in line with recognised benchmarks (taking account of patient preferences) ■ reduced variation in treatment.*
9. Knowledge of and access to services, especially primary care, is improved.	
10. Variation and duplication of service provision is reduced*.	

*It was noted that reduced variation in treatment does not automatically lead to cost savings, given that the system currently involves a mix of under and overuse of treatment and the extent to which these balance each other out is not known.

Participants also identified the importance for funders of evidence of sustainability. However, it was agreed that this would not necessarily be an outcome of coordinated care, rather a requirement of strategies to implement coordinated care.

Measures for assessing the effectiveness of coordinated cancer care

The outcomes identified at each level were grouped according to common themes. Participants were asked to consider each outcome and to identify what measures could be used to show that progress towards these outcomes was being made. The outcomes, measures and suggested tools for measuring progress are provided below. The measures do not represent performance indicators, but rather point to broad dimensions that can be used to show whether an outcome is being achieved.

Outcome	Measures	Tool
1. Clear referral pathways are in place for patients irrespective of location or service delivery setting.	<ul style="list-style-type: none"> ■ Existence of a documented referral pathway for each patient. 	<ul style="list-style-type: none"> ■ Audit of patient records. ■ Assessment of compliance of treatment with protocols.
2. Transfer points are well managed across networks and sectors.	<ul style="list-style-type: none"> ■ Frequency of involvement of primary care and the patient in decisions at key transfer points. ■ Proportion of patients who report that transfer has been smooth. ■ Proportion of patients who have a patient-held record. 	<ul style="list-style-type: none"> ■ Survey of levels of involvement of the GP and patient. ■ Patient survey data.
3. Patients receive appropriate treatment.	<ul style="list-style-type: none"> ■ Proportion of patients for whom care is planned by a multidisciplinary team based on current standards. 	<ul style="list-style-type: none"> ■ Audit of patient records. ■ Analysis of situations where care is not aligned with evidence of best practice. ■ Quality of life tools.

Outcome	Measures	Tool
4. The patient experience is positive.	<ul style="list-style-type: none"> ■ Proportion of patients who report being involved in decisions about their care. ■ Frequency of repetition by patients of their medical history to different service providers. ■ Level of consumer involvement in service planning and education for health professionals (indirect measure). 	<ul style="list-style-type: none"> ■ Patient surveys about their experience. ■ Documentation of patient preferences. ■ Analysis of complaints.
5. Patients have access to multidisciplinary care.	<ul style="list-style-type: none"> ■ Proportion of newly diagnosed patients who are referred to and discussed by a multidisciplinary team for prospective treatment planning. ■ Number of protocols that exist about referral to multidisciplinary teams. 	<ul style="list-style-type: none"> ■ National Breast Cancer Centre Indicators of Multidisciplinary Care and Audit tool. ■ ACHS MDT indicator.
6. Multidisciplinary teams function effectively (and practitioner perspectives are positive).	<ul style="list-style-type: none"> ■ Proportion of multidisciplinary meetings that are attended by appropriate health professionals. ■ Evidence that the documented treatment plan is actioned. 	<ul style="list-style-type: none"> ■ Multidisciplinary meeting attendance log. ■ Growth/sustainability of teams. ■ Audit of case notes.

Next steps

The workshop identified a range of outcomes and measures that could be used to show whether care coordination was being achieved. The outcomes from this one-day workshop were developed through a consultative process, rather than through a comprehensive analysis of available evidence in this field. The outcomes and measures identified provide a useful starting point to guide those with an interest in improving care coordination. They require ongoing refinement and validation.

A number of actions were agreed, some requiring action at a service level, others requiring national input and some requiring coordination at a jurisdictional level.

1. At a service level, it will be important for health professionals to determine relevant referral pathways to guide how patient care will be provided. Existing frameworks, such as the Victorian Patient Management Frameworks, and examples of pathways developed by individual teams will be helpful in guiding discussions.
2. At a patient level, it will be important to increase awareness by patients and the broader community of the critical nature of multidisciplinary care in the management of cancer.
3. At a national level, it will be important to determine the key elements of cancer care coordination and to develop clear outcomes and indicators that can be

adopted across jurisdictions. Decisions about what roles are important in implementing cancer care coordination need to be taken at a jurisdictional level.

Attendees requested ongoing forums to facilitate sharing of knowledge and information about what is and is not working effectively and about what is happening at a policy level to inform care coordination.

Acknowledgements

The workshop was sponsored by Cancer Australia and The Cancer Council Australia. COSA gratefully acknowledges the input and support of the workshop facilitator, Lynette Glendinning from PALM Consulting and the Chair of the workshop committee, Professor Patsy Yates. Thanks also to Dr Madeline King and Dr Marion Haas for their input to the workshop presentations.

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- 1 National Cancer Control Initiative. *Optimising Cancer Care in Australia*. Melbourne: NCCI, 2002.
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- 3 National Cancer Strategies Group. *Priorities for action in cancer control 2001-2003*. Canberra: Department of Health and Ageing, 2001.
- 4 National Health Priority Action Council. *National Service Improvement Framework for Cancer*. 2004.
- 5 Yates P. *Achieving Coordinated Cancer Care: Report on the Clinical Oncological Society of Australia Care Coordination Workshop*. *Cancer Forum*, 2007; 31(3): 169-172.

Appendix I: Principles of cancer care coordination

Patient Focus

Care co-ordination should:

- be patient, carer and family-centred
- be a key focus across the entire cancer journey
- enable patient choice (to not receive care co-ordination)
- emphasise patient empowerment
- improve patient access to services
- address equity of access
- improve care outcomes.

Team Focus

Care co-ordination takes a **multidisciplinary team** approach and is inclusive of medical and allied health professions as well as management and administrative staff. Care co-ordination:

- focuses across the continuum of care
- is a shared responsibility, and is not solely the responsibility of an individual co-ordinator
- relies on the sharing of information and knowledge.

Systematic Approach

Care co-ordination should:

- be evidence-based
- be sustainable and supported
- take a system-based approach
- be capable of use across different platforms, including public and private systems, metropolitan and rural and remote geographical settings and various care settings
- be built on a sound and robust evaluation framework.

Appendix II: List of attendees

Name	Affiliation
Ms Kristin Linke	Cancer Clinical Network, Royal Adelaide Hospital
Mr Ray Araullo	Social Worker, Cancer Services, Royal North Shore Hospital
Professor Bruce Barraclough	Medical Director, Australian Cancer Network
Mr Douglas Bellamy	Area Cancer Care Coordinator, NSW
Ms Sharon Bowering	Cancer Care Coordinator AYA, Children's Youth & Women's Health Service, SA
Dr Stephen Byrne	GP, Goolwa Medical Centre, SA
Ms Philippa Cahill	Manager Clinical Workforce, The Cancer Institute NSW
Ms Sandy Cleghorn	Paediatric Care Coordinator, Department of Health SA
Ms Shoni Colquist	Manager, Queensland Cancer Control Analysis Team
Ms Angela Cotroneo	President, Oncology Social Work Australia (OSWA)
Professor David Currow	CEO, Cancer Australia
Ms Tracey Doherty	Oncology Nurse Practitioner, Flinders Medical Centre
Ms Cecilly Dollman	Royal Adelaide Hospital
Ms Maeve Downes	Nurse Unit Manager, Paediatric Haematology/Oncology, Children's Youth & Women's Health Service, SA
Ms Mary Duffy	Peter MacCallum Cancer Centre
Ms Jacinta Elks	Cancer Care Coordinator, Sunshine Coast Health Service District
Ms Rita Evans	National Manager, Cancer Australia
Ms Kate Fernandez	Cancer Care Coordinator, Central Nervous System Tumours, Women's and Children's Hospital, CYWHS, SA
Dr Linda Foreman	GP, Chandlers Hill Surgery SA
Ms Spiri Galetakis	Acting Director, Integrated Cancer Services, Department Human Services Victoria
Ms Alanna Geary	Nursing Director Cancer Care Services, Royal Brisbane and Women's Hospital
Ms Phillipa Hartney	Program Manager, Bendigo Regional Breastscreen
Ms Lauren Holland	Network Development Manager, Cancer Clinical Network, Department of Health, SA
Ms Beth Ivimey	Cancer Care Coordinator, Cancer Care Centre, Prince of Wales Hospital
Ms Lena Leone	Cancer Support Programs, The Cancer Council South Australia
Ms Alison Love	Cancer Care Coordinator
Ms Mirela Mathews	Project Officer, North Eastern Metropolitan Integrated Cancer Service (NEMICS)
Mr Adam Monkhouse	Clinical Service Planning, Cancer Clinical Network, SA
Ms Caroline Nehill	Program Manager, National Breast Cancer Centre
Professor Ian Olver	CEO, The Cancer Council Australia
Ms Megan Plaster	AYA Cancer Care Coordinator, WA Cancer & Palliative Care Network
Ms Violet Platt	Director of Nursing, WA Cancer & Palliative Care Network
Ms Sharon Reinbrecht	Rural Cancer Care Coordinator, Southern Adelaide Health Service
Ms Nicole Robert	Cancer Support Nurse, Royal Darwin Hospital
Dr Ian Roos	Chair, Cancer Voices Victoria
Ms Margaret Ryan	Coordinator Cancer Support Programs, The Cancer Council South Australia
Ms Gayle Salkield	Director of Nursing Cancer Services, Southern Area Health Service
A/Prof Tim Shaw	Director, Program Development, Centre for Innovation in Professional Health Education and Research, University of Sydney
Ms Heather Shepherd	PhD Candidate/Research Nurse, Medical Psychology Research Unit University of Sydney
Ms Helen Smith	Director of Cancer Services, The Cancer Council Northern Territory
Professor Bernard Stewart	Director of Cancer Services, South Eastern Sydney and Illawarra Area Health Service, NSW
Ms Maggie Stowers	Cancer Coordination Manager, Barwon South Western Regional Integrated Cancer Service (BSWRICS)
Ms Pauline Tanner	Cancer Care Coordinator (Gynaecology), WA Cancer & Palliative Care Network
Ms Celia Taylor	Director, The Cancer Council Tasmania
Ms Janet Thoseby	Cancer Nurse Coordinator, Gosford Hospital
Ms Dagmar Voss	Cancer Care Coordinator, Wagga Wagga Community Health, Greater Southern Area Health Service, NSW
Dr Pauline Wachtel	GP, The Medical Clinic Millicent
Ms Liz Wilson	Nursing Director, Medicine, Nambour Hospital
A/Prof Marion Haas	Deputy Director, Centre for Health Economics Research & Evaluation (CHERE), University of Technology Sydney
Professor Patsy Yates	Director of Research, School of Nursing, Queensland University of Technology
Ms Lynette Glendinning	Workshop Facilitator, PALM Consulting
Dr Alison Evans	Report author, Alison Evans Consulting

OVARIAN CANCER IN THE CENTRE – WHAT'S IN A NAME?

Dr Helen Zorbas ■ National Breast and Ovarian Cancer Centre, Sydney, Australia.

In February 2008, National Breast Cancer Centre incorporating the Ovarian Cancer Program (NBCC) changed its name to National Breast and Ovarian Cancer Centre (NBOCC). What were the factors that contributed to this change?

Ovarian cancer has been part of our core work, funded by the Australian Government since 2001, when our name became National Breast Cancer Centre incorporating the Ovarian Cancer Program.

The NBCC Board decided in 2007 that the name National Breast and Ovarian Cancer Centre would more accurately reflect our work and mission to improve outcomes across both breast and ovarian cancer. Since 2001, ovarian cancer and its manifold challenges have been, and continue to be a key focus for NBOCC.

The 2006 Senate Inquiry into Gynaecological Health also brought into sharp relief many of the key challenges in ovarian cancer and this presented important strategic opportunities for NBCC to address those challenges.

NBCC was established in 1995 by the then Labor Government to improve outcomes for women with breast cancer through the translation of research into evidence-based information, best clinical practice, policy recommendations and improvements in health service delivery.

Since its inception, our breast cancer program has pioneered an innovative approach to the translation of evidence into practice, centred on a systematic evidence-based model, which includes a strong consumer focus and the application of inclusive and collaborative processes to work with stakeholders in undertaking its role. Through this approach, NBOCC contributes to national cancer control through behavioural, social, organisational, systems, policy and population-level initiatives. It works across the continuum of care, including risk reduction, early detection, treatment, supportive care, follow-up and end-of-life care, as defined in the National Service Improvement Framework for Cancer (2005).

In September 2001, in recognition of the impact of ovarian cancer on Australian women, the Australian Government committed funding to improve the health outcomes of women with ovarian cancer. Due to the success of its breast cancer control model, NBCC was chosen to manage a national ovarian cancer initiative which has been an integral component of our program of work since that time.

At that time, the name and logo was changed to 'National Breast Cancer Centre incorporating the Ovarian Cancer Program', to reflect this commitment. However, the organisation was commonly referred to as the National Breast Cancer Centre and NBCC remained the commonly used acronym. The Senate Inquiry was

critical of the fact that the NBCC name did not accurately reflect or convey to the community its work in and commitment to ovarian cancer.

Ovarian cancer – the challenges

This added remit in ovarian cancer provided an opportunity to demonstrate the successful transferability of the 'NBCC model' and approach to another cancer.

However, while there are obvious areas of congruence and similarity of issues in breast and ovarian cancer – both women's cancers, treatment induced infertility for younger women, psychosocial care, treatment induced premature menopause, secondary lymphoedema, survivorship issues and communication skills – there are some significant differences and challenges in ovarian cancer.

- There is no screening test for ovarian cancer, yet NBCC's 2006 survey revealed that 56% of women mistakenly believe a Pap test will detect the disease.
- The early detection message is highly complex to communicate, due to the vague and common symptoms of ovarian cancer and the fact that over 70% of cases are advanced at diagnosis.
- Ovarian cancer is a relatively uncommon disease and the impact in terms of awareness is very different to that of breast cancer: around 12,000 cases of breast cancer diagnosed each year in contrast to 1200 cases of ovarian cancer.
- Ovarian cancer survival rates also contrast sharply with breast cancer. A high percentage (70%) of ovarian cancers are advanced at diagnosis and this is reflected in poorer outcomes. Only about 42% of women with ovarian cancer will survive five years or more from diagnosis,¹ less than half the survival of women with breast cancer.
- While thousands of breast cancer survivors play an important role in reducing the impact of the disease, as advocates, consumer representatives, spokespersons and awareness ambassadors, the ovarian cancer consumer voice is far more limited due to lower incidence and a high mortality rate.

Breaking the silence

In October 2006, the Senate Standing Committee on Community Affairs published its report *Breaking the silence: a national voice for gynaecological cancers*. The report delivered a range of recommendations based on submissions from a broad range of clinical, cancer and consumer stakeholders to the Senate Inquiry into gynaecological cancer in Australia.

Submissions to the Senate Inquiry generally recognised the significant contribution of NBCC's 'extremely effective model of the outcomes that gynaecological cancer is seeking across the board'.

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The inquiry also identified a range of gaps and deficiencies in care and management of ovarian cancer and made recommendations to address them. These included advice that ovarian cancer had a lower profile than other cancers such as breast, that the low levels of awareness in women and the medical community impacted negatively on outcomes, that ovarian cancer care was often deficient, uncoordinated, not funded or unavailable to certain women, that data collection and management was often uncoordinated, that psychosocial issues often remained unaddressed, that a need existed for the application of the principles of multidisciplinary care and improved education and communication skills in health professionals.

Some of the committee's recommendations included:²

- development of a system for national data collection and management system to ensure the appropriate and accurate collection of gynaecological cancer data;
- educational material to be provided to general practitioners to aid diagnosis and referral, and address the psychosocial and emotional needs of women;
- that consumer and community agencies and representatives have greater involvement in decision-making of national health agencies;
- the uptake and implementation of multidisciplinary care models in gynaecological cancer care;
- development of strategies and targets to improve referral rates from general practitioners to gynaecological oncologists for women with ovarian cancer;
- multi-layered approach to national education strategy to increase knowledge and awareness of gynaecological cancers.

Addressing needs and delivering results

NBOCC has addressed these recommendations in a number of ways. It has developed a national Data Strategy for breast and ovarian cancer, linked to its 2007-2011 Strategic Plan. In collaboration with the gynaecological section of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, we conducted a review of data items collected by gynaecological oncologists to inform the development of a minimum data set (MDS) for gynaecological cancers. This MDS is now being developed in partnership with Cancer Australia.

We have developed and implemented a range of clinical practice guidelines for specialist and GP clinicians and associated consumer guides. These include clinical practice guidelines on the management of epithelial ovarian cancer, recommendations on the familial aspects of breast and ovarian cancer, a GP guide on the assessment of symptoms of ovarian cancer and a module on ovarian cancer as part of NBOCC's General Practitioner Education Series.

In addition NBOCC is soon to launch an interactive online version of the popular *Advice on familial aspects of breast and ovarian cancer* to aid GP referral of women at increased risk of ovarian cancer due to their family history.

We have also developed, with the guidance of an expert steering committee, standards for facilities providing

intra-peritoneal chemotherapy for women with ovarian cancer.

Our ovarian cancer fact sheet has been translated into five languages. In 2007, NBCC raised awareness and promoted understanding of ovarian cancer to well women from five culturally and linguistically diverse backgrounds through a multi-faceted information campaign, which included a series of multi-lingual forums in Arabic, Greek, Vietnamese, Italian and Chinese around Australia.

During 2008 Ovarian Cancer Awareness Week, NBOCC will launch an ovarian cancer awareness campaign.

The multidisciplinary care model is a major platform of NBOCC's work and has applicability across all cancers. NBOCC has developed multidisciplinary care principles for advanced disease which have application in determining best practice treatment and care of women with ovarian cancer. NBOCC is currently completing an audit of multidisciplinary care in five tumour streams including breast and gynaecological cancer across Australia to identify where gaps in care exist.

We have conducted a number of surveys to provide insight into levels of awareness and understanding of ovarian cancer in Australian women. NBOCC's 2008 Well Women's Survey will update the evidence on Australian women's knowledge, attitudes and behaviour in relation to ovarian cancer.

NBOCC is working with the Queensland Institute of Medical Research to investigate current referral pathways for women with ovarian cancer from general practitioners to gynaecological oncologists. This study is using data from the Australian Ovarian Cancer Study.

NBOCC's Ovarian Cancer Program website, www.ovariancancerprogram.org.au, provides a one-stop shop of information about ovarian cancer.

Where to from here?

Extensive consultation with a broad range of stakeholders guided the development of NBOCC's 2007-2011 Strategic Plan, *Vision for the Future*, which identifies the promotion of ovarian cancer as one of its key focus areas.

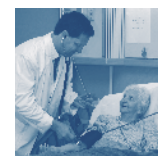
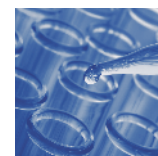
We aim to ensure that by changing our name to National Breast and Ovarian Cancer Centre, clinical and community audiences can more readily identify us as a national authority and source of reliable information on ovarian cancer, and as an organisation which is actively promoting a range of evidence-based initiatives to bring about real improvements in outcomes for women diagnosed with this disease.

Addressing the challenges of breast cancer, however, will remain a key focus for National Breast and Ovarian Cancer Centre as 2008 rolls out and the new name takes effect.

References

- 1 National Breast Cancer Centre and Australian Institute of Health and Welfare. Ovarian cancer in Australia: An overview 2006.
- 2 Senate Standing Committee on Community Affairs October 2006. Breaking the silence: a national voice for gynaecological cancers.

BOOK REVIEWS



Brachytherapy Applications and Techniques

Phillip M. Devlin

Lippincott Williams & Wilkins, 2007

ISBN: 9780781762774

420 pages

RRP: \$295.00

Brachytherapy refers to the use of sealed radioisotopes near or within the tumour volume and this book provides a fully comprehensive understanding of the importance and techniques of this treatment modality in cancer control. As Professor Harris states in the forward of this book "the field of brachytherapy is a largely evolving one and is often relegated to a small chapter in a standard radiation oncology textbook," however this book puts brachytherapy as the 'main star'.

Brachytherapy Applications and Techniques is written in an easy style suitable for any medical personnel to understand, from a novice to a professional expert. There are many diagrams, tables and colourful illustrations to complement the text and which help to provide a greater understanding of the treatment. It describes the types of brachytherapy available and gives a clear understanding of the differences between high and low dose rate brachytherapy.

The first part of the book explains the radiobiological concepts of brachytherapy, including dose rate and fractionation. There are substantive mathematical

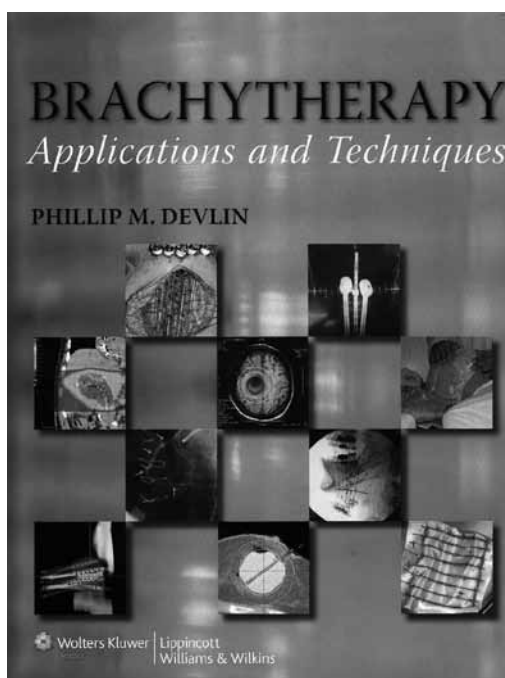
resources for the physicists, as well as case studies for examples. The book also delves into detail of the treatment-planning system requirements, which is clear to understand.

The ensuing chapters detail brachytherapy by disease site. These chapters attribute the benefit of brachytherapy by the contribution of an experienced multidisciplinary team and the basic principles of suitable patient selection, radioisotope selection and implant and technique. The treatment toxicity is fully discussed and in most cases is usually low, according to clinical based evidence of more frequently published study results. With each chapter there is also a plethora of references to validate chapters.

There is a large chapter detailing the continuing evolution of prostate brachytherapy, as a chosen treatment modality due to advances in imaging and procedural technologies, which allows for a more rapid and minimally invasive treatment approach. The next chapter discusses the use of gynaecological brachytherapy when combined with other standard therapeutic approaches to improve local-regional control and survival.

Overall this book is an excellent addition to any radiation oncology department where brachytherapy is used as a mode of treatment.

Carol Hook, Department of Radiation Oncology, Prince of Wales Hospital, Sydney NSW.



BOOK REVIEW

Cancer Pain: Pharmacological, Interventional and Palliative Approaches

Oscar de Leon-Casasola

Saunders Publishing (2006)

ISBN-13:9780721602615

591 pages

Price: \$125.00 (Inc GST)

Cancer pain can be a complicated issue to deal with, from pressure on nerves to direct tumour invasion. This edited text is a comprehensive look at the whole issue both in adult and paediatric patients.

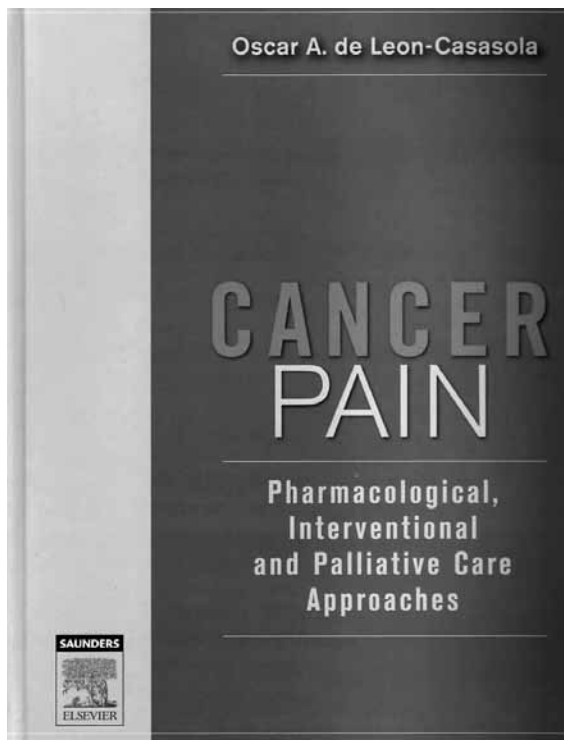
It has 27 chapters that have been broken into eight sections. The first section looks at the mechanisms of cancer pain and gives a mechanistic approach to pain assessment and patient evaluation. Section two covers cancer pain syndromes, including base of skull metastatic extension and the sequelae of this issue. Section three looks at the pain syndromes that can be the result of anti-cancer treatments from surgery to chemotherapy. Section four discusses the radiological evaluation of the patient, as well as looking at behavioural assessment and dealing with psychiatric complications.

Section five is the largest section and is the meat of the book for those who want only the drug references for cancer pain. Section six follows with a look at non-drug interventions for dealing with cancer pain, from psychology and physiotherapy to acupuncture. Section seven explains the invasive techniques that can be used, from nerve blocks to chemotherapy and radiotherapy. There are several specific chapters on techniques, but the one on forgotten techniques is a reminder that all technology started somewhere.

The final section tackles the terminal phase of cancer care. It reminds us to focus on patient comfort and on the need to rationalise medications and make use of non-oral routes of medication. The final chapter on skin care is a useful reminder of the practical care that is needed at this time.

Overall, the book is a great compilation on cancer pain; it is well referenced and is thought provoking of the holistic issues that cancer patients and practitioners face. There are good examples of the reality of what needs to happen to get people home and keep them in their own surrounds. The book is logical in sequence and while it has the feel of being a collection of journal articles, this does not detract from the fact that this is a useful text for all practitioners.

Fred Miegel, Alice Springs Hospital, NT.



BOOK REVIEW

Cancer Survivorship Sourcebook 1st Edition – Health Reference Series

Karen Bellenir (Ed)

Omnigraphics (2007)

ISBN: 978-0-7808-0985-7

661 pages

RRP: \$US78.00

The *Cancer Survivorship Sourcebook* is one of many general reference books printed as a resource for the general reader by Omni-graphics, though it is their first edition for cancer patients. The tag line on the back of the book advertises the series as, 'helping the layperson understand, manage, and avoid serious illness'.

I found the book to have a very easy to follow index with a helpful section at the front explaining the information contained in each chapter. This would be handy for those of our client base who are not used to navigating their way through many modern textbooks. Included at the back of the book is a handy glossary of cancer care terms. Though the book discusses American statistics and resources, there is a section in the first chapter aimed at those readers not in the United States. The non-US reader is directed to the website for the International Cancer Information Service Group (ICISG) in order to make inquiries about local cancer treating facilities. The section then continues to explain to the reader how to get a second opinion in the US and what they need to obtain before visiting the US for treatment.

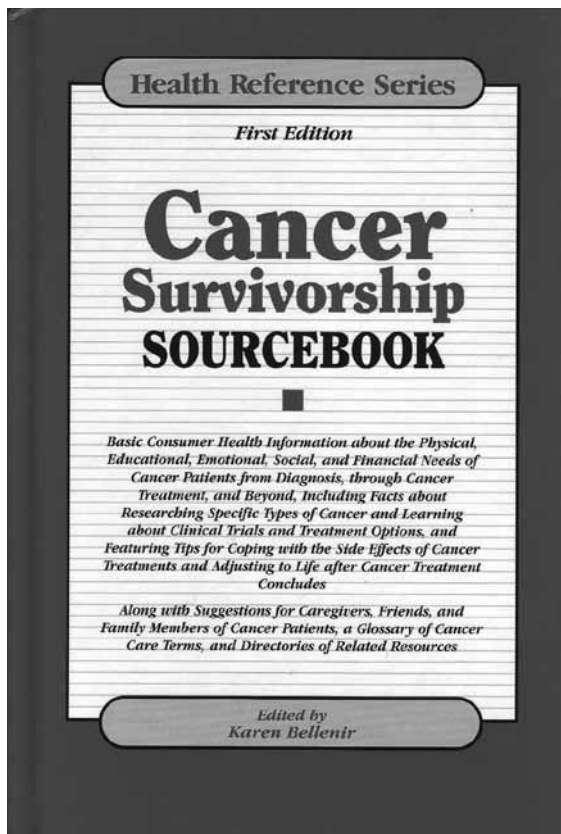
The book progresses in a logical manner from 'If your Doctor says it's cancer', to treatment decisions and psychosocial management, to talking to friends and family about the diagnosis and treatment. The authors have included a very easy to follow explanation of numerous examinations and pathology, with normal values listed. A large proportion of terminology used in cancer treatment is mentioned and explained in a fairly easy to understand way, starting all the way from cell structure, through tumour markers to staging classifications.

Sexuality and reproductive concerns for cancer patients are also addressed. The discussion is broken into a disease specific format and then progresses on to treatment related causes. Overall sexuality is discussed in a very normal manner to help remove some of the stigma generally associated with sexuality and cancer treatment.

Issues of symptom control and survivorship are also covered and I was impressed with a chapter dedicated to palliative care, with the explanation that it "starts at the beginning of the cancer process and may change over time to reflect each persons priorities and needs. Palliative care is not giving up on treatment."

Overall, I think the book is a good basic reference for those who have been affected by cancer in some way, whether it is themselves or their loved one.

*Katherine Cox, Medical and Radiation Oncology Unit,
Westmead Hospital, NSW.*



BOOK REVIEW

Cancer Survivorship: Today and Tomorrow

Patricia A. Ganz

Springer 2007

ISBN: 978-0-387-34349-5

304 pages

RRP: □62,95

Cancer Survivorship: Today and Tomorrow is a comprehensive text comprising 22 chapters written by over 40 authors, all experts in their field. With the ever-increasing number of cancer survivors and the subsequent increased risk of these survivors developing late or delayed effects of treatment, the attention of health care professionals has been increasingly drawn to survivorship issues. This book presents a timely addition as a resource text.

As suggested by the title, this book describes what is currently known about cancer survivorship and what knowledge the future might bring to this topic. It identifies the many, often complex medical and psychosocial needs of cancer survivors, emphasising the importance of health professionals providing comprehensive and coordinated survivor care, a theme consistent throughout the book.

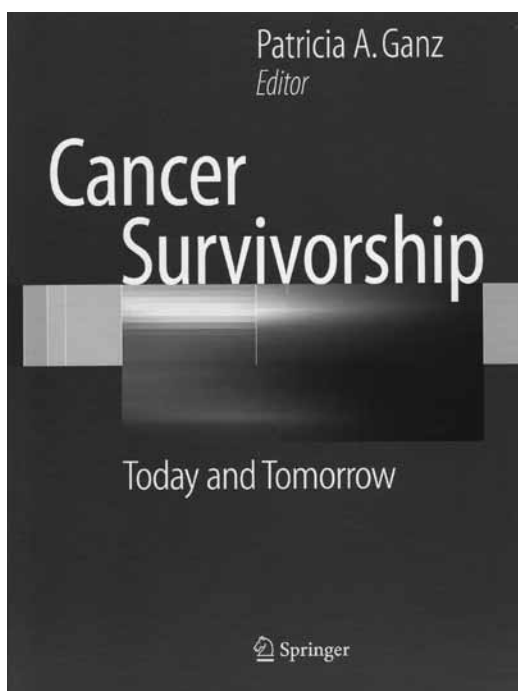
The first three chapters provide the reader with medical, nursing and social work perspectives on issues related to survivorship, detailing the professional's role in the care of the cancer survivor. Subsequent chapters focus on general topics such as, survivorship research, surveillance after primary treatment and late effects of cancer treatments, to the more specific topics of survivorship issues in childhood cancers and older adults.

Eight of the chapters are devoted to disease-specific cancer sites. Several of these include more detail than others, with the breast, lung and transplant survivor chapters providing comprehensive and current research evidence on such survivorship issues as early and late effects of treatment, functional status after treatment and quality of life. A limitation of the chapter discussing medical and psychosocial issues in gynaecologic cancer survivors is the author's lack of reference to lower limb lymphoedema as a potential survivorship issue. Likewise, another disappointing omission in this text is the absence of primary site cancer chapters on head and neck cancer, and melanoma.

The final three chapters deal with more diverse topics, such as the employment and insurance concerns of cancer survivors, cancer advocacy and the development of survivorship care plans, highlighting the complexity of survivorship issues. The presentation of the research evidence in most chapters is in table format, which provides an easily accessible reference tool. All chapters conclude with a comprehensive and current reference list, affording the reader an opportunity to undertake a more in-depth literature review.

Overall, this is an informative and interesting book, despite some of the limitations previously discussed. Health care professionals interested in cancer survivorship will find it a relevant text. Although it is written from a predominately North American viewpoint, the information can generally be transposed to the Australian health care setting. The editor should be justifiably proud that she has achieved her aim in providing a 'concise' and 'focused' resource for health care professionals.

*Ellen Barlow, Gynaecological Cancer Centre,
The Royal Hospital for Women, Sydney, NSW.*



BOOK REVIEW

Clinical Radiation Oncology 2nd Edition

Leonard L. Gunderson, Joel E. Tepper (Editors)

Elsevier 2007

ISBN-13: 978-0-443-06840-9

1827 pages

RRP: \$US259.00

The second edition of the classic text *Clinical Radiation Oncology* by Gunderson and Tepper was much anticipated by this reviewer and certainly did not disappoint. It is a completely revised and updated version of the original text with an emphasis on an evidence-based approach. While it is directed mainly at radiation oncologists and trainees, it is without doubt an invaluable reference resource for surgical and medical oncologists as well.

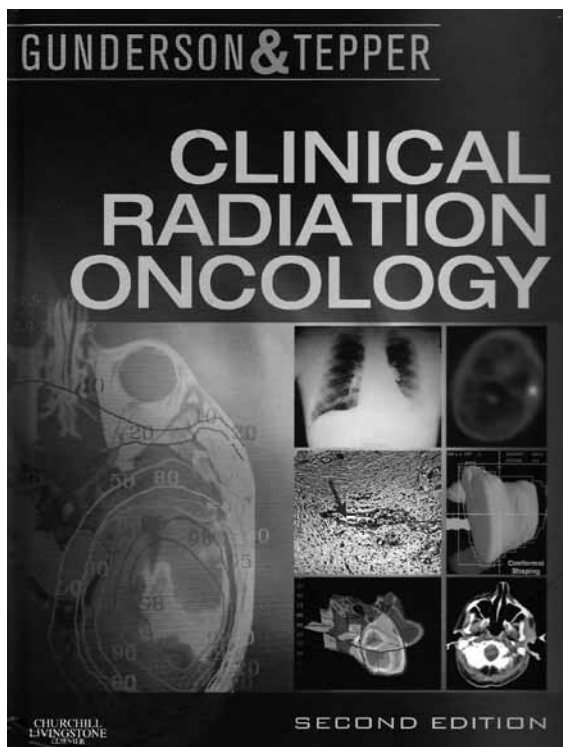
Featuring a multi-disciplinary perspective, it examines the role of single and combined modality treatment of specific disease sites. The format is clear and logical, with a consistent thread running through all chapters. Initial chapters deal with the scientific foundations of radiation oncology: radiobiology, physics, and radiation techniques and modalities. The physics chapter is especially well-written and provides an excellent overview of the various aspects of physics unique to different radiation modalities.

In addition, there are short chapters that deal with key concepts of surgical oncology, chemotherapy and the interactions between chemo and radiotherapy. The

clinical units are divided into tumour specific chapters covering: the central nervous system, head and neck, thoracic, gastrointestinal, genitourinary, gynaecologic, and breast tumours; soft tissue sarcomas; childhood cancers; and lymphoma and haematologic malignancies. Each clinical unit is preceded by a short overview segment. While some might find this repetitive, this reviewer found these sections essential for students of the field to help place treatment principles in context and focus on fundamental concepts, despite the overwhelming amount of data one needs to assimilate. In this regard, the authors have to be commended for having clearly developed a rationale for treatment recommendations, which are based on key clinical trials for the respective fields. Suggested treatment algorithms are provided for each section, which are concise and invaluable, especially for rapid reference. Important aspects of pathology and radiology are also reviewed as necessary.

In short, the text is easy to read, user-friendly and practical in orientation rather than an esoteric, all-encompassing manual. The layout is logical and together with excellent indexing and full-colour design makes reference fast and easy. There is no doubt that it is a well-produced resource that should be read by all trainees and be part of every practicing radiation oncologists' library.

Anu Thiagarajan, Department of Radiation Oncology, Westmead Hospital, Sydney, NSW.



BOOK REVIEW

Essentials of Clinical Oncology

R Marsh & J Samuel (Editors)

McGraw Hill Publishers

677 Pages

ISBN: 9780071485807

RRP \$140.00

This book is described as a comprehensive, yet concise guide to cancer written by international experts. The contents are divided into three sections with 56 chapters 'General Principles in Cancer', 'System or Organ Specific Cancer' and 'Treatment of Cancer'.

On first impression, the size of the book and format give the appearance of a quick and easy reference guide for most cancers. However, when I started to read I soon realised that it was written for health care professionals trained and working in the Indian medical system.

Attitudes and values therefore reflect the beliefs of authors from an Indian culture and the roles of staff working within this culture in the Indian health care system. I therefore could not recommend this as a worthwhile book to purchase for health professionals working in the Australian oncology setting.

The book describes the etiology and epidemiology of cancer in India, dividing incidences into site, gender and

religion. Many comments are simplistic and open to challenge, for example in the preface it is written that children (including a 17 year-old boy) "accept their diagnosis of cancer without emotion" and "succumb to death quietly" and that "death, after all, is not a painful experience but the final and true freedom".

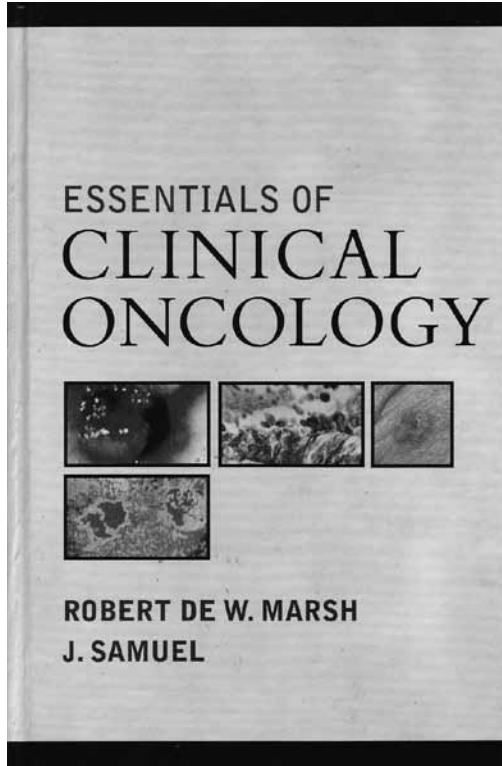
Chapters in the second section entitled 'System or Organ Specific Cancer' have clear headings, with some worthwhile tables, but the information is minimal and sometimes hard to follow.

The final chapter entitled 'The Journey's End' briefly describes end of life care in the Indian setting, including practices such as intravenous pethidine on demand. It concludes with the authors' attempt to highlight the thoughts on death and dying from the perspective of the major religions in India.

To summarise I would describe this book as an overview of cancer, written for the Indian health care setting and for those working within that setting. I should also conclude that though the quality of the paper used appears good, the binding was not, and unfortunately during my review pages soon became loose and started falling out.

Pauline Tanner,

WA Cancer and Palliative Care Network, WA.



BOOK REVIEW

Essentials of Surgical Oncology

MS Sabel, VK Sondak, JJ Sussman (eds)

Mosby (2007)

ISBN: 0-8151-4385-0

RRP: \$160.00

Essentials of Surgical Oncology presents as a concise textbook, tailored for a broad audience. The text follows a logical and sequential format, building on the concepts of molecular biology, aetiology and diagnostics to the specificity of oncology surgery. The distinct narrative quality of this text embraces the techniques, approaches and rationale used during surgery, whereby the voice of the surgeon is not lost in the print. It is this narrative genre that has a more personal tone and leaves the reader with a sense that the authors have 'shared their expertise' using a problem-solving perspective.

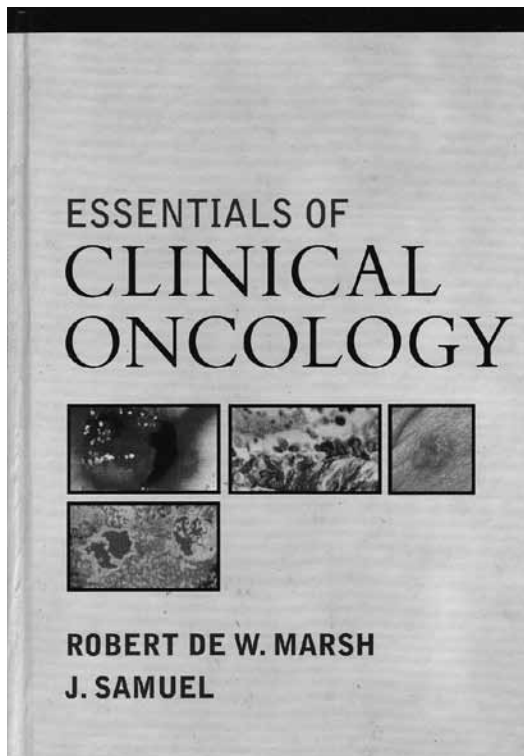
The principles traversed through the text are emphasised in an uncomplicated dialogue which is very readable. The focus on the specificity of oncology surgery provides quality content without too many over-arching details. In saying this though, the detail provided maintains 'the essentials' as its core, in concert with the text's title. Seventeen specialty surgical domains are included in the chapters, which are underpinned by a presentation of disease aetiology and management considerations including adjuvant treatment. There is a holistic quality and perspective in content that is weaved through each chapter, presenting a balanced and congruent coverage of the topic.

The chapter on 'Surgical Emergencies in the Cancer Patient' is an important addition to the text and warrants particular mention. The chapter tackles some of the efficacy considerations associated with emergency intervention outside the tenets of general surgery. There is a strong, personable and individualised tone in this coverage, whereby patient uniqueness provides the basis for broad and vigilant decision-making. This chapter discusses the more common emergencies that can arise and provides the scope for operative and palliative options.

In essence, this text deviates somewhat from the more voluminous and traditional resources available and is less formal overall. It is this compactness in quantity that underpins its practicality and readable style. Its format has been carefully considered whereby the tables, exploratory diagrams and photos are evenly spaced through the text in a complementary arrangement. General principles and salient points are summarised in concise tables, which can be easily scanned for ongoing reference through the text.

The text's strength lies in its ability to navigate the reader along a trajectory that is engaging in its quality rather than exhaustive in its volume. The detail provided in the chapters on specialty surgery gives a clear and directive view towards potential post operative sequelae. For this reason, the text is recommended for those surgeons and nurses involved in the management of the surgical oncology patient.

*Dee Maguire, Surgical Unit,
Westmead Hospital, Sydney, NSW.*



BOOK REVIEW

Innovations in Cancer and Palliative Care Education

Lorna Foyle, Janis Hostad (Editors)

Radcliffe Publishing 2007
ISBN: 978-1-84619-056-8
280 pages

Innovations in Cancer and Palliative Care Education aims to provide a practical guide for teachers of cancer and palliative care. This book is part of a series which highlights best teaching practices within both the cancer and palliative care specialisation.

Written predominantly for the British audience and focusing upon related UK social and health policy, I initially expected this book would have limited use for the Australian cancer or palliative care teacher. However, much of what is written about what to teach, how to teach it and to whom do you teach, fits with challenges and innovations within the Australian context. For example, the book refers to the use of competencies and simulation as learning and assessment tools for achieving competency in chemotherapy administration and pain management.

Internationally there appears to be the same reality of delivering effective education in a rapidly changing and challenging care environment and difficulties in being released to attend educational programs. To accommodate the difficulties and challenges, clinical education and e-learning are suggested as teaching strategies and these methods are realistically appraised in relation to cost and the need for collaboration to produce material

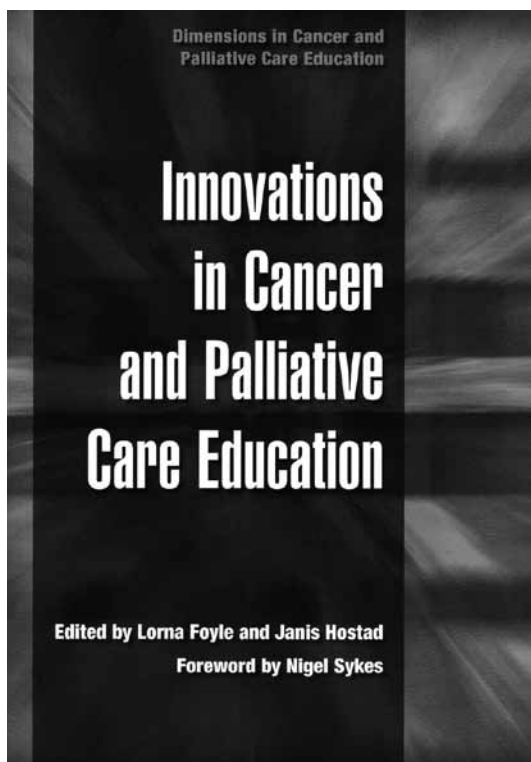
and assessment that is of a suitable standard. For example, when using e-learning as a teaching method, the reliance of such a project upon computer literacy among nursing staff and access to computer equipment is flagged as a major consideration. This resonates with my own experience of delivering education in a busy cancer and palliative care setting alongside the pressing need for accessible education.

The format of the text includes aims, learning outcomes, key points and implications of the points discussed to the readers own practice, making the reader reflect upon their own practice experience. As an example of the need for all nurses to be involved with education, the authors highlight the fact that the level of chemotherapy education is often dependant upon workplace standards.

I would therefore suggest that the book would be of interest not only to nurse teachers or educators but to all cancer and palliative care nurses. This is largely due to the fact that within both the Australian cancer and palliative care contexts, there is a formal acknowledgement that each nurse has a responsibility to educate junior staff and for promoting health and independence amongst patients and carers.

I found the book relevant and thought provoking and the format accessible. I would recommend this text as a starting point for stimulating thinking about how practice competency, attitudes and holistic care can be promoted.

*Lynda Prescott, Cancer Services,
Westmead Hospital, Sydney, NSW.*



BOOK REVIEW

Oncology Nursing Secrets 3rd Edition

Rose A. Gates, Regina M. Fink

Mosby 2007

ISBN: 978-0-323-04457-8

658 pages

RRP: \$US44.95

The experts who have compiled this great resource book are both registered nurses and medical practitioners with extensive experience in oncology within the United States. The book opens with '75 top secrets of Oncology Nursing' – some of these secrets are not as interesting or relevant as the remainder of the content, so don't stop there when beginning to read it.

The book is thoughtfully set out in a question and answer style. This style can greatly assist the novice oncology/ haematology nurse in answering both basic questions as well as covering fairly complex concepts. For the experienced nurse it serves as both a refresher and an addition to their knowledge base.

There is a logical pattern to the presentation of questions and answers. They cover a wide variety of topics, including an overview of cancer, treatment modalities,

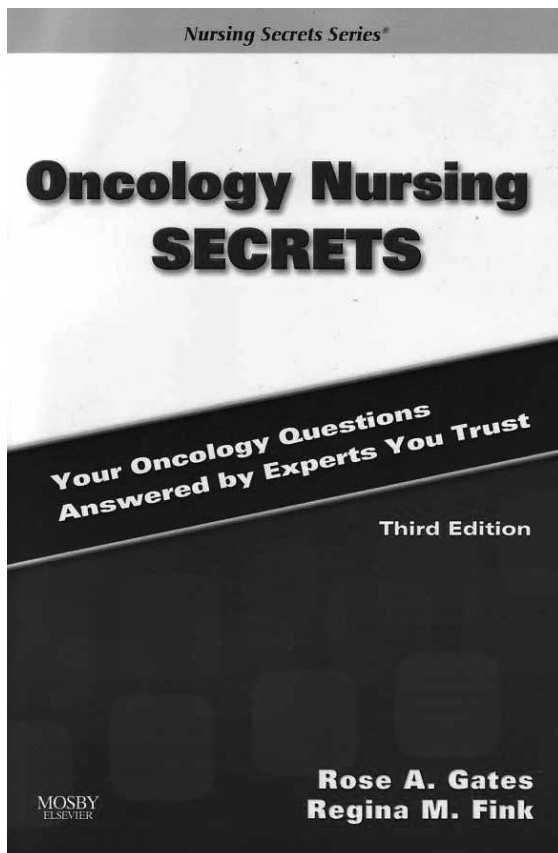
haematological malignancies and solid tumours. It includes sections covering symptom management and some excellent guides for treating symptoms to make the patient's cancer experience more tolerable. It discusses oncologic emergencies in some depth and closes with a section which looks into the spectrum of psychosocial issues when caring for the person with cancer. This part of the book includes racial, ethnic, religious and spiritual issues, along with survivorship, hospice care and some ethical dilemmas.

At the conclusion of each chapter the author has presented a summary of important information in point form. It is accompanied by listings of resource links from the internet for further searching. As the book is authored by Americans, the internet resources are mostly for US sites, however this does not present any drawbacks.

Overall this book contains many facts which I found interesting and useful in my clinical practice and will be helpful in teaching novice and experienced nurses alike. I would not hesitate to recommend it to my colleagues.

Marie Condon,

St John of God Health Care, Murdoch, WA.



BOOK REVIEW

Oral Cancer – Diagnosis, Management and Rehabilitation

John W. Werning

Thieme Medical Publishers

2007

ISBN: 978-3-13-135811-0

354 pages

RRP: \$129.95

This American text provides the health practitioner with a very detailed overview of management approaches to cancers of the upper aerodigestive tract. The editor and co-author, Randal Weber, emphasises that the successful management of head and neck cancer relies on multidisciplinary collaboration. Thus, the 46 mainly American contributors hail from the fields of radiology, radiation oncology, surgery, dental care, prosthodontics, orthodontics, medical oncology, pathology, otolaryngology and epidemiology. The result is an essentially medically-focused text, aimed at those who either require or desire in-depth explanations of the diagnosis and treatment of head and neck cancer.

With this in mind, I found this book a very interesting and informative read. There is a logical progression from the initial chapter on epidemiology, through those covering the evaluation of premalignant lesions, staging, examination of the different anatomic regions, reconstruction, multimodality treatment and the management of side-effects. Pleasing is the underpinning of all material with an emphasis on enhancing quality of care and quality of life for patients.

We know that the head and neck area is complex in structure and function and that cancer in this area can have enormous functional implications for patients. The purpose of this text is to critically examine: the lip; buccal mucosa; tongue and floor of mouth; lower alveolar ridge and retromolar trigone; hard palate and upper alveolar ridge; and neck. The epidemiology is considered on a background of US statistics and highlights the importance of investing in screening techniques and future prevention strategies. There is a neat discussion on oral pre-cancer and malignant lesions of the oral cavity, considering genetic and molecular

characteristics as well. Anatomic considerations are extremely detailed, written from a surgical perspective, but are very well illustrated. In fact, this book is loaded with diagrams and clinical photos that support and clarify the text very well.

The role of imaging in the diagnosis and treatment of oral cancer is an important current and future consideration. Werning's publication includes a good comparison of the essential qualities of CT, MRI and PET in this setting.

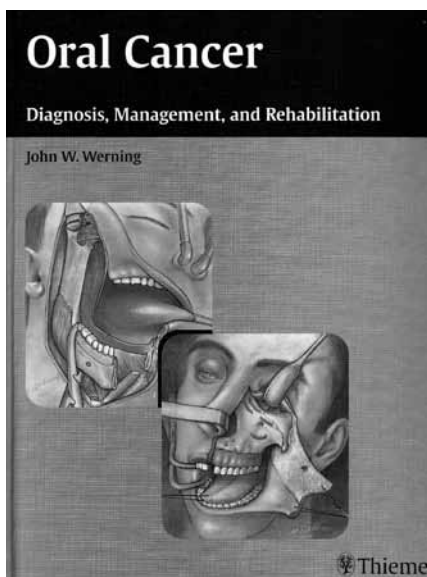
The upper aerodigestive tract is well defined with a chapter devoted to each area. Within these discussions, epidemiology and presentation is reviewed again. Staging and then treatment options are explored with a focus on preservation techniques. In line with best practice, recent data are quoted throughout and concluding summaries are short and pertinent.

The chapters devoted to reconstruction recognise the dynamic and complex functions of the anatomic areas. The discussion is very detailed, but does make very interesting reading if relating it to a current patient. Again, a holistic approach to the patient is adopted.

The indications for radiotherapy and chemotherapy are easy to follow and provide a good basis for understanding when the different treatment modalities may be offered to patients. The aetiology of therapy side-effects is concise and draws the conclusion that there is no universally accepted treatment to reduce the toxicity of xerostomia, mucositis and desquamation.

In summary, *Oral Cancer – Diagnosis, Management and Rehabilitation* is a detailed and well-presented text for those health professionals working with, or interested in, head and neck cancer. Chapters can be read in isolation or as a universal management approach. The concluding chapter focuses entirely on managing litigation – an interesting concept indeed. Perhaps it would have been better if a nursing perspective had been included instead, as part of the multidisciplinary approach to head and neck patient care.

*Megan Nutt, Head and Neck Cancer Unit,
Capital Region Cancer Service, ACT.*



BOOK REVIEW

The Lymphomas 2nd Edition

George P. Canellos, T. Andrew Lister, Bryan Young

Elsevier 2006

ISBN-13: 978-0-7216-0081-9

582 pages

RRP:

This medical and scientific text book offers a comprehensive investigation of the pathophysiology, diagnostic procedures and principles of therapy in relation to the malignant diseases classified as Hodgkin's Lymphoma (HL) and Non Hodgkin's Lymphoma (NHL). The editors, Canellos, Lister & Young, have brought together over 60 international contributors that ensure this medical text represents teachings based upon current international research, the associated advances in new biological discoveries and improved targeted therapies.

Divided into four sections, this book is targeted at the haematology/oncology clinician or scientist in its entirety. Sections of the text book provide detailed clinical perspectives of specific lymphoma subtypes which would be useful as a reference book to haematology/oncology nurses and medical students.

Section one provides the reader with comprehensive pathophysiology of individual disease subtypes. Included are chapters on classification and histopathology, cytogenetics, molecular biology, molecular monitoring, diagnosis and gene expression profiling. Epidemiology is also included in this section, given the unexplained substantial increase in incidence of NHL over the last two decades; the authors have provided insight into current scientific opinion of associated risk factors – including aspects of genetics, immunodeficiency, infectious agents and occupational and environmental exposures that may have some causal link to lymphoma.

Section two provides current trends on how the patient is best approached when diagnosed with malignant lymphoma. This is a purely medical approach, including pre-treatment assessments and use of imaging for disease staging, such as use of PET scan, following with individual chapters of common therapies offered to lymphoma patients. Therapies discussed include radiation therapy, chemotherapy, allogeneic stem cell transplant and biological therapies (including monoclonal antibodies), radio-immunotherapy and other novel therapies used in treatment of NHL in particular.

Section three, examining specific disorders, gives a thorough summary of a range of lymphomas from the aggressive Burkett's lymphoma, through to indolent Follicular Lymphoma. Each disease specific chapter highlights pathophysiology, clinical presentation, treatment choices and follow-up. At times however, this section appears to repeat some information offered in sections one and two of the text. Important information on the less common lymphomas is also found here.

Section four covers lymphoma in special populations. It includes the elderly, the young, the immuno-suppressed (in a setting of HIV Infection) and a fascinating chapter of lymphoma and pregnancy, highlighting the diverse group of people living with lymphoma and the different approaches necessary to successfully treat those with special considerations.

As a medical text, this book is a useful tool to expand knowledge of the pathophysiology, diagnosis and treatment of those involved in the care of people diagnosed with malignant lymphoma. However, at a time when world best practice in cancer care promotes early psychological/psychosocial assessment and intervention, the editors appear to have failed to include this vital aspect of care in their text book.

*Sandy McKiernan,
Leukaemia Foundation of WA.*

