# Does living better also mean living longer?

## *Quality of life and cancer*

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It seems to be a universal law of human nature that we are all interested in 'a happy life' or perhaps 'quality of life' (QOL) as it is more usually termed. According to our beliefs we look for it in varying ways. Cicero, the orator and statesman from ancient Rome wrote a series of books, Discussions at Tusculum, on the subject. He introduces them in the following way:

They examine the essentials for a happy life. The first volume shows that death is not to be feared, and the second that pain is endurable. The third indicates how sorrow can be alleviated, the fourth deals with other disturbances of the mind, and the fifth ... the proposition that moral goodness, by itself, is sufficient to make anyone happy.[1]

Exactly what constitutes QOL could be the subject of many articles but for now let us focus on a contemporary application of old principles in the relationship between QOL and illness. In a previous article[2] the role of stress in the development of cancer has been discussed but what is the current state of thinking with regard to interventions aimed at improving QOL and cancer survival? One noted researcher in the field suggests there might be a relationship.

> Living better also seemed to mean living longer.
>
> David Spiegel

Poor coping, distress and depression have long been linked to poor survival for a number of cancers including lung cancer,[3] breast cancer,[4] malignant melanoma,[5] and bowel cancer. Elsewhere, global QOL has also been linked to survival in a variety of cancers.[6-8] As an example, one study showed that a number of factors including the perceived aim of treatment, QOL, marital status and anger all influenced survival.[9] Some studies however, have not confirmed this link.[10]

Nonetheless, if psychosocial factors might be important in the aetiology and progression of cancer then psychosocial interventions such as support groups, CBT, communication strategies, relaxation and meditation, and pain management might be able to produce better prognoses.

One of the first studies of its type was done by David Spiegel on women with metastatic breast cancer. Women were randomised to receive either usual care or an intervention which included group support, 'supportive expressive therapy', and some simple relaxation and self hypnosis techniques.[11] After one year the intervention group showed a significant improvement in QOL but he was surprised to find some 10 years later that there was a doubling of average survival time for the intervention group. At 10 year follow up three women in the intervention group were still alive but none in the control group who had the usual management alone survived. Importantly, divergence between the survival curves of the two groups did not take place until some 20 months after entry into the trial.

Fawzy and his team studied 68 patients with early stage malignant melanoma.[12] They were divided into two groups, one receiving usual care alone and one also receiving a six week stress management intervention. At six year follow up the intervention group showed a much lower recurrence (7/34 vs. 13/34) and death rate (3/34 vs. 10/34; p=0.03) than the group with only the usual management. Monitoring of immunity showed that with baseline comparable immunity, the stress management group had significantly better immune function six months into the study. This provided a plausible mechanism to explain the difference in survival. Both studies suggest there is a lag time between interventions and clinical outcomes.

Other studies have also yielded promising results in terms of survival for liver[13] and other gastrointestinal malignancies[14] and lymphoma[15] but others have shown equivocal or negative results.[16-20]

Why do some studies show the positive results and not others? The answer may lie with the effectiveness of the intervention in improving QOL. Of the negative trials Goodwin's was only the second to have shown a positive effect on

mental health not translating into a significant benefit for survival. Studies showing a positive effect on survival were all associated with improved QOL and mental health as a result of the intervention. So the trend seems to be that where the psychosocial intervention has marginal or no long term benefit on mood or QOL it does not seem to translate into longer survival.

- What are the factors leading to 'false positive or negative results'?
- Does psychosocial support help all forms of cancer or only some (eg. those which are aggressively attacked by the immune system like melanoma)?
- Does psychosocial support help all patients, only those who are most distressed, or only those who strongly comply with the intervention?
- Are positive findings only found with the best targeted and run programs?
- What should doctors tell their patients on the basis of the presently available data?

Just being in a program is probably not protective in itself but it appears it is the level of patient participation which is important. This is demonstrated by a study finding that only high involvement in the program was associated with better survival.[21] If studies do not control for this factor they may find ambiguous results. Also important are the different interventions used and the different styles of group support and meditation etc.

Not all interventions, it would seem, are equal. A lot more work needs to take place in determining what sorts of interventions work and what is the best way of administering them. But on the basis of the present direct evidence one would have to express cautious optimism about the prospect of effective psychosocial interventions improving survival.

To measure an outcome is one thing but to explain it is another. The potential mechanisms for longer survival in those with better mental health and QOL fall into a number of categories:

- via stress reduction effecting the HPA axis, cortisol and other stress hormones
- genetic mutation and expression
- stress causing suppression of immunity leading to reduced host defences
- induction of protective 'anticancer' hormones such as melatonin
- angiogenesis, ie. interfering with the ability of cancers to make their own blood supply.

The answer is likely to lie with an interplay of a number of mechanisms rather than any one. For example, recent research has demonstrated that poor social support, chronic stress and depression are associated with higher cortisol levels and a flattening of the natural diurnal rhythm in women with breast cancer[22,23] which is highly predictive of poor long term survival. These patterns of cortisol secretion were also associated with suppressed activity of NK cells. It had commonly been thought that the body's main defense against cancer is a tumour 'rejection' response mediated through the NK cells so the hypothesis was that immuno-enhancement through better stress management potentiated this effect. This mechanism may well explain some of the beneficial effects for some tumours, but not all. In some cases, like malignant melanoma, the immune system has been shown to recognise and aggressively attack the tumour but it has also been noted that many other tumours do not wear their antigens on their surface and therefore the immune system cannot recognise them.[24] Other potential mechanisms whereby stress reduction can help against cancer include reducing the chemical mediators of the stress response which can stimulate tumour growth, almost like a 'fertiliser'. Many stress mediators when induced inappropriately 'float' around the body and act on rapidly replicating cells, like cancer cells. Even the physiological stress associated with surgery has been shown to increase the growth of tumour metastases at distant sites via these hormones.[25] The evidence for the effect of stress on cancer gene expression is presently more circumstantial than definitive. We do know however, that we can have genetic dispositions to cancer and that there are protective genes such as 'cancer suppressor genes.' It has also been shown that stress reduces DNA repair capacity. Therefore it is being increasingly postulated that our approach to cancer has ignored 'the aberrant signaling on control pathways malignant cells manifest.'[26] Reducing stress hormones[27] and inducing hormones associated with wellbeing and relaxation, like melatonin, may be another reason why stress reduction and psychosocial interventions may help cancer survival.[28]

Does living better also mean living longer? It is highly likely that it does. If so then it suggests that the aim of a holistic approach to cancer treatment is to improve quality of life; better survival may just be a side effect, albeit a useful one. If it doesn't then perhaps it would have made little difference to the likes of Cicero or Leonardo da Vinci in any case because surely making the most of the life we have is more important than merely living longer.

> Just as a well used day brings a happy sleep, so a well used life brings a happy death.
>
> Leonardo da Vinci

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