

# Cancer, lifestyle and chemotherapy

Dr Ian Gawler OAM, BVSc, MCouns&HS

Prepared with assistance from Dr Craig Hassed MBBS, FRACGP, Senior Lecturer, Department of General Practice, Monash University.

June 2007

## Cancer in context

Cancer is an illness which has an enormous impact upon the wellbeing of patients, their families, the healthcare system, and the wider community. Managing cancer requires a multi-disciplinary and holistic approach utilising evidence-based medical and surgical treatments, lifestyle advice and complementary therapies. This approach is best described as Integrative Medicine. The Gawler Foundation and its members are committed to working within the context of Integrative Medicine. This approach aims to foster the best outcomes for cancer patients, families and the community through informed decision making and the provision of quality skills, resources and information.

As difficult a problem as cancer is for patients and clinicians alike, the 2005 Senate inquiry into the management of cancer in Australia suggested that there is much room for improvement. Some of the main recommendations included:

- •Setting up and funding existing multidisciplinary cancer centres integrating holistic and Complementary Medicine (CM)
- •Recognising the need for patients to be informed about CM
- •NHMRC dedicating funding, personnel and support to CM cancer research
- •Making quality information more available to assist patients in making informed decisions about cancer management
- •That Cancer Australia examine funding mechanisms for programs and activities like those operated by The Gawler Foundation and give

consideration from a health and equity point of view of providing Medicare deductibility for cancer patients accessing these services.

**Incidence** Around 88,000 people are diagnosed with cancer annually.<sup>1</sup>

At any one time, about 267,000 people are living with cancer in Australia.<sup>2</sup>

This means that for every 100,000 people in the community, about 1,250 are living with a diagnosis of cancer, and about 440 new cases will be diagnosed annually. Currently about 56% of all people diagnosed with cancer are cured of their disease.<sup>3</sup> By gender, 60% of women and 52% of men are cured. This means that 44%, or around 38,720 people are diagnosed annually with a potentially incurable cancer.

There are about 32,000 GPs in Australia.<sup>4</sup> On average therefore, each GP will diagnose around three new people with cancer annually and have around eight people living with cancer amongst their patient list.

## **Definitions**

To facilitate effective communication, it is important that definitions are clear and used consistently. Everyone needs to be aware that many in the public and media, and even some in the medical system are using definitions in cancer medicine loosely and that this may lead to misunderstandings amongst the public regarding the potential benefits and risks of treatment options.

### *Curative treatment*

Curative treatment aims to render the person clinically free of detectable cancer and restore the person to their normal life expectancy.<sup>5</sup>

### *Palliative care*

Palliative care is an umbrella term for assisting those approaching death - a fundamental need and right. It is generally used in the context that death is imminent and inevitable and aims to make dying as easy and comfortable as possible.

## *Palliative treatment*

Palliative treatment is a specific but integral part of palliative care. Palliative treatment can be more interventionist. It is non-curative by definition but aims to extend life, ameliorate symptoms and increase quality of life in situations where cure is not medically feasible.

## *Prognosis and statistics*

When it comes to evaluating the benefits of any treatment, whether curative or palliative, it is important to understand the difference between *relative* or *absolute* benefits. For example, a treatment that reduces a risk of dying from 4% to 2% may be expressed as a relative reduction in risk of 50%, as it halves the risk of dying and sounds good, or, an absolute reduction in risk of 2%, as it reduces the risk of dying by 2% which does not sound like much.

Prognosis is best assessed using statistics rather than making a statement such as “you have 3 months to live”. A method for this is to answer the following questions.<sup>6</sup>

Q1. If 100 people had no treatment

- How many would be alive after 1 year and what would their health be like?
- How many would be alive after 5 years and what would their health be like?

Q2. If 100 people had this treatment

- How many would be alive after 1 year and what would their health be like?
- How many would be alive after 5 years and what would their health be like?

Q3. If 100 people had this treatment

- What side effects are possible and how many people would have them?

Q4. What impact will my own responses have?

- What can I do to help myself?
- What will my state of mind be like?
  - fear and loathing, or gratefully embracing
  - how committed will I be to this treatment?

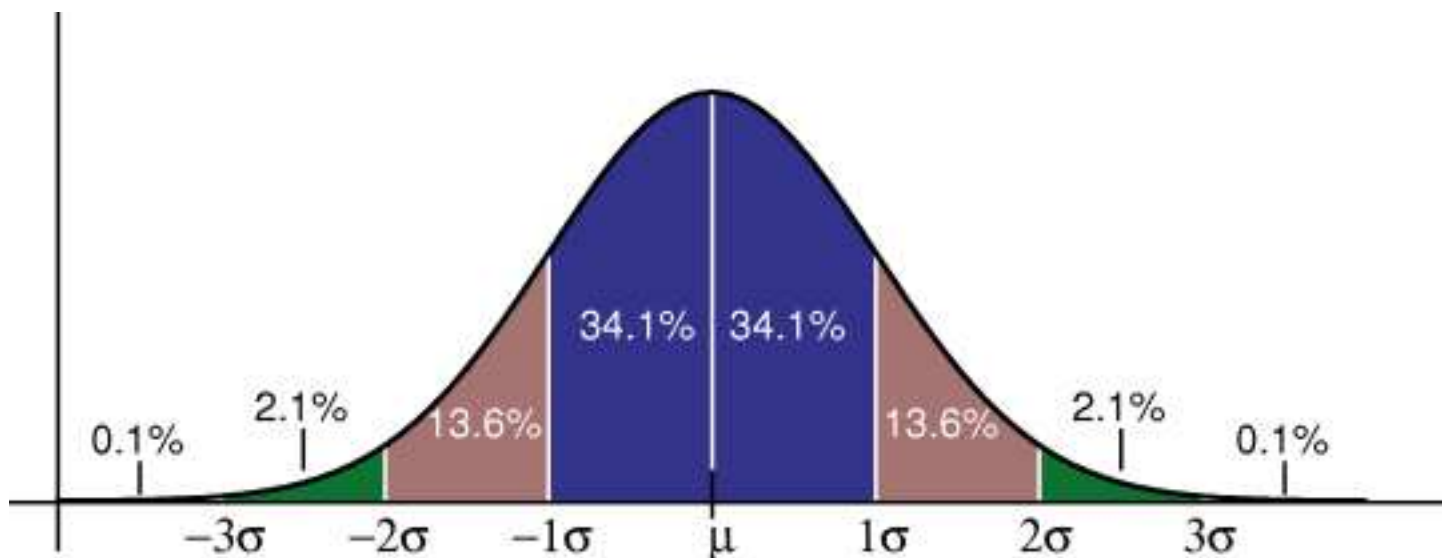
□ What are my support systems like? - personal - external

Once these questions are answered (with the best quality information available) then the equation of pluses and minuses can be discussed, balanced, considered, contemplated and an informed decision made.

### *The bell curve*

The bell curve helps people to understand so called “normal distributions” and to consider what factors may influence where a given individual may end up on the curve. For example, a good diet and regular exercise is highly likely to affect a shift to the right.

### **No. of Deaths**



### *Survival*

Survival refers to how long a person lives with a particular condition (e.g., they survived 6 months or 6 years). This is different to cure which implies surviving the cancer and dying of something else; but in fact means returning to a normal life expectancy. A person does only know for sure that they are cured of cancer when they die of something else.

### *Response*

A response to treatment could refer to any response. However, in cancer medicine it usually implies reduction in the size of a tumour. Doctors need to be aware that “response” is often mistaken by patients as a “cure”.

### *Integrative Medicine*

The term Integrative Medicine refers to a style of medical practice which is holistic and integrates the best and safest of conventional medical care with lifestyle advice and evidence-based complementary medicines and/or therapies. It aims to use the most appropriate of all available modalities and to help each individual patient make informed choices.

### *Orthodox or Conventional Medicine*

Orthodox or conventional medicine generally describes medical interventions that are taught at medical schools, generally provided at hospitals, and meet the requirement of peer accepted mainstream medicine and standards of care.

### *Complementary Medicine*

Complementary medicine refers to a medicine or therapy that is used in addition to, or complements conventional medicine. Complementary medicine is increasingly taught in medical schools and practiced in hospitals and is steadily gaining widespread support. More research is needed, to better evaluate it.

## *Lifestyle Factors*

Lifestyle factors are concerned with what a person can do for themselves in the context of their daily life. They are diverse, have a major impact upon health, and include physical, psychological, social and spiritual factors including diet, exercise, stress management, social support, leisure or work. Although they warrant being a core element in conventional medical care, many patients perceive, rightly or wrongly, that doctors do not take sufficient time or interest in lifestyle factors, hence, it is one of the main reasons for patients attending CM practitioners. Although cancer patients often seek help with lifestyle factors from complementary therapists and self-help programs as a part of their treatment, lifestyle factors benefit from being distinguished from complementary therapies for a range of reasons.

- a. They have a stronger evidence-base supporting their use.
- b. Their safety is high and has been more clearly defined.
- c. The 'side-effects' of appropriate lifestyle change tend to be beneficial.
- d. They should be seen as integral to conventional medical care rather than being a secondary option.

## **Complementary medicine and usage**

The use of natural, complementary and alternative medicines and therapies in Australia is considerable and increasing. Complementary medicine generally involves a person seeking help from a practitioner and/or the taking of medications and/or utilising products.

It has been estimated from a South Australian survey that in 2000 approximately 52% of the Australian population used complementary medicines and that 23% consulted practitioners of complementary medicine. This represents an estimated out of pocket spending of \$2.3 billion which is a 62% increase since 1993 and four times the out of pocket spending on pharmaceutical drugs.<sup>7</sup> Also, in 2000, 23% had consulted at least one alternative non-medical practitioner in the South Australian survey.<sup>8</sup>

Among cancer patients, it is estimated that 7-64% of adults use CM.<sup>9</sup> Figures vary with country, time and definition of CM. 31-87% of paediatric cancer patients use CM as a result of parental choice.<sup>10</sup>

Complementary and alternative medicine, as defined by the National Center for Complementary and Alternative Medicine (NCCAM) is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.<sup>11</sup>

NCCAM classifies natural, complementary and alternative medicines into five categories, or domains:

#### *Alternative medical systems*

Alternative medical systems are built upon complete systems of theory and practice such as homeopathic and naturopathic medicine, traditional Chinese medicine and Ayurveda.

#### *Mind-body interventions*

These interventions include patient support groups, cognitive-behavioural therapy, meditation, prayer, spiritual healing, and therapies that use creative outlets such as art, music, or dance.

#### *Biologically based therapies*

These therapies include the use of herbs, foods, vitamins, minerals and dietary supplements.

#### *Manipulative and body-based methods*

These methods include chiropractic or osteopathic manipulation, and massage.

#### *Energy therapies*

These therapies involve the use of energy fields. They are of two types:

- a. biofield therapies such as qigong, reiki, and therapeutic touch
- b. bioenergetic therapies involving the use of pulsed electromagnetic fields,

such as pulsed fields, magnetic fields, or alternating-current and/or alternating and direct-current fields.

## **Differentiating between complementary medicine and lifestyle factors**

By contrast, lifestyle factors are concerned with what a person can do for themselves in the context of daily life. The Gawler Foundation focuses upon lifestyle factors; providing professionally led psycho oncology groups that are based upon health education (e.g., what to eat, how to meditate, mindfulness) and which include a range of psychotherapeutic interventions (e.g., cognitive behavioural therapy).

Life factors include:

### *Physical interventions*

□ Nutrition - food □ Exercise □ Sunlight □ Hobbies

### *Mind-body interventions*

□ Group therapy - support, self help, etc □ The power of the mind - positive thinking, etc □ Meditation □ Yoga, qigong, tai chi, etc □ Creative activities - art, music, dance, gardening □ Emotional health - relationships, sexuality □ Personal development and transformation

### *Spiritual pursuits*

□ Exploring meaning and purpose □ Prayer □ Spiritual healing □ Religious practice

□ Spiritual development

Although there is growing evidence that a number of CAMs can be safe and helpful in cancer management, particularly in the area of symptom control, there are a number of legitimate concerns regarding the use of CAM among cancer patients.

These concerns include: □ Heightened concerns for vulnerable cancer patients and families □ The suggestion of false hope □ The potential for monetary



exploitation□ Delayed use of effective conventional treatments□ Little scientific evidence for some therapies□ Potential dangers, interactions and side-effects□ Poor training and regulation of some practitioners.

Of course, these issues are just as relevant for the conventional cancer care as they are for complimentary therapies and lifestyle factors.

## **Chemotherapy**

### *Chemotherapy and its efficacy*

Chemotherapy is associated with significant cure rates for 50% or more of childhood cancers, 50% or more of Hodgkin Lymphoma and certain aggressive lymphomas, 75% or more of carcinoma of the testes, 90% of choriocarcinoma in woman, 15 to 20% of adult acute leukemia, and 15 to 20% of ovarian carcinoma.

Chemotherapy provides substantial improvement in survival times, but is rarely curative, for a number of cancers, including carcinoma of the breast and osteogenic sarcoma. Chemotherapy may substantially palliate symptoms in some cancers, even though survival benefits are unknown or negligible, including carcinoma of the prostate. It may occasionally produce responses and modest survival benefits at the expense of moderate to severe toxicity, including brain cancers and malignant melanoma.<sup>12</sup>

In 2004, a meticulous analysis of the published data by Morgan of 22 types of cancer in adults, including breast, prostate, bowel & lung found that the overall benefit of chemotherapy to 5 year survival was a mere 2.3% in Australia.<sup>13</sup>

Morgan stated that “the minimal impact on survival in the more common cancers conflicts with the perceptions of many people who feel they are receiving a treatment that will significantly enhance their chances of cure”.

According to Segelov (2006), the aim of the great majority of chemotherapy is palliative, not curative.<sup>14</sup> This being so, the question then is what is the most effective form of palliation and in individual cases, do the side effects of chemotherapy warrant its use in palliative treatment?

### *Chemotherapy and side effects*

The Adverse Drug Reaction Advisory Committee (ADRAC) collects reports of suspected adverse drug reactions. Chemotherapy reactions are so common that they are generally considered normal and not regularly reported.

However, despite this, for the platinum group of chemotherapy agents, ADRAC has listed 346 different and specific reactions ranging from nausea to cardiac arrest to depression, and 65 incidents of deaths.<sup>15</sup>

Sir Charles Gairdner Hospital, Perth, sees 50,000 patients per annum. For the period July to December 2005, it saw 68 patients with sepsis (acute infections) following chemotherapy. All required hospitalisation.<sup>16</sup>

### *Chemotherapy and its acceptance*

People with advanced cancer are more willing to accept chemotherapy with a lower chance and a shorter duration of benefit than others imagine. Health professionals must recognise this when discussing treatment options with patients.<sup>17</sup>

Duric et al in 2006 researched women with early breast cancer who had received chemotherapy at least 3 months prior.<sup>18</sup> They were asked if they were given another round of chemotherapy and it were to add just one more day to an imagined 5 year survival without chemotherapy, would they have it? Over 50% said yes.

### *Chemotherapy and breast cancer - a specific example*

In 1998, out of 10,661 women who were diagnosed with breast cancer, 4,638 were considered eligible for chemotherapy. From this group only 164 gained some survival benefit, i.e., chemotherapy increased 5 year survival in early breast cancer by 3.5%.<sup>19</sup>

Whilst newer chemotherapy regimes (inc taxanes & anthracyclines) may increase survival by 1% at the expense of the risk of cardiac toxicity & nerve damage, to date there is no convincing evidence that newer and more expensive regimes are more beneficial.<sup>20</sup> Morgan et al conducted two

systematic reviews that have shown no survival benefits for chemotherapy in secondary breast cancer.

### *Chemotherapy summary*

Tables 1 and 2 summarise the benefits of chemotherapy.

#### **Table 1. Chemotherapy in general**

- ·Is curative for a good percentage of childhood cancers and some of the adult cancers.
- ·Taken overall, for most common cancers, improves 5 year survival rates.
- ·Generally speaking, can be regarded as palliative.
- ·Does have considerable cost in side effects and financial terms.

#### **Table 2. Chemotherapy for breast cancer**

- Improves survival in early stages by 3.5%.
- Has no evidence for survival benefits for secondary breast cancer.
- Has considerable costs in side effects and financial terms.

### **Lifestyle factors**

Lifestyle factors have the potential to assist people diagnosed with cancer during every phase of the disease. Just as with heart disease and diabetes, Lifestyle Factors relate directly to the cause and prevention of cancer, provide real support for anyone diagnosed with the disease and may well improve outcomes significantly.

#### *Lifestyle as a cause of cancer*

Cancer is essentially a lifestyle disease, with around 80% of the recognised causes being lifestyle related and about 10% related to inherited, genetic

factors.<sup>21</sup> People need to be aware that recent research identifies lack of sunlight as a major risk factor for cancer. For example, 25% of breast cancers in Europe are now linked to lack of sunlight.<sup>22</sup> The strongest relationship between lack of sunlight and cancer is for breast, colon & ovarian cancers. Other cancers identified as being affected are: bladder, uterus, oesophagus, rectum & stomach.

### *Lifestyle and cancer prevention*

People need to be aware that the best way to treat cancer is to prevent it! The best prevention is a healthy lifestyle. There is a good body of evidence to support this proposition, the detail of which is outside the scope of this paper.

### *Lifestyle factors and efficacy*

Do lifestyle factors reduce recurrence rates and mortality? No solid evidence to date has been produced that proves that a change in lifestyle cures cancer. Only a little definitive research in this area exists which is of great interest. What research there is points to a distinct possibility of significant gains but more specific trials are needed urgently.

## **Research on lifestyle factors and cancer**

Considerable research has been undertaken exploring the impact of a number of lifestyle factors on people with cancer.

### *The Ornish Prostate Study*

One randomised controlled trial to date is the Ornish Prostate cancer study.<sup>23</sup> Men in the watchful waiting group of the Ornish study utilised group support, meditation, low fat, vegetarian diet, stress management, and yoga.

Results proved a 4% reduction in PSA levels whilst the control group had a 6% increase in PSA levels, a difference of 10% between groups. Further, by contrast to the control group, no men in the intervention group went on to require major medical treatment which in prostate cancer is commonly quite invasive. However, more time is needed to observe if these early benefits are sustained. Therefore it is too early to claim this as a potential cure, but these results are encouraging. This trial needs

replicating - both in prostate cancer and other cancers.

There exists a good body of supportive evidence in the literature for the therapeutic benefits of lifestyle interventions, with a specific focus on breast cancer (where most of this type of research has been carried out).

### *Vegetable intake*

A study by Rock et al on women with breast cancer found that long term high level vegetable intake (as measured by plasma carotenoids) reduced the risk of recurrence by 40%.<sup>24</sup> This study supports previous findings.

### *Exercise*

A study by Holmes et al<sup>25</sup> found that three to nine hours of exercise per week halved the risk of dying in women with breast cancer, whilst nine hours or more per week reduced absolute mortality risk by 6% at 10 years. Hayden et al found that regular exercise halved the risk of dying for people with stage II and III colon cancer.<sup>26</sup> Similar findings were reported by Giovannucci for prostate cancer.<sup>27</sup>

### *Sunlight*

Sunlight and vitamin D may improve prognosis for breast cancer, as well as colon, prostate, leukemia, lymphoma and even melanoma.<sup>28</sup> Vitamin D levels may be checked by simple blood tests and ideal calcidiol levels are probably 100-250 n mol/l<sup>29</sup> or more specifically 120-150 n mol/l.<sup>30</sup>

### *Marriage*

Tominaga found that following surgical treatment of primary breast cancer, being a widow reduced survival by one third whilst having a hobby doubled survival.<sup>31</sup>

### *Group therapy*

Spiegel reported in the Lancet 1989, that attending a group based upon emotional expression, weekly for one year, doubled survival time for women with secondary breast cancer and some participants survived over 10 years.<sup>32</sup>

Another trial was performed by Fawzy with 68 patients with early stage malignant melanoma.<sup>33</sup> At 6-year follow-up those who had usual care plus stress management showed a halving of recurrence (7/34 vs 3/34) and much lower death rate (3/34 vs 10/34;  $p=0.03$ ) than the group with only the usual surgical management. Both groups also had their immune function monitored which showed that after being originally comparable, the stress management group had significantly better immune function after six months.

Other studies have also yielded promising results in terms of longer survival for liver,<sup>34</sup> gastrointestinal malignancies,<sup>35</sup> and lymphoma<sup>36</sup> but others have shown equivocal or negative results.<sup>37</sup><sup>38</sup><sup>39</sup><sup>40</sup><sup>41</sup> The last of these trials was a large-scale attempt to replicate the findings of Spiegel. The results of this trial were negative despite the fact that the effects of the intervention had a positive effect on quality of life and mental health.

Of the five negative or equivocal trials mentioned above only two reported a positive effect on mental health and quality of life while all the studies that showed a positive effect on survival reported improved mental health and quality of life. Therefore, the trend seen in eight out of ten cancer studies seems to be similar to the findings in studies of psycho-social support in heart disease; where a psychosocial intervention improves quality of life and mental health it has the 'side-effect' of prolonging survival, while if there is marginal or no long-term benefit on mood or quality of life there is no corresponding improvement in survival.

### *Meditation*

There are no properly conducted, specific trials to date investigating the survival benefits of meditation, but Meares published case reports of remission from secondary breast cancer (in the liver and the breast) following intensive meditation.<sup>42</sup><sup>43</sup><sup>44</sup>

More recent research is suggesting a range of physiological and psychological benefits from practicing meditation many of which have implications for cancer. These include improved sleep<sup>45</sup>, elevation of melatonin levels<sup>46</sup>, improved pain control<sup>47</sup>, improvement of depression<sup>48</sup>, anxiety and coping<sup>49</sup><sup>50</sup>, and improved immunity.<sup>51</sup> As such, independent of potential effects on survival, meditation

should be considered as an option offered to patients to improve their coping with cancer and symptom control.

### *Traditional techniques*

Yoga and qigong are two therapies that have been utilised extensively in the East over many centuries. Quality of life studies affirm benefits, but again survival benefits remain to be studied using Western scientific methods. Massage falls into the same category.

### *Creative activities*

Art, music and dance are amongst another range of therapies waiting to be studied more analytically.

### *Personal development and transformation*

Faller found that poor coping, distress & depression was linked to lower survival<sup>52</sup>, while Penninx found that depression in the elderly doubles the risk.<sup>53</sup> Greer found that women with breast cancer who demonstrated a “fighting spirit” as compared to denial or stoic acceptance, increased their chance of survival significantly.<sup>54</sup> Likewise, psychotherapy and involvement in self help techniques proportionally associated with quality of life experience and survival duration have been demonstrated by Cunningham.<sup>55</sup>

### *Spiritual factors*

A review of 71 research articles by Hawka indicated that imagery, meditation and group support activities may address spiritual health, resulting in beneficial outcomes of enhanced physical and emotional health and decreased cancer mortality.<sup>56</sup>

### *Lifestyle factors and side effects*

The side-effects of healthy lifestyle change are by-and-large healthy. It is obviously important to tailor the lifestyle change to suit the cancer patient’s personal preferences, level of fitness or motivation and at the same time to take care that the patient does not form unrealistic expectations nor forgo important treatment.

- <sup>1</sup> Australian Institute of Health and Welfare and Australasian Association of Cancer Registries. Cancer in Australia 2001, Canberra 2004.
- <sup>2</sup> Cancer in Australia. A snapshot. 4822.0.55.001, Australian Bureau of Statistics, 1 September 2004.
- <sup>3</sup> English D. Cancer Survival in Victoria, 2003; Cancer Council of Victoria.
- <sup>4</sup> 2001 Census of Population and Housing, Generalist Medical Practitioners from the Australian Bureau of Statistics.
- <sup>5</sup> Caociao DA.. Manual of Clinical Oncology 5th Ed 2004.
- <sup>6</sup> Gawler I. You Can Conquer Cancer. Anderson Publishing, 2001, Pages 14-15.
- <sup>7</sup> MacLennan AH, Wilson DH, Taylor AW. The escalating cost and prevalence of alternative medicine. Prev.Med. 2002;35:166-173.
- <sup>8</sup> MacLennan AH, Wilson DH, Taylor AW. The escalating cost and prevalence of alternative medicine. Prev.Med. 2002;35:166-173.
- <sup>9</sup> Lowenthal RM. Public illness: how the community recommended complementary and alternative medicine for a prominent politician with cancer. Med J Aust. 2005;183(11-12):576-9.
- <sup>10</sup> McLean TW, Kemper KJ. Complementary and alternative medicine therapies in pediatric oncology patients. J Soc Integr Oncol. 2006;4(1):40-5.
- <sup>11</sup> National Center for Complementary and Alternative Medicine (NCCAM), 2002. What is Complementary and Alternative Medicine (CAM)?, May 2002, USA. Last Modified: 21 October 2002. <http://nccam.nih.gov/health/whatiscam/>.
- <sup>12</sup> Morgan G et al. Clin Oncol 2004; 16:549-60.
- <sup>13</sup> Morgan G et al. Clin Oncol 2004; 16:549-60.
- <sup>14</sup> Segelov E. Aust Prescriber 2006;29(1)2-3.
- <sup>15</sup> [www.tga.health.gov.au/adr/adrac.htm](http://www.tga.health.gov.au/adr/adrac.htm).
- <sup>16</sup> Pers comm Prof G Jelinek, Sir Charles Gairdner Hospital, Perth.
- <sup>17</sup> Pers comm. Prof G Jelinek, Sir Charles Gairdner Hospital, Perth.



- <sup>18</sup> Duric V et al. *Ann Oncol* 2005 Nov;16(11):1786-94. Epub 2005 Aug 26.
- <sup>19</sup> Morgan G et al. *Clin Oncol* 2004;16:549-60.
- <sup>20</sup> Morgan G et al. *Clin Oncol* 2004;16:549-60.
- <sup>21</sup> Doll & Peto: *The Causes of Cancer*. Oxford Uni Press 1981.
- <sup>22</sup> Grant: *Cancer* 2002; 94:272-81
- <sup>23</sup> Ornish D et al. *The Journal of Urology*, Vol 174, 1065-1070. Sept 2005.
- <sup>24</sup> Rock CL et al. *J Clin Oncol*. 2005 Sep 20;23(27):6631-8.
- <sup>25</sup> Holmes MD et al. *JAMA*, 2005 May 25;293(20):2479-86.
- <sup>26</sup> Haydon A et al. *Gut* 2006 Jan;55(1):8-10
- <sup>27</sup> Giovannucci E et al. *Arch Intern Med*. 2005 May 9;165(9):1005-10.
- <sup>28</sup> Robsahm TE et al. *Cancer Causes Control*.2004 Mar;15(2):149-58.
- <sup>29</sup> Moan J, Porojnicu AC. *Tidsskr Nor Laegeforen*, 2006 Apr 6;126(8):1048-52
- <sup>30</sup> Pers comm Prof G Jelinek, Sir Charles Gairdner Hospital, Perth.
- <sup>31</sup> Tominaga K. *Jpn Clin Oncol*. 1998 Jan;28(1):36-41
- <sup>32</sup> Spiegel D et al. *Lancet* 1989;2:888-891.
- <sup>33</sup> Fawzy F. et al. Malignant melanoma; Effects of an early structured psychiatric intervention, coping and affective state on recurrence and survival six years later. *Arch Gen Psych* 1993;50:681-89.
- <sup>34</sup> Richardson JL, Shelton DR, Krailo M, Levine AM. The effect of compliance with treatment on survival among patients with hematologic malignancies. *J Clin Oncol* 1990;8:356-64.
- <sup>35</sup> Kuchler T. Henne-Bruns D. Rappat S. et al. Impact of psychotherapeutic support on gastrointestinal cancer patients undergoing surgery: survival results of a trial. *Hepatogastroenterology*. 1999;46:322-35.
- <sup>36</sup> Ratcliffe MA, Dawson AA, Walker LG. Eysenck Personality Inventory L-scores in patients with Hodgkin's disease and non-Hodgkin's lymphoma. *Psycho-oncology* 1995;4:39-45.
- <sup>37</sup> Cunningham AJ. Edmonds CV. Phillips C. et al. A prospective, longitudinal study of the

relationship of psychological work to duration of survival in patients with metastatic cancer. *Psychooncology*. 2000;9(4):323-39.

<sup>38</sup> Edelman S, Lemon J, Bell DR, Kidman AD. Effects of group CBT on the survival time of patients with metastatic breast cancer. *Psycho-Oncology*. 1999;8(6):474-81.

<sup>39</sup> Ilnyckyj A, Farber J, Cheang MC, Weirnerman BH. A randomized controlled trial of psychotherapeutic intervention in cancer patients. *Ann R Coll Physicians Surg Can* 1994;27:93-6.

<sup>40</sup> Linn MW, Linn BS, Harris R. Effects of counseling for late stage cancer patients. *Cancer* 1982;49:1048- 55.

<sup>41</sup> Goodwin PJ, Leszcz M, Ennis M, et al. The effect of group psychosocial support on survival in metastatic breast cancer. *N Engl J Med* 2001;345:1719-26.

<sup>42</sup> Meares A. *Med J of Aust*. 1976, 2:184

<sup>43</sup> Meares A. *Med J of Aust*. 1977, 2:132-133

<sup>44</sup> *Meares A. Med J of Aust. Correspondence, 10 Sept 1977*

<sup>45</sup> Sephton S, Spiegel D. Circadian disruption in cancer: a neuroendocrine-immune pathway from stress to disease? *Brain Behav Immun*. 2003;17(5):321-8.

<sup>46</sup> Mahmoud F, Sarhill N, Mazurczak MA. The therapeutic application of melatonin in supportive care and palliative medicine. *Am J Hospice & Palliative Care*. 2005;22(4):295-309.

<sup>47</sup> Kabat-Zinn J et al. *J Behav Med*. 1985;8(2):163-90.

<sup>48</sup> Teasdale JD, Moore RG, Hayhurst H, et al. *J Consult Clin Psychol*. 2002;70(2):275-87.

<sup>49</sup> Tacon AM, et al. *Family & Comm Health*. 2003;26(1):25-33.

<sup>50</sup> Speca M, et al. *Psychosom Med*. 2000;62(5):613-22

<sup>51</sup> Davidson RJ *Psychosom Med*. 2003;65(4):564-70.

<sup>52</sup> Faller H et al. *Arch of Gen Psychiatry*. 1999;56(8):756-62.

<sup>53</sup> Penninx BW et al. 1998;90(24):1888-93.

<sup>54</sup> Greer S et al. *Lancet*. 1990;1:49-50

<sup>55</sup> Cunningham AJ et al. *Adv Mind Body Med* 2000;16(4):276-87.

<sup>56</sup> Hawka SR et al. Am J Health Promot. 1995 May-Jun;9(5):371-8