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This Issue in the Journal

The control of melanoma in New Zealand
M Sneyd, B Cox

From the literature we identified activities which could reduce the burden of melanoma in New Zealand, and estimated the effect of each on the numbers of new cases and deaths. The best methods for reducing this burden in New Zealand are avoidance of excessive sun exposure and early diagnosis of melanoma. A reduction of 10% in the numbers of people getting severely sunburnt could reduce the number of melanomas by about 28 per year; about 4 deaths per year could be prevented by follow-up of people at high risk; and diagnosing 10% more melanomas earlier, when they are thin, could prevent approximately 29 deaths per year.

Confirming a diagnosis of hereditary colorectal cancer: the impact of a Familial Bowel Cancer Registry in New Zealand
P James, S Parry, J Arnold, I Winship

New Zealand has a high incidence of colorectal cancer of which at least 5% will have a known genetic cause. The New Zealand Familial Bowel Cancer Registry, or specialised multidisciplinary unit, was established in 1996 to facilitate the identification of families likely to have a genetic cause of bowel cancer. The Registry maintains a confidential national register of participating families, and facilitates education, genetic testing, bowel screening, and optimal management for affected individuals and their relatives.

Multidisciplinary treatment of colorectal cancer in New Zealand: survival rates from 1997–2002
J Keating, D Yong, G Cutler, J Johnston

Bowel cancer, comprising colon and rectal cancer, is second only to lung cancer in the “league table” of cancer deaths in New Zealanders. This paper documents the results of treatment of bowel cancer in metropolitan New Zealand in the period 1997 to 2002. The chance of cure of bowel cancer, usually taken as surviving to 5 years, is approaching 60%. Significant gains have been made in the safety of surgery and in the reduction of local recurrence of rectal cancer following surgery. Further reduction in the death toll of bowel cancer will need detection of the disease at an earlier stage or screening as has started in the last two months in Australia.
H Curry, G Horne, P Devane, H Tobin

Osteosarcoma is a form of cancer which arises from bone. It is rare, affecting up to 20 people per year in New Zealand. This study has looked at how many people survive for more than 5 years after having treatment for this type of cancer. We compared a group of patients from 1981–1987 with a group from 1994–1999. We found there was a trend of improved survival in the 1994–1999 group. The survival of patients with a cancer in a single limb only (who were younger than 40 years) had a 60% likelihood of surviving for greater than 5 years. This is similar to international standards. These results are encouraging for patients with this type of cancer.
Melanoma control: few answers, many questions

Rod Dunbar, Mike Findlay, Graham Stevens

Malignant melanoma exerts a high toll in New Zealand, and now looms large in the public consciousness, perhaps due to its relatively high incidence in younger people and its cruel association with the pleasures of the outdoors. Strategies are needed to control this disease.

In this issue of the Journal, Sneyd and Cox\(^1\) calculate the likely effect of various cancer control activities on melanoma incidence and mortality in New Zealand. They conclude that prevention of excessive sun exposure and early diagnosis of melanoma are the options likely to have the greatest effect.

These conclusions are likely to find broad acceptance, but the detail in their analysis highlights how much more work is necessary if we are to seriously tackle melanoma.

Early detection of melanoma is a good start. Recent data from Australia suggest that earlier detection of melanoma\(^2\) is beginning to impact on melanoma mortality.\(^3\) Anecdotal reports abound in New Zealand that primary melanomas are being excised “thinner” these days, but as yet there are no good studies to support this impression.

Monitoring the distribution of melanoma depths over time might help measure whether public education initiatives are successful in driving earlier detection. Breslow depth is available in the New Zealand Cancer Registry data, and has been analysed previously for the period 1995 to 1999.\(^4\) However more timely release of these data will be necessary if they are to be useful in monitoring cancer control strategies: as noted by Sneyd and Cox, the 2002 data has only just been published by the New Zealand Health Information Service (NZHIS).

Prevention of excessive sun exposure seems logical, although the science supporting this approach is surprisingly weak. Indeed, despite more than 20 years of primary prevention programmes in Australia, there is as yet little evidence of any effect on melanoma incidence.\(^3\) Such evidence is crucial because clinical trials testing the effect of modulating sun exposure are notoriously difficult to perform well, due to long timelines and low numbers of melanoma “events”.

It is not entirely unexpected that population-based reductions in sun exposure might take more than a decade to affect incidence rates, given the long time required for populations to change their behaviour, and for melanoma to become clinically apparent. But a lesson for New Zealand is immediately clear: it is highly unlikely that any influence of sun exposure education on melanoma incidence rates will be measurable for a considerable time.

In measuring incidence, it is important to note the limitations of the melanoma data available from the Cancer Registry prior to 1996. As highlighted by Sneyd and Cox\(^1\) (and also observed for some other cancers) there is a “spike” in apparent incidence in 1994 and 1995 when registration became compulsory under the Cancer Registry Act 1993.
It seems likely that melanoma was significantly under-reported before 1994, and that reporting did not stabilise under the new regime until 1996 or 1997. Hence, by the end of this year, the Cancer Registry will probably have accumulated 10 years of reliable incidence data. As noted above, if the 4-year delay in data publication persists, this first 10-year dataset might not become available until 2010. Monitoring the effects of changes in sun exposure will require a long-term commitment to the provision of accurate, timely, and complete data for subsequent analysis.

Regrettably, there remains the possibility that preventing excessive sun exposure will not prevent melanoma. Sneyd and Cox estimate that a 10% reduction in the number of people who experience blistering sunburn could prevent 28 cases of melanoma per year in New Zealand. One reason why this figure is so modest is that the relative risk used in their calculations is only 1.4: according to Sneyd’s New Zealand-based case control study, this kind of sunburn only increases the risk of melanoma by a factor of 1.4. This surprisingly small relative risk is borne out by many other studies: one authoritative review of the reliable studies available estimated that excessive childhood sun exposure conferred, at most, a 1.95-fold increase in the risk of melanoma. The available studies also vary so much in their definition of excessive sun exposure, that the precise patterns of sun exposure conferring increased risk are uncertain, as are their interplay with different skin phenotypes.

While it is certainly prudent to promote the reduction of sun exposure and sunburn in New Zealand, there remains a possibility that this strategy will have only a moderate impact on melanoma incidence. More work is urgently needed to better define the relationship between sun exposure and melanoma, and New Zealand is an environment very well suited to such studies.

Even if strategies for prevention or early detection are highly successful, the long lead-times mean other strategies need to be considered to deal with the melanoma burden. Better therapy is a realistic medium-term target.

Sneyd and Cox rightly highlight the lack of recent New Zealand guidelines for the management of melanoma. Approaches to melanoma treatment vary dramatically, not just across the country but within regions and cities. However, a recent initiative has seen New Zealand clinicians (under the umbrella of the New Zealand Guidelines Group) collaborating with their Australian counterparts to produce high-quality evidence-based guidelines for the management of melanoma.

The release of these trans-Tasman guidelines in 2007 will help to unify and promote best practice. Several centres are also pursuing multidisciplinary management of local recurrences and metastases, and such approaches seem likely to improve quality of life, if not survival.

Surgery is still the mainstay of melanoma therapy, and it can be successful at arresting metastatic disease while radiotherapy can be helpful for local control. Even current chemotherapeutic agents can occasionally induce remission, although the low response rates have meant that they have had little impact overall. Although only a small minority of patients respond to these drugs, occasional complete responses suggest fundamental differences in the biology of the responding and non-responding tumours.
As with other types of cancer, melanoma is not a single disease in terms of its cell biology, and certainly not at the molecular level. One of the most fruitful areas of investigation in melanoma therapy may be the definition of molecular markers that correlate with responses to agents already available. Identifying even 10% of melanoma patients who are likely to have strong responses to such agents would substantially reduce the melanoma burden in New Zealand.

Recent advances in molecular medicine have also opened up new therapeutic possibilities for melanoma, including chemotherapy, biological therapy, and immunotherapy. The recent identification of the BRAF pathway, as a common source of molecular perturbation in melanoma,\(^9\) has offered hope that kinase inhibitors might be designed to specifically target the disease.

Numerous clinical trials are also underway testing novel agents that modulate aspects of melanoma biology or the immune response to melanoma (www.cancer.gov/clinicaltrials). While hopes have often been raised (and subsequently dashed) about these kinds of therapies, a body of evidence is building that suggests they will produce substantial clinical gains in at least a proportion of melanoma patients. Again, molecular typing may be required to determine which patients are likely to respond to which agents, but such patient stratification is rapidly becoming routine in modern cancer treatment.

In summary, what is needed to control and manage melanoma in New Zealand? In addition to the measures recommended by Sneyd and Cox, at least four other steps seem advisable: more detailed study of the relationship between sun exposure and melanoma incidence; timely release of accurate and complete data from the Health Information Service to allow changes in melanoma incidence and thickness to be tracked; development and adoption of agreed melanoma management guidelines across New Zealand; and intensive research into new therapeutic options and the molecular classification of melanomas.

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References:


Improving outcomes in ovarian cancer

Michelle Vaughan, Peter Sykes, Carol Johnson, Bernie Fitzharris; on behalf of the New Zealand Gynaecologic Cancer Group

Ovarian cancer is the fourth most common cause of cancer mortality in New Zealand women. In 2001, there were 300 new cases of this disease and 175 deaths. While the incidence of ovarian cancer is slowly increasing, mortality is decreasing and the expected survival for women with this disease is lengthening.\(^1\)

Unfortunately, at diagnosis, the majority of women have advanced disease, and there is no screening test that has been shown to improve mortality. Improvements in treatment are therefore largely responsible for improved survival. Currently, despite advanced disease, many women survive several years beyond their initial diagnosis.

Surgical staging, the surgical debulking of intra-abdominal tumour, leaving minimal residual disease (‘optimal debulking’), followed by intravenous (IV) platinum-based chemotherapy, is the cornerstone of the modern management of this disease.\(^2,3\)

Carboplatin, with or without paclitaxel, is the current accepted standard chemotherapy regimen. This optimal management is most easily achieved with a multidisciplinary team approach including gynaecological oncologists (gynaecological cancer surgeons) and medical oncologists.

In January 2006, Armstrong and her colleagues on behalf of the Gynecologic Oncology Group (GOG) in North America reported a large randomised trial.\(^4\) This showed an improvement in the survival of women with optimally de-bulked ovarian cancer when they were treated with chemotherapy which was in part delivered via an intraperitoneal (IP) catheter. Patients were given intravenous paclitaxel, followed by either IV cisplatin, or IP cisplatin plus IP paclitaxel. A 16-month survival advantage was reported for the IP arm.

Publication was accompanied by a Clinical Announcement from the National Cancer Institute (USA), which suggested…*strong consideration should be given to a regimen containing IP cisplatin (100 mg/m\(^2\)) and a taxane whether given IV only, or IV plus IP.*\(^5\)

Intraperitoneal therapy in ovarian cancer has been the subject of research for some years. As ovarian cancer is a disease that tends to spread to peritoneal surfaces rather than solid organs, it is hypothesised that the direct contact of intraperitoneal chemotherapy with the tumour nodules offers a more effective route of delivery of drugs than intravenous therapy, particularly in women with small volume residual disease.

Drugs also tend to have a longer half life in the peritoneum. The first positive randomised trial in intraperitoneal (IP) therapy for ovarian cancer was published in 1996, and there have been at least five other randomised trials published since. The practice, however, had not been adopted as standard treatment because of three reasons; firstly not all of the studies have been positive, secondly some of the studies...
have been flawed methodologically, and lastly intra-peritoneal administration is associated with significant morbidity.

An independent (Cochrane) review has also recently been published, supporting the role of IP therapy in women with optimally debulked ovarian cancer. The meta-analysis reports a relative risk of recurrence and death of 0.79 in the patients who received IP therapy. This review, however, cautions that catheter related complications and toxicity need to be considered, and that more work needs to be done to determine optimal dose, timing, and mechanism of administration.

Publication of the most recent trial has led to IP chemotherapy being adopted widely in North America, however many centres have substantially modified the regimen because of toxicity. This toxicity is widely felt to be prohibitive, with 19% of patients developing neuropathy interfering with activities of daily living, and 46% developing grade 3 or 4 gastrointestinal complications (i.e. requiring hospitalisation).

Evidence in favour of IP therapy, particularly from European Oncologists, has been criticised, and while the three largest trials have all been positive, each has also been flawed in some way.

The first trial used an obsolete control arm, and paradoxically found no significant survival advantage in those patients with the greatest expected benefit of IP therapy (those with minimal residual disease <0.5 cm). The second trial used a higher dose of platinum in the IP arm, and the benefit was of only marginal significance (one-tailed p value 0.05 for overall survival). The most recent trial also used higher platinum and paclitaxel doses in the IP arm, leaving open the possibility the benefit is dose rather than delivery-related. In this trial, only 42% of the IP patients received the planned 6 cycles of IP therapy, and 44% of patients in the IP arm went on to get non-protocol IV carboplatin and paclitaxel.

Again, the control arm of cisplatin and paclitaxel used in this trial is no longer standard IV therapy. Therefore there is no study demonstrating an IP regimen which is superior to the current standard IV therapy, and the regimen which has produced the most encouraging results can not be delivered to the majority of patients because of toxicity.

Most New Zealand specialists regularly treating gynaecological cancers are members of the New Zealand Gynaecological Cancer Group (NZGCG) whose aim is to improve the care of women with gynaecological cancer throughout New Zealand. Having reviewed the evidence, the opinion of the NZGCG is that trial results of IP chemotherapy are encouraging, and require further study. However this is a new treatment approach with documented morbidity, without direct evidence of superiority over the current standard of care; IV carboplatin with or without IV paclitaxel. The technique should therefore be further investigated in a standard, monitored fashion. The ideal way to do this is to take part in a large, well-governed, multi-centre clinical trial.

In the immediate future, further improvements in the outcome of ovarian cancer in New Zealand depend on a multifaceted approach; ensuring patients throughout the country have access to optimal surgery and chemotherapy. The NZGCG is committed to facilitating this process, and welcomes technological advances such as IP therapy.
However the data supporting IP therapy is open to interpretation, and is therefore incomplete.

We believe that (by opening a trial of IP treatment) we can contribute to increasing the body of knowledge about this treatment modality. We are working actively with the Australia New Zealand Gynaecological Oncology Group (ANZGOG) to implement an appropriate clinical trial of intraperitoneal chemotherapy in New Zealand in the next few months.

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References:


The control of melanoma in New Zealand

Mary Jane Sneyd, Brian Cox

Abstract

**Aims** This study estimated the impact of prevention, screening, early diagnosis, and treatment on the burden of melanoma in New Zealand.

**Methods** Cancer control plans and management guidelines were reviewed to identify activities that could reduce the burden of melanoma in New Zealand and an estimation was made of their effects on incidence and mortality. The base year for estimating changes in incidence and mortality was the published melanoma data for 2002.

**Results** The registration of melanoma increased from 1037 new registrations in 1993 to 1487 in 1994 and peaked at 1759 in 1995. In 2002 a further increase occurred, to 1842 new registrations and 235 deaths from melanoma. It is likely that 328 of the 1842 new cases of melanoma in 2002 were directly attributable to severe sunburn. A reduction of 10% in the number of people getting severely sunburnt could prevent 28 melanoma cases per year. If 2% of melanoma deaths occur in high-risk individuals, approximately 4 deaths per year could be prevented by surveillance of high-risk groups. Thin melanoma has a very good prognosis: a 10% shift in the depth distribution into the thinnest depth category would result in about 29 deaths from melanoma prevented each year.

**Conclusions** The best avenues for reducing the burden of melanoma in New Zealand are prevention of excessive sun exposure and early diagnosis. Reducing severe sunburn and diagnosing a greater proportion of melanomas when they are thin would have the greatest impact on the incidence of and mortality from melanoma.

The incidence and mortality rates of malignant melanoma have shown large increases in New Zealand over the past 30 years.\(^1,2\) Similar trends have also been observed in many other developed countries,\(^3,4\) but New Zealand and Australia still have the highest incidence rates in the world. While smaller increases in both incidence and mortality have been observed in people born after about 1950 in New Zealand, they have continued to increase for older people and in particular those aged over 60 years.\(^5\)

Until the Cancer Registry Act 1993 came into force in New Zealand in July 1994, the Cancer Registry had been based primarily on public hospital records and so had missed many tumours excised outside hospital and many patients treated privately. Several studies\(^6-8\) have shown that incidence rates of melanoma estimated directly from pathology reports were considerably higher than was apparent from registered cases provided by the New Zealand Cancer Registry. Since the introduction of the Cancer Registry Act 1993, statutory notification has greatly increased the numbers of melanomas registered.
Multiple strategies will be required to combat the increasing burden of melanoma. A cancer control strategy encompasses all aspects of cancer: prevention, screening, early detection, diagnosis, treatment, rehabilitation, and palliative care. It also includes cancer surveillance and research. The results in this report focus on the likely effects of four different interventions (prevention, screening, early diagnosis and treatment) in reducing the burden of melanoma in New Zealand.

Methods
Cancer control plans and management guidelines, both from New Zealand and overseas, were reviewed to identify potential activities that could reduce the burden of melanoma in New Zealand. Their effects on the incidence of and mortality from melanoma in New Zealand were estimated.

Service provision depends on actual numbers of cases or deaths, not rates of disease or death, whereas comparisons over time or place require standardised rates of disease. Absolute numbers and age-standardised rates, standardised to Segi’s world population, have been presented. Registration rates are used as the closest approximation to the national incidence rate available in New Zealand.

Estimates of projections in incidence and mortality have been used to estimate the future burden of disease. The projection models separately relate cancer incidence and mortality data to three time dimensions: age, period, and cohort. Estimates of the future burden used the average projection from a set of models rather than relying on any individual model alone.

The base year for the estimations of changes in incidence and mortality resulting from cancer control activities was the data published for 2002. The number of deaths prevented by cancer control activities has been calculated for 2002 as if the nominated interventions were already in existence. This, in effect, standardises their impact to the 2002 calendar year.

Life expectancy tables were used to calculate person-years of life lost from death due to melanoma. Population attributable risk percent (PAR%) was calculated in the usual way:

\[
PAR\% = \frac{P_e (RR - 1)}{P_e (RR - 1) + 1} \times 100
\]

…where \( P_e \) = proportion exposed in the population and \( RR \) = relative risk for the exposure of interest.

Further details of the methods are available in another report of this work.

Results
Incidence and mortality—In 2002, melanoma accounted for 1842 new cancer registrations, of which 933 were in men and 909 in women (Figure 1). The registration of melanoma increased from 1037 new registrations in 1993 to 1487 in 1994 and showed a peak at 1759 in 1995 due to the effects of compulsory cancer registration. Registrations of melanoma then decreased in 1996 and 1997, but in 2001 and 2002 the numbers of registrations increased, to approximately the same level as in 1995 for women and slightly higher than in 1995 for men.

In 2002 there were 235 deaths from melanoma (Figure 1); 149 in men and 86 in women. In this year, death from melanoma accounted for 3.6% of all male cancer deaths and 2.3% of all female cancer deaths. Numbers of deaths from melanoma have increased since 2002, to 174 in men and 111 in women in 2003.
Figure 1. Melanoma registrations and deaths by year

Age-standardised registration rates (ASR) for melanoma show a very similar pattern (Figure 2). ASRs peaked in 1995 (40.2 per 100,000 population for men and 37.5 per 100,000 population for women) after the introduction of the Cancer Registry Act, declined in the following few years and then recently have shown a slight increase. Prior to 1992, men had a lower registration rate than women, but since 1993, men have had higher age-standardised registration rates than women (Figure 2).

Melanoma is reasonably common in younger age groups with significant numbers of melanomas diagnosed between 25 and 39 years of age in both men and women (Figure 3). Melanoma is the commonest cancer in adolescence. In 2002, the greatest number of registrations in women occurred in those aged 45–49 years and in men occurred at 70–74 years of age. However, the highest age-specific rate for men occurred in those aged 85 years or more, and in women occurred in those aged 75–79 years. The average age at diagnosis in 2002 for men was 61.2 years and for women was 57.1 years.

Many deaths from melanoma occur at a younger age than for most other solid tumours, with the average age at death of 65.5 years for men and 66.7 years for women in 2002. In the same year, 2,354 person-years of life were lost for men and 1,573 person-years of life were lost for women due to melanoma.
Melanomas were considerably under-registered before 1 July 1994 when the Cancer Registry Act 1993 came into force, so estimations of projections have used adjusted rates, where the adjustor was the average incidence to mortality ratio pre- and post-1994.\textsuperscript{12} Between 2001 and 2011, the absolute number of registrations for men over the age of 15 was expected to increase by 32%, to 1,148 per year and the number of deaths was expected to increase by 17%, to 183 per year.\textsuperscript{12}

When these calculations were made it was estimated that, for women over the age of 15 years, the absolute number of registrations would increase to 799 per year and the number of deaths was estimated to increase to 113 per year by 2011.\textsuperscript{12} However, in 2002, melanoma registrations for women were already higher than the projection, at 909 new cases, and in 2003, deaths in women had almost reached the projection for 2011.

Cancer control activities—The estimated impact of cancer control activities for melanoma are summarised in Table 1.

Primary prevention—The main causal factor for the development of melanoma is exposure of the skin to ultra-violet (UV) light. Using the relative risk for ever versus never being sunburnt (with blisters) as 1.4, and the prevalence of ever being sunburnt (with blisters) as 54%,\textsuperscript{14} the population attributable risk per cent (PAR%) due to being sunburnt with blisters was 17.8%. So it is possible that 328 of the 1842 new cases of melanoma in 2002 were directly attributable to severe sunburn.
### Table 1. Estimate of the potential for changes in the incidence of and mortality from melanoma

<table>
<thead>
<tr>
<th>Components of cancer control</th>
<th>Change in incidence rate</th>
<th>Change in numbers of registrations per year</th>
<th>Change in mortality rate</th>
<th>Change in number of deaths per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention</td>
<td>Decrease</td>
<td><em>28 new cases prevented</em></td>
<td>Decrease mortality</td>
<td><em>4 deaths prevented</em></td>
</tr>
<tr>
<td>Screening</td>
<td>Increase</td>
<td>Increase slightly</td>
<td>Not known</td>
<td><em>4 deaths prevented</em></td>
</tr>
<tr>
<td>Early diagnosis</td>
<td>None</td>
<td>None</td>
<td>Decrease if 10% shift to &lt;=0.75mm depth category</td>
<td><em>29 deaths prevented</em></td>
</tr>
<tr>
<td>Treatment</td>
<td>None</td>
<td>None</td>
<td>None predicted in the near future</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>None</td>
<td>None</td>
<td>None predicted in the near future</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy/Immunotherapy</td>
<td>None</td>
<td>None</td>
<td>None predicted in the near future</td>
<td></td>
</tr>
<tr>
<td>Radiation</td>
<td>None</td>
<td>None</td>
<td>None predicted in the near future</td>
<td></td>
</tr>
</tbody>
</table>

Removal of thin melanomas means ~95% cure.
If severe sunburn (with blisters) in the population is decreased by 10%, to a prevalence of 48.6%, then the PAR% decreases to 16.3%. If we apply this PAR% to the 2002 incidence rate, 300 cases of melanoma could be directly attributable to severe sunburn. Thus a reduction of 10% in the prevalence of severe sunburn could result in approximately 28 fewer cases of melanoma per year. With a mortality to incidence ratio of 12.8% in 2002, this could result in a reduction of about 4 deaths from melanoma each year.

**Screening**—Population screening by skin examination has the potential to reduce mortality but there is currently no data to assess the potential benefits of population screening in New Zealand.

Surveillance (including screening by skin examination) of high-risk people is possible. If 80% of the melanomas that occur in high-risk individuals were found early enough to prevent death and we assume that 2% of melanoma cases and 2% of deaths occur in these individuals, approximately 4 deaths per year would be prevented by screening of high-risk groups. That is, about 1.6% of all deaths each year from melanoma.

**Early diagnosis**—Survival decreases with increasing melanoma depth, but melanoma has a very good prognosis (about 95% 10-year survival) for tumours less than 1 mm thick. Prognosis is poor for tumours thicker than 3.5 mm: the 5-year disease-free survival is less than 50%.  

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**Figure 3. Melanoma registrations and deaths by age, 2001**

![Graph showing melanoma registrations and deaths by age](image)

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In 1998 and 1999, approximately 50% of invasive melanomas in New Zealand were diagnosed at ≤0.75 mm. Using survival data from the USA\textsuperscript{17} and Australia\textsuperscript{15} (comparable figures for survival by depth in New Zealand are not available), if patients with melanomas diagnosed at ≤0.75 mm depth (the previous cut-off point for ‘thin’ melanomas) have a 10-year melanoma-specific survival rate of about 96% and an average survival rate of 64% for depths greater than 0.75 mm, then a 10% shift in the depth distribution from >0.75 mm into the ≤0.75 mm depth category would result in about 29 deaths prevented per year, based on the melanoma registration figures for 2002.

**Treatment**—A reduction in death rate from improvements in treatment is possible but likely to be small in the near future. Surgical excision of early lesions is currently the main curative treatment for melanoma.\textsuperscript{18} Elective lymph node dissection is no longer recommended, and the value of sentinel node biopsy is currently still under investigation.\textsuperscript{19–21} There are as yet no adjuvant therapies of proven benefit for melanoma.\textsuperscript{19,21} Interferon-α treatment has been shown to increase disease-free survival but is also associated with severe side effects. Melanoma is usually responsive to radiation but only in certain circumstances is radiation the treatment of choice.

**Discussion**

Reducing the impact of melanoma in New Zealand requires a planned, systematic, and coordinated approach to multiple activities. Underpinning this approach is the requirement to collect information on incidence, prevalence, mortality, diagnosis, stage, and survival of melanoma patients.\textsuperscript{9} Research seeks to identify and evaluate means of reducing melanoma morbidity and mortality, and thus research is a fundamental element for the production of evidence needed for effective prevention and control of melanoma.

Prior to the Cancer Registry Act which made notification of cancer compulsory, many melanomas had not been notified to the Cancer Registry and this appears to have been greater for men than women. The system for registration of cancer in New Zealand prior to mid-1994 was a voluntary system, and notifications came predominantly from public hospitals. Thus, melanoma was considerably under-reported in New Zealand until 1995–1996 and the interpretation of trends over time is thereby restricted.

As expected, both the numbers of registrations of melanoma and the ASRs increased dramatically after the introduction of the Cancer Registry Act. However, in 1996, the rates declined, but not to pre-Cancer Registry Act levels. The reason for this decrease, which was greater in women, is not clear, although it appears that prevalent rather than incident cases were initially being registered in 1995. It is possible that before 1994, recurrences were registered as new cancers because of a failure to register the original diagnosis in earlier years.

After the Cancer Registry Act, recurrences were easier to identify because of more complete registration and thus less likely to be registered as incident cases. Since 1997, the registration rates in men have remained reasonably stable albeit with a suggestion of an increase in recent years, whereas the registration rates in women increased slightly in 2000, 2001 and 2002. Incidence rates of melanoma in both men
and women have also increased in Queensland\textsuperscript{22} and South Australia\textsuperscript{23} from 1998 to 2002.

Cancer prevention should be a key element in all cancer control programmes; it is often the most cost-effective form of cancer control.\textsuperscript{9} The main aetiological factor for melanoma is exposure of Caucasian skin to ultra-violet (UV) light, particularly intermittent exposure and particularly during childhood. The best avenue currently for melanoma prevention is believed to be by encouraging protection against sunburn, particularly in children, and in fair-haired and fair-skinned people.\textsuperscript{18}

The efficacy of sunscreens in reducing exposure to sunlight has not been proven. A randomised controlled trial (RCT) of sunscreen use and a review by the International Agency for Research on Cancer have shown that sunbathers often use sunscreen to extend their time in the sun, thus increasing their exposure to UV light and their risk of melanoma.\textsuperscript{24,25} Frequent sunbed use is also suspected of increasing the risk of melanoma.

Coordinated public health policies and comprehensive interventions are needed to encourage and support healthy environments.\textsuperscript{9} There is reasonable evidence that knowledge about skin cancer can be increased by health education and health promotion, but there is no evidence that sun exposure behaviour can be easily altered.\textsuperscript{18,26} Neither is there data to support the suggestion that health promotion of sun avoidance has substantially altered the incidence of melanoma.\textsuperscript{18}

Even Australia, which has had comprehensive health promotion messages about skin cancer prevention for more than 30 years, shows little decrease in the incidence of melanoma, except possibly in younger women in New South Wales and Queensland.\textsuperscript{27} Moreover, a recent Australian study\textsuperscript{28} of adolescent sun exposure and sun protection behaviours showed a significant increase in sun exposure and sunburns from 1993 to 1999.

Melanoma meets many of the criteria of a cancer whose outcome could be improved by screening. Population screening by skin examination has the potential to identify a high proportion of people with early melanomas and reduce mortality by early treatment, but there is as yet no conclusive evidence of improvement in survival.\textsuperscript{18,29}

The efficacy of early detection or screening programmes for melanoma has not been tested by randomised trials anywhere in the world.\textsuperscript{30} A systematic review of papers published between 1994 and 1999 on screening for skin cancer\textsuperscript{31} found no direct evidence that screening by physicians reduced morbidity or mortality from melanoma. Nevertheless, melanoma prevention and control programmes, including education campaigns and screening, have started in many other countries over the past decade although data on their effects are only beginning to be collected.\textsuperscript{32}

Organised population screening has not been introduced into Australia as there is little evidence for its survival benefit, and its cost-effectiveness is poor. A cluster RCT underway in Queensland, Australia, is investigating a community-based screening programme versus normal practice, but any effects on mortality may not be evident for 10 years.\textsuperscript{33}

Approximately 10\% of melanoma patients in Australia had a first-degree relative who had had a confirmed melanoma.\textsuperscript{18} Many of these familial clusters will be due to chance, but about 2\% of all melanoma cases occur in high-risk kindreds. Assuming
the same proportion in New Zealand, high-risk kindreds are thus relatively rare, so surveillance, including screening, of these high-risk individuals will (while of potential benefit to these individuals) make little impact on the overall burden of melanoma.

It is also important to educate health professionals and the public about early signs of melanoma and to encourage early presentation. Development of techniques of skin surface microscopy may help health professionals diagnose pigmented skin lesions early. The recent decrease in mortality in younger cohorts in Australia may be due to earlier presentation and improvements in early diagnosis.

Breslow thickness at diagnosis has decreased from the 1980–1986 to 1994–2000 time periods. However, about half the improvement in survival from melanoma was unexplained by the change in depth distribution. There is no comparable data series yet available for New Zealand. However, in 1998 and 1999, only 50% of invasive melanomas in New Zealand were diagnosed at ≤0.75 mm depth (thin melanoma), whereas in South Australia between 1994 and 2000, 57.8% were thin at diagnosis.

Optimising survival and quality of life for patients with melanoma requires having access to treatments that (on the basis of current evidence) are known to provide the best outcomes. The use of guidelines, protocols, and interdisciplinary management of melanoma patients may achieve consistent treatment standards. Surgical excision of early lesions is currently the main curative treatment for melanoma. Melanomas <1 mm deep are treated definitively by excision with a 1 cm margin. In situ tumours and those <0.76 mm deep, and with no vertical growth phase, are commonly excised with a 0.5 mm margin or less. More recent guidelines have recommended that lesions up to 2 mm deep be excised with a 1 cm margin.

Elective lymph node dissection is no longer recommended. Although recommended by some groups to be carried out in specialist centres, the value of sentinel node biopsy is currently still under investigation. There are as yet no adjuvant therapies of proven benefit for melanoma. Interferon-α therapy has been shown to increase disease-free survival but is associated with severe side-effects.

The UK guidelines state there is no place for isolated limb perfusion whereas the Swiss guidelines and the European Society for Medical Oncology recommend its use in specialist centres. Melanoma is usually responsive to radiation. It may be used for large unresectable lesions or for lentigo maligna in elderly frail patients, but it is not usually the first treatment of choice.

The number of melanoma cases and deaths from melanoma have been projected to significantly increase in the following years and there is evidence that the number of deaths in women have already exceeded the projections. If future mortality from melanoma in New Zealand is to be controlled, then it is important that a greater proportion of new cases are diagnosed when they are thin and when the chances of a complete cure are high.

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References:


Confirming a diagnosis of hereditary colorectal cancer: the impact of a Familial Bowel Cancer Registry in New Zealand

Paul James, Susan Parry, Julie Arnold, Ingrid Winship

Abstract

Aims The optimal management of familial bowel cancer is thought to involve specialised familial cancer units and registries that facilitate a multidisciplinary approach. We studied the impact this approach had on the investigation and management of affected families in our register.

Method A review of the outcomes of assessment for 25 families was undertaken. These families have completed assessment by the Northern Regional Genetic Service Familial Bowel Cancer Registry because of the possibility of a hereditary bowel cancer syndrome. Details of the cancer history and screening advice known at the time of initial referral to the genetic service, and at the end of assessment, were compared.

Results Detailed family history revealed 130 cancers, 90 of which were known at referral. Eighty-four cancers were confirmed, of which 73 belonged to the spectrum of cancers associated with hereditary nonpolyposis colorectal cancer (HNPCC). The mean age of diagnosis was 56.3 years. Eight families met the modified Amsterdam Criteria for the diagnosis of HNPCC, compared to four families at the time of referral. Familial hyperplastic polyposis was diagnosed in one family. 164 asymptomatic at-risk first-degree relatives were identified, 48 from families who met the Amsterdam criteria and were thereby recommended to have intensive colonoscopic screening.

Conclusion Assessment by the Familial Bowel Cancer Registry increased the number of cancers identified in families, thus facilitating a diagnosis of HNPCC in a third of the referred families and a diagnosis of hyperplastic polyposis in one other. Consequently specialised genetic testing and intensive colonoscopic surveillance could be targeted to the asymptomatic first-degree relatives most at risk. Ongoing coordination of colonoscopic surveillance by the registry for those individuals identified to have disease causing mutations or to be at-risk, is anticipated to reduce the number of deaths from colorectal cancer in these families.

Familial forms of colorectal cancer account for 5–10% of bowel cancers in countries of high incidence of sporadic colorectal cancer. Although only a minority of the total cases, this represents around 200 cancers per year in New Zealand which through timely investigation and intervention could potentially be prevented. Consequent ly, specialised services have been developed to investigate and manage affected families. Familial Bowel Cancer Registries facilitate the collection of accurate family data, identify at-risk individuals, and coordinate the provision of evidence-based colonoscopic surveillance for this cohort. Registry-based programmes have been effective in achieving gratifying improvements in both the incidence of colorectal cancer and the overall survival in families affected
by either of the two most common genetic conditions causing bowel cancer—namely, hereditary nonpolyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). 2–5

A Familial Bowel Cancer Registry was established as a clinical service in Auckland in 1996. To evaluate the impact of registry assessment on the management of families with an inherited predisposition to bowel cancer, we used the registry records to compare the available information, and resulting management advice, at completion of assessment with that available at the time of initial referral.

Methods

The study was performed through an audit of the records of the Familial Bowel Cancer Registry of patients referred for evaluation, by the Registry team.

The multidisciplinary Registry team is comprised of a clinical geneticist, gastroenterologist, registry coordinator, and a researcher, as well as associated members from the colorectal and oncology teams. Following referral to the service, a family pedigree involving at least three generations was constructed initially using information provided by the proband and augmented by other available family members who consent to be involved. Details of all cancers in the pedigree were confirmed where possible through medical records, death certificates, or the National Health Index database—all of which were accessed with written consent.

In each instance where a cancer was confirmed, histology was sought for review. The Registry team then reviewed all information and an assessment of the families’ colorectal cancer (CRC) risk status made. Specific recommendations regarding colonoscopic and appropriate extracolonic surveillance procedures were then advised.

Twenty-five consecutive families who completed their assessment from November 2000 until June 2002 were included in the review. Information compiled during the assessment was compared to the family history as known at the time of referral and to any information present in the medical records of the proband.

Results

In the 25 families reviewed there were 90 cancers known to the referring doctor at the time of referral. Following assessment by the Registry, a history of 130 cancers was established in these families—an average of just over 5 cancers per family (Table 1). In a further 9 cases there was a history of colonic polypectomy for adenomas associated with at least moderate dysplasia. In two-thirds (85/130) of the cases of malignancy it was possible to obtain direct confirmation of the diagnosis. In 56 of the 66 confirmed cases of colorectal cancer histology was obtained for review.

Table 1. Number of cancers per family and median age at diagnosis

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Number of cancers</th>
<th>Median age (years)</th>
<th>All</th>
<th>Confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At referral</td>
<td>On assessment</td>
<td>All</td>
<td>Confirmed</td>
</tr>
<tr>
<td>Total cancers</td>
<td>90</td>
<td>130</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>HNPCC spectrum</td>
<td>87</td>
<td>97</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>77</td>
<td>82</td>
<td>66</td>
<td></td>
</tr>
</tbody>
</table>

Amst.=Amsterdam criteria; +ve=positive; HNPCC=hereditary nonpolyposis colorectal cancer.
The large majority of the confirmed cancers (87%) belonged to the spectrum of malignancy that makes up the diagnostic criteria for HNPCC. Ten of the 25 families had histories of extracolonic tumours from this spectrum. Furthermore, 3 cases of endometrial adenocarcinoma, 2 small bowel tumours, and 1 case each of gastric cancer and transitional cell carcinoma were confirmed (Table 2).

Table 2. HNPCC-associated extracolonic tumours per family

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Extracolonic tumours</th>
<th>Confirmed</th>
<th>Unconfirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial</td>
<td></td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Gastric cancer</td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Transitional cell cancer</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td></td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Renal cell cancer</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>4</td>
<td>19</td>
</tr>
</tbody>
</table>

Table 3. Site of colorectal cancer (CRC) in families compared with site distribution CRC in general population

<table>
<thead>
<tr>
<th>Variable</th>
<th>RC</th>
<th>LC</th>
<th>Rectum</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>25 (47%)</td>
<td>10 (19%)</td>
<td>18 (34%)</td>
<td>14</td>
</tr>
<tr>
<td>Amsterdam +ve</td>
<td>9 (70%)</td>
<td>1 (8%)</td>
<td>3 (22%)</td>
<td>8</td>
</tr>
<tr>
<td>Jass 1991</td>
<td>2908 (37%)</td>
<td>2124 (27%)</td>
<td>2850 (36%)</td>
<td>415</td>
</tr>
</tbody>
</table>

RC=right colon (caecum and transverse colon to the splenic flexure); LC=left colon.

Eight of the 25 families at completion of assessment met the modified Amsterdam Criteria for the diagnosis of HNPCC compared to four families at the time of referral. These 8 families were referred directly for genetic testing to detect mutations in the mismatch repair genes identified to cause HNPCC.

In 6 of the 25 families, the Amsterdam criteria for a diagnosis of HNPCC were not met—but in line with the Bethesda Criteria, tumour immunohistochemistry (or microsatellite status), to support the involvement of the mismatch repair genes in these families, was requested. In one other family, review of the histology led to a diagnosis of FAP.

164 asymptomatic individuals were identified on the basis of their family history or the age (<55 years) at which a first-degree relative developed CRC to have a least a moderate increase in their lifetime risk for developing CRC. Of these, 48 individuals were from families meeting the Amsterdam criteria.
Individuals were referred to the Registry mostly by their oncologist or surgeon, and accounted for two-thirds of referrals. Other individuals were referred severally by gastroenterologists, general practitioners, or self-referral.

Discussion

Causative factors for familial bowel cancer include several inherited disorders that are distinct at both the clinical and molecular level from the common forms of sporadic bowel cancer.

Overall, 3–5% of bowel cancers are due to HNPCC and a further 0.5–1% to FAP. The remaining familial cases are due to either rare genetic conditions such as Peutz-Jeghers syndrome or familial hyperplastic polyposis (HP), or represent familial clustering for which the underlying inherited basis is unknown.

HNPCC and FAP are autosomal dominant single gene disorders where first-degree relatives of an affected individual have a 50% risk of inheriting the predisposing mutation. Research and confirmation of the family cancer history is an essential component of the investigation of affected families. Histological review of the location and nature of colonic tumours and confirmation of the profile of extracolonic tumours allows a more accurate assessment of the true likelihood of an autosomal dominant cancer syndrome in a family and facilitates the diagnosis of the more unusual polyp syndromes—e.g. attenuated FAP or HP.

Verification of both the tumour site and age at diagnosis is a requirement for a diagnosis of HNPPC according to the modified Amsterdam criteria.

This study has shown that referral to the Familial Bowel Cancer Registry has a large impact on the amount of information available for the assessment and management of individuals belonging to families with a history of CRC. In the 25 families studied, the Registry assessment process identified 40 (44% of total) additional cancers, to the 90 reported at the time of referral. This is consistent with other studies which have shown that as many as 25% of individuals are unaware of a diagnosis of colorectal cancer in a first-degree relative.

At the completion of assessment, one-third of our referred families met the modified Amsterdam criteria for a diagnosis of HNPCC. This is a high proportion in comparison with data from other familial cancer registries, thus suggesting that (in our local setting) referrals to the Registry are only made when there is a high index of suspicion for the existence of a familial syndrome.

We also found that the Registry has an important public health function in that a large number of relatives were identified on the basis of their family history or the age (<55 years) at which a first-degree relative developed CRC to have a least a moderate increase in their lifetime risk for developing CRC.

Of the 164 at-risk first-degree relatives identified from the 25 families and offered colonoscopic surveillance, less than a third (48 of 164 individuals) were from families meeting the modified Amsterdam criteria for HNPCC. Registry assessment restricted the recommendation for intensive colonoscopic surveillance to this smaller group in line with the evidence that in HNPCC families such surveillance results in a significant reduction in both the incidence of colorectal cancer and overall mortality.
For the majority of at-risk first-degree relatives identified at assessment (116 of 164), 5-yearly colonoscopic surveillance beginning at the age of 50 years (or at an age 10 years before the earliest age at which CRC was diagnosed in the family) was advised. In some cases this represented a reduction in their current surveillance recommendations. The Registry also provided education and reassurance to many individuals in the wider families of people affected by bowel cancer, although this benefit is difficult to quantify.

HNPCC has been documented to be caused by mutations in one of four mismatch repair genes, with the majority of mutations being identified in two of the four genes (hMLH1 and hMSH2). These genes normally repair errors that occur in DNA as a result of cell replication.

In New Zealand, the limited resources for predisposition genetic testing need to be targeted to those most likely to benefit. Registry assessment facilitated this with the eight families (meeting the modified Amsterdam criteria for HNPCC) being referred directly for genetic testing to detect germline mismatch repair gene mutations.

Molecular techniques that detect microsatellite instability or immunohistochemical tests revealing loss of expression for hMLH1, hMSH2 or hMSH6 proteins can aid in the detection of tumours resulting from defective mismatch repair. This is particularly helpful in families where the Amsterdam criteria for HNPCC are not met, but clinical features (as outlined in the Bethesda Criteria) suggest this diagnosis.

Of the 25 families assessed, 6 are in this category but genetic testing will only be requested if tumour immunohistochemistry or microsatellite status supports the involvement of the mismatch repair genes.

Referral to the Familial Bowel Cancer Registry facilitated the diagnosis of a dominantly inherited bowel cancer syndrome with appropriate targeting of specialised genetic testing and intensive colonoscopic surveillance.

Ongoing coordination of colonoscopic surveillance by the Registry, for those individuals identified to have disease-causing mutations or to be at-risk, is anticipated to reduce the number of deaths from CRC in these families.

The New Zealand Guidelines on the surveillance and management of groups at increased risk of CRC advise offering individuals or families with hereditary CRC syndromes referral to a Familial Bowel Cancer Registry. To facilitate these referrals, a National Registry based in both Auckland and Christchurch is now being established.

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References


Multidisciplinary treatment of colorectal cancer in New Zealand: survival rates from 1997–2002

John Keating, David Yong, Glenda Cutler, James Johnston

Abstract

Introduction The surgical and oncological treatment of colorectal cancer has undergone steady evolution over the last 20 years, however nationally derived survival figures have been disappointingly slow to improve. This study is an analysis of prospectively collected data (taken over a 6-year period) on the outcome of colorectal cancer management from a single university surgical unit in New Zealand.

Methods A comprehensive dataset was prospectively collected on all patients seen with colorectal cancer by a single surgical team, and complete follow-up was obtained. Details of surgical and oncology treatment of the primary lesion and of any subsequent disease and treatment were recorded. Survival was analysed by clinical and pathological variables.

Results Over 6 years, 244 new patients with a total of 263 primary colorectal cancers were seen.; 97% of these patients had an operation and 95% had the primary tumour resected. The mortality after elective operation was 0.5% (1/197) and 8% (3/39) after urgent or emergency surgery. After a median follow-up of 32 months, recurrence in the pelvis was apparent in 1 of 72 patients after curative resection of rectal cancer and 4 of 18 after palliative resection, thus giving a total pelvic recurrence rate of 6% at 30 months. The 5-year survival rate of all new patients seen with a rectal cancer was 58% and 56.5% for patients with a colon cancer.

Conclusions A combination of low operative mortality rates, low local recurrence rates in rectal cancer, the increasing use of adjuvant therapies, and careful follow up to detect (and where possible resect) metastatic disease at an early stage is associated with good cancer-specific survival figures. However further improvement in survival will need a shift to earlier stage at diagnosis and more effective chemotherapy (both in the adjuvant setting and for advanced disease) if significant gains in survival are to be made.

Colorectal cancer (CRC) is second only to lung cancer as a cause of years of life lost due to cancer in Australia and New Zealand.\(^1\)\(^2\) Despite screening initiatives for high-risk patients, improvements in the surgical management of rectal cancer, the introduction of novel active chemotherapy agents, and advances in the treatment of liver metastases, survival statistics have been relatively slow to improve.\(^3\)

National incidence and survival figures provide an overall picture of the outcome of patients with CRC, however large differences in survival have been found between countries, hospitals, and individual surgeons treating CRC.\(^4\)\(^6\) Against this background, a detailed database was set up to analyse the outcome of patients seen and treated with bowel cancer in a university teaching hospital. The database was designed to capture information on the patient, the pathology, and the treatment variables that might impact on ultimate survival.
Methods

All patients seen with a new CRC from January 1997 to January 2003 by a single colorectal surgical team were entered into the database. The great majority were treated in a public university hospital with the remainder treated in adjacent private hospitals. 100 data fields were assigned to each patient and the collected data included basic demographics, detailed information of initial treatment and pathological variables, perioperative blood transfusion, complications, and ultimate survival.

Tumours were staged according to the Australian Clinicopathological Staging (ACPS) system. Comprehensive data were also collected on sites of, time to, and treatment of metastatic disease. Data was entered into an EPI6 program and analysed in a EPI 2004 program (CDC, Atlanta, Georgia). The current status of all patients is known. Patients treated by other surgeons and referred with recurrent disease were not included in the analysis.

There was a close liaison between the surgeon and medical and radiation oncologists over the period of the study in the care of patients with colorectal cancer. An inclusive definition of pelvic recurrence was adopted.

Local pelvic recurrence after rectal cancer surgery was defined as any documented clinical, radiological, or histological evidence of recurrence in the pelvis at any time after surgery.

Curative surgery was defined as the absence of macroscopic evidence of disease at the completion of the primary operation.

Perioperative blood transfusion was defined as any transfusion in the 2 weeks prior to surgery or during the index admission.

Patient follow-up consisted of 3-monthly carcinoembryonic antigen (CEA) estimation and 6-monthly clinical review for 5 years—at which point patients were referred back to their primary physician.

Colonoscopy was performed at the time of resection, at 1 year in patients with multiple adenomatous polyps in addition to their cancer, and thereafter 3 yearly. Imaging of the abdomen, pelvis, and chest was only performed on the basis of a rising CEA or on clinical suspicion of recurrence and not as a routine. Patients with metastatic liver disease suitable for resection were referred to the hepatobiliary team.

All patients with mid and low rectal cancers had a total mesorectal excision (TME). A colonic pouch was constructed in all patients having a TME from early 1998. Adjuvant preoperative radiotherapy or chemoradiation was given to extraperitoneal rectal cancer patients if the clinical examination and preoperative imaging suggested that the tumour was infiltrating the mesorectum or if it was thought that downstaging would facilitate a restorative resection.

In patients receiving preoperative chemoradiation, postoperative chemotherapy was completed regardless of lymph node status. Adjuvant chemotherapy was offered to node-positive colon and rectal cancer patients deemed fit for treatment. On completion of adjuvant chemotherapy, patients had an abdominal and pelvic CT scan and subsequent follow-up was undertaken by the surgical team.

Operative mortality was defined as any death within 30 days of surgery. Urgent and emergency cases were defined as cases operated on out of hours or on a non-elective list.

Patients with multiple cancers, either synchronous or metachronous, had only a single entry in the database and analysis of prognostic factors was carried out for the most pathologically advanced tumour.

Results

244 patients were seen with a new primary colorectal cancer (CRC) in the 6-year period. Twenty patients had more than one primary cancer at presentation (9%) and 1 developed a second primary over the period of follow-up. The median age at operation was 68 years.

The 5-year survival rate of all new patients seen with a rectal or colon cancer was 58% and 56.5% respectively. The corresponding cancer-specific survival rates were 65% and 71% for rectal and colon cancer respectively.
The majority (87%) of patients were treated in the one public university hospital. Patients treated in the private system were younger than public patients by an average of 7 years (p=0.004). Thirty-nine of 233 (17%) operations were performed as emergent cases. No patients had a laparoscopic resection of CRC in this series.

One of 197 patients (0.5%) having an elective resection died after a myocardial infarction following an elective right hemicolectomy; and 3 of 39 patients (8%) died following emergency resection, 2 from pulmonary emboli and 1 from an aspiration pneumonia.

Twenty-two percent of patients having surgery had postoperative morbidity. The anastomotic leak rate was 1.5% (2/130) for patients having a colon cancer resection and 11.5% (6/52) for patients with rectal cancer undergoing restorative resection. All six rectal leaks occurred in patients with a coloanal anastomosis with a proximal defunctioning ileostomy. There were no deaths from sepsis.

The stage distribution is shown in Table 1 and is characteristic of a predominantly unscreened population with only 16% cancers being at stage A. The stage at presentation was significantly different between patients with colon and rectal cancer (p<0.0015).

**Table 1. Stage distribution (%) at presentation or resection of 244 primary colorectal cancers**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Rectum</th>
<th>Colon</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>24</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>B</td>
<td>24</td>
<td>46</td>
<td>37</td>
</tr>
<tr>
<td>C</td>
<td>28</td>
<td>25</td>
<td>36</td>
</tr>
<tr>
<td>D</td>
<td>22</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>CPR</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100%</strong></td>
<td><strong>100%</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

CPR=Complete pathological remission.

Rectal cancers were more likely to be resected at stage A than colon cancers (24% vs 11%), however the percentage of early stage disease (A+B) was higher for colon cancers 57% vs 48%. There was no difference in survival between patients with colon and rectal cancers (Figure 1).

Screen-detected cancers were the most likely to be detected at stage A (6/8, 75%) followed by presentation with rectal bleeding (18/76, 24%), whereas emergency cases presenting with obstruction or perforation had the lowest percentage of A cases (2/28, 7%).

The crude survival by ACPS stage at 5 years was A 77%, B 71%, C 63%, and D 0%, with the cancer specific survival being A 100%, B 92%, C 65%, and D 0% (Figure 2).
Figure 1. Survival of patients with colorectal cancer by tumour location (C=Colon, R=Rectum)
Figure 2. Cancer-specific survival by the Australian Clinicopathological Staging (ACPS) system

Stage A: the cancer is confined to the bowel wall; Stage B: the cancer has spread to the outer surface of the bowel wall; Stage C: cancer is found in lymph nodes in the area of the bowel; Stage D: cancer is found at distant sites—for example, in the liver or lungs; N: no residual cancer (complete pathological remission).
On univariate analysis stage, vascular invasion, perineural invasion, emergency operation, perioperative blood transfusion, and tumour grade all significantly influenced survival (Table 2), however in a multivariate model only stage remained an independent predictor of survival.

**Table 2. Prognostic factors on univariate analysis for death from colorectal cancer in addition to stage**

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>Hazard ratio</th>
<th>Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perineural invasion</td>
<td>4.4</td>
<td>2.3–8.7</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td>4.2</td>
<td>2.3–7.5</td>
</tr>
<tr>
<td>Emergent surgery</td>
<td>2.9</td>
<td>1.6–5.5</td>
</tr>
<tr>
<td>Differentiation (P vs M)</td>
<td>2.4</td>
<td>1.3–4.7</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>2.0</td>
<td>1.1–3.8</td>
</tr>
</tbody>
</table>

P=Poor; M=Moderate.

Sixty-three patients had complete resection of a lymph node-positive colon or rectal cancer, of whom 32 (53%) received adjuvant chemotherapy. Patients receiving adjuvant chemotherapy were significantly younger with a median age of 60 years as opposed to non-recipients with a median age of 73 years (p<0.0001).

Of 56 patients with metastatic disease, 43% were treated with systemic chemotherapy, 25% had no active treatment, and 16% had metastectomy as their initial treatment. One patient each had cryotherapy and selective internal radiation therapy.

Twelve patients (21%) have undergone surgery for metastatic or recurrent disease; of these, eight are alive and disease-free after a median of 31 months following resection (Table 3). In addition, 7 of these patients were found to have surgically resectable disease on imaging (undertaken to investigate a rising CEA as part of their routine follow-up). Repeat metastasectomy was performed in 2 of these 8 patients for recurrence again on the basis of a rising CEA, with a third currently awaiting a repeat liver resection.

Of 103 patients seen with a new rectal cancer, 95 were resected. Of these 95 patients, 50 had an anterior resection and 16 an abdominoperineal excision (APE) of the rectum; 6 patients had a local excision of whom 1 (the only patient with a T2 lesion) recurred and was treated by a salvage APE and remains well 2 years later.

One-third of patients in this series with a rectal cancer had neoadjuvant treatment; chemoradiation in 20, long course radiation in 7, and short course in 3 patients respectively. Two out of 20 patients (10%) having chemoradiation had a complete pathological remission (CPR). One patient had postoperative radiation.

Local recurrence in the pelvis was apparent in one patient after curative resection and four patients having palliative resection giving a total local recurrence rate of 6% at a median follow-up of 32 months.
Table 3. Details of surgical resection of metastatic/recurrent disease in 11 patients

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Site (1st)</th>
<th>Site (2nd)</th>
<th>F/U</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>57</td>
<td>Liver</td>
<td>Nil</td>
<td>63</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>50</td>
<td>Liver</td>
<td>Liver</td>
<td>50</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>47</td>
<td>Liver</td>
<td>Adrenal</td>
<td>31</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>57</td>
<td>Liver</td>
<td>Nil</td>
<td>25</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>67</td>
<td>Liver</td>
<td>Nil</td>
<td>14</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>64</td>
<td>Pelvis</td>
<td>Nil</td>
<td>01</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>64</td>
<td>Wound</td>
<td>Nil</td>
<td>05</td>
<td>Alive, disease-free</td>
</tr>
<tr>
<td>70</td>
<td>Pelvis</td>
<td>Nil</td>
<td>43</td>
<td>Alive, disease-free*</td>
</tr>
<tr>
<td>71</td>
<td>Liver</td>
<td>Nil</td>
<td>31</td>
<td>Alive, with disease</td>
</tr>
<tr>
<td>74</td>
<td>Liver</td>
<td>Nil</td>
<td>11</td>
<td>Dead</td>
</tr>
<tr>
<td>73</td>
<td>Wound</td>
<td>Nil</td>
<td>24</td>
<td>Dead</td>
</tr>
<tr>
<td>54</td>
<td>Liver</td>
<td>Nil</td>
<td>49</td>
<td>Dead</td>
</tr>
</tbody>
</table>

The follow-up (F/U) time is in months from the resection of metastatic disease; *Recurrence after local excision of rectal cancer treated with an abdominoperineal excision (APE).

Discussion

Although the age-specific incidence of CRC has plateaued (and looks set to fall) the burden of the disease is likely to continue to increase due to the effects of an ageing population and a growth in population size. In spite of the continued evolution of most aspects of colorectal cancer management, regional and national mortality rates have been slow to improve and improvement has been more marked in women than in men. Indeed, New Zealand survival rates for a number of malignancies including CRC have been compared unfavourably with Australian outcomes.

A colorectal cancer database with comprehensive fields was set up in January 1997 to collect data on treatment and outcome of all new patients seen with CRC to test the hypothesis that “optimised management” of CRC could improve on nationally derived figures on survival. The 5-year survival of all new patients in this series with a rectal or colon cancer was 58% and 56.5% respectively with a cancer-specific survival of 65% and 71% respectively. This represents a modest improvement on nationally derived figures covering the same period.

On univariate analysis, the clinical variables and urgency of operation and blood transfusion—as well as the pathological variables, tumour stage, tumour grade, vascular and perineural invasion—predicted a worse outcome. In a multivariate model however, only stage remained as a significant predictor of survival. The failure of these same variables to show an independent effect on prognosis in a multivariate model is likely explained by the relatively smaller sample size in subset analysis as in larger series these factors persist as being of independent prognostic value.

The difference in the stage distribution between colon and rectal cancer cases is of interest. Significantly more rectal cancers were resected at stage A than colon cancers, largely at the expense of fewer B cases, whereas the percentage of advanced cases (stages C and D) was similar in the two groups. This suggests that an effect similar to the ‘lead time bias’ seen in screening programmes is at play in patients presenting with rectal bleeding.
Operative mortality was low in this series, a factor that is important in ultimate survival. However, the rate of postoperative morbidity at 22% remains a significant problem in keeping with other series.

Rectal cancer is a tumour now widely recognised to be best managed by surgeons with an interest and expertise in its treatment. The total local recurrence rate for patients who had a resection of rectal cancer in this series, after a median follow-up of 32 months, was 6%. This compares favourably with contemporary reports which often only report on rates of pelvic recurrence following “curative” resection and ignore the recurrence rate in the 25% of patients who have a palliative resection.

A third of patients in this series had preoperative radiotherapy, however our current practice is to refer all patients with an extraperitoneal rectal cancer for preoperative radiotherapy prior to resection.

The use of adjuvant chemotherapy in this study was disappointing, with only 53% of patients with a lymph node-positive cancer receiving treatment. Age, and therefore presumably comorbidity, was a major factor in determining who received treatment.

Age in itself is not a barrier to completing adjuvant chemotherapy for CRC, and this underutilisation of adjuvant chemotherapy has been addressed by leaving the decision-making for adjuvant therapy with the medical oncologists. If it is assumed that the absolute survival benefit from adjuvant therapy in patients with a lymph node-positive CRC is currently 15% and given that only just over half of the 26% of eligible patients received chemotherapy, then the absolute potential gain from adjuvant chemotherapy in this series of patients was approximately 2% at 5 years.

The utility of follow-up after curative resection of CRC is a topic of ongoing interest. Regular follow-up serves the interests of the surgeon for audit purposes and is generally liked by patients, however the rationale for follow-up is principally to detect and treat early recurrent disease. Such a strategy can only be effective if pre-symptomatic recurrent disease is detected and resected in a timely manner.

Three-monthly CEA and 6-monthly clinical review revealed 13 patients in this series with surgically resectable disease of whom 12 underwent surgery (1 patient with resectable liver disease was deemed unfit for liver surgery). After a median follow-up of 31 months, 8 of these 11 patients who received surgery remain disease-free, of whom 2 have had a second resection both again detected on rising CEA. These results have encouraged us to continue with this protocol. Regular liver imaging may have lead to a further small incremental gain but was not a practical proposition at our institution.

The results of this series leaves no room for complacency. Perioperative morbidity remains a common problem for patients having a colorectal cancer resection. Adjuvant chemotherapy has been underutilised.

A low operative mortality, a low rate of local recurrence in rectal cancer, and careful follow-up all make small but incremental gains in survival, however the stage at diagnosis is the overriding predictor of ultimate survival. Further gains in survival will require a shift to an earlier stage at diagnosis and more effective systemic therapy.
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Acknowledgements: I gratefully acknowledge the expertise of the medical and radiation oncologists of the Wellington Blood and Cancer Centre as well as Peter Johnston (hepatobiliary surgeon) for his care of these patients.

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References:


Hamish Curry, Geoffrey Horne, Peter Devane, Helen Tobin

Abstract
Aim To review the data and outcome of patients with osteosarcoma in New Zealand from 1994 to 1999 and to compare this to data retrieved from a similar study from 1981 to 1987.

Methods Data from 1994–1999 was obtained from the New Zealand Cancer Registry; raw data was also retrieved from the 1981–1987 study.

Results There were 96 cases in the 1981–1987 cohort and 84 cases in the 1994–1999 cohort. Overall, 5-year survival from osteosarcoma improved from 32.3% to 44.0% between the cohorts. When the cohorts were compared, there was a trend toward improved outcome in most subgroups.

Conclusions The outcome in patients with osteosarcoma in New Zealand has improved over the study period and is similar to that seen in the overseas literature.

Osteosarcoma is the most common non haemopoietic primary tumour of bone. The estimated incidence is approximately 4–5 per million, occurring most commonly in the second decade of life (ages 11–20).1

The most recent WHO Classification of Tumours defines eight different types of osteosarcoma: conventional osteosarcoma which is further delineated into three subtypes depending on the predominant matrix present—osteoblastic (50%), fibroblastic (25%), and chondroblastic (25%); telangiectatic, small cell, low grade central, parosteal, periosteal, high grade surface, and secondary osteosarcoma.

The treatment of osteosarcoma is changing as the knowledge of chemotherapy advances, and surgical techniques and prosthetics improve. The treatment commonly involves pre- and post-surgical chemotherapy in combination with surgery (either limb salvage or amputation).

In this study, we wanted to compare the data on patients with osteosarcoma treated in New Zealand from 1994–1999 to data collected from a similar study of a cohort from 1981–1987, and then assess if there had been an improvement in 5-year outcomes.3

In particular, we wanted to assess if a more specific histological classification had lead to improved outcomes being reported in certain groups.

Method
Data was collected from the Cancer Registry at the Ministry of Health. From 1994, reporting of documented cancers became a legal requirement; data was collected from 1994 until July 1999. The raw data from 1981–1987 was also retrieved and analysed for comparison.

Information was gathered on patient age at diagnosis, age at death, sex, tumour site, histological classification, and treatment type. The coding of information and classification systems used by the
Cancer Registry had not changed between the two cohorts and this was used to enable comparison. The overall 5-year outcome was collated.

Parosteal and periosteal osteosarcomas were excluded because of their different behaviour and better outcome. In addition, osteosarcoma of the skull, facial bones, and mandible were excluded (as they are not treated by orthopaedic surgeons) as well as soft tissue osteosarcomas and osteosarcomas of an unknown site.

Statistical analysis was performed on the 5-year outcome results using the Fisher’s exact test to analyse whether a statistically significant improvement had occurred. Patients with Paget’s osteosarcoma were excluded from this analysis.

**Results**

**1981—1987 data**

Of the original 104 cases in the 1981–87 study period, 4 skull osteosarcomas, 1 mandibular osteosarcoma, 1 soft tissue osteosarcoma, 1 osteosarcoma from an unknown site, and 1 sarcoma not specified were excluded, thus leaving 96 cases of osteosarcoma (61 males and 35 females).

The age distribution of the cases is typical; it shows a peak in the second decade of life and a further smaller peak in the seventh and eighth decades (Figure 1).

**Figure 1. Age distribution of New Zealand osteosarcoma cases**

As shown in Figure 2, there were 76 tumours in the appendicular skeleton and 20 in the axial skeleton.

There were 89 cases of osteosarcoma which were not specified histologically. Four osteosarcomas originated from Paget’s disease, and 3 were telangectactic osteosarcomas.
Figure 2. Sites of osteosarcoma
Staging was documented at the time of diagnosis. Of the 98 cases, 66 were tumours were intracompartmental. There were 11 cases where the tumour was extracompartmental and 17 cases had metastases. The staging was not specified in 4 cases.

Treatment consisted of combinations of chemotherapy, surgery and radiotherapy. No specific data was available for the type of surgery performed or the chemotherapy regime used.

**1994–1999 data**

In the 1994–1999 study period there were 97 registered cases of osteosarcoma. Of the original cohort, 6 mandibular osteosarcomas, 2 maxillofacial osteosarcomas, 1 abdominal osteosarcoma, and 1 soft tissue osteosarcoma were excluded. In addition, 3 cases were excluded because the diagnosis was made at autopsy. Thus 84 cases remained (46 males and 38 females). A similar bimodal age distribution to the 1981–1987 cohort was found (Figure 1).

There were 73 tumours in the appendicular skeleton and 11 tumours in the axial skeleton (Figure 2). Histologically, there were 67 cases of osteosarcoma not otherwise specified; 6 cases were chondroblastic osteosarcoma, 5 were fibroblastic osteosarcoma. Four osteosarcomas originated from Paget’s disease and there were 2 telangectactic osteosarcomas.

The tumour was intracompartmental in 22 cases while 8 cases were extracompartmental and 23 cases had metastases. The staging was not specified in 31 cases.

The modality of treatment of cases in the 1994–1999 cohort was similar to the 1981–1987 cohort. No specific data was available on the type of surgery performed or the chemotherapy used. Compared to the 1981–1987 cohort, many more patients had chemotherapy combined with surgery plus there was a significant reduction in the use of radiotherapy (Table 1).

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Surgery</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>23</td>
<td>1</td>
</tr>
<tr>
<td>Chemotherapy + surgery</td>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>Chemotherapy + surgery + radiotherapy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chemotherapy + radiotherapy</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Surgery + radiotherapy</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Treatment not specified</td>
<td>5</td>
<td>18</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>96</td>
<td>84</td>
</tr>
</tbody>
</table>

**Outcome**

All patient groups demonstrated an improved outcome in the later cohort, except those with metastatic disease.
Patients with axial tumours had a poorer outcome when compared to those with appendicular tumours. However both those with axial tumours and those with appendicular tumours showed an improvement in outcome in the later cohort.

There were twice as many pelvic osteosarcomas in the earlier cohort which may partially account for the improved outcome in the later cohort.

Outcome was also broken down in terms of histological classification for the later cohort. Cases of osteosarcoma in Paget’s disease had the poorest 5-year outcome (25%). The group of osteosarcomas not otherwise specified had a 5-year outcome of 42.3%—this is lower than the 5-year outcome of cases with fibroblastic osteosarcomas (60.0%), chondroblastic osteosarcomas (50.0%), and telangectactic osteosarcomas (50.0%).

**Statistical analysis**

Using Fisher’s exact test, the improvement in 5-year outcome between age groups within the cohorts reached statistical significance in only those patients older than 40 years (Table 2).

**Table 2. Outcome statistics**

<table>
<thead>
<tr>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>5-year outcome</td>
<td>Cases</td>
<td>5-year outcome</td>
<td></td>
</tr>
<tr>
<td>All tumours (total cohort)</td>
<td>96</td>
<td>31 32.3%</td>
<td>84</td>
<td>37 44.0%</td>
<td>0.12</td>
</tr>
<tr>
<td>Primary tumours*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;40 years</td>
<td>60</td>
<td>28 46.7%</td>
<td>54</td>
<td>28 51.9%</td>
<td>0.71</td>
</tr>
<tr>
<td>Age &gt;40 years</td>
<td>32</td>
<td>3 9.4%</td>
<td>26</td>
<td>8 30.8%</td>
<td>0.050</td>
</tr>
<tr>
<td>Appendicular skeleton</td>
<td>73</td>
<td>29 39.7%</td>
<td>70</td>
<td>32 45.7%</td>
<td>0.50</td>
</tr>
<tr>
<td>Axial skeleton</td>
<td>19</td>
<td>2 10.5%</td>
<td>10</td>
<td>4 40.0%</td>
<td>0.14</td>
</tr>
<tr>
<td>Metastatic disease all ages</td>
<td>16</td>
<td>2 12.5%</td>
<td>22</td>
<td>2 9.1%</td>
<td>1.00</td>
</tr>
<tr>
<td>&lt;40 yrs non metastatic †</td>
<td>51</td>
<td>26 51.0%</td>
<td>20</td>
<td>13 65.0%</td>
<td>0.31</td>
</tr>
<tr>
<td>&gt;40 yrs non metastatic †</td>
<td>21</td>
<td>3 14.3%</td>
<td>9</td>
<td>2 22.2%</td>
<td>0.62</td>
</tr>
<tr>
<td>&lt;40 yrs non metastatic appendix †</td>
<td>45</td>
<td>24 53.3%</td>
<td>20</td>
<td>12 60.0%</td>
<td>0.79</td>
</tr>
<tr>
<td>&gt;40 yrs non metastatic appendix †</td>
<td>15</td>
<td>3 20.0%</td>
<td>7</td>
<td>2 28.6%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Cases of Paget’s osteosarcoma excluded; †Unspecified staging not included; ‡Probability that the difference in 5-year outcome is significant.

**Discussion**

The most important finding in this study was the improved 5-year outcomes for patients presenting in New Zealand with osteosarcoma. This improvement was seen throughout most age ranges and stages at presentation but did not reach statistical significance, except in those patients older than 40 years.

The outcome of osteosarcoma continues to improve with better treatment. Kotz et al have demonstrated an improvement in survival rates in primary osteosarcoma from 24% in 1965 to 62% in 1994. Despite ongoing developments in the field of...
chemotherapy and surgery, the overall survival rates of 55–70% have not changed significantly in the last 15 years, however.\textsuperscript{4}

One of the aims of this study was to assess if histological classification had any effect on the outcome. This was not possible due to the small numbers of specific histological subtypes. No comparison could be made between the two cohorts, as the classification had changed in the intervening period to become more specific. The review of subtypes found a poorer outcome of osteoblastic osteosarcomas compared to other subtypes. The reason for this is unclear.

There has been little literature surrounding this topic. Hauben et al found that (in 570 patients less than 40 years of age) survival was not affected by histological type.\textsuperscript{5} Our results of overall outcome in the 1994-1999 cohort are comparable to other studies.

For patients aged less than 40 years with a primary osteosarcoma of an extremity, the 5-year survival rates range from 55–71% in prospective trials.\textsuperscript{6–9} Our results compare favourably (60% for similar patients).

Older patients (>40 years) with osteosarcoma generally do not survive as long as younger patients. Our 5-year survival results for older patients are lower than those in other studies in the literature where a 5-year survival rate of 41.6% is quoted in one study.\textsuperscript{10}

Patients with metastatic disease also have poorer outcomes. In two studies, the 5-year survival was 24% and 29%, respectively.\textsuperscript{11,12} Again, this rate is higher compared to our results.

Caution is necessary when comparing our outcome results with other studies, as the patient inclusion criteria in those studies are often very specific and they have higher numbers of cases. Specifically, the numbers of patients older than 40 years and those with metastatic disease are much smaller in the New Zealand cohorts, which makes comparison difficult.

Indeed, the main limitation of this study is its small number of cases. Furthermore, incomplete data was available on the staging of these tumours, histological grade, and on the presence of skip lesions which thus made comparisons difficult.

We also acknowledge that more accurate results could have been obtained if more defined data about histological grade, staging, and treatment regimes were available.

Despite these reservations, we have shown a trend toward an improved outcome of patients with osteosarcoma treated in New Zealand which is similar to reports in the literature from other countries.

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Acknowledgement: We thank Gordon Purdie (Wellington School of Medicine) for the statistical analyses.

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References:


Palliative Care Partnership: a successful model of primary/secondary integration

Bruce Stewart, Simon Allan, Barry Keane, Bridget Marshall, Jane Ayling, Tai Luxford

Abstract
The health reforms of the 1990s and early 21st century have seen unheralded change in the delivery of health services in New Zealand, and the concept of integration of primary and specialist or secondary services into a seamless health delivery service is one of the key planks of national and regional healthcare planning in New Zealand.1,2

This paper reports on a successful primary secondary integration project. Starting with commentary on the historical difficulties that acted as a catalyst to this initiative, it reports on the development process, how the model works in practice, and outlines some initial evaluation work done as part of its quality improvement component. Given the collaborative nature of this project and its scope across primary and specialist care sectors, the authors believe this model has implications and relevance across a wide spectrum of the New Zealand health service.

The concept of partnership between palliative care services and primary care is a well established internationally.3,4 The consensus has been that a partnership approach to palliative care provision has many benefits in terms of maximising existing services in the face of rising referral rates5 and preventing fragmentation of services.6,7

Clarke and Neale8 suggested that building palliative care services exclusively around a specialist hospice service only served to de-skill general practitioners and district nurses which had a flow on effect regarding the standard of care delivery.

An ideal of general practice involvement is suggested by Thomas:9,10

Caring for the dying is a challenging but rewarding business. Many GPs and district nurses feel that palliative care represents the best of all medical care, bringing together the clinical, holistic, and human dimensions of primary care, and bonding us with our patients in a very special way.

In the same way as it matures as a specialty, specialist palliative care has been defining its relationship with primary care:

Specialist palliative care builds on the palliative approach adopted by primary care providers and reflects a higher level of expertise in complex symptom control, loss grief and bereavement. Specialist palliative care works in two ways: first by providing the direct care to referred individuals and their families and secondly by providing a consultancy service to primary care providers and therefore supporting their care of the patient and family.11

These ideals are consistent with the New Zealand Palliative Care Strategy12 which states that the provision of palliative care should happen across a range of agencies and involve a partnership between primary care and a specialist palliative care provider.
The perception of Manawatu general practice providers in the early 21st century was that their situation was less than the international ideal. General practice perceived that the Hospice Service had ‘captured’ palliative care, often to the exclusion of general practice.

Contemporaneously, in response to a growing awareness of the need to find a more integrated approach to manage the growing palliative care need, Arohanui Hospice staff looked for ways to work more closely with general practice teams (GPTs), and the scene was set for open dialogue.

In 2002, Arohanui Hospice in conjunction with the Manawatu Independent Practice Association (MIPA) commissioned a survey of GPTs in the greater Manawatu, Horowhenua, and Tararua region.13 This survey demonstrated that although Arohanui Hospice was respected as a specialist palliative care service, the earlier perceptions of general practice providers were reinforced and responses clearly signaled:

- GPTs feeling marginalised in palliative care provision;
- Cost as a barrier for patients accessing GPTs;
- Acknowledgement of a need for ongoing learning in palliative care by GPT members; and
- A strong willingness on the part of GPTs to participate in meeting the palliative care needs of their patients.

Arohanui Hospice and MIPA responded with the establishment of a multidisciplinary working party to address the issue of provision of community-based palliative care. The working party developed a set of key aims for the project:

- Enhance patient and family access to palliative care services;
- Remove financial barriers for those with a terminal illness in their region;
- Maximise the appropriate use of specialist palliative care services;
- Promote a coordinated service responsive to patient and family needs;
- Increase knowledge of GPTs in palliative care principles and practices; and
- Promote a highly effective working relationship between specialist palliative care services and primary healthcare providers.

Following on from these aims, the working party developed the concept of the Partnership of Care—with a vision for palliative service delivery in the MidCentral region (see Box 1).
Box 1

**Partnership of Care** between:

*Specialist palliative care*: an essential service of quality, evidence based, specialist care provided by a qualified interdisciplinary team.\(^{12}\)

*Generalist palliative care*: the patient and family’s primary professional carers providing palliative care as a vital and integral part of their routine clinical practice.\(^{14}\)

**Vision**

“The Palliative Care Partnership attempts to maximise the skills and experience of both generalist and specialist services to provide the best possible palliative care to the community”

As this partnership model was consistent with the MidCentral District Health Board’s vision for primary secondary multidisciplinary service integration, the project was able to attract significant district health board funding as a new primary care initiative. This funding provides for equitable access to primary level palliative care by reducing financial barriers to patients accessing general practice care.

**The Palliative Care Partnership (PCP)**

In essence, the PCP is community palliative care based on a partnership between GPTs and the Specialist Palliative Care Service. The cornerstone of the PCP is the effective working relationship between the GPTs and Arohanui Hospice. Central to the effectiveness of the model is the role of the Palliative Care Coordinator (PCC), an advanced nursing role within the Arohanui Hospice interdisciplinary team. The PCC has the twin responsibilities of bringing specialist palliative care assessment and nursing support to patients and families and facilitating coordination of care between providers. This creates the true ‘partnership’ between primary care and specialist care for the benefit of the patient and their family/whānau.

Key aspects of the partnership are:

- Good communication.
- Joint decision-making.
- Respect of all providers’ skills.
- Specialist resource and support.
- Shared responsibility for the care plan.
- Ongoing case management review.
- Appropriate use of ancillary services (including MidCentral District Nursing Service and Arohanui Hospice day stay).

**Partners**

The Palliative Care project has three main partners: the Arohanui Hospice Palliative Care Service, General Practice Teams (general practitioners, practice nurses, and support staff), and the Manawatu Independent Practice Association.
Key linkages

Supporting and interacting with the partners are several key groups. The most important linkage is with the MidCentral Health District Nursing Service. This service often plays a significant role by providing 24-hour clinical and personal care for patients and their families/whānau during the final phase of care.

Other linkages include the Cancer Society, Aged Residential Care, and Māori and Iwi health providers.

Components

There are four main components to this Partnership:

- **Participation framework**, which describes
  - the providers’ roles and responsibilities.
  - how patients will move through the Partnership of Care.

- **Education programme**
  - which includes a resource folder.

- **Partnership administration**
  - which provides the business framework and funding information.

- **Governance Group**.

Participation framework

Patients are referred to the partnership via the following health providers:

- MidCentral Health or other secondary care provider.
- General Practice Team.
- District Nurse.
- Private medical or surgical consultant.
- Self referral.

All referrals are made to Arohanui Hospice; the hospice team conducts an initial assessment which integrates physical, spiritual, cultural, and psychosocial elements of the patient and family/whānau. This assessment is usually conducted by the PCC but may involve any member of the Hospice team—doctor, nurse, social worker, or other (as appropriate to each case).

As part of this assessment, a care plan is developed to which all parties are encouraged to contribute to and update. The care plan is held by the patient who takes it to all care review discussions.

Depending on need, ongoing care is then provided across the agencies involved with the PCC as the primary coordinator of care and the GPT as the patient’s first point of contact. Patient review by the specialist hospice team is provided as required. This review may be requested by either the GPT, PCC, the patient and/or family/whānau, District Nurse, or hospice staff. The PCC will usually be the communication conduit for key decisions made.
As part of the partnership, after-hours availability (including weekend and annual leave cover) is discussed, agreed, and documented in the patient’s care plan. In situations where patients cannot be managed effectively in the community, admission to the Arohanui Inpatient Unit may be required and will be negotiated between the PCC and/or GPT and the Inpatient Unit Team.

The GPT is informed of a patient’s admission, discharge from and/or death in the hospice and is encouraged to visit and contribute to the management plan, however the Hospice team has overall responsibility for inpatient management.

The participation pathway (Figure 1) outlines the roles and responsibilities within the partnership model, and how the patient moves through the Partnership of Care. The PCCs provide the link between the GPTs and the specialist interdisciplinary team at Arohanui Hospice.

Figure 1: Participation pathway

To encourage an interdisciplinary approach, registration for participation in the PCP by interested GPTs is only accepted if both general practitioners and practice nurses participate. Completion of the education programme and yearly updates is mandatory for registration on the programme.
Education programme

The education component of the partnership programme is framed around the Gold Standard Framework (GSF) developed by Keri Thomas. The GSF was developed in the United Kingdom as a tool to support and facilitate the primary care practice team to 'raise their game' towards the highest quality care for patients with any diagnosis in the last stages of life.

The education programme is able to cover a comprehensive range of material necessary to explore a palliative approach within primary care. It highlights all aspects of care and goes beyond physical symptom control and management issues which could have easily become the focus of a standard GPT education programme.

The three 2-hour education workshops cover areas such as:

- Communication.
- Symptom control.
- Continuity of care (including after-hours responsibilities).
- Coordination of services.
- Carer support (respite care).
- Care of the dying.

Delivery of the education sessions utilises the expertise of the wider interdisciplinary team within the specialist palliative care service and is supported by a resource manual of area-specific information written by the interdisciplinary team.

Update sessions are an annual requirement of the partnership; so far they have focused on case reviews and medication updates as well as being used as a vehicle for introducing initiatives developed by the specialist palliative care service.

Partnership administration

MIPA provides the administration support for the partnership, this involves ensuring compliance with contractual requirements, facilitating the ongoing education sessions, organising on going robust evaluation, and administering the monetary payments to general practice providers.

MidCentral District Health Board provided funding under the following formula:

- General practitioners and practice nurses are paid for attendance at the education sessions.
- A funding envelope of up to $400 per registered patient is paid on a fee for service basis under the following formula:
  - General practitioner consultation $30
  - General practitioner home visit $40
  - Practice nurse consultation $25
  - Repeat prescription $15

  The Practice Nurse consultation includes significant telephone consultations.

  If need exceeds the $400 per patient limit, then additional funding is negotiated between the provider and the project coordinator.

- Administrative support.
Governance group

The PCP working party now maintains a role as the management group for the programme with administrative support provided by MIPA.

The governance is shared, with the Arohanui Hospice Community Reference Group providing the palliative care philosophical direction and the recently formed Midcentral DHB Cancer District Management Group responsible for the long-term sustainability of the partnership.

Outcomes

During 2005, a provider feedback survey was conducted. This survey suggested there has been a positive change in the culture of palliative care service delivery in the primary care setting.

Outcomes so far can be explained using the following themes.

Participation

Recruitment of MidCentral District general practice teams for the programme was done through MIPA networks and the project coordinator.

<table>
<thead>
<tr>
<th></th>
<th>Practices</th>
<th>General practitioners</th>
<th>Practice nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (% of total)</td>
<td>30 (73%)</td>
<td>54 (62%)</td>
<td>73 (67%)</td>
</tr>
</tbody>
</table>

Communication

Both GPTs and PCCs response to the staff survey (Figure 2) suggested that historically the relationship had generally been a good one and that communication had improved since the introduction of the partnership programme. Specifically, more face-to-face and telephone contact resulted in their relationship having a greater sense of partnership.

I think that there is more of a partnership feel in the care, less of patients being taken over (GP)

It has opened the door for freer [sic] communication (PCC)

Some GPTs’ responses still suggested that Hospice ‘take over’ was still a concern, but comments from the PCCs suggested that (in terms of ways of working) they were much more likely to involve GPT involvement than in the past.
In your experience how effective has communication been between yourself and PCC’s?

- Of little use
- Extremely useful

RATING SCALE

<table>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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</tbody>
</table>

**Professional development**

The training component of the programme appears to have been well received by the GPTs and well supported by the PCCs themselves (Figure 3).

Feedback from the survey indicated that the training programme had two main benefits; the first being enhanced knowledge and confidence in management of patients with palliative care need and secondly familiarity with the Hospice staff and its way of working:

[I] feel more confident and more personally involved in treatment management—more comfortable using hospice and discussing progress with staff (GP)

**Funding**

The project is well within budget for the first year.

GPT feedback suggests that the removal of cost as a barrier to visiting the general practitioner may have been a significant component in the success of this programme. From the GPT perspective, it has meant that general practitioners felt more comfortable about visiting palliative care patients knowing that they don’t have to charge.
Hospice impact

Referrals to the specialist palliative care outpatient clinics have decreased, however their complexity increased. This suggests a greater number of less complex problems are being resolved in the community.

Patient impact

In the first 14 months, 255 patients were part of the partnership. Of these, 82.5% were cancer patients, 8.2% were cardiovascular disease patients, 3.9% were respiratory patients, and 6.1% had another (including renal, dementia, and neurological) disease. Approximately 60% of partnership patient deaths occurred in the community; very few occurred within the hospital setting [<5%].

Linkages

An important (though unexpected) outcome has been the strengthening of service relationships with the Midcentral Health District Nursing Service via increased communication and teamwork with general practice and hospice staff. The coordination role of the PCC has been pivotal to this enhancement.

The limited evaluation completed in 2005 has not addressed the impact of the partnership on patients and families or fully addressed the impact on providers.

The Midcentral District Health Board and the working party are currently working with the Wellington School of Medicine to develop a robust and detailed reporting and evaluation package that will examine the outcomes of the partnership in much greater depth. This process will be completed in late 2006.
Summary

The care of patients with palliative care needs presents us with considerable challenges. This partnership initiative supports and enhances the provision of palliative care by both specialist and generalist providers within our region. The patient and family/whānau remain at the centre of this partnership, and the special relationship between the patient and their primary healthcare providers is maintained and integrated within the provision of palliative care. Coordination of care between providers is a key element of effective palliative care provision.

While more evaluation is required, early indications suggest that the main benefits to emerge from this partnership (at the ‘coalface’) are effective communication, a better understanding and respect of roles, and responsibilities between providers, which enhances patient choice and coordination of their care. In this regard, the partnership has partly met its original goals.

A factor that has helped provide a sound foundation for this programme is the often under-recognised administration component. Utilising the networks of a well-organised IPA, the partnership has succeeded in achieving a 73% participation rate for GPTs, which is impressive by any standards.

Other spin-offs include consolidation of Arohanui Hospice’s role as a provider of community palliative care education, and (through the PCP management group) a forum to address ongoing interface issues such as after hours care, referral criteria, or scope of practice.

Another benefit has been the recognition by the MidCentral District Health Board of the value of such a partnership in the provision of community palliative care. This recognition is important to the partnership’s long-term sustainability.

The success of this integrated care model has attracted interest from outside the Midcentral region. For instance, in July 2005, representatives of the PCP working party were invited to present the partnership model to the Hawke’s Bay District Health Board’s Community Public Health Advisory Committee.

We believe that this model has relevance across a broad spectrum of primary/secondary interfaces, not just palliative care. Indeed, the model could be adapted for use as a blueprint for a wide range of health services.

The detailed reporting and evaluation to be undertaken in 2006 will, we believe, validate the approach taken with this model further enhancing its position as an integration model.

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References:

Back to the future: postoperative pain management beyond COX-2 inhibitors

Ole Naesh

Abstract

In the aftermath of the heated dispute on COX-2 selective nonsteroidal anti-inflammatory drugs (NSAID) that led to the national and international withdrawal of several of the recently introduced coxibs a balanced discussion of pros and cons for their short term use is warranted. Further debate and research has highlighted risks with both classical NSAIDs and coxibs when administered to patients with cardiovascular disease. For several decades discussion about indications, risks and contraindications for the perioperative use of classical NSAIDs has been ongoing. The COX debate has further added some uncertainty amongst practitioners. With a vast amount of research available on this topic, it should however be feasible to reach some consensus for the perioperative use of NSAIDs as well as for coxibs. This would ensure that the right patients take advantage of our present knowledge of NSAIDs as part of a multimodal and balanced perioperative analgesic regimen and at the same time that the patients at risk are not prescribed such drugs. Rational use of NSAIDs in the perioperative period would benefit a major group of patients who at present are deprived of such therapy due to unfounded fears of side effects and lack of knowledge among prescribers. This review highlights some of the aspects of short term (i.e. less than 5 days) perioperative use of NSAIDs.

Recent debate has highlighted severe cardiovascular side effects from COX-2 selective nonsteroidal anti-inflammatory drugs (COX-2 inhibitors or coxibs). This has led to a withdrawal from the New Zealand (NZ) market of rofecoxib and valdecoxib in accordance with international recommendations.

The bulk of evidence for the potentially harmful effects of COX-2 inhibitors is based on long-term trials in rheumatoid populations. An extensive database is available on the analgesic efficacy of COX-2 inhibitors for postoperative pain. While only a few studies have focused on adverse effects of the short-term perioperative use (1–5 days) of these drugs, the main impression seems to be of a high general tolerability apart from a cluster of cardiovascular adverse events reported after coronary by-pass surgery.

Anaesthetists have been advocates of the COX-2 inhibitors as they have allowed more patients to get the benefits from a nonsteroidal anti-inflammatory drug (NSAID) as part of a multimodal perioperative analgesic regimen offering superior analgesia with opioid sparing effect and reduced opioid-related side effects.

In the aftermath of the recent COX-2 debate it is however appropriate to revisit the rationale perioperative use of NSAIDs. The extent upon the prolonged use of NSAIDs outside the perioperative period will not be elaborated.
Pharmacology

The synthesis of prostaglandins is the primary target of all NSAIDs. Prostaglandins are known to be involved in numerous physiological systems (Table 1). The regulation of vascular tone and platelet aggregation is affected by endothelial prostacyclin and platelet-derived thromboxane. Prostaglandins of the E-series exert protective effects on the gastric mucosa.\(^7\)\(^-\)\(^11\) Prostaglandins are also of major importance in the regulation of the inflammatory cascade and they act as sensitisers of peripheral nociceptors.\(^12\)

The synthesis of prostaglandins (PG-series), thromboxane, and the leucotrienes is initiated (e.g. after tissue trauma) by the conversion of arachidonic acid to intermediate PGG\(_{2}\) and PGH\(_{2}\), which are the substrates for the several other prostaglandins (Figure 1).

The two first metabolic steps are catalysed by cyclo-oxygenase (COX) which is the enzyme responsible for the velocity of the reaction and thus the rate limiting factor. Cyclo-oxygenase is known to be present in at least two isomeric forms (COX-1 and COX-2) with different physiological effects.\(^9\)\(^,\)\(^10\)

### Table 1. Prostaglandins: their organ-specificity and effects

<table>
<thead>
<tr>
<th>Prostaglandin type</th>
<th>COX-1</th>
<th>COX-2</th>
<th>Organ specificity</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGE(_1)</td>
<td>++</td>
<td>+</td>
<td>CNS / peripheral nerves</td>
<td>Sensitisation and hyperalgesia</td>
</tr>
<tr>
<td></td>
<td>++</td>
<td>+</td>
<td>GI-tract</td>
<td>Motility, mucosa protection</td>
</tr>
<tr>
<td></td>
<td>++</td>
<td>++</td>
<td>Kidney</td>
<td>Medullary blood flow, Na(^+)/K(^+) exchange</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>++</td>
<td>Peripheral tissues</td>
<td>Inflammatory response</td>
</tr>
<tr>
<td>PGE(_2)</td>
<td>++</td>
<td>+</td>
<td>CNS / peripheral nerves</td>
<td>Sensitisation and hyperalgesia</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>++</td>
<td>Peripheral tissues</td>
<td>Inflammatory response</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>+</td>
<td>GI-tract</td>
<td>Mucosa protection, H(^+) secretion</td>
</tr>
<tr>
<td></td>
<td>++</td>
<td>++</td>
<td>Uterus</td>
<td>Labour onset</td>
</tr>
<tr>
<td>PGI(_2)</td>
<td>-</td>
<td>++</td>
<td>Vessel wall</td>
<td>Smooth muscle relaxation</td>
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<tr>
<td></td>
<td>++</td>
<td>?</td>
<td></td>
<td>Fibrinolysis, platelet aggregation</td>
</tr>
<tr>
<td></td>
<td>++</td>
<td>+</td>
<td>GI-tract</td>
<td>Mucosa protection, H(^+) secretion</td>
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<td></td>
<td>++</td>
<td>++</td>
<td>Kidney</td>
<td>Cortical and glomerular blood flow</td>
</tr>
<tr>
<td>TXA(_2)</td>
<td>++</td>
<td>-</td>
<td>Platelets</td>
<td>Pro-aggregatory</td>
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<tr>
<td></td>
<td>++</td>
<td>+</td>
<td>Vessel wall</td>
<td>Contraction</td>
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<tr>
<td></td>
<td>++</td>
<td>-</td>
<td>Kidney</td>
<td>GFR regulation</td>
</tr>
<tr>
<td>PGF(_2\alpha)</td>
<td>-</td>
<td>++</td>
<td>Uterus</td>
<td>Contractility ↑ in labour</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>++</td>
<td>Kidney</td>
<td>Na(^+)/water excretion</td>
</tr>
</tbody>
</table>

The predominant COX-enzyme involved in their metabolism is marked ++; + indicates that the enzyme is present but in lower concentrations under normal non-inflammatory conditions; GFR=glomerular filtration rate; GI=gastrointestinal; CNS=central nervous system.

COX-1 is a costitutive enzyme (i.e “daily household”) and is involved in the production of “physiological” prostaglandins. COX-2 is classically described as inducible and is expressed in inflamed/traumatised tissues, but is lacking in others (e.g. platelets) (Figure 2). Recent evidence, however, points to a more complex picture, with the COX-2 enzyme being constitutively expressed in several tissues as e.g. brain and kidney (cf. Table 1). A third isomeric form (COX-3) has recently been proposed as being expressed in the restitutinal phase of inflammation.\(^13\)
The classic, non-selective NSAIDs are not more specific for either isomeric form of the COX enzyme as opposed to the newer and selective COX-2 inhibitors. A hydrophilic side-pocket unique to the COX-2 isoenzyme allows the active site to accommodate only the coxibs due to their added side chain. Classic NSAIDs block arachidonic acid access to both isoforms. However the degree of COX-1 or COX-2 selectivity (i.e. COX-1: COX-2 inhibitory ratio) warrants caution in the interpretation due to methodological differences of currently available test systems, of which biological models have more clinical relevance. Of the various coxibs, celecoxib has a ratio of 1:30 whereas rofecoxib, for example, has a ratio of 1:276 and lumaricoxib a ratio of 1:433.

The analgesic effects of NSAIDs are ascribed primarily to COX-2 inhibition, whereas several adverse effects are believed to be mediated by COX-1 inhibition. The inhibition of COX-1 prolongs the bleeding time due to an inhibition of TXA2 synthesis from platelets and may lead to the formation of gastric ulcerations due to PGE2 inhibition. COX-1 inhibition may, under certain circumstances, decrease renal glomerular filtration rate. COX-2 selectivity may theoretically attenuate such adverse effects.14

Figure 1. Tissue injury activates the arachidonic acid cascade through membrane bound phospholipase A2 (PA2). Through the action of cyclooxygenase various prostaglandins (PG) are formed according to tissue specific pathways. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the COX enzyme.
Figure 2. Cyclo-oxygenase (COX) exists in at least two forms (COX-1 / COX-2). In a simplified model, various normal physiological stimuli induce COX-1 activity and inflammation induces COX-2 activity. By the enzymatic action of COX, arachidonic acid is converted into prostaglandins (TXA₂=thromboxane; PGI₂=prostacyclin; PGE₁/PGE₂=prostaglandin E)

Cyclooxygenase (COX)

Inhibition of COX-3 by the non-selective NSAIDs may theoretically interfere with restitution after tissue trauma but the clinical relevance remains to be elucidated. The above mentioned pharmacological effects of NSAIDs are widely accepted. Central (CNS) effects have recently been suggested but the exact mechanism has not been fully clarified. NSAIDs are strongly ionized at physiological pH, and have difficulties passing the blood-brain barrier. However endothelial cells in the brain were recently shown to possess interleukin receptors coupled to COX-2 activity.

Provided the proper stimulus (e.g. interleukin 1), such receptors would allow PGs to be expressed in the brain. An inhibition by NSAIDs at this level could explain an intracerebral effect. Finally, an interaction with opioid receptors in the CNS has been suggested.

Selective COX-2 antagonism affects the balance between PGI₂ and TXA₂ in favour of TXA₂, and might thus act as a prothrombotic principle due to unopposed inhibition of endothelial PGI₂. Early warnings of this potential mechanism were given by several groups but it took larger patient materials in order to realize that COX-2 antagonism might increase cardiovascular events in predisposed patients.
Several recent large-scale studies have unraveled this side effect and have led to a heated debate on the use of these new drugs and to the withdrawal of some (but not all) coxibs.\textsuperscript{21–25}

The inherent potential for serious cardiovascular events with the use of coxibs seems to be a class effect but may still differ among the coxibs (e.g. rofecoxib $\gg$ celecoxib). However, as would be expected, it becomes evident in patients at risk of such events.

Recent debate has focussed on an interference of coxibs with the mechanisms of myocardial preconditioning (i.e. a preceding minor ischaemic episode offering protection towards a following ischaemic event) and on the impact of coxibs on renal physiology as underlying coxib-induced adverse cardiovascular events.\textsuperscript{24} Indeed, the increased cardiovascular risks are acknowledged in the recent national and international recommendations on the continued use of COX-2 inhibitors.\textsuperscript{26}

To paraphrase George Orwell, \textit{all NSAIDs are not created equal}. Indeed, possibly due to several variant forms of the COX enzyme,\textsuperscript{27} NSAIDs differ in their effects and side effects profile. Of the four major pharmacological groups of classical NSAIDs (salicylic acid, propionic acid, acetic acid, and oxicams), there are differences in platelet inhibitory activity (e.g. diclofenac being less active than comparator NSAIDs) and in gastrointestinal side effects profile (e.g. ibuprofen showing best GI tolerability).\textsuperscript{28}

Interaction (e.g. decreased effect) with low-dose regimens of salicylic acid is seen with some but not with others (e.g. ibuprofen may interact whereas e.g. diclofenac does not).\textsuperscript{29} Furthermore, NSAID-induced side effects show a strong dose, time, and age dependence.

\textbf{Clinical use of COX-2 inhibitors}

So in which patients are COX-2 inhibitors indicated for perioperative pain management?

As an inflammatory tissue response to surgery is involved in sensitisation of peripheral and central pain pathways, NSAIDs / coxibs should be used as facilitating analgesics as part of a multimodal regimen. Coxibs should be used at the lowest recommended dosage and for short periods of time only (i.e. $< 5$ days). A lower “ulcerogenic” potential and a platelet-sparing effect must be taken into consideration.

Where the nature of the surgical intervention “contraindicates” use of classic NSAIDs due to risk of bleeding (e.g. ENT surgery, plastic surgery, or neurosurgery) coxibs may well be used.\textsuperscript{30}

There is, however, no valid evidence for any superior analgesic benefits of the coxibs as opposed to the classic NSAIDs in the majority of surgical patients.\textsuperscript{1,31–34}

In NZ, there is access to five COX-2 selective NSAIDs: meloxicam, etoricoxib, lumiricoxib, celecoxib, and parecoxib. The latter is for parenteral use and is the only available intravenous (iv) COX-2 inhibitor in NZ. Primarily used by anaesthetists during the immediate perioperative period, it has not proven superior to any classical iv NSAIDs.

Meloxicam has a long record as anti-inflammatory drug with a relatively long half-life ($\sim 20$ h) and a favourable gastrointestinal (GI) profile (ulcerogenicity and GI bleeding)
in long-term studies in osteoarthritis. The database for its perioperative use is limited, and its COX-2 selectivity at clinically relevant perioperative doses has been questioned (Virtual Anaesthesia Textbook: http://www.virtual-anaesthesia-textbook.com).

Etoricoxib has not been trialled in the perioperative setting. Lumericoxib was recently introduced, but is only scarcely documented for postoperative pain.

This leaves us with celecoxib as the only available true COX-2 selective, oral NSAID for perioperative analgesia. A one-off premedication dose of 400 mg (as opposed to 200 mg) of celecoxib (elimination $T_{1/2}$ ~ 4–8 hr), followed by 200 mg once to twice daily for postoperative analgesia, has recently been advocated as optimal in adults (cf. Straube et al 2005). Intraoperatively, the only available intravenous COX-2 inhibitor is parecoxib (elimination $T_{1/2}$ ~ 8 hr) at a normal adult dose of 40 mg. No further NSAIDs should be administered until after at least 12 hours.

**Contraindications and adverse effects of NSAIDs**

Anecdotes and myths are often quoted when discussing NSAIDs. Clear and updated guidelines for the perioperative use of NSAIDs (including COX-2) are imperative to ensure that patients get the full benefit of their inclusion into a multimodal analgesic regimen. There are, however, some clear contraindications to the use of NSAIDs and some more controversial relative contraindications (Table 2).

The national advisory board of NZ (Medsafe: http://medsafe.govt.nz/hot.htm), in agreement with international consensus, recommends that COX-2 NSAIDs are contraindicated in patients undergoing cardiac or vascular surgery, and in patients at high risk of cardiovascular disease (including patients with diabetes, ischaemic heart disease, cardiac failure, hyperlipidaemia, hypertension, or smokers) who are undergoing major surgery.

**Table 2. Absolute contraindications to NSAIDs**

| • Ischaemic cardiovascular disease |
| • Severe hypertension |
| • Severe liver disease |
| • Severe diabetes |
| • Allergy to NSAIDs / (sulphonamide ~ COX-2) |
| • Peptic ulcer disease (COX-1) |

There is, however, no indications as to the severity of such risk factors and the perioperative team is left with a recommendation to weigh the risks and benefits in each individual case and an obligation to inform the patient of any intended perioperative use of coxibs.
It is worth remembering that all NSAIDs hold a potential to aggravate any pre-existing heart failure and hypertension due to fluid retention through renal effects. It is also worth noting that patients should continue low-dose acetylsalicylic acid if a COX-2 inhibitor is prescribed to maintain a cardioprotective/antiplatelet effect, as this is not offered by COX-2 inhibitors.

Ibuprofen and indomethacin may impede access of aspirin to platelet COX-1 enzyme and inhibit this protective effect. Furthermore, the addition of low-dose acetylsalicylic acid will remove any “gastroprotective” effect of the COX-2 inhibitor.

Patients with a history of peptic ulcer disease may well benefit from the perioperative use of coxibs if a NSAID is indicated. An alternative approach to coxib prescription for the patient with gastrointestinal intolerance to NSAIDs is the concomitant use of a proton inhibitor or misoprostol as mucosal protection. Patients on continued perioperative acetylsalicylic acid should also receive gastroprotection during COX-2 inhibitor treatment.

Another major concern of perioperative NSAID use is the potential for renal impairment. Both COX-1 and COX-2 activity is expressed in the kidney, and in the marginally failing kidney, any class of NSAIDs may cause deterioration of such failure. It has been stated that the physiological function of COX-1 in the kidney is mainly in maintaining the glomerular filtration rate (GFR), whereas COX-2 is primarily involved in water and electrolyte haemostasis.

Side effects such as acute renal failure, papillary necrosis, and nephrotic syndrome are extremely rare with NSAID therapy in the uncompromised patient. Although mild side effects such as hyperkalaemia and fluid retention, and minor increases in blood pressure, are seen they are readily reversible with discontinuation of the drug. Furthermore, interactions with antihypertensives and diuretics warrant caution in patients concomitantly treated with these drugs.

Patients who should not receive either non-selective nor COX-2 selective anti-inflammatory are the ones with preoperative renal dysfunction or a renal perfusion compromise (e.g. hypovolaemia, severe liver or heart failure, and advanced hypertension or diabetes).

Continuous perioperative monitoring of creatinine and urea during NSAID therapy is warranted in patients with hypertension and mild diabetes and also in the very elderly. There are some indications, however, that COX-2 inhibitors may prove safer in these patient groups, but more data is needed before any recommendations can be made.

NSAIDs are contraindicated in patients with a known allergy to this group of drugs. As celecoxib and parecoxib contain a sulphonamide moiety, they are contraindicated in patients with a known allergy to sulphonamides. Of the asthmatic population, only 10–15% are actually reactive to the effect of NSAIDs, partly related to their diversion of the arachidonic acid cascade towards bronchoconstrictory leucotrienes.

A simple questioning of the patient prior to surgery of any NSAID usage in the past will often solve the concern. If the patient is an asthmatic and never challenged with NSAID, the perioperative period is perhaps not the ideal time to test the system. In addition, COX-2 selectivity does not seem to confer any advantage in these patients.

The use of NSAIDs in orthopaedic surgery is controversial—some experimental work points to NSAIDs having an inhibitory effect on bone healing. However long
experience and a widespread use of NSAIDs after fracture surgery has not highlighted any clinical problem.

Some evidence points to a negative impact of NSAIDs after spinal fusion surgery but most of the scarce literature has not corrected for confounders such as smoking which has a major impact on bone and soft tissue healing.\textsuperscript{39–41} Whilst awaiting prospective, randomised clinical trials, no clear recommendations can be given, although the prudent healthcare professional might consider avoiding NSAIDs in orthopaedic cases involving bone grafting.

As the coxibs may interfere with the cytochrome P-450 enzymatic system, other drugs depending on this enzyme for their metabolism may be adversely affected.\textsuperscript{42} Anticoagulation therapy with warfarin can thus be potentiated and the dosage may have to be adjusted in those cases where a NSAID (COX-2) is deemed of major benefit—but the classic NSAIDs are contraindicated due to their antithaemostatic effect.

The risk of haematoma formation with the use of neuraxial blocks (i.e. spinals and epidurals) and the concomitant use of NSAIDs has been a matter of concern. International consensus holds that non-selective NSAIDs (including acetylsalicylic acid) do not per se contraindicate neuraxial techniques. But as combined with low-molecular weight heparins and/or other “weak” anticoagulants, the risks of bleeding does increase.

Full anticoagulation (e.g. coumarins) contraindicate neuraxial techniques irrespective of NSAIDs. Combination of NSAIDs and the newer anti-platelet drugs (e.g. clopidogrel, ticlopidine) markedly increase the risk of perioperative bleeding and should be avoided. Interestingly, several complementary and alternative medicines (e.g. garlic, ginko, ginseng) are platelet inhibitors so it is currently recommended that their use is stopped before surgery and that the are not used together with classic NSAIDs.\textsuperscript{43}

**Perioperative use of classic NSAIDs**

NSAIDs are an integral part of a multimodal and preventive, perioperative analgesic regimen. It is, however, only a relatively small proportion of patients who will benefit from selective COX-2 inhibition for perioperative analgesia.

Gastric ulcer disease (GI intolerance to non-selective NSAIDs) or surgical request for minimal platelet inhibition (e.g. plastic surgery, neurosurgery, ENT surgery) may warrant the use of perioperative selective COX-2 inhibition. The combined use of NSAIDs and paracetamol has proven highly cost-effective and with a desirable opioid sparing effect, not least in day-case surgery.\textsuperscript{1,37,44–45}

Of the classic NSAIDs, ibuprofen in appropriate oral dose (i.e. 400–800 mg tds), diclofenac (50 mg tds), and iv tenoxicam (e.g. 20–40 mg intraoperatively) have a long and well-established place in perioperative analgesia. Together with paracetamol, a NSAID can be incorporated into a cost-effective “take-home pack” for day-case surgical patients (e.g. paracetamol 1 g qid with ibuprofen 400 mg tds for 3 days’ use).

It is notable that merely being a child is no contraindication to the use of NSAIDs. Indeed, no evidence suggests that paediatric surgery patients tolerate NSAIDs to any
lesser extent than adults; otherwise healthy children may well benefit from the perioperative use of NSAIDs, often in combination with paracetamol.

Judicious consideration of indications, side effects, and contraindications is as appropriate as in the adult surgical patient.\textsuperscript{46,47} Interestingly, a recent study showed less analgesic efficacy of a COX-2 inhibitor (rofecoxib) than ibuprofen in a paediatric tonsillectomy population although any potential haemostatic advantage of a COX-2 inhibitor was not further discussed.\textsuperscript{48} COX-2 selective NSAIDs are currently not recommended in NZ for age groups under 18 due to lack of valid data on dose-effect relations.

Supplemental drugs such as $\alpha_2$-agonists (e.g. clonidine), NMDA receptor antagonists (e.g. ketamine), tramadol, and gabapentin are emerging as facilitating perioperative analgesics and their possible combination with NSAIDs is under intense scrutiny. A more procedure-specific approach to perioperative analgesia has recently been suggested.\textsuperscript{49} Eventually, recommendations for analgesic regimens involving or not involving NSAIDs or COX-2 inhibitors may emerge.

We may have gone two steps forward and one step back, but the judicious use of the entire group of NSAIDs (selective and non-selective) in postoperative pain remains to be determined in the future.

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**Acknowledgement:** I am grateful to Dr R Rarity for his valuable input and proofreading.

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**References:**


Managing squamous cell carcinoma of the bulbomembranous male urethra with genital-preserving surgery and chemoradiotherapy

Alison Finall, Martha Nicholson, John North, Kampta Samalia

Invasive squamous cell carcinoma (SCC) of the bulbomembranous urethra is rare. Radical disfiguring surgery is often recommended to control this aggressive disease, with subsequent 5-year survival rates of 5–15%.1 Evidence regarding treatment using genital preserving surgery and coordinated chemoradiotherapy is scarce. We report a case of SCC of the bulbomembranous urethra managed using this less mutilating method; results were encouraging.

Case report

A 62-year-old sexually active man presented in December 2004 with a recurrent episode of obstructive urinary symptoms secondary to a benign stricture of the bulbomembranous urethra. The stricture was related to traumatic postoperative urinary catheter insertion in July 2000 and was initially diagnosed by rigid cystoscopy.

Eight subsequent dilatations were required over the next 4 years, each time with a benign cystoscopic examination. Abdominal, perineal, and per rectal (PR) examination were normal. A buccal patch urethroplasty was planned as definitive treatment for February 2005.

Figure 1. Descending urethrogram of patient showing stricturing of the bulbomembraneous urethra
During surgery, examination of the stricture had become abnormally hard in texture. Frozen section suggested transitional cell carcinoma with extension into periurethral tissues. Consequently, the urethra was excised from the base of the prostate to meatus with adjacent periurethral tissue. A postoperative staging CT scan of the chest, abdomen, and pelvis showed no evidence of lymph node or distant metastases.

A definitive diagnosis of poorly differentiated squamous cell carcinoma was made on haematoxylin and eosin (H&E) histological section. There was microscopic involvement of the proximal resection margin, in addition to perineural and lymphovascular invasion. He had significant risk of occult metastases to pelvic and inguinal lymph nodes and was staged as having T4 N0 M0 disease (Stage C, Ray’s classification).¹

The patient subsequently received 40 Gy / 20 fractions to the lower pelvis and urethra, plus a 10 / 5 boost to the perineum, and 2 cycles of mitomycin C (10 mg/m² stat day 1) and 5 fluorouracil (5FU) (1000 mg/m² daily x 4 days, days 1–4), 4 weeks apart. He had no evidence of recurrence 13 months from diagnosis.

Discussion

The aetiology of SCC of the male urethra appears to have an association with the presence of HPV 16.² Other chronic inflammatory conditions, such as urethral condylomas and urethral stricture disease, as in this case, also have an association.³ Definitive diagnosis is made by biopsy. Voided urine cytology is not a useful diagnostic tool.⁴

Patients with locally advanced squamous cell carcinoma of the bulbomembranous urethra fare poorly with radical surgery or primary radiotherapy.¹

The use of chemoradiotherapy in the treatment of SCC of the anus, penis, and oesophagus has a well-established base in evidence.³ There is a small amount of evidence regarding a variety of chemoradiotherapy regimes in the treatment of urethral SCC.⁵–⁷ For comparison, we describe two using mitomicin-C and fluorouracil specifically.

Lutz and Huang (1995) treated a 47-year-old man with gonococcal urethritis and a poorly differentiated SCC (Stage 4, T4N2M0).⁸ Mitomycin C, 5-fluorouracil, and radiotherapy caused marked regression of the tumour. He had no clinical evidence of disease 16 months after diagnosis.

The second publication by Oberfield et al (1996) describes two similar cases.³ A 42-year-old man with moderately differentiated stage C disease (T4N0M0) was given 5FU, mitomycin C and radiation of 45Gy to the primary site and groin regions. The patient went into full remission for 18 months. The second patient, a 49-year-old man diagnosed with a 6 x 4 cm proximal bulbous urethral SCC (Stage C, T4N0M0) was treated similarly. This man survived disease-free for 4 years.

Our findings add to the evidence in favour of using chemoradiotherapy in conjunction with genital-preserving surgery for the treatment of this unusual malignancy.
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References:


Quality improvement in New Zealand healthcare. Part 6: keeping the patient front and centre to improve healthcare quality

Gillian Robb, Mary Seddon; on behalf of EPIQ*

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Abstract

Patient-centred care is arguably the most important of the dimensions of quality as it is likely that a healthcare system which is patient-centred will also perform well against the other dimensions—safety as well as timely, accessible, effective, and efficient care. What does it mean to be patient-centred and how can it be achieved?

This article explores several definitions of patient-centred care and discusses two interpretations—the expert patient and shared decision-making. Being sick is inherently a vulnerable position to be in and our current healthcare system does little to recognise and alleviate this vulnerability. But the patient-centred approach is about more than making the journey for patients less tortuous, it has actually been shown to improve outcomes. The evidence of benefit for a patient-centred approach is reviewed, along with some of the challenges in implementing the concept in practice.

Most providers will see themselves as patient-centred—patients are the reason for coming to work. But many of our structures, particularly in hospital-based care, conspire against effective patient-centred care. For example, restrictive visiting hours create barriers for family to support patients at times of great anxiety and limit opportunities for providers to discuss management options with patients and their families.

A simple rule of “keeping patients and their loved ones together through the care process” would lead to entirely different designs compared with the rule that patients don’t belong in technical areas or that wards should be quiet in the mornings.1

In primary care, lack of timely access to care and short rushed visits create dissatisfied patients and frustrated doctors. Alternative reimbursement systems could provide greater flexibility in the delivery of care. For example, team members other than doctors, using web and email patient portals, could perform routine preventive care and manage some patients with chronic conditions.2 This would free up time for doctors to provide better access for visit-based care (where appropriate), and to improve the quality of the consultation.

Recognition that non patient-centred care is rife has contributed to the call for patient-centred care to become a policy priority in most healthcare systems. This has been reinforced by challenges to traditional medical paternalism and increased access to health information, along with the rise of consumerism and knowledge that patients experiences are potentially powerful levers for quality improvement.3,4
In New Zealand, the Code of Health and Disability Services Consumers’ Rights Regulation 1996, developed in response to the Cartwright Report of 1988, established patient-centred care as a priority. The Bristol Enquiry led to the British Government placing improving patients’ experiences higher up the agenda, thus making it the central theme of its plan for the National Health Service (NHS) in 2000.

In the United States, following publication of the report *To Err is Human*, the Institute of Medicine (IOM) published a second report calling for a complete redesign of the healthcare system to make it more patient-centred. They analysed the needed changes in terms of four levels of healthcare:

- **Level A**: The experience of patients.
- **Level B**: The functioning of small units of care delivery (microsystems).
- **Level C**: The functioning of organisations.
- **Level D**: The environments of policy, payment, regulation, accreditation, and professional training.

Levels A and B are where patients and the healthcare system interact; organisations support the microsystems that deliver care and these in turn are supported by the healthcare environment. While changes are required at all levels to improve quality, it is the “experience of patients, their loved ones, and the communities in which they live” which are the “true north” of the model.

In other words, actions taken at levels B, C, and D should be measured in terms of their effects on the patient experience “and in no other way”. This message has been reiterated by Ron Paterson, Health and Disability Commissioner for New Zealand. He suggests that the first question whenever a policy issue arises for public debate should be:

“How will this proposal affect the health and wellbeing of the community?”

**Definitions**

Patient-centred care—a simple “sound bite” but a complex concept. It is most commonly described in terms of what it is not—disease-, doctor-, technology-, or hospital-centered. Various terms are often used in association with the concept of patient-centred care, such as “shared decision making”, “integrated medicine”, “empowerment”, “informed choice”, “dignity in healthcare”, “concordance”, and the “expert patient”.

In New Zealand, the Ministry of Health’s *Improving Quality* document talks about “people-centred” rather than patient-centred care, and defines this as:

…the extent to which a service involves people, including consumers, their families and whanau and is receptive to their needs and values. It includes participation, appropriateness and adherence to the Code of Health and Disability Services Consumer Rights 1996 and adherence to other consumer protections such as the Health Information Privacy Code 1994.

By alluding to the Code of Health and Disability Services Consumer Rights 1996, it acknowledges patients rights’ as integral to patient-centred care, a common omission in other definitions. The words “the extent to which a service involves people” implies an application of patient-centred care beyond the patient practitioner.
interaction, thus reflecting to some extent the importance of collaboration between patients, families, healthcare practitioners, and hospital leaders in all aspects of healthcare at all levels of the healthcare system.\textsuperscript{12}

The Picker Institute, an international organisation which seeks to improve the quality of healthcare by considering the patient experience, has identified what they believe a patient-centred service should deliver:\textsuperscript{13}

- Fast access to reliable health advice.
- Effective treatment delivered by trusted professionals.
- Participation in decisions and respect for preferences.
- Clear, comprehensible information and support for self care.
- Attention to physical and environmental needs.
- Emotional support, empathy, and respect.
- Involvement of and support for family and carers.
- Continuity of care and smooth transitions.

This definition is useful to the extent that it operationalises (to a degree) the definition of patient-centred care for a service.

These definitions of patient-centred care demonstrate similar themes (see Box 1), and are indicative of a fundamental shift in the balance of power in the patient-practitioner relationship—from patients as passive recipients of healthcare to patients as active participants with guaranteed rights.

There is, however, now an emerging discussion in the literature however about patients’ responsibilities, particularly with reference to the growing costs of unhealthy lifestyles and the fact that patients can actively influence the outcomes of care both for good and for bad.\textsuperscript{14} These are important issues, but such discussions must take account of the fundamental inequality of information, expertise, and power that persists in the patient practitioner relationship.

Being sick is inherently a vulnerable position to be in. Kelley argues that placing more emphasis on professional responsibility is “largely correct” and emphasises the importance of a cautious approach to patient responsibility based on persuasion and encouragement rather than blaming patients for past behaviour.\textsuperscript{15}

\textbf{Box 1. Common themes in patient-centred care}

- Informing and involving patients.
- Eliciting and respecting patient preferences.
- Engaging patients in the care process.
- Treating patients with dignity.
- Designing care processes to suit patient needs, not providers.
- Ready access to health information—both paper and electronic.
- Continuity of care.
Models of patient-centred care

Patient-centred care has mostly been described in the context of chronic disease management (e.g. diabetes) in primary care. The concepts of the expert patient and shared decision-making are models of patient-centred care.

**The expert patient**—The “Expert Patient Programme” (EPP) is an initiative implemented in the UK by the NHS. Its intent is to enhance patient autonomy and reduce reliance on limited healthcare resources by promoting the need for patients to be more actively engaged in managing their own conditions.\(^{16}\)

The EPP is based on models of chronic disease self management developed at Stanford University\(^{17}\) and successfully tested in the 1990s.\(^{18}\) It involves a structured 6-week training programme designed to give people the confidence, skills, and knowledge to manage their disease and to minimise its impact on their everyday lives. Expert patients are those who “take responsibility for the day-to-day decisions about their health and who work with healthcare providers as collaborators and partners to produce the best possible health given the resources at hand.”\(^{17}\)

The UK NHS piloted and evaluated the EPP between 2001 and 2004. Self reported data from participant questionnaires before and after the programmes suggested improvements in levels of confidence in managing pain, tiredness, depression, and breathlessness; reductions in GP visits, A&E attendances, and outpatient appointments; and improved compliance with medication and other treatment regimes.\(^{18}\)

The programme has not, however, been without its critics.\(^{16,19}\) Questions have been raised about the extent to which a patient can be considered an “expert” and the implications for healthcare practitioners in accepting patients taking a more active role in their care.\(^{19}\) Some of these concerns can be addressed by understanding the distinction between illness and disease, as expressed in the old adage, “you go in to the doctor with an illness and come out with a disease.”\(^{16}\)

Illness is what the patient experiences. They bring the knowledge of their condition (gained from a variety of sources) to the patient/practitioner encounter, as well as their unique experience of their illness described in terms of symptoms; how these impact on their quality of life, how they manage these on a day-to-day basis, and what recovery or healing might mean to them. In this respect, they may indeed be considered “expert” in the sense that they understand their illness as they experience it and manage it.

In contrast, doctors understand and manage diseases. This requires a technical expertise based on knowledge about the pathophysiology of disease as well as diagnostic and treatment procedures. This technical expertise is enhanced by the skill that experienced practitioners, in particular, have in coping with uncertainty and atypical presentations. This key professional attribute, important in medical decision-making, has been called “phronesis”, defined as “the ability to make good decisions and take effective action in unfamiliar situations”.\(^{16}\)
In the context of the EPP which calls for collaborative partnerships between patients and practitioners, more effective collaboration is possible when there is a clear demarcation of areas of expertise and responsibility.\textsuperscript{16}

Ashkam and Chisholm elaborate further on this distinction in their paper \textit{Patient-centred medical professionalism}. They explore the basic concepts underpinning the notion of patient-centred care, namely what it means to be a patient (lay medical role) and what it means to be a doctor (medical professionalism). Furthermore, they identify where the interests and preference of each intersect and where further research is needed to resolve areas of conflict.\textsuperscript{20} This type of research should contribute to a better understanding of the issues at stake, and facilitate the implementation of structures and processes that support collaborative partnerships between patients and practitioners in any setting.\textsuperscript{20}

\textbf{Shared decision-making}—Shared decision-making is another model of patient-centred care which has relevance across a broader spectrum of healthcare provision including prevention, acute, chronic, and palliative care. From an ethical perspective, it promotes patient autonomy and self determination and promotes trust in the patient/practitioner relationship. A more informed patient has more realistic expectations, having weighed their personal preferences and values with information about the benefits and harms of the proposed management.\textsuperscript{21}

Shared decision-making is the process of interacting with the patient to assist the patient to make an informed choice.\textsuperscript{22} Various models have been described, most of which include the patient’s right to relinquish the decision in varying degrees to the clinician, recognizing that the extent to which patients contribute to the decision-making process will vary according to the patients personal characteristics (age, gender, education, and ethnicity), the practitioners communication style, the health condition, and the clinical setting.\textsuperscript{23}

There also needs to be some consideration of the of the differential power in the relationship, given the doctor’s role in legitimising the ability to work, drive, and receive benefits and the fact that they are the gate keepers for healthcare resources.\textsuperscript{19}

The World Health Organization’s\textsuperscript{24} “5 As” framework (Box 2) offers a systematic approach to shared decision-making which has particular application in preventive and chronic care to ensure consistency of care.\textsuperscript{21} Many clinicians will recognise these steps as part of their everyday practice.

\textbf{Box 2. A systematic approach to shared decision-making}

<table>
<thead>
<tr>
<th>ASSESS</th>
<th>Patient’s health needs and their desired role in decision-making.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVISE</td>
<td>Inform the patient about recommended preventive service or management options. If needed, provide balanced evidence-based information about the service, the benefits, harms, alternatives, and areas of uncertainty.</td>
</tr>
<tr>
<td>AGREE</td>
<td>Elicit the patient’s values and determine preferences, then negotiate a course of action.</td>
</tr>
<tr>
<td>ASSIST</td>
<td>Deliver service or prescribe appropriate management.</td>
</tr>
<tr>
<td>ARRANGE</td>
<td>Organise follow up and continuity of care.</td>
</tr>
</tbody>
</table>

Adapted from Sheridan et al.\textsuperscript{21}
The shared decision-making model is particularly relevant when there are two or more medically reasonably alternatives, such as ‘radical prostatectomy versus radiation treatment for prostate cancer’ or ‘watchful waiting versus surgery for chronic cholecystitis’. This has been called “preference-sensitive” care. Evidence-based decision tools (designed to provide up-to-date information about the risks and benefits of the available options) assist patients in the decision-making process and help patients clarify their values and preferences. Failure to base the choice of treatment on the patients’ preferences and values in this case has been termed “misuse” which sits alongside underuse and overuse as examples of poor quality care.

The success of achieving an informed and joint decision can be measured in terms of the extent to which the patient:

- Understands the risk or seriousness of the disease or condition.
- Understands the risks, benefits, alternatives, and uncertainties of the preventive service or management options.
- Has weighed his or her values and preferences.
- Has engaged in decision-making at the level he or she desires and feels comfortable with.

What is the evidence for a patient-centred care approach?

In terms of health outcomes, the evidence base for patient-centred care is growing (see Box 3). Studies have shown that there are benefits in terms of patient satisfaction, adherence to best-practice protocols, reduction of anxiety, and improved quality of life.

### Box 3. Benefits of patient-centred care

- Improved patient satisfaction.
- Improved patient compliance and engagement in health process.
- Reduced anxiety.
- Improved quality of life.
- Improved efficiency of care (decrease in inappropriate tests, treatment, and GP visits).

Interventions that have provided patients with training in information-seeking and negotiating skills have resulted in improvements in symptoms and outcomes. Expert patient models of care in diabetes has resulted in better blood sugar control and quality of life. There have also been benefits in terms efficiency through fewer diagnostic tests, unnecessary referrals, and treatment.

A Cochrane review of interventions to promote a patient-centred approach in clinical consultations found some evidence for improved patient-centredness of care, but also found mixed evidence about the effects of such interventions on patient healthcare behaviours or health status. The review noted that the included studies varied...
considerably in terms of types of interventions, the clinical conditions, the comparisons made, and outcomes assessed; and methodological quality was generally poor.

A comprehensive review of studies relating to chronic care management (560 systematic reviews, randomised trials, and other studies) found evidence for involving people with long-term conditions in decision-making, providing accessible information, self management education, and self monitoring and referral systems.\textsuperscript{31}

**Barriers**

Numerous barriers to achieving patient-centred care have been described: the design of healthcare systems, poor communication skills, attitudes of doctors, inadequate training of health professional, limited resources (people, time, and money), lack of information in an accessible format to patients, failure to involve family and friends, lack of integrated care, lack of patients rights, and so the list goes on.\textsuperscript{11}

In addition to physician and structural barriers to patient-centred care, there are also barriers for patients in actively engaging in making decisions about their healthcare. Lack of understanding about the nature of medicine as an “inexact science” and limited understanding of medical concepts such as “risk”—and what words such as “some” and “likely” mean—are confusing even for the more numerically literate patients.\textsuperscript{21} Lack of awareness of treatment alternatives, coupled with inexperience and discomfort in engaging with clinicians in this way represent common reasons why patients may fail to engage fully in healthcare decisions.\textsuperscript{21}

Social, linguistic, and cultural attributes have also been cited as barriers.\textsuperscript{3} It is worth remembering that the concept of patient-centred care originated in North America and Europe and may have limited relevance for some patients.\textsuperscript{11} For example, ethnic groups who do not value autonomy may also be reluctant to engage in shared decision-making.\textsuperscript{21}

**Conclusions**

Patient-centred care is one of the most important dimensions of quality; in fact adhering to its principles can help drive those dimensions—making healthcare safer, more accessible, and timely; more equitable and effective (including the concept of appropriate care); and even more efficient. However, it is clear that the concept of patient-centred care is complex and contested. Its effective implementation is impeded by the variety of understandings, lack of leadership from policy makers, and the divergence of views between clinicians and managers.\textsuperscript{3}

The expert-patient approach has been adopted in the UK and is best suited to patients with chronic care conditions. Shared decision-making is another approach and is useful when there are competing alternatives. These approaches do not decrease the importance of practitioners skilled in biomedical science with up-to-date knowledge of evidence-based diagnosis and management. But they do require additional skills—especially in effective communication—that allow practitioners to be guides to their patients.

For the clinician this is not about ‘behaving correctly” but about practicing sound medicine by engaging the patient in a way that provides additional information to achieve the desired outcome for the patient.\textsuperscript{33}
Some of the structures and the way that we organise care are in conflict with patient-centred care. For this to change, the meso and macro levels of healthcare need to pay more than lip-service to patient-centred care. In the broadest sense, the phrase “nothing about me without me” expresses the ideal of patient-centred care in which patients work together with health professionals as “full partners to design and implement change”.

**Conflict of interest:** No conflict.

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**References:**

Notes on cholelithiasis—Case 3

This case report was one of several written by Dr Martin and published in the New Zealand Medical Journal 1907, Volume 5 (21), p9.

Case 3 was that of a young woman of 35, whom I saw during an attack of bilious colic. She was screaming with agony when I saw her, and tossing about from one side of the bed to the other. She would not let me examine her on account of the great pain. She was deeply jaundiced, the whole body was of a dusky yellow, and the conjunctiva was yellow with 2 or 3 small spots of haemorrhage in it dotted over either eye.

I at once administered chloroform, and when she was, half under it, gave ½ grain of morphia hypodermically. That evening I again saw her, and the pains were again coming on. She was again given another ¼ grain of morphia and sent to the Public Hospital.

A week afterwards, under an anaesthetic administered by Dr. McIntire, the usual incision was made, and the gall bladder and ducts exposed. Three small facetted calculi were removed from the gall bladder and one from the common bile duet. The common bile duct was opened directly on the calculus, which was then removed by squeezing it out. The incision into the duct was then closed by two layers of cat-gut stitches A tube was fixed into the gall bladder and the bladder was then stitched to peritoneum and fascia in the usual way The lower part of the wound was stitched, and no strain of any sort was left round the incision made into the duct. She left the Hospital quite well six weeks after the operation.

This woman had been a martyr to the terrible attacks of biliary colic for the three years previously. Latterly they came on about every month. His life was a misery till after the operation.

The gall bladder was small and shrunken, and its walls were very thick. There were no adhesions except some omentum round the gall bladder. This woman was extremely collapsed after the operation. For 24 hours she had a weak thready pulse, was semi-conscious, and was bathed in a cold clammy perspiration. Strychnine and camphor were given freely, rectal saline and nutrient enemata, every four hours. She then gradually recovered from the shock of the operation.
Extensive oral ulcerations

Nadir Goksugur, Fahrettin Yilmaz

A 40-year-old woman presented with fatigue and labial crusts, ulcerations, blister remnants, and multiple painful ulcerations in the floor of her mouth, tongue, buccal mucosa, and soft palate, all on a background of an erythematous mucosa for 1 week (Figure 1).

Figure 1

The medical history revealed that the patient had had psoriatic arthritis and psoriasis vulgaris for 12 years. She commenced a once-weekly dose of methotrexate 10 mg 6 months earlier. Although she had responded well initially, her psoriatic arthritis had worsened 1 month before admission. Then, by her own decision, she took methotrexate 10 mg daily for about 20 days.

On admission, laboratory studies showed hematocrit 34.9%, white blood cells 1,700/mm$^3$, platelets 168,000/mm$^3$, erythrocyte sedimentation rate (ESR) 45 mm/h,
C-reactive protein 20.5 mg/dL, ALT 980 UI/L (N<45), AST 587 UI/L (N<40), GGT 85 UI/L (N<35), and LDH 556 UI/L (N<190).

Initial clinical impression was suggestive for erythema multiforme or Stevens-Johnson syndrome but our patient did not have any other skin finding such as target lesions.

Other mucosal surfaces (genital and ocular) were intact and viral infections were ruled out. So we assumed that methotrexate was the culprit for toxic hepatitis and oral mucositis and thus it was stopped.

Mupirocin ointment for lips, chlorhexidine gluconate, and benzydamine hydrochloride mouthwashes for oral mucosa were started for symptomatic relief. One week later, all blood parameters returned to normal levels and mucosal ulcerations were partially resolved (Figure 2A). At review (after 3 weeks), the patient’s symptoms and ulcerations had resolved almost entirely (Figures 2B, C, D).

Figure 2

Methotrexate is increasingly being used in the management of chronic inflammatory disorders, however practitioners should be mindful of possible liver toxicity and mucosal side effects.

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High-dose atorvastatin for stroke prevention

Statins, in general, are widely accepted as appropriate treatment for those with cardiovascular and cerebrovascular risk factors. In this report, the results of treatment with high-dose atorvastatin (80 mg/day) vs placebo are assessed in patients who have had a recent stroke or transient ischaemic attack (TIA). Unsurprisingly, 80 mg of atorvastatin per day reduced the overall incidence of strokes and of cardiovascular events, but there was a small increase in the incidence of haemorrhagic stroke.

An accompanying editorial was critical of the patient inclusion criteria and remarked that “the absolute benefit of treatment with atorvastatin was relatively modest.” Although the editorial commentator was not rapt with the high-dose atorvastatin, he strongly favoured the adoption of statin therapy into guidelines for treatment of ischaemic stroke.


And more about statins—atorvastatin vs simvastatin

Statins are one of the great success stories of preventive medicine. Extensive evidence, excellent safety, and high efficacy have resulted in an exponential rise in prescriptions for statins, currently increasing at 30% a year in England. Statins represent the largest drug cost to the NHS (£78 million [Euros1.1bn; US$1.4bn] in 2004).

Similar trends in New Zealand also—simvastatin is the second most prescribed medicine (945,783 scripts in 2005) and the total cost of lipid-modifying agents in 2005 was over NZ$60,000,000. We, in New Zealand, use simvastatin as it is fully funded. Atorvastatin can be obtained under special authority—albeit, with difficulty.

The author of this paper advocates the replacement of atorvastatin with simvastatin. In support, he quotes a head-to-head comparison of atorvastatin and simvastatin, which although underpowered, showed no difference between the drugs. And a meta-analysis of clinical trials using simvastatin 40 mg and atorvastatin 10 mg and 20 mg showed no significant differences in mortality, death from coronary heart disease, or stroke. And the punchline—using generic simvastatin as first line could save £2bn over five years in England.

PS—Paradoxically, in New Zealand, 40 mg of simvastatin is more expensive than 10 mg of atorvastatin.

BMJ 2006;332:1344–5
C-reactive protein (CRP) and cardiovascular disease

CRP, the classical acute-phase protein, is well known as a marker of inflammation and tissue damage. It is commonly used to detect subtle inflammation and some believe that it is predictive of impending myocardial infarction.

In this report, British researchers assert that CRP binds to ligands exposed in damaged tissue and then activates complement and increases myocardial infarct size in rats subjected to coronary artery ligation. They have developed a specific small-molecule inhibitor of CRP which abrogates the increase in infarct size and cardiac dysfunction produced by injection of human CRP.

Excellent, but, only in rat experiments! However, you have to start somewhere.

Nature 2006;440:1217–21

Use it or lose it—again

Observational studies have shown that older adults who report low physical activity levels are at elevated risk of mortality compared with those who report moderate or high levels of activity.

So what about the reverse? Does activity prolong life? An international gerontology study group documented the free-living activity energy expenditure in 302 high-functioning, community-dwelling older adults (aged 70–82 years). And you guessed it—those elderly US adults, who burned more energy, had a significant lower risk of death over a mean follow-up of six years.

Very encouraging for the healthy elderly, but unhelpful for those who cannot burn energy because of ill health.

JAMA 2006;296:171–9

Emerging emergency-medicine crisis

Overcrowding, hospital-bed shortages, and lack of specialist coverage in many emergency departments is a frequently heard theme, not only in New Zealand but elsewhere. Why? For a variety of reasons but the most compelling is that these departments provide far more than just urgent care for trauma and medical emergencies. Increasingly, they are called on to offer services that in the past were provided by personal physicians. As a result, emergency department staff and resources are often stretched to the limit.

Apparently it is particularly bad in the USA where it is sometimes necessary to direct ambulances to other facilities farther away, putting critically ill patients at increased risk.

In some respects, the situation in the USA is unique. Because 41 million people (about one in seven) have no health insurance, many seek help in emergency departments when they need medical care.

Lancet 2006;367:2033
New Zealand should control *Campylobacter* in fresh poultry before worrying about flies

The possible role of flies in the aetiology of human campylobacteriosis in New Zealand was the focus of a recent *Journal* article by Nelson and Harris.\(^1\) This is not a new hypothesis,\(^2\) so we were surprised to see it being raised again without specific data to support it.

Such speculation contrasts with the well established role of contaminated food products (and particularly fresh poultry) as the major risk factor for campylobacteriosis in New Zealand as detailed in recent reviews.\(^3\)\(^4\) This evidence is based on New Zealand case-control studies of sporadic disease, one of which was a large multi-centre study.\(^5\)

Other published and unpublished New Zealand epidemiological studies of sporadic campylobacteriosis, and of outbreaks, provide additional support for the importance of food-borne transmission.\(^4\) Further to the epidemiological evidence, serotyping has revealed strains common to cases and poultry from New Zealand stores (including those stores at which cases shopped),\(^6\)\(^7\)\(^8\) and links with sausage,\(^10\) sheep liver,\(^11\) and sheep and beef offal.\(^12\) However, such serotyping work may still be of somewhat limited value owing to the likely genetic instability of the *Campylobacter* genome (e.g. uptake of extracellular DNA and DNA recombination). Even when considering campylobacteriosis outbreaks alone, food dominates over water-borne transmission.\(^4\)

None of the 13 published outbreak and 16 unpublished outbreak reports in New Zealand (that met the quality criteria for inclusion in a review) identified flies or fly-contaminated environmental surfaces as risk factors for campylobacteriosis.\(^4\)

Nelson and Harris suggest cow faeces as the major environmental source with a flies-fomites-fingers link to humans. If this was the case, we would expect to see much higher rates of illness in rural areas. Such a pattern is not observed.\(^13\)

There is no need to propose a role for flies to explain the elevated summer rates of campylobacteriosis in New Zealand.

Many other factors may be more important, including:

- The seasonal load of *Campylobacter* contamination in poultry flocks;
- Higher summer consumption of contaminated food used on barbecues and in salads (when it is not hygienically handled or thoroughly cooked); and
- Higher levels of contact with outdoor environments (including contaminated water) and with livestock.

However, the impact of the latter point may be minor, since notification and hospitalisation rates are highest in New Zealand cities,\(^13\) again consistent with the importance of food-borne transmission rather than from contaminated environments.

Nelson and Harris’ article also failed to explain how flies could account for the huge rise in campylobacteriosis over the past 20 years. Instead, it presented data showing
how the rise in campylobacteriosis notifications appeared closely correlated with increased consumption of chicken, which is a far more plausible explanation.

Informed scientific debate is highly desirable, but the kind of unsubstantiated speculation contained in the Nelson and Harris article can have negative consequences for public health. Indeed, it can reinforce a public perception that the sources of human Campylobacter infection are highly speculative, that every surface in their home environment is potentially contaminated, and that this disease is virtually unstoppable. This ‘miasma’ viewpoint is paralysing and easily exploited by interest groups which seek to divert attention from potential interventions.

Given the research evidence detailed above, the emphasis in this country should continue to be on reducing the levels of Campylobacter contamination in the food supply (e.g. particularly on poultry farms, in poultry processing plants, and in poultry in the distribution system). In fact, the bulk of government-funded research into campylobacteriosis control appears to relate to the food-borne transmission pathway (see the New Zealand Food Safety Authority website: http://www.nzfsa.govt.nz/).

Studies on the possible role of flies might be justified in the distant future, but only once the major sources of campylobacteriosis have been successfully controlled and control programmes evaluated.

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References:


Response

Eating raw or undercooked chicken and associated food contamination is not disputed as a risk for campylobacteriosis. Neither is suggesting another transmission route to be taken as justification for the chicken industry to make no attempt to reduce or eliminate Campylobacter contamination of their product. If we are to get on top of the problem though, we need to have an honest evaluation of facts.

We repeat, chicken production interruption in both Belgium (1999) and the Netherlands (2003) cut reported Campylobacter rates significantly, a calculated 40% reduction. That still leaves 60% with an unexplained source. Our flies/fomites/fingers hypothesis offers an alternative transmission route to explain a chicken-consumption link to illness, while at the same time also taking into account the many factors strongly discounting the source as being only and directly chicken.

Chicken as a direct source is heavily entrenched in the medical mindset. The “well established direct link” claimed is, at best, circumstantial. In its favour is the common knowledge that chicken meat is frequently contaminated, very low levels of organism constitute an infectious dose, and people who get sick have commonly eaten chicken recently. Chickens can provide some of the same strains as found in human cases, but this is not evidence of direction of transmission.

Outbreaks and their associated food or water-borne transmission routes represent about 10% of campylobacteriosis cases. Our paper focussed solely on the much more common sporadic cases. Food-borne causes of gastroenteritis frequently result in outbreaks of cases, not sporadic incidents as is usual with Campylobacter.
We made no claim to be first to involve flies in the transmission of *Campylobacter* to humans, nor for the idea that dairy cows are a significant source for *Campylobacter* in the environment. Prior credit is clearly indicated. We do however propose a fomite, finger addition to the transmission pathway.

The rural/urban aspect needs investigating, but no New Zealand city is far from a rural source of disease. Urban pets may yet prove a more common source than is currently fashionable to consider. An interesting coincidence to fomites and fingers is the hand to mouth suggestion recently postulated, although this retains chickens as source.¹

The marked increase in campylobacteriosis cases over the last 20 years was not part of our investigation. However, the increase in chicken consumption noted fits our hypothesis of food-associated transmission. The increase in dairy cow numbers also shows a somewhat similar trend (Figure 1). Far from being a paralysing viewpoint, washing hands before touching food is a key hygiene factor. We have merely tried to determine a plausible transmission route that also fits the known epidemiology and risk factors associated with eating chicken and sporadic campylobacteriosis.

**Figure 1. Campylobacter data as before, with dairy cow numbers added**

![Data from Livestock Improvement Company (http://www.lic.co.nz). Least squares linear regression fitted.](image)

The supposed genetic instability of *Campylobacter* is not supported by evidence. Specific subtypes are common from the Far East to Europe.² Genotype overlap
between humans and chickens has been reported as between 20% \(^3\) and 6%. \(^4\) Some virulence markers in *Campylobacter jejuni* show little commonality between humans and chickens.\(^5\) This should come as little surprise as a chicken flock is often colonised by a single or very few strains of *Campylobacter*.\(^6\)

Flies being eaten or contaminating food are a known source of *Campylobacter* for chickens.\(^7\) Flies are therefore a highly plausible vector between other environmental sources and chickens, or between chicken houses. Thus cows are a plausible source of environmental *Campylobacter* for both chickens and humans. Flies represent a common transmission agent too, although direct consumption by humans of flies is rare, hence the indirect fomite/fingers suggestion.

Recent calls for banning the sale of fresh chicken meat in New Zealand based on our high rate of campylobacteriosis do not have experimental evidence on their side.\(^9\) The weekly pattern of disease in the UK supports a hypothesis of food-associated (but not necessarily food-borne) transmission.\(^10\) Unfortunately, we cannot repeat this here as New Zealand statistics are on a monthly basis.

With the bulk of research funding already going on a food-borne approach, yet with only rising rates over 20 years to show for it, perhaps a broader target is justified. *Campylobacter*-free chicken meat is a desirable aim, but this is likely to only target the outbreak (10%) side of the equation. Chicken-association appears to be about 40% of cases.

Wilson et al seem to have missed the point of our paper and the authors apologise for apparent obscurity of expression. We hope this response will also aid others who might have missed these points. However, we are delighted with the widespread uptake of our main points by the popular press as it is individual diners who control what they ingest from their own fingers.

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Modern treatment for cholecystostomy

I was fascinated to read of the case report from 100 years ago in the 8 September 2006 issue of the NZMJ where a 42-year-old man, who suffered intermittent biliary colic for 1 year, was treated successfully by cholecystostomy.

The treatment these days is much easier. He would simply be removed from the waiting list after 6 months.

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What is health?

Health is metabolic efficiency. Sickness is metabolic inefficiency. Nobody is totally healthy or totally sick. Each of us is a unique combination of health and sickness. And each of us has a unique combination of abilities and disabilities, both emotional and physical.

As we grow up, we learn that we are loved for our abilities but hated for our disabilities. This happens at home, at play, at school, and at work. Sometimes, this even happens with our doctors, especially if our disabilities mystify them or remind them of their own disabilities.

So, we try to hide our disabilities from people and from ourselves. This charade undermines our relationships and our self-esteem. We learn to fear society and hate ourselves.

Self-hatred is the most debilitating sickness. It interferes with our ability to seek and accept help. And everybody needs help. How do we free ourselves from self-hatred?

First, we reclaim our disabilities, whether society accepts them or not. This means that we learn to accept ourselves. Then, we cope with our disabilities. This means that we learn to take care of ourselves.

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Eczema: What Really Works (the treatments and therapies that really work)


It is rewarding to be asked to review a book that I will be able to thoroughly recommend to patients. There is a profusion of well-intended but erroneous information about eczema in the community, and this book provides a practical, balanced, and evidence-based guide for patients and their parents.

The emphasis of the book is on atopic eczema in children as this disease forms a large proportion of clinical work, although mention is made of the other types of eczema. It is written mostly in a question and answer style.

The authors are a consultant dermatologist and a specialist dermatology nurse. Together they have covered the breadth and depth of eczema answering the “frequently asked questions” in an easily readable style with language that avoids medical jargon. There is a useful glossary at the back. The 14 chapters cover the pathogenesis, investigation, and both orthodox and alternative treatments. The final three chapters focus on school, social life, leisure, and importantly the psychosocial impact of eczema.

The book is up-to-date and with a chapter devoted to topical immunomodulators. The 2005 FDA black box warning about topical pimecrolimus and tacrolimus is not discussed, however. The authors work in the United Kingdom, and whilst both generic and commercial drug names are used, a number of the drugs mentioned are not available in New Zealand. The comprehensive resource section at the end only lists UK-based organisations.

This is a good book filling an important need. I suggest recommending it to enquiring, motivated families and patients who want good quality information, particularly if they have atopic eczema. My reviewer’s copy is just about to be donated to one such family!

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Verbal Medicine: 21 Contemporary Clinician-Poets of Australia and New Zealand

Tim Metcalf (ed). Published by Ginninderra Press (Canberra), 2006.

As Lois Lane retorted when Superman swooped down to save her from falling to certain death, “Yes, but who’s got you?” While the clinician-as-super-being protests a public image of unique resilience, the clinician-as-poet projects a more vulnerable persona.

Beyond the mythical and the political, Tim Metcalf’s anthology of 21 New Zealand and Australian clinician-poets offers poignant insights into the humanity that the mass media prefer to overlook. From Glenn Colquhoun’s “Haka to be used when reversing the effects of a general anaesthetic” to Andrew Leggett’s “Shower Scene” reflections of the infamous Mengele, Metcalf provides an intense glimpse into the all-too-mortal self-revelation of the empathetic clinician.

Metcalf’s clinician-poets have borne their practice beyond that shock/horror stage where self-medication, alcohol, and denial mask feelings of futility to a more reflective pinnacle. Nevertheless, recurrent images abound. Snatches of conversation imagined, “Now, Bubby, I’ve turned the electricity off …” culminate too frequently in Shen’s “…silence/ disrupted only by the twitching/ of the second hand of a wall clock.”

Fear, elemental tragedy and two in the morning images, however, contrast with lighter moments—as when incomprehension meets information overload, when metaphorical explanations of how pills work meet righteous indignation and the physician-frustrated, suggests that the “active metabolites in each pharmaceutical … worked by magic./ She asked me why I didn’t say that in the first place.”

Seeking to illuminate the empathy of the clinician, Metcalf’s selection balances Doris Brett’s powerful reflection on her own cancer, “Losing your hair as the year bled/ leaves, streaming and drifting,” with the torment of John West’s trainee surgeon who, against best advice, sees a dying baby on the table as a chrysalis who “had wings/ but the glue of her birth was keeping them closed.”

The personal is never far from the surface. Craig Powell’s ECT patients, who “glaze on their cool beds/ like dynamited fish.” suggest the reflective capacity that permeates the anthology. In contrast, Saxby Pridmore’s Coroner’s Delight where “Another patient hung himself/ in our ward today … Someone will have to pay.” offers the lighter side of this ‘laugh or you’ll cry’ selection.

As Metcalf observes in his introduction, “Only experience can make the voice lucid.” In consequence, “the scope of the poem … broadens and strengthens our human field, our reply to chaos, which is our intellectual life.”

The 21 clinicians offering various doses of Verbal Medicine provide a powerful collage of experience filtered and sensibilities unlocked to create a stimulating, even
challenging read. For those seeking a “reply to chaos”, Verbal Medicine offers an “essential interconnectedness”.

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