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QUALITY OF LIFE IN PATIENTS WITH METASTATIC BREAST CANCER: A SOUTH AFRICAN PERSPECTIVE

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by

MAGARETHA SUSARA MERTZ
B.PHARM (1979) P.U. for CHE
MSc. PHARM (1983) P.U. for CHE

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PROMOTER:

Carla Isadora Falkson, MB ChB, MMed(Int), MD

Professor and Head: Department of Medical Oncology
Faculty of Medicine, University of Pretoria, Pretoria.

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One of the wonderful characteristics of human existence is that we do not exist in isolation, but are all very dependent on one another. There is therefore no such thing as achievement that has been attained independently by one person. We inspire each other, learn from each other and support each other. It is often by means of the teamwork of ordinary people, that meaningful and valuable projects are conceived and executed.

There are a few wonderful people whom I would like to thank for their support and contribution to this study: Firstly my parents Robbie and Bella, who instilled in their children a culture of learning and a love of knowledge. Who supported us in our studies even when they didn't know how on earth it would be financed. Then the three PBs in my life: My husband Paul-Bolko who encouraged me every step of the way. My two statisticians Dr. Peter Braun and Dr. Piet Bekker without whose valuable input and seemingly endless hours of hard work this thesis certainly could not have seen the light. I would like to thank my promoter professor Carla Falkson.

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Our patients for the wonderful strength, dignity and courage that they bring to the fight with the cancer demon. I often wish that we could eradicate this dreadful adversary and take away all the suffering of our patients, but mostly in the metastatic setting, we can't. We can however improve the quality of our patients' lives very significantly and in this way lighten their burden and ease their way.

I do think that a revolution in the treatment of cancer will take place in the next ten to twenty years, given the great strides that are being made in our understanding of the molecular and genetic basis of the disease. But the psychosocial input that can be made just by caring and taking time for another human being will always remain the foundation upon which our entire endeavor in this field will be built.

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INTRODUCTION

The advances made in medical science this century have completely transformed the practice of medicine. At the beginning of the century there were few efficacious treatments available and the primary role of doctors was to provide comfort. Nowadays the availability of sophisticated diagnostic procedures, therapies, drugs and surgical techniques have revolutionized the management of hitherto fatal conditions. Specialists today display a highly scientific and technical role. Unfortunately, the impressive list of advancements in the *science* of medicine has lead to a decline in the *art* of medicine. Patients complain increasingly that "high-tech" medicine dehumanizes them. There are actually states of life that are worse than death and few people accept the "life-at-any-cost" philosophy assumed by many doctors. We must consider both the quality as well as the quantity of life for any individual who requires medical treatment (Fallowfield 1990).

There has been a rapid increase in the interest of clinicians in the study of quality of life. Index Medicus citations about quality of life have increased as follows in the last few years:

- 20 in 1976
- 65 in 1984
- 1974 in 1996
- 2170 in 1997
- 1328 in 1998

Health-related quality of life has been defined as a concept for more than three decades. Despite the relative longevity of the quality of life concept, it's utility is often unclear. Quality of life data can be usefully employed in a multitude of ways:

- To improve clinical practice.
- As an integral tool for clinical trials.
- To help formulate health policy.

Unfortunately "Quality of Life" is not well conceptualized in the medical and health literature. Additionally clinical researchers are searching for a single best measure of quality of life and created a confusing multitude of measuring tools, most of which require sophisticated statistical analyses.

When one investigates the South African situation, the position becomes even more precarious. Up to date, no general studies have been published to reflect the quality of life of South African cancer patients. There are unique factors influencing the quality of life of this patient group:

- Huge cultural differences between black and white patients as well as between the different black racial groups (Pedi, Tswana and Zulu to name just the main groups). There is also a chasm in the way in which these different groups view the impact of diseases such as cancer on their lives.
- The political and social situation in the post-apartheid era.
- The dire financial position in which the health services find themselves currently. This is leading to the type of situation where decisions have to be made in a scientific way about whether to embark on costly medical interventions or not.

Breast cancer is the second most prevalent cancer among South African females and because advances in treatment have improved survival, it uses a sizeable part of the available health budget for cancer patients. It was therefore decided to investigate the quality of life of South African patients with breast cancer and to try and establish the utility of this measurement tool within the South African health service context. If some of these findings can be applied to more universal quality of life issues, then this discipline can also benefit from this current endeavor.

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SUMMARY

The purpose of my study was to establish norms and general trends of quality of life issues as they relate to South African breast cancer patients. The effect of race on quality of life was also of special interest.

An Afrikaans translation of the FACT-B was developed and found to be reliable. The previously translated versions of the FACT-B into the South African ethnic languages were re-assessed for reliability. Low reliability for the social/family well being scale was found.

The advantages of the Zulu, Pedi and Tswana translations were that the quality of life of these patients could be assessed in their own language for the first time. An added advantage was that the QOL of illiterate black patients could be assessed by means of the interview method, in their own language. We learnt a lot about the cultural differences between the black and white South African patients.

The interim analysis showed prominent differences in the quality of life of black and white patients. The multivariate analysis however, corrected for the factors that influenced the quality of life of the patients. These factors were baseline quality of life scores, performance status, race, disease stage, treatment time, marital status and educational status. The factors that were found to be significant predictors of the change of quality of life over time, were performance status, disease stage and total FACT-B score. Marital status, educational status and race showed a tendency towards significance.

Analysis of the patient demographics yielded interesting and useful information. The management of breast cancer in the black population needs to be improved. Concerted efforts should be made to educate the black population about breast cancer and about the benefits of early intervention.

A bimodal distribution for the age-related incidence of breast cancer in the black population was found for our patients in this area. This is unusual, because it is not found in other parts of South Africa. The reasons for this finding are unclear at the moment.

A previous analysis of the first two hundred patients showed that twelve percent of these patients had complained of pain at their first visit, but that no pain medication had been prescribed. During the course of the study, it became clear that specific problems or needs of patients were in fact identified by means of the quality of life questionnaire. An intervention program was then started.

A better understanding of the cancer patient and the impact of quality of life and related issues has been established. Quality of life norms for South African breast cancer patients have been established. Race-related issues have been explored and clarified.

The problems facing patients diagnosed with cancer are huge and very real. It is therefore imperative that we develop meaningful solutions to these problems and keep striving to improve patient care.

OPSOMMING

Lewenskwaliteit is 'n komplekse en veelkantige konstruk. Faktore so uiteenlopend as ouderdom en huweliksstatus kan dit beïnvloed. Ander faktore is die impak van slegte gesondheid, die kankersoort, die tipe behandeling, tyd sedert diagnose en stadium van die siekte. Die geskooldheid van pasiënte, of daar iemand met hulle saamwoon, geslag, verlies van rol, sosiale en familie verhoudings, vehoudings met mediese personeel en emosionele en geestelike faktore kan ook 'n rol speel. Die diagnose van 'n lewensbedreigende siekte as sulks, het sonder twyfel 'n geweldige impak op die lewenskwaliteit van 'n pasiënt. Swak gesondheid *per se* is 'n deursslaggewende faktor in die lewenskwaliteit van enige mens.

Die oomblik wanneer 'n pasiënt met kanker gediagnoseer word, verander haar lewe onherroeplik en moet sy die lang proses van aanpassing tot haar veranderde omstandighede aanpak. Sy moet woede, ontkenning en smart ervaar en uiteindelik die siekte en die impak daarvan op haar lewe aanvaar.Tydens hierdie proses moet sy vaardighede aanleer sodat sy haar fisiese swakheid en die onaangename aspekte van haar kanker en die behandeling daarvan kan baasraak.

Langs hierdie weg is daar 'n menigte terugslae wat sy mag ervaar. Sy moet die probleme wat in haar verhoudings met haar lewensmaat, haar familie en vriende kan ontwikkel, probeer oplos. Sy kan tydelike of permanente emosionele gebreke ervaar.

Vanuit die literatuurstudie het dit duidelik geword dat 'n verwarrende versameling van lewenskwaliteit instrumente tans beskikbaar is vir navorsing in hierdie veld. Dit is belangrik om tydens die beplanning van 'n studie oor die impak van bepaalde faktore op lewenskwaliteit, 'n instrument of instrumente te kies wat by die kankersoort onder bestudering pas. Enige studie-spesifieke aangeleenthed moet ook aangespreek word. Die instrument of instrumente moet psigometries aanvaarbaar wees, asook multidimensioneel. Twee voorbeelde van lewenskwaliteit instrumente wat geldig, betroubaar en multidimensioneel is, is die "Factual Assessment of Cancer Therapy" (FACT) skaal en die skaal wat deur die "European Organization for Research and Treatment of Cancer" (EORTC QLQ-C30) onwikkel is. Daar bestaan baie publikasies wat oor studies wat hierdie skale gebruik het, verslag lewer. Hierdie skale is gekonstrueer deur middel van die gebruik van 'n modulêre benadering. Dit beteken dat

die kern vraeboog vir die meet van lewenskwaliteit wat met enige soort kanker gepaardgaan, geskik is. Kanker spesifieke modules kan aangelas word, vir meer siektegerigte doeleindes.

Omdat die meeste behandelings teen kanker 'n geweldige impak op lewenskwaliteit veroorsaak, het die bestudering van lewenskwaliteit 'n belangrike studierigting geword. Dit is 'n onomwonde feit dat geen fase III studie sonder die insluiting van 'n lewenskwaliteit module aangepak behoort te word nie. Die waarde van die bestudering van lewenskwaliteit tydens fase II studies is ook al goed gedokumenteer.

Ongelukkig is die probleme wat met die bestudering van lewenskwaliteit gepaard gaan 'n werklikheid. Die insluiting van die assessering van lewenskwaliteit vergroot die werkslading van die kliniek personeel. As lewenskwaliteit assessering gedoen gaan word, moet dit op 'n gekontroleerde manier gedoen word. Al die korrekte tegnieke om te verseker dat data van 'n hoogstaande gehalte versamel word, moet toegepas word. Die pasiënte se samewerking is ook nodig, omdat verlore data 'n kritieke uitvloeisel in hierdie navorsingsveld geword het. Die statistiese analises kan ook duur en tydrowend word. Vereenvoudiging in hierdie veld sal die bestudering van lewenskwaliteit meer aantreklik vir navorsers maak.

Die nuttigheid van die bestudering van lewenskwaliteit kan as volg opgesom word:

- As 'n addisionele parameter in kliniese proewe, waar die lewenskwaliteit data dikwels die vernaamste faktor in die uitkoms van die navorsing kan wees.
- Die resultate van lewenskwaliteit studies kan 'n direkte impak hê op die hantering en behandeling van kankerpasiënte wat sjirurgie en/of radioterapie en/of chemoterapie ontvang.
- As 'n prognostiese faktor kan lewenskwaliteit data as 'n voorspelling van oorlewing gebruik word.
- Om standaarde van sorg en pasiënt funksionering te verbeter.
- As 'n hulpmiddel in die diagnose van emosionele en ander probleme.
- Om ingeligte besluite betreffende die risiko-voordeel ruiltransaksies ("risk-benefit trade-offs") te maak en as 'n hulpmiddel in kliniese besluitneming.
- As 'n hulpmiddel by die formulering van gesondheidsbeleid.

Psigososiale evaluasie word as een van die basislyn ondersoeke in 'n standaard onkologie teksboek beskryf, reg tussen die volbloedtelling, borskas x-straal en die beenskandering. Dit bly die ideaal waarna ons moet strewe en sal effektiewelik 'n baie betekenisvolle bydrae tot optimale pasiëntsorg maak.

Die doel van my studie was om norme en algemene neigings vir lewenskwaliteit aangeleenthede, soos wat dit van toepassing op Suid Afrikaanse borskanker pasiënte is, daar te stel. Die effek van ras op lewenskaliteit was ook van spesiale belang.

'n Afrikaanse vertaling van die FACT-B is ontwikkel en betroubaar bewys. Beskikbare vertalings van die FACT-B in die Suid Afrikaanse etniese tale is ge-hervalideer deur middel van Chronbach se aplha. Probleme met die betroubaarheid van die sosiale/familie welstand skaal was tot 'n groter mate gevind as wat Mullin (1999) bevind het. Redes vir die onvoldoende betroubaarheid en moontlike oplossings om betroubaarheid to verbeter, word verskaf. Hierdie area is definitief 'n veld vir verdere navorsing.

Die voordeel van die Zulu, Pedi en Tswana vertalings was dat die lewenskwaliteit van hierdie pasiënte vir die eerste maal in hulle eie taal bepaal kon word. 'n Bykomende voordeel was dat die lewenskwaliteit van ongeletterde pasiënte in hulle eie taal bepaal kon word, deur middel van 'n onderhoud. Ons het baie geleer betreffende die kultuurverskille tussen swart en blanke Suid Afrikaanse pasiënte.

Die interim analise het prominenete verskille in die lewenskwaliteit van swart en blanke pasiënte aangetoon. Die meerverandelike analise ewenwel, het vir die faktore wat die lewenskwaliteit van pasiënte beïnvloed, gekorrigeer. Hierdie faktore was die basislyn lewenskwaliteit telling, werkverrigtings status ("performance status"), ras, stadium van siekte, behandelingstyd, huweliksstatus en opvoekundige peil. Die faktore wat as betekenisvolle voorspellers van die verandering in lewenskwaliteit oor tyd gevind is, was werkverrigtings status, stadium van siekte en die totale FACT-B punt. Huweliksstatus, opvoedkundige peil en ras het 'n neiging tot betekenisvolheid getoon.

Analise van die pasiënt demografiese gegewens het interessante en nuttige informasie getoon. Die hantering van borskanker onder die swart bevolking moet verbeter word. Gesamentlike optrede om die swart bevolking oor borskanker en die voordele van vroeë ingryping in te lig, moet gemaak word. Die waarskynlikheid dat swart pasiënte adjuvante chemoterapie sal ontvang is baie klein, meestal omrede hulle geografiese onbereikbaarheid. In my studie was daar nie een enkele swart pasiënt wat adjuvante chemoterapie gehad het nie.

'n Bimodale distribisie vir die ouderdoms-verwante insidensie van borskanker is vir ons pasiënte in die swart populasie gevind. Dit is ongewoon, omdat dit nie in die ander dele van Suid Afrika die geval is nie. Die redes vir hierdie bevinding is tans onbekend.

'n Vorige analise van die eerste tweehonderd pasiënte het aangetoon dat twaalf persent van hierdie pasiënte tydens hulle eerste besoek oor pyn gekla het sonder dat daar vir hulle enige pynmedikasie voorgeskryf is. Gedurende die verloop van die studie het dit duidelik geword dat spesifieke probleme of behoeftes van die pasiënte deur middel van die lewenskwaliteit vraeboog geïdentifiseer word. 'n Intervensie program is gevolglik begin. Sommige van die belangrikste intervensies was: die verskaffing van addisionele informasie, identifikasie en fasilitasie van die behandeling van depressie en slapeloosheid, raadgewing oor medisynegebruik, ongeskikheidspensioene, behandelings newe effekte en praktiese aspekte soos pruike en prosteses.

'n Beter begrip vir die kankerpasiënt en die impak van lewenskwaliteit en verwante uitkomste is daar gestel. Norme vir lewenskwaliteit vir Suid Afrikaanse borskanker pasiënte is bepaal. Ras-verwante aangeleenthede is verken en verklaar.

Ek het probeer om vir ander navorsers in die veld 'n omvattende oorsig oor die huidige lewenskwaliteit instrumente te gee. Sommige van hierdie instrumente is as addenda aan hoofstukke twee en vier aangeheg. Duidelikheidshalwe is die lewenskwaliteit instrumente in tabel nege van hoofstuk twee opgesom. Hierdie tabel lys die lewenskwaliteit instrumente en die spesifieke weergawe daarvan, watter domeine die instrument aanspreek, en die voordele en nadele van die instrument. Ek het probeer om my taalgebuik eenvoudig te hou sodat die tesis tot die breë publiek kan spreek. Ek het lyste met nuttige inligting spesifiek vir gebruik deur pasiënte ingesluit as addenda.

Alle huidige lewenskwaliteit instrumente het sekere tekortkomings. Bestaande instrumente is tans nog maar growwe benaderings van wat dit behoort te wees. Ons is beslis nog vêr weg van die verfynde meting van al die faktore wat 'n impak op die lewenskwaliteit van ons pasiënte kan hê. Bestaande lewenskwaliteit instrumente spreek geensins die meting van subtiele persoonlikheids- en houdings-verskille van pasiënte aan nie. Laasgenoemde is dalk nog belangriker as al die huidiglik bekende faktore. Maar elke bydrae in hierdie veld bring ons uiteindelik 'n klein stappie nader aan die ideaal. Die probleme wat kanker pasiënte ondervind is enorm en baie werklik. Daarom is dit noodsaaklik dat ons sinvolle oplossings vir hierdie probleme ontwikkel en aanhou om daarna te streef om pasiëntsorg te verbeter.

CHAPTER 1: THE PATIENT

1.1 INTRODUCTION

When the suspicious lump is diagnosed as cancer, the former citizen becomes a patient. Suddenly she has to decide about different treatment modalities and cope with the impact that this will have on her life. She has to contend with unpleasant side effects and try to adjust to an altered body image. She may experience a loss of role and suffer ostracism in the workplace and socially. This chapter explores the impact of these and other related issues on the patient and on her quality of life. It investigates anxiety and depression, sexual problems, the impact of cancer on family and social life, the role of supportive care and lists helpful tips and strategies for helping patients cope.

It has been found that quality of life is a much bigger issue in cancer than in other equally life threatening diseases.

1.2 PSYCHO-ONCOLOGY

Psycho-oncology has been a formal discipline for just over a decade. It embodies a range of activities about the phenomenology, prevalence, the role of psychological factors in the onset and progression of cancer, the stress response in relation to cancer, quality of life, improved pain control, researching a healthy population who may be at genetic risk for developing cancer, etc. as well as treatment of psychological problems in cancer patients among whom psychological treatment features prominently. Research in psycho-oncology has burgeoned during the last decade, but this is not the case in Africa and South Africa (Schlebusch 1998).

Given the projected increase in the number of cancer patients and cancer survivors, there are pressing needs to further research the implications of psychological factors as one of the groups of modulators in the etiology and management of cancer (Schlebusch 1998).

1.3 PROBLEMS THAT CANCER PATIENTS EXPERIENCE

When people are invited to talk about cancer and the feelings that it evokes, a number of dominant themes emerge (Ray 1982):

1. Fear of death as either an inevitable or a possible outcome of cancer.

This theme is elaborated in terms of the pain and suffering that is thought by many to be a necessary part of the process of dying from cancer. People also associate weakening and loss of dignity with death.

2. Cancer is regarded with abhorrence because of its invasiveness.

People describe the disease as similar to "a tree spreading its branches" or refer to it as "eating you away".

3. A third theme is the uncertainty associated with the disease.

Few people have much knowledge of cancer and its implications. Although tremendous advances have been made in the scientific knowledge that exists about cancer, predictions about the prognosis and course of a patient's disease can only be made in broad terms. This uncertainty leads to feelings of helplessness and vulnerability.

4. Cancer creates feelings of conflict and ambivalence.

People express inconsistent attitudes and are often aware of this inconsistency. It is in part a reflection of personal ignorance, but it also represents a conflict between what the person thinks he or she knows rationally and what, on the other hand, the person feels subjectively. For example, the same person might profess a strong faith in the achievements of medicine, including the treatment of cancer among these, and yet at the same time feel that cancer is all-powerful and synonymous with death.

Mertz (1998) listed the following problems that cancer patients experience:

Invasive tests
Loss of autonomy
Pain and fatigue
Physical mutilation
Physical limitation
Loss of job
Financial problems
Emotional restriction
Side effects of treatment
Relationship with staff
General relationships
Insurance denied

Many of these issues will be discussed in depth further on in the chapter.

In a descriptive study of breast cancer patients undergoing adjuvant therapy following surgery, a sense of emotional disruption, stemming from fatigue, nausea and irritability, was described. Most patients also underwent major decreases in their levels of work and social activities coupled with major increases in emotional distress. Worsening family and sexual relationships were reported by 25 to 40 % of patients (Meyerowitz 1983).

A number of factors have been identified that consistently predict low quality of life. Patients with a poorer prognosis have reduced life satisfaction. Unpleasant and debilitating treatments, such as chemotherapy and radiotherapy, also reduce quality of life, although these effects appear to be reversed once the treatment ends. However, for some patients who take medications on a regular basis, quality of life can be substantially and chronically diminished by the treatment side effects. Treatment side effects are a particular problem for patients suffering from cancer (Taylor 1990).

1.3.1 ADJUSTMENT TO CANCER- GENERAL

Individuals living with cancer have the following needs: Practical, spiritual, psychosocial, informational, emotional and physical.

Coping is directed towards the resolution of difficulties, but it can be effective or ineffective, adaptive or maladaptive, in terms of its outcome. Can ways of coping be used to distinguish those patients who do adjust well from those who do not? First, we can predict that those who have coped unsuccessfully in the past, with the challenges of life as a whole, would be less able to cope with the demands of cancer and mastectomy. High neuroticism and trait anxiety are in fact correlated with poor adjustment to cancer, as are low ego strength, depression, low well being, pessimism, poor self-esteem and a discrepancy between expectations and actual attainment in life. General measures of personality however, make no reference to the nature of the immediate situation and cannot take into account specific factors, and patients who are generally well adjusted may sometimes react atypically to the threat of cancer and treatment. Unfortunately the patient's response to other and totally different situations of stress in the past is not very helpful in understanding or predicting her response to the stress of having breast cancer. Each stress experience has a very specific meaning (Ray 1985).

Because it is a chronic and mostly life–threatening disease, cancer poses a series of both physical and psychological threats to its victims, the intensity of which can sharpen and ease repeatedly throughout the treatment process and long thereafter. In recent years, the focus of medical care in cancer has broadened to incorporate not just basic issues of survivorship, but also quality of life (Knapp 1995).

Knapp (1995) has identified the following steps in the adjustment to cancer: These tasks represent some of the core psychosocial areas of quality of life and they are also at significant risk of disruption throughout the cancer experience:

1. Numbness occurs at initial diagnosis and recurrence.
2. Periods of anxiety will overlie the emotional shock. Individuals in this state of mind often process medical information inadequately or incorrectly (Heinrichs 1983).
3. Fear of pain, disfigurement and death.
4. Fears specific to the treatment: surgery, radiotherapy or chemotherapy often develops. Many patients believe that the treatment is worse than the disease.
5. Transient mood disturbances and periods of anticipatory grieving. Even when the prognosis is good, the patient may mourn the loss of sense of immortality and control over the course of his life.
6. Searching for explanations of the illness.
7. Episodes of externally directed anger occur.
8. The patient is at high risk of developing psychological morbidity.
9. The ability to manage stress and loss become a critical factor.
10. Any therapy that compromises reproductivity or sexuality may pose added psychological consequences, because these domains are a partial basis of self-image for many adults.
11. Negative psychological impact may then spill over into interpersonal functioning, not only in the area of sexuality but also into family and social relationships.

Good psychological functioning permits an individual to adapt and cope with an awesome array of physical and social assaults. Healthy psychological functioning, that is freedom from anxiety and the ability to adapt and adjust to different illness states, is crucial for the maintenance of a good quality of life (Fallowfield 1990).

In certain circumstances illness can be seen as a reaction to stress, loss or other psychodynamic events (Jaffe 1977). According to Moos (1977) seven major adaptive tasks must be confronted and managed at the time of an illness:

The illness – associated tasks are:

1. Dealing with pain and incapacitation.
2. Dealing with the hospital environment and treatment procedures.
3. Developing functional relationships with the hospital staff.

The general tasks are:

1. Preserving an emotional balance.
2. Preserving an adequate self-image.
3. Maintaining relationships with family and friends.
4. Preparing for uncertainty.

Tarr & Pickler (1999) conducted a study to explore the process by which families of children with acute lymphocytic leukemia "become" cancer patients. The central process of "becoming" was defined as trying to live as "normally" as possible; accepting that life is not the same; understanding what you have to do; accepting what you can't change and living with dissatisfactions. This process was mediated by families' external contexts, including marital relationships and support networks, experiential contexts, including positive and negative experiences during treatment and previous illness experiences, and internal contexts, including personal survival strategies and personal outlooks and attitudes. The process illustrates the pattern of experience that occurs in families faced with the diagnosis of their child's acute lymphocytic leukemia. Understanding this process may be useful to care providers when treating patients with cancer.

1.3.2 COPING WITH STRESS

Coping refers to the "things people do to avoid being harmed by life's strains". They try to overcome difficulties and minimize the impact of unpleasant events by using skills and habits that have been developed over a lifetime. It is behavior directed towards the solution or mitigation of a problem, and the term coping should not strictly speaking be used, as it sometimes is, to describe emotional responses that lack this purposive element (Ray 1985).

Types of goals in coping:

1. Instrumental coping:

Brings about an objective change in the situation.

2. Meaning-directed coping (palliative):

Even without any objective change in the situation, the person may be able to change the way in which she perceives the situation to make it more acceptable for her.

3. Emotion-directed coping (palliative):

Anxiety, anger or depression interferes with the person's behavior in the situation. It may be beneficial to tackle these emotions even when nothing can be done to change outcomes or the way in which they are evaluated.

Both instrumental and palliative coping serve to protect the person from distress, and the latter may in many situations be the only possible way in which adaptation can be achieved and psychological equilibrium be maintained. Indeed it is forms of coping that modify meanings and emotions, rather than objective events, that have been most emphasized in the past literature. It is these forms of coping that are primarily reflected in the "defense mechanisms" first proposed by psychoanalytic writers (for example Freud), but which, since then, have been very widely adopted by clinicians and researchers in the field of adjustment. Within this psychoanalytic framework the defenses are viewed as mechanisms that protect the ego from conflict, achieving this aim by "deceiving" the self and distorting reality (Ray 1985).

The most commonly found mechanisms include the following:

Repression: inhibiting the awareness and expression of impulses or feelings that would cause anxiety.

Denial: disavowing unwelcome impulses from within or unwelcome facts in the outside world; focusing on the pleasant.

Reaction formation: acting out the opposite of unacceptable feelings.

Displacement: attaching an unacceptable motive or emotion to an alternative object. This can provide some release without the conflict that would be involved in directing the feeling at its original object.

Sublimation: channeling an unacceptable impulse into a socially acceptable behavior.

Rationalization: disguising the true reasons for a behavior; presenting plausible but distorted accounts of beliefs.

Isolation: cutting off the unpleasant emotional aspects of a total experience; acknowledging unpleasant ideas, but not the unpleasantness associated with them.

Intellectualization: focusing on abstract ideas or detailed minutiae and adopting an objective and "scientific" attitude towards the situation.

Projection: disowning thoughts and feelings that a person has and projecting them onto others; attributing to others his or her own unacceptable motives.

Regression: acting inappropriately for a person's age; not accepting self-responsibility and turning to others for emotional support.

Suppression: directing awareness away from a conflict, threat, or unpleasant experience.

Alternatively these reactions can be analyzed in terms of general styles or dispositions: Repression-sensitization: Repressors are those people who characteristically take an ostrich-like stance when threatened. The significance of the situation is discounted in some way and the person tries to maintain her present equilibrium rather than adjust to a new one by simply not recognizing that circumstances have changed.

Sensitizers are open to and even on the lookout for unpleasantness. They recognize and focus on threat and make an attempt to find a new equilibrium that takes account of changed circumstances.

Locus of control: The person with an external locus of control tends to see their fate as being determined by chance or by powerful others, rather by than their own efforts. In contrast, the person with an internal locus of control is typically one who sees herself as "holding the reins", with her own actions determining outcomes. Both these dimensions are useful, in that they can predict behavior, but the character of a given person's coping is not necessarily consistent across either time or situation. It is now widely acknowledged that personality variables such as these indicate only broad tendencies. Thus, the same person may be both a repressor and a sensitizer, or have either an external or an internal locus of control, depending on the context (Ray 1985).

1.3.3 COPING IN CANCER PATIENTS

Denial is most often discussed in the literature in connection with cancer patients:

- Patients may fail to draw the obvious conclusion from the evidence of the treatment they are receiving and avoid taking the opportunity of confirming any suspicions that they have.
- Some may even deny the fact of their cancer even though this has been communicated to them directly.
- Alternatively, denial can take the form of an acceptance of the diagnosis but with a refusal to acknowledge its implications.

Though denial is an important strategy for dealing with cancer, it may not be quite as prevalent as it seems. In some vulnerable patients it may be the only viable response, where the alternative would be fragmentation and despair. Where there is little possibility of controlling the objective threat, then its open acknowledgement may serve little purpose. This is generally true of cancer and denial may enable the patient to face the future with hope and optimism at little cost. However denial before diagnosis, when delay may worsen the prognosis by giving the cancer a chance to grow and metastasize, is maladaptive.

A study of coping in breast cancer described defense employed in terms of six basic styles:

- Displacement: For example where the patient showed an excessive concern for her husband but not for herself.
- Projection: In the form of hostility to the staff.
- Denial with rationalization: The most common strategy found in the study. Patients adopted the view that all was well and provided justifications for this view.
- Stoicism and fatalism.
- Prayer and faith.
- A style where several of these defenses were employed simultaneously.

The researchers attributed the apparently good adjustment of patients in their sample to the use of the coping devices described, emphasizing that distress does not automatically follow from exposure to a stressor, but depends on how this is perceived, interpreted and defended against (Ray 1985).

In a sample of 90 women, their responses were analyzed in terms of a number of ego-defenses and then related to delay in presenting with the breast symptom. Denial and suppression were found to be positively associated with delay, while intellectualization and isolation were negatively related (Ray 1985).

In another study, coping strategies were defined in terms of patients' general attitude towards their illness:

- Denial.
- A fighting spirit.
- Stoic acceptance. Over half the responses obtained were stoic acceptance. Patients who coped in this way were less likely to change the nature of their response.
- Anxious-depressed acceptance.
- Helplessness and hopelessness (Ray 1985).

An analysis of general coping responses to serious illness by Verwoerdt (1972) suggests three categories, oriented towards cognitive ways of coping with the situation:

1. Strategies that involve a retreat from threat.

Examples are withdrawal and regression.

2. The exclusion of threat or its significance.

For example suppression, denial, rationalization and depersonalization.

3. Mastery of the threat.

Includes strategies such as intellectualization and acceptance of loss.

Ray and coworkers (1982) described a schema of the coping strategies of patients, which incorporates features of many of the other approaches, but within a structured framework:

- Rejection-assertion:

Rejection-assertion is a way of coping that reflects a view of the situation as basically unacceptable. The patient rejects its implications and attempts to revise these to meet her personal needs and desires. In the context of cancer, there may be little that the patient can do to assert her demands over the facts. Her attempts at control are often frustrated and lead to bitterness and resentment.

- Control:

When control is the coping mechanism, the situation is not seen as a battle but as a challenge. The patient rather than rebelling against it, view it as a problem to be managed.

- Resignation-helplessness:

This patient faces the threat, but sees herself as relatively powerless, with events and outcomes being determined by fate. There is a sense of "what will be will be" and so there is no incentive to struggle against the situation or to attempt to control it.

- Trust-dependency:

Trust-dependency is related to resignation helplessness in that the patient regards herself as relatively powerless, but events and outcomes are seen here as being determined not by fate but by other people. She relies on her faith in the physicians and the nursing staff.

- Avoidance:

The patient acknowledges the existence of the threat, but avoids situations or thoughts that will remind her of it. Withdrawing attention from it neutralizes the threat.

- Minimization-denial:

The patient sees the situation as relatively secure. As far as she is concerned there is little or nothing to worry about and nothing that needs to be done.

Successful coping requires a balance between what one can accept and confront and what can harmlessly be ignored or postponed. There is some evidence that coping that is oriented towards control has a positive role in adjustment. Confrontation was associated with low distress, while suppression, fatalistic submission, social withdrawal and passivity characterized patients who did less well (Weisman 1976). Information seeking was one way of establishing control and a study of coping, showed that this was associated with less negative effects, in contrast to recourse to wish-fulfilling fantasy. The latter is an avoidance strategy and is associated with a poor acceptance of the illness.

The coping strategies of patients that facilitate psychological adjustment must be identified next: There is some evidence that avoidant coping is associated with increased psychological distress. On the other hand, cognitive restructuring is associated with good emotional adjustment. Coping by fantasizing, expressing emotion or blaming the self is associated with poor adjustment. Information seeking and threat minimization is not related to adjustment. Weisman and Worden (1976) found poor adjustment to be associated with efforts to forget the cancer, fatalistic views of cancer, passive acceptance, withdrawal from others, blaming of others and self-blame.

The previously mentioned findings concerning denial imply that coping strategies may be most effective when they are matched to the particular problems or points in time when they may be most useful. There is evidence that people spontaneously match coping strategies to aspects of a stressful event. For example, people are more likely to use problem-solving strategies for aspects of a stressor that are amenable to direct control and to use emotion-focused coping for aspects of a stressful event that remain uncontrollable. Also, research suggests that multiple coping strategies may be most effective in managing some stressful events. In conclusion, active coping strategies seem to be more consistently associated with good adjustment than avoidant strategies, so long as there are aspects of the disease amenable to active coping efforts (Taylor 1990).

One of the criteria for successful adjustment has been the length of time it takes people to return to their pre-stress activities. Often a chronic illness interferes with the conduct of daily life activities. To the extent that a person is able to resume those activities, adjustment is said to be better. However, there is an implicit bias in this criterion to the effect that the person's prior living situation was in some sense an ideal one. This is not always true. In fact, substantial life change may follow a stressful event and this may be a sign of successful rather than unsuccessful adjustment. Most frequently, researchers have measured adjustment in terms of psychological distress. When a person's anxiety or depression is low, adjustment is judged to be successful. In summation, then, there have been several criteria of successful adjustment, which were formally incorporated into quality of life measures (Taylor 1990).

1.4 HEALTH AND PERSONAL CONTROL IN QUALITY OF LIFE

After cancer, a person's sense of security and well being in their internal and external environments may be permanently altered. Often the meaning given to cancer is more destructive than the disease itself. Leigh's (1992) physical recovery from cancer treatment took six months, but her psychological, emotional and social recovery took years.

Research has also found lower psychosocial morbidity to be associated with positive active responses to stress, to high internal locus of control and to beliefs that one can personally exert direct control over an illness. Similarly, low levels of helplessness have been associated with superior psychological and behavioral functioning and reduced symptom severity (Taylor 1990).

Campbell (1976) conducted a large-scale study on quality of life. Good health was found to be the most important domain and there was a strong relationship between health status and satisfaction. Poor health seems to be a condition of life that is uniquely difficult to accept. Most people seem to have a capacity to live with economic or personal vicissitudes and to develop some degree of satisfaction with their circumstances. But poor health is a condition that people find very difficult to feel satisfied with.

Not surprisingly, age and socioeconomic status were correlated with health status. Nevertheless, a certain amount of accommodation appeared to take place during the aging process. This moderated the negative impact of poor health in later life, so that relatively high levels of life satisfaction were reported. Furthermore, a strong sense of personal or internal control over life was also associated with good health, happiness and life satisfaction (Campbell 1981).

According to Knapp (1993) there appears to be evidence that a perception of personal control is often associated with positively reported quality of life. Overall control was found to relate to both psychological and physical outcomes. Those who generally found more control over their lives experienced less depression, less impairment of activities of daily living, less pain and less severe symptomatology. Individuals with a stronger sense of internal overall control were less likely to report decreases in their social and recreational activities. The cancer diagnosis and treatment process may negatively affect specific aspects of quality of life, such as sexuality. She also found that cancer patients frequently indicate that they have a good quality of life, with the exception of those in chronic pain or those in active therapy.

1.5 THE PERSONAL MEANING OF ILLNESS

Unconsciously, if not consciously, we feel that anything can be achieved as long as we try hard enough or want it badly enough. We regard death as something that comes to other people; or to ourselves, but in some far distant future. An illness like cancer cuts through these illusions of omnipotence and immortality and courage is needed to carry on without them and somehow not only to accept but also to transcend our limitations. Illness provides opportunities for growth on the part of both the physician and the patient. It provides a context in which the nature of the human condition can be learned and the character necessary to negotiate reality can be developed. This is of course an ideal as opposed to a description of what actually occurs (Ray 1985).

The most obvious interpretations of a cancer diagnosis are negative ones – a loss, a threat, or a punishment. Their unfavorable impact is likely to be especially marked for patients with other risk factors such as social isolation, low socioeconomic status, past history of psychiatric illness, alcohol or drug abuse, other recent life stresses and a tendency to be rigid and pessimistic in outlook. However, striking exceptions are sometimes seen, when a diagnosis of cancer seems to enable a patient to transcend longstanding emotional maladjustment. Many patients see positive aspects to their illness as well as negative ones: it may represent a challenge to be fought and overcome (Barraclough 1994).

"I had lost my innocence and in the fullest sense I realized how very close I'd come to my own mortality (Runowicz 1995)."

Even people who have a good prognosis after a relatively uncomplicated course of treatment did not experience cancer as a limited episode. The person enters what can meaningfully be described as a new stage of life as a consequence of the crisis (Mages 1979).

Rijken et al. (1995) compared the structure of the concept subjective well being between three groups of elderly women (cancer patients, women with chronic ailments and healthy women). Physical health is extremely important to elderly populations. It is crucial to maintain a state of independence, which is highly valued by the elderly. The most notable finding was that perceived physical health appears to be more strongly related to global subjective well being, when the objective health status is worse.

When a woman first learns she has cancer, she and her loved ones turn to the oncologist for information about her illness, leaning on the combined strength of her medical support team for direction and encouragement in the demanding fight simply to stay alive. The woman who survives cancer faces rocky, uncharted territory. Often she must contend with the disabling consequences of therapy and face the ongoing concerns about living with a frightening chronic disease. Slowly she beings to realize that her body may not look, feel or function exactly the way it did prior to her illness. And she may find herself reevaluating her relationships, her career, her goals, and even her sense of purpose. On top of this comes the ever-present threat of recurrence, a fear that stalks, to varying degrees, every cancer survivor (Runowicz 1995).

1.6 GENERAL FACTORS WHICH INFLUENCE QUALITY OF LIFE

Rustoen and coworkers (1999) used the Ferrans and Powers Quality of Life Index and the Cancer Rehabilitation Evaluation System (short form), to examine which domains of quality of life are most strongly affected in patients with newly diagnosed cancer. Additionally they examined whether quality of life was related to gender, age, educational level, cohabitation, time since diagnosis, treatment or type of cancer. The patients were satisfied with their lives, especially with the family and marital domains. They were least satisfied with health, functioning and sex life. Those cohabiting had significantly higher quality of life compared with those living alone. In contrast the younger group (19 – 39 years) living alone had significantly lower quality of life than the older groups living alone. Elderly people reported their quality of life to be better in almost all sub-scales. Time since diagnosis was not associated with quality of life, while treatment was associated with quality of life. Gender and educational level were only associated with one or two domains in quality of life, respectively.

The major concerns and needs of breast cancer patients was assessed by Wang and coworkers (1999). Their major concerns and needs were health, family, finances, work, the future, self-esteem, counseling and support for themselves and their family. Married women and those younger than 50 were more likely to have concerns about their family. Nonwhites had more concerns about finances and work than white women did. Older women and married women, however, had fewer concerns about finances and work than younger women did and those who were not married. Fewer nonwhites than white patients expressed concerns about their future. Young women were more concerned with self-esteem than older women. More nonwhites than whites and more married than unmarried women expressed needs for family counseling and support. Help for interpreting information was required more frequently by nonwhites than whites. Nonwhite women also tended to require more referrals than whites.

1.7 THE RELATIONSHIP WITH MEDICAL PERSONELL

1.7.1 GENERAL

Stefaneck (1994) assessed the psychological consequences of communication problems between patients and providers. A substantial portion of patients (84%) reported difficulties communicating with their medical team. The difficulties reported suggest that although providers offered information and explanations, many patients had problems comprehending information. Many patients reported problems with asking questions and expressing feelings to providers, behaviors that could prompt clarification of the information received. Also, communication problems were more common among less optimistic patients. Patient-reported communication problems were associated with increased anxiety, depression, anger and confusion at a three-month follow-up. The data suggests that interventions to enhance communication between patients and providers may improve psychologic adjustment to treatment.

Cancer impacts on all aspects of the patient's life. Most cancer patients have special concerns about their physical appearance, self-esteem and sexual lives. Too often health professionals focus their attention only on the disease process, its diagnosis and treatment. Often it is the lack of information and an inability to communicate with cancer patients about these concerns which lead physicians and other health professionals to neglect important aspects of patients' care (Vaeth 1980).

Patients rely heavily on their physician to weigh the potential benefits and risks of therapy alternatives and provide clear treatment recommendations (Fetting 1988).

There are certain things about how patients operate that would be useful for physicians to know. The first is that patients' fears and more rational expectations may be strongly influenced by the experiences of a relative or close friend with cancer. These expectations may be in the form of a general belief that cancer cannot be stopped or in the form of specific expectations about the possible spread or complications of the disease. Physicians could find out what those expectations are simply by asking whether the patient knew anyone with cancer and what had happened to them. This would enable the doctor to clarify mistaken ideas and to gain a picture of how the patient may interpret certain events or symptoms during chemotherapy. It might also be possible to pick out those patients who have very distressing and pessimistic expectations about cancer and treatment so that they can be watched more carefully.

A second fact that medical personnel need to be aware of is that patients are constantly making inferences from details of their physical state, treatment procedures, and remarks by their doctors, about what the disease is doing. The patient as evidence of therapy success or failure may interpret things such as levels of side effects or changes in these, low or high white cell counts. The doctor or nurse needs to be aware of this possibility, and to be ready to offer explanations where none are asked, and to also question patients about their interpretations of things, which are happening in the treatment. For example, patients should be told, before they start chemotherapy, about the schedule of tests they will be given, so that they will not assume something is wrong when given a routine bone scan.

Thirdly, physicians need to know that most patients with metastatic disease are able to face what is happening with their disease. When they have adequate information, they make accurate judgements about how well their treatment is working. If patients appear to deny or be unaware of what is happening with their disease, this may be more a social pretense than what they actually think.

Finally health care workers need to know that the disease and treatment may create family problems which are serious enough to need outside assistance. For example withdrawal or acting out in children, because they are angry with their parent for being sick (Ringler 1983).

Poor communication, rather than poor treatment, is the basis of most complaints and most patients simply want to be treated with respect and sensitivity (Cousins 1989).

1.7.2 RELATIONSHIP WITH THE SURGEON

The treatment of illness does not take place in a vacuum, but within the framework of the relationship between the patient and the physician responsible for her care. A key aspect of this relationship is its hierarchical nature. The degree of inequality varies depending on the people involved, but the physician inevitably does have the more powerful role. There are a number of bases to his power. He can first, provide resources that even it they cannot promise a cure, still offer the patient some hope of return to health. The patient is in a sense, a supplicant for these resources. Second within our social system physicians are cast as figures of authority, having the right to make important decisions regarding their patients' welfare, within the constraints of a general ethical code and certain limits prescribed by law. It has been suggested that the profession is "invested at the level of bodily health, with powers similar to those exercised by the clergy over men's souls". Third, the physician has a competence acquired through training and experience that most patients undeniably lack, giving his pronouncements a greater weight than those of any layman.

When a patient consults a physician, the latter makes recommendations for action and the patient is generally regarded as having to comply with these recommendations. A lack of compliance is regarded as a failure to comply. It takes more determination to tell a physician outright that you are not going to regard his advice than, to accept a prescription and subsequently discard the tablets. Hospital treated illness is more serious and the possible costs of noncompliance in terms of health are therefore greater.

Without this authority the physician would have less prospect of persuading patients to accept treatment whose rationale they do not understand, or treatments that are unpleasant, and from this point of view can be regarded as a quality to be fostered. It can also be of psychological benefit to the patient, by lifting from her shoulders the responsibility of evaluating courses of action and making decisions, a responsibility that she might not be able to cope with intellectually or emotionally.

This portrait of a relationship in which the physician has the authority and the patient is passive and dependent, is one that is conflict free. It assumes that the perspectives of the physician and the patient are compatible, and their roles are complementary, and that the patient is willing to hand over control to the physician in return for his efforts to define and solve her problems. However, although some patients conform to this model, others are more questioning in the relationship and seek to preserve their autonomy. Medicine is a specialized subculture in which the layman and the professional inhabit "separate wolds of experience". While the patient may respect the physician's greater expertise, she may have reservations about how this expertise is being applied to her own particular situation. Her perspective on illness may be very different from his. He applies general rules and categories and functions as a professional on the basis of his training and experience. The patient, in contrast, is personally involved and brings to her role other aspects of her being. Thus, while the physician and the patient may agree in the abstract on the ultimate goal of cure, they may have different ways of defining the problem and different ideas about viable solutions. Some consultations can thus involve a struggle for control, from these different perspectives, even though the struggle may be subtly expressed. Its existence is recognized whenever physicians talk of persuading patients to do something for their own good, or of overcoming their resistance. The struggle for control is also manifest when patients complain that they have not been sufficiently informed of the facts about their illness and treatment, thus depriving them of the opportunity to make their own judgement.

In the case of breast cancer and mastectomy, the kind of conflict that might arise is one where the surgeon recommends the operation on the basis of its curative potential, while the patient is concerned also with that treatment's personal, social and sexual implications. Many patients are happy to take their surgeon's advice on trust, assuming that he knows what is best for them. But there are patients who refuse mastectomy or who acquiesce with misgivings. The latter may be resentful and bitter after surgery, never having been truly convinced that the extra safety to be derived from the removal of the breast would compensate for the distress they feel at its loss (Ray 1985).

Some surgeons would like a patient to participate in the decision-making process. They may hope that she will agree to whatever recommendation is made, but would like to feel that this agreement has the force of an informed consent (Ray 1985).

1.7.3 RELATIONSHIP WITH THE NURSE

Generally speaking nurses have a more explicit and well-articulated concept of their role than physicians do. This role has two distinct but interwoven aspects: a technical function in taking care of the physical needs of patients and an expressive function that comprises the kinds of concerns implicit in a personal orientation. The former refers to the support of the patient's physical treatment and care and the latter refers to the effort she makes to reduce the patient's emotional tensions. The importance of caring for the total patient, that is for her psychological as well as her physical needs, is very commonly recognized. The nurse informs the patient, reassures her, conveys warmth and interest, and helps to clarify problems and solve them but this is to some extent an ideal, as opposed to actual practice. Nurses may want to provide total care, but feel that they do not have the opportunity to do so. Most of the available time may be taken up by physical tasks and even if it is not, it is often seen as inappropriate for the nurse to stay by the patient just to talk (Ray 1985).

A nurse may be reluctant to give information and have detailed discussions with patients, for fear of incurring the displeasure and criticism of a physician who regards himself as responsible for what to disclose and what guidance to give. Another problem is that nurses, like physicians, may have emotional difficulties in coping with their role, and these may be greater because of the closer and more extended contact that they have with patients. In caring for the sick, nurses are routinely exposed to grief, doubt and uncertainty and such stresses are particularly acute when working with cancer patients (Ray 1985).

Specialist nurses counsel mastectomy patients from the time of diagnosis and maintains contact after she has left the ward. This continuity of care enables her to deal with problems

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as they arise and she can talk to the patient about her feelings when she is ready to do so. Often, just the fact that the patient has the opportunity to express her fears and is encouraged to think in an objective manner about them seems to alleviate her distress. If the patient's reaction to the mastectomy is extreme, the specialist nurse will enlist the help of a consultant psychiatrist.

1.7.4 RELATIONSHIP WITH OTHER PROFESSIONALS

Professionals with training in psychology or social work can also support the patient in the same way as the specialist nurse. Counseled patients' anxiety, hostility and depression declines more rapidly. They are more active and realistic in their outlook and they are more open about the difficulties that they face because of their illness. Counseled patients show reduced denial and less negative affect.

1.8 THE PATIENT'S OPINION, NEEDS AND WISHES

1.8.1 GENERAL

Patients need to be treated as individuals because for each person, the cancer is a very personal experience. A cancer patient often feels that the cancer is a threat to her life, her courage and her faith in God: her entire existence. She sometimes feels that she is treated as a carcinoma left breast and not as a human being. She needs to maintain some measure of control over her life and she needs to come to terms with her illness. She also needs to be able to discuss her feelings and experiences.

Patients often need the acknowledgement that they are respected as human beings. This is especially true when medical staff is trying to put up intravenous lines, or carry out other potentially painful procedures without success and procedures have to be attempted repeatedly. One kind word can often make a huge difference.

A growing body of evidence indicates that believing one has control over outcomes in life plays an important role in maintaining and improving an individual's health and sense of well being. Street (1997) investigated patients with early breast cancer with regard to relationships among patient involvement in deciding treatment (i.e. whether to undergo breast removal or breast conservation), perceptions of control over treatment decisions and subsequent health-related quality of life.

Sixty patients with stage I or II breast cancer allowed their consultations with surgeons to be audio recorded. Following these visits, patients reported on their involvement in the consultation, optimism for the future, knowledge about treatment and two aspects of perceived decision control, the perception of having a choice of treatment and the extent to which the doctor or patients was responsible for the decision. The patients who had more actively participated in their consultations, particularly in terms of offering opinions, assumed more responsibility for treatment decisions during the year following surgery than did less expressive patients. Also, the patients who reported more involvement in their consultation later believed they had had more of a choice for treatment. The patients who believed they were more responsible for treatment decisions and believed they had more choice of treatment reported higher levels of quality of life than did the patients who perceived themselves to have less decision control (Street 1997).

1.8.2 PARTICIPATION IN CLINICAL TRIALS

According to Williamson (1996) there can be important mismatches between what clinicians and local health services provide and what some patients would have wanted. There are also concerns about the way research is conducted and how patients come to take part in it (Batt 1994). Both in treatment and research, patients sometimes conclude that they and their interests meet with scant respect (Hancock 1996). Therefore research that picks up trends in patients' views and detects new issues, as professional practices or patients' expectations change, is a necessary complement to professional assumptions and aspirations (Williamson, 1996).

Ambiguities between the "objective" world of science and the inner world of feeling come to the fore when participation in clinical trials are discussed. Alderson (1994) explored dilemmas between accepting randomization to a treatment arm of a randomized controlled trial and wanting "the treatment that is best for me". The results also suggested that greater knowledge led previously treated patients to reject certain research trials. Approximately half of the previously treated patients wanted to make their own decision.

Patients wanted to take part in treatment or research that would fit with their moral values, their work and social circumstances, and their responsibilities. Evidence is increasing that involving patients in making decisions and choices improves outcomes. But it is imperative to remember that the personalities of patients vary (Alderson 1994).
From the patients' point of view, the highest ethical standards must always be in place. Informed consent must be obtained from all participants (Williamson, 1996). Psychosocial and psycho-oncological research should learn from patients not merely study them (Pickering, 1995).

1.9 TREATMENT MODALITIES FOR CANCER AND THEIR IMPACT ON THE PATIENT

It must be remembered that patients with advanced disease have a limited life expectancy irrespective of treatment. Therefore, of the two objectives – palliation of symptoms and prolongation of life – the main emphasis has to be given to improving the quality rather than the length of the patient's remaining life. A point may be reached where aggressive active therapy diminishes the quality of life to a level where stubborn perseverance ceases to be humane.

All three general areas of human functioning: physical, social and psychological, can be affected by cancer treatment. Unfortunately, treatments without side effects are presently virtually non-existent. Some degree of morbidity is caused with every kind of cancer treatment and this, together with progressing disease, has clear implications for issues of quality of life (Knapp 1995).

Given the recognition that cure is not a realistic expectation for stage IV disease with conventional treatments, the patient and her physician should then define the goals and expectations of therapy. These goals could then help to define the philosophical approach to staging and treatment priorities. One would logically assume that the order of the priorities would most likely be: (1) comfort, (2) function and (3) longevity. Most patients and physicians would likely agree that achieving survival longevity without comfort and function would not be worthwhile (Aisner 1994).

Most women with advanced disease treated with combination chemotherapy regimens, whose disease responds, experience only a partial response of their disease. A minority of the women has a complete response, i.e. complete disappearance of all signs and symptoms of disease. For those women whose disease responds to therapy, one might reasonably ask how long such toxic or potentially toxic therapy should continue. There are no good studies to define the answer to these questions and many of the cooperative group trials have continued the therapy until the time of progression, sometimes in excess of two years. Such an approach seems contrary to the initial priority goals set out for the treatment of metastatic disease: comfort, function and then longevity. An alternative approach may be to give a fixed number of cycles (e.g. four to six, or until a maximum response is achieved) and then allow a woman a "rest" period off all chemotherapy to enjoy the benefits of response (Aisner 1994).

It has been found with prostate cancer patients that all areas of quality of life are significantly better for patients in remission and on treatment than patients with disease progression (Albertsen 1997). Disease symptoms under control are therefore very important for a good quality of life.

1.9.1 SURGERY

Hospitalization and surgery may be as terrifying, for some patients, as other concerns. Surgery has been described as "a planned physical assault" on the body, although one to which the patient has consented. After she leaves the hospital, the post-mastectomy patient moves toward adjustment to her illness and to the loss of the breast. Many women have difficulty in making the adjustment and postoperative depression is a common sequel to mastectomy and is marked by anxiety, insomnia, depressive attitudes, occasional suicidal thoughts and feelings of shame and worthlessness (Ray 1985).

The breast does not have a well-defined physiological function at the time of life when a woman is most at risk from breast cancer, but its loss can cause difficulties of adjustment at a number of other levels. It can affect a woman's body image, her perception of her identity as a woman, her social image and the way in which she presents herself to others and her marital or other sexual relationships (Ray 1985).

No matter how much a woman reads about breast surgery or how much support she receives from relatives and friends, it never is enough to prepare her for the shock of looking down at her own mastectomy scar. Each person experiences a different and unique level of grief when she loses a breast to cancer. And every woman needs time to mourn her loss and reconcile her feeling. We live in a society that worships breasts, not for their function, but for their form. The decision to undergo reconstruction after surgery has to do with a woman's sense of self, with restoring what has been lost (Runowicz 1995).

Patients, who are offered a choice regarding the type of surgery that will be performed, have been found to have less anxiety and depression, than those who were not offered a choice. However, offering the patient a choice of surgery is not a simple matter and it has been recommended that discussion should be supported by written or tape-recorded information. This information provided the patient the ability to discuss issues with family, friends and the patient's general practitioner (Stefanek 1994).

Indications for breast reconstruction following mastectomy begin with a reasonable assurance that the primary cancer has been eradicated. Therefore, stage I patients without evidence of spread beyond the breast either locally or distantly are the best candidates for reconstruction. But the possibility that a patient may succumb to a distant metastasis in the future is no justification to deny reconstruction in the intervening years (Harvey 1980).

The old-fashioned concept that women seek reconstruction because they cannot adjust psychologically to their plight is outrageous. People want to look and feel normal. Feeling good about oneself is terribly important to all people (Harvey 1980).

Surgery may have sequelae beyond the initial post-operative period. Axillary clearance can lead to painful and often permanent swelling of the arm (lymphedema). Lymphedema can be disfiguring and may have serious consequences if a cut or abrasion on the affected limb causes subsequent infection. Surgery for cancer is often deforming and follow-up surgery is often required to try and correct these deformities. One example is reconstructive surgery after mastectomy.

1.9.2 CHEMOTHERAPY

Despite the clinical benefit that may be associated with reduction of tumor volume, chemotherapy may produce physical or psychological distress that could compromise a patient's quality of life. Conversely, chemotherapy may palliate symptoms produced directly by the tumor, such as pain, dyspnea, or cough, or lessen psychological distress by reducing hopelessness. These effects may improve quality of life, providing benefits that are not reflected by the traditional outcomes assessed in cancer clinical trials, including tumor response, toxic effects and performance status (Seidman 1995).

Chemotherapy is a systemic treatment directed at rapidly growing cancer cells. The basis for cell death is generally targeted at the level of cell division. Therefore all normal cells that have a rapid turnover are also affected. Additionally, most chemotherapeutic agents have a narrow therapeutic index, which means that the difference between the effective dose and the toxic dose is extremely small.

Chemotherapy provided women with a sense of control over their lives and a feeling that they were doing something active to deal with the cancer. The patients identified that receiving chemotherapy helped them to deal with the sense of helplessness that accompanied the diagnosis of breast cancer (Levine 1988).

Most chemotherapy regimens are administered intravenously, some by continuous infusion over days or weeks, necessitating the insertion of a port and that the patient wear a continuous infusion pump. Frequent blood tests and counts need to be performed, so that needles are continuously assaulting the patient, which can be very distressing to some people.

Although more effective methods of controlling some of chemotherapy's side effects are available, it is not unusual for a patient to undergo periods of anxiety, depression and nausea in anticipation of each course of treatment (Knapp 1995).

The treatment of metastatic breast cancer involves the sequential selection and delivery of hormonal therapies and cytotoxic chemotherapies. The available therapies for metastatic breast cancer are rarely curative, although high rates of response and modest prolongation of survival may be achieved in association with varying degrees of treatment-related toxicity. Therefore, the selection of appropriate therapy requires a reasoned consideration of the likelihood of benefit from therapy balanced with the impact of therapy on the patient's quality of life. Several instruments have been developed to measure quality of life in cancer patients, but none has been universally accepted, and they require time and resources to administer. Few randomized trials have incorporated quality of life assessments. Thus the clinicians must balance the antitumor activity, performance status and the usual toxicity measures, as surrogates for quality of life associated with each specific therapy. Studies have confirmed the clinical impression that antitumor activity of treatment generally correlates with quality of life outcome (Carlson 1998).

A number of cytotoxic agents have activity in the treatment of metastatic breast cancer. Although the active single agents differ substantially in their toxicity profiles, the dose-limiting toxicity is usually myelosuppression. Recently, several agents with substantial activity in breast cancer have become available, including the taxanes (paclitaxel and docetaxel), vinorelbine and gemcytabine (Carlson 1998). The benefit of these agents needs to be carefully balanced with the quality of life that patients experience while receiving these treatments.

For many cancer patients, chemotherapy, radiation or surgery causes a drop in estrogen production that leads to premature menopause. The symptoms and consequences of menopause can be disturbing: hot flashes, vaginal dryness, diminished bladder capacity, insomnia, as well as an increased risk for osteoporosis and heart disease (Runowicz 1995). Estrogen replacement for patients with hormone-related cancers is contra-indicated and therefore the options to try and control the symptoms of menopause are limited. This may further impair the patient's quality of life. Additionally menopause can lead to decreased sexual desire, mood swings, irritability and an inability to concentrate. Hot flashes are usually worse at night, resulting in loss of sleep, which in turn leads to irritability and moodiness during the day.

Although continuous therapy significantly prolongs the time to disease progression, it does not result in improved survival. Coates et al. (1987) demonstrated that continuous therapy resulted in improved quality of life compared with intermittent therapy.

1.9.3 RADIOTHERAPY

The patient referred for radiotherapy for the treatment of advanced disease or following surgical treatment for breast primary, encounters a complex of psychological and social problems. First, it is still quite common for "radium treatment" to be stigmatized. Any mention of damaged nuclear plants or disasters involving radiation is, usually accompanied by information explaining the potential dangers of the invisible rays. Patients get scared, but since patients receiving irradiation instead of extensive surgery, usually chose to do so, they are inhibited from discussing their fears. One of these irrational fears is that the patient herself may become radioactive and a danger to her family. Other popular myths are that radiotherapy to any part of the body can make the hair fall out, that it is painful and that it inevitably burns the skin. With modern techniques, radiation burns are usually avoided, although women with sensitive skin may expect transient erythema and desquamation. Radiotherapy can cause exhaustion, nausea and vomiting, and much of the distress experienced by patients may be linked to this (Ray 1985).

It was demonstrated by Parsons and coworkers (1961) that 75 percent of patients exposed to sham radiotherapy developed symptoms of nausea and fatigue, and this suggests that many symptoms may be a function of anxiety produced by the procedure and patients' expectations of its effects.

Radiotherapy is employed either curatively or palliatively. It is a local or regional treatment and side effects depend on the body-site involved. Commonly fatigue and local skin reactions occur in the short term. Chest radiation may produce cardiac irregularities. Whole brain radiation causes hair loss and decreased mental faculty. Long-term sequelae such as incontinence, fibrosis of critical organs like the lung or even pain and skin burns can add to the patient's distress.

"When my radiation treatments began, I was fitted with a body mold to immobilize me during therapy and my chest was tattooed with little black dots so that the nozzle of the radiation machine lined up exactly with my tumor. The walls of the room were two feet thick and lined with lead. And although the technicians were very nice, explaining every adjustment they made, I was terrified. From the moment they turned to close the vaultlike doors behind them, it was all I could do not to run behind them, screaming" (Runowicz 1995). Runowicz is a gynaecological oncologist.

There is the social inconvenience of radiotherapy, which involves long distances to travel, particularly if the patient lives in a rural area, since radiotherapy centers are usually situated in large towns. As treatment is often five days a week for up to six weeks, then the additional expense and fatigue associated with travel, particularly among older women, presents a genuine additional burden (Ray 1985). The alternative is hospitalization that could also be stressful to certain patients.

It is difficult to assess the impact of radiotherapy independent of the life threat following the diagnosis of cancer and the impact of a mastectomy. Forester and coworkers (1978) tried to evaluate psychiatric aspects of radiotherapy among 200 patients receiving radiotherapy for a variety of disorders. These patients were interviewed before, during and after treatment and assessed using the Schedule for Affective Disorders (SADS). Unfortunately they chose psychiatric patients as controls. The patients receiving radiotherapy had increased scores for depression and anxiety throughout treatment, but similar levels for anorexia, fatigue and insomnia as in the psychiatric control group were found. In addition the treated patients scored more frequently for social isolation. An interesting and unlooked for finding from this study was the type of radiotherapy machine influenced the grade of change in affective disorder. The patients treated on the linear accelerator seemed to adapt very well and scores for depression and anxiety returned to normal toward the end of treatment. In contrast, those patients treated on the betatron, a noisy and somewhat threatening piece of equipment, tended to fare worse.

Another relevant study is that of Margolis et al (1983). They interviewed patients who had chosen radiotherapy as an alternative to mastectomy and found that these patients seemed well adjusted and grateful for the treatment. Since the patients self-selected for this therapy, they must be considered a biased sample and their reactions may be different from those of the general population.

It is likely that radiotherapy can have distressing effects, but that these are mostly of short-term duration (Ray 1985).

1.9.4 ENDOCRINE THERAPY

Endocrine therapy holds an important place in the treatment of breast cancer as it does for other hormone-sensitive cancers. The aim of endocrine therapy in breast cancer is to decrease or eliminate estrogen activity, as estrogen sustains the growth of hormone-dependant tumors. In premenopausal women this can be achieved by removal of the ovaries (surgically, radiotherapeutically or chemically), often in combination with antiestrogen therapy. In postmenopausal women, however, estrogen is produced predominantly by peripheral tissues rather than by the ovaries. Therefore, estrogen deprivation in this patient group is achieved by antagonism of estrogen at the receptor or reduction of estrogen levels by inhibition of aromatase (Lamb 1998).

In patients with advanced breast cancer endocrine therapy is considered to be the most important systemic treatment. The response rates to different endocrine treatment alternatives seem to be similar, but the drugs vary somewhat with respect to their side effect profiles.

The hormonal therapies have the quality of life advantages of limited and non-threatening acute toxicity, rare chronic toxicity, need for infrequent visits to health care providers, oral administration and, in appropriately selected patients, response and duration of response rates equivalent to those of the cytotoxic agents.

Tamoxifen is currently the treatment of choice for postmenopausal women with hormonally responsive breast cancer. It has a response rate of 76% in ER+ PR+ (hormone receptor positive) breast cancer and has very few side effects. Tamoxifen binds reversibly with the estrogen receptor, forming an inert complex that blocks estrogen-mediated protein synthesis. The toxicity is usually minimal but headaches and/or hot flashes sometimes occur. Development of endometrial cancer and corneal changes has been found in long term users and needs to be monitored carefully.

For patients with hormone-dependent breast cancer, inhibition of estrogen production is an effective form of therapy. Aromatase is an enzyme that is responsible for the peripheral manufacture of estrogen from androgens and cholesterol. Aromatase inhibitors like aminoglutethimide, letrozole, anastrozole, formestane and vorozole inhibit peripheral aromatase and suppress estrogen levels in postmenopausal women. Second-line treatment options, for locally advanced or metastatic breast cancer, include megestrol and anastrozole, with aminoglutetimide available as a third-line agent (Lamb 1998).

In the only trial to report quality of life (Dombernowsky 1998), no major differences were observed between patients receiving letrozole or megestrol. Letrozole was found to be significantly superior to megestrol with respect to overall survival and consistently achieved better response rates than megestrol.

1.9.5 PALLIATIVE CARE

For patients with metastatic disease, the aim of treatment is not curative but palliative. The most important endpoint is therefore a good quality of life.

The aim of the palliative treatment of cancer is to control the disease in order to make life as active and as symptomless for as long as possible with the least adverse effects of treatment. There is no intention to eradicate the cancer and so it has been accepted that the patient's life will almost certainly be severely shortened as a result of the disease. Communication is therefore a particularly sensitive issue and requires much skill and compassion and understanding (Rubens 1993).

Important aspects of communication:

- Adequate, frequent and sensitive communication with the patient.
- There has to be precise and frequent communication between different members of the medical team.

- Communication with the patient's family, keeping in mind that patients can become isolated under these circumstances.

General principles of communication (Rubens 1993):

- Honesty at all times, but this does not mean unsolicited candour.
- Attention must be paid to signals from the patients which indicate that there is a limit to how much information they wish to receive.
- For a satisfactory basis for communication there must at least be:
  An explanation of the disease status.
  What the aims of treatment are and its likely side-effects.
  Emphasis on quality of life.
  Fostering of realistic hope.

Within the various approaches to palliative care, the most contentious is the use of cytotoxic drugs. Rubens (1993) devised a scoring system to attempt to assess what the utility of treatment has been. Points are awarded for symptom relief, objective response, improved activity status and the reversal of immediately life-threatening disease. Points are deducted for physical toxicity, psychological morbidity and social disruption. There must be a positive score for treatment to be worthwhile. Findings were that: for first line chemotherapy for advanced breast cancer, it was deemed to be worthwhile in 34% of patients, for second line treatment in only 11%; third and fourth line treatments were not worthwhile in any patient. A highly significant correlation has been found between these criteria and standard objective response criteria.

1.10 SYMPTOM DISTRESS

Symptom distress can be defined as the degree of discomfort reported by a patient in relation to their perception of the symptoms being experienced (McCorkle 1987). Alternatively it can be seen as the physical or mental anguish or suffering that results from the experience of symptom occurrence and/or the perception of feeling states (Rhodes 1987). The reasons for assessing symptom distress include the identification of patients' needs and problems, and determining the effectiveness of different modalities of treatment.

Symptom distress refers to the meaning that illness holds for an individual (Kleinman 1978). Symptom distress alters the cancer experience and the individual's quality of life. Quality of life is often grouped in four domains: physical, functional, emotional and social well being. Factors that influence symptom distress are: disease state, gender, age, marital status, sense of coherence (an enduring and dynamic feeling of confidence), the type of treatment and the availability of home care nursing (McClement 1997). Additionally socioeconomic status, race, culture, role, education, health, knowledge, values and past experience may influence symptom distress. Considering the negative effect symptom distress can have on the patient and family, the management of symptom distress should be a priority of health professionals (Northouse 1995).

Symptom distress appears to be a significant prognostic indicator even when other psychosocial variables are considered (Germino 1987). High symptom distress scores can therefore alert clinicians to those patients who have limited time in which to deal with life completion issues (Degner 1995). This finding is also important because it may help to identify whether or not interventions do in fact improve patients' quality of life and/or survival.

1.11 EMOTIONAL PROBLEMS

The diagnosis and treatment of breast cancer are considered critical life-events leading commonly to depression, anxiety, problems in body image and self-concept and consequently social isolation (Fourie 1996).

The diagnosis of a chronic disease not only produces the need for behavior change; it also evokes many emotional changes that may require attention. The impact of chronic illness on the individual can be pervasive, affecting physical and emotional well-being work, sex and family life. Chronic disease can produce a variety of adverse outcomes, including pain and discomfort, fear and uncertainty about the future and a variety of adverse emotional effects, such as anxiety and depression. When left untreated, the emotional distress associated with chronic illness represents a substantial reduction in patients' quality of life and may further interfere with physical rehabilitation and return to work, leisure and social activities. Researchers are documenting the high prevalence of emotional distress in chronically ill patients and are designing interventions to prevent or reduce this distress (Taylor 1990).

Of particular concern in this regard is the patient's premorbid personality and any chronic history of depression or anxiety disorders prior to the onset of chronic illness. Those with prior histories of such disorders have a higher risk for exacerbated emotional responses to chronic illness, because chronic illness becomes an additional stressful event for them. Their psychological resources may leave them unprepared and their coping skills may be insufficient to deal with these adverse effects (Taylor 1990).

Practicing clinical psychologists have extended their concern beyond the treatment of specifically psychiatric disorders, to include the psychological care of people experiencing distress through illness or injury. Traditionally these patients have tended to fall through the net, unless their distress is so great that it assumes the proportion of a psychiatric disorder that can then be treated in its own right. Because the physical disorder is the primary one, its existence has detracted from the salience of the very real emotional disturbance to which it can give rise. Moreover, emotional reactions in this setting, being the norm, seem to have been regarded as not meriting special attention and care. This situation is changing. Within general medicine, there is now renewed emphasis on the care of the whole patient and not just the disease (Ray 1985).

Some degree of depression following treatment is normal for all cancer survivors. Studies have shown that while major mental illness is uncommon, cancer survivors do have an increased incidence of emotional problems in coping with the trauma of their disease. Cancer survivors need time to mourn their life before cancer and to grieve over the fact that after cancer things are never quite the same. Having cancer changes a person in many ways. Each patient must work through her feelings of sadness and loneliness, isolation and fear. The mind can sometimes take much longer to recover from cancer than the body (Runowicz 1995).

What helps patients keep emotional distress under control may be very individualized. What patients can do to make chemotherapy less difficult may be quite similar for all patients, while what they can do that makes it less distressing may vary considerably from patients to patient. For example, some patients reported that it was a great relief to talk to their husbands or friends about things that were upsetting them. In other patients, sharing sadness or worries with other people would only make them feel out of control. For them, it worked much better to conceal their upset from other people, and to keep busy with work so they didn't have too much time to think (Ringler 1983).

Most cancer patients, with the help of various coping strategies, manage to come to terms with their illness in ways that work reasonably well for them. Some, however, are unable to achieve a satisfactory emotional adjustment. Instead they develop reactions which impair their relationships with other people and prevent them from obtaining optimum benefit from anticancer treatments (Barraclough 1994).

Massie (1989) found that not all of the emotional distress found in cancer patients could be labeled as "psychiatric illness". Additionally, several of the common problems, like excessive anger or denial, do not fit with formal classification systems for psychiatric disorders. Nevertheless, psychiatric disorders occur more frequently in cancer patients than in the general population, and it is important to recognize them, as there may be specific treatment available.

The findings of several large-scale surveys have reported on the frequency of psychiatric disorder in large populations of cancer patients. The findings can be roughly summarised as follows:

• No psychiatric disorder	50%
• Adjustment reaction	30%
• Formal psychiatric diagnosis	20%

"Adjustment reactions " can be found in about one third of patients and usually take the form of anxiety and/or depression. These reactions are not serious mental disorders and usually improve on their own accord over time. Anxiety and depression do produce significant extra suffering. Humane and well-organised general clinical care could often do much to minimise this distress. Depression and/or anxiety are also the most common forms of disorders that are found in patients with a formal psychiatric diagnosis. It has been shown that the treatment of a patient's psychiatric illness often improves his physical condition as well.

Prevention of emotional problems (Massie 1989):

- Offer information about the illness and its treatment: "too little" information is a far more frequent complaint than "too much". Do not delay in passing on new information to the patient. Information given on one occasion is often forgotten or misinterpreted and may need to be repeated, or backed up with written material.
- Allow the patient to participate in treatment decisions, if they wish to do so.
- Let the patient express emotional distress, making it clear that it is perfectly normal to do so.
- Ongoing care from a few key doctors and nurses who will be there to monitor physical progress and emotional wellbeing throughout the course of the illness. The patient's own general practitioner should be one of these.

Research evidence shows that emotional problems among cancer patients often go unrecognised, unless they are specifically sought out, either through personal interviews or by means of screening questionnaires. Ideally such screening should be repeated at regular intervals for each patient because emotional problems can start at any time during the illness. Putting this apparently simple recommendation into practise requires consistent effort on behalf of the staff. Whether or not a formal screening programme is in place, it is important that all patients are asked from time to time how they are coping with the emotional side of their illness. They should also be given frequent opportunities to discuss their current concerns.

1.11.1 DEPRESSION

Depression is among the most frequent of emotional problems in cancer patients and it important to recognise this because it can often be treated successfully. Surveys show that up to 50% of patients at any one time report some depressive symptoms. Of these, 10 to 20 % have clinical depression. Depression is estimated to be four times as frequent in patients with cancer than in the population as a whole. Depression in cancer patients can be difficult to diagnose and can be easily missed (Massie 1989b).

This high rate of depression may be partially accounted for by either a premorbid propensity for depression, neurological damage or reactions to the stressors associated with chronic illness. Depression is important not only because of the distress that it produces, but also because it may have an impact on long-term rehabilitation and recovery. Depression has also been linked to suicide in the chronically ill (Taylor 1990).

Because depression can continue in certain patients after physical recovery, it is important that the patient and the physician be aware of it. It has been shown that there is a significant tendency by physicians to miss the diagnosis of depression in their patients, when compared to the patients' own assessment of their condition (Fourie 1996).

Assessment of depression in the chronically ill can be problematic. First, many of the physical signs of depression, such as fatigue, sleeplessness, or weight loss, may also be symptoms of the disease or a side effect of its treatment. If depressive symptoms are attributed to the illness itself, depression may be masked and infrequently diagnosed. These problems are exacerbated in illnesses that can affect brain function such as cancer (Taylor 1990).

Mental symptoms of depression	Physical symptoms of depression
Low mood with diurnal variation.	Weight loss.
Tearfulness.	Anorexia.
Guilt.	Insomnia (with early morning waking).
Feeling a burden to other people.	Tiredness.
Loss of interest.	Malaise.
Inability to feel pleasure (anhedonia).	Pain.
Poor concentration.	
Agitation or retardation.	
Irritability.	
Social withdrawal & suicidal thoughts.	

Seven items that identify severe depression have been described (Taylor 1990):

Indecision.
Sense of failure.
Dissatisfaction.
Loss of social interest.
Suicidal thoughts.
Crying.
Sense of punishment.

Depressed patients may consider themselves too worthless to merit help and do not complain about the symptoms of either the depression or the cancer. Additionally depression in the chronically ill often goes untreated because many people believe that one is supposed to be depressed after a diagnosis of chronic illness. Clearly guidelines must be developed concerning how much depression can be expected after diagnosis of a life-threatening illness and the point at which depression becomes severe enough to warrant intervention (Taylor 1990).

Physicians and clinicians should ask about family history of depression and prior episodes of depression in their patients. Screening instruments to identify depression can also be used. Although disease severity reliably accounts for part of the variance, it does not fully account for depression in chronically ill patients. Studies that control for disease severity have found that other negative life events, social stress and lack of social support are associated with depression in chronically ill patients. It is also possible that depression reduces the quality of social support during a prolonged illness (Taylor 1990).

Unlike anxiety, which appears to be episodic, depression can be a long-term reaction to chronic illness. For many illnesses, depression lasts a year or more following surgery or the diagnosis of the illness. The evaluation for these potential problems should be a standard part of care. A variety of interventions, from informal communication with a health care professional, to antidepressant drugs, have been proposed to alleviate emotional distress in chronically ill patients (Taylor 1990).

Biological complications of cancer such as hypercalcaemia and cerebral metastases, as well as steroids and chemotherapy, may lead to depression in vulnerable people. Additionally hypothyroidism and other physical illnesses can mimic depression (Massie 1989b).

1.11.2 ANXIETY

Chronically ill patients often experience anxiety and heightened levels of anxiety can interfere with physical and psychosocial functioning. For example anxiety is associated with poor functioning following radiotherapy. Some of the documented anxiety may be a premorbid propensity for anxiety, but there are also clear specific sources of anxiety during rehabilitation and treatment (Taylor 1990).

The following sources cause high anxiety during rehabilitation and treatment:

A diagnosis of cancer.
Invasive procedures.
Life-style alterations.
Fear of recurrence.
Waiting for test results.
The side effects of treatment.
Dependency on health professionals.

A certain degree of anxiety among patients with cancer is understandable. When anxiety develops for no apparent reason or persists in a disabling form long after the initial cause has passed, an anxiety disorder may be diagnosed. Some cancer patients remain disabled by anxiety about their illness even if they are doing well from a physical point of view. In someone with cancer, anxiety is often due to unexpressed fear of progressive disease and of death.

Mental symptoms of anxiety

Worry.
Irritability.
Restlessness.
Difficulty in falling asleep.
Sleep disturbed by nightmares.

Physical symptoms of anxiety

Breathlessness.
Palpitations.
Sweating.
Headaches.
A "lump in the throat"(that impedes swallowing).
Nausea.
Abdominal pain.
Diarrhea.

High levels of anxiety are generally associated with coping mechanisms. A finding that has consistently been made for breast cancer patients is that they show strong coping mechanisms in relation to the effect that their illness has on them.

Another consequence of high anxiety levels is that it interferes with patients' understanding and assimilation of the information that the physician is trying to communicate to them. This can be especially problematic during the time when the diagnosis is being made.

While some cases of suicide among cancer patients may be understandable and justified, others represent the tragic culmination of distress which might have been relieved.

Once a woman has suffered through the rigors of treatment and faced the prospects of her own mortality, the fear of battling cancer again is almost too frightening to consider. Yet in the back of every cancer survivors' mind is the terrifying possibility that one day the disease will return. That's why many survivors tend to panic whenever some new bump or lump surfaces or they experience a small ache or pain. The risk of developing a second cancer is also higher for someone who has had cancer before (see Addenda 1, 2, 5 and 7).

No person can come through an experience as traumatic as cancer without changing. On the positive side, many patients actually come to see a beneficial side to their illness. The experience of cancer often leads many survivors to critically review their values and life's priorities. In confronting their own mortality through sickness and the hard-fought struggle for health, many women find they are better able to accept both themselves and the smaller glitches of life. It can be called "life rekindled" (Runowicz 1995).

Recent studies, however, indicated that although the diagnosis and treatment of breast cancer are emotionally traumatic events its effects are generally of limited duration. It seems as if the majority of patients recover well from this experience without serious long-term emotional impairment. There are indications that this adjustment takes place within the first three months after surgery (Fourie 1996).

1.11.3 ANGER

Besides depression and anxiety, breast cancer patients may also experience feelings of guilt and anger with associated aggression.

Anger, a typical reaction that is often found in conjunction with depression, is often directed at the physician who is held responsible by the patient for the loss of her breast and other unpleasant medical procedures like chemotherapy and radiotherapy. Some patients direct their anger at their spouses. But some breast cancer patients do not show any signs of anger or aggression because of the very strong denial of their condition (Fourie 1996).

Anger should be managed by listening to the patient's point of view, without responding in a defensive fashion, and, however ungrateful and unrewarding the patient may be, to try to offer consistent professional concern (Barraclough 1994).

1.11.4 GUILT

Feelings of guilt are a less common, but not an atypical emotional phenomenon for breast cancer patients. They regard the illness as a punishment for the sins of the past. Alternately feelings of guilt may result from misconceptions about cancer, for example that it is contagious or can be caused by a blow or an injury. Other possible reasons for feelings of guilt are anger towards medical personnel, jealousy of the good health of family members or her realisation that she has a greater dependency on them (Fourie 1996).

Others even feel guilty because they do not recover soon enough and are therefore disappointing those who are treating and caring for them. Feelings of guilt are also sometimes found in connection with anger and depression (Fourie 1996).

1.12 LOSS OF ROLE

"Overnight, survival became my one and only goal. I cancelled most of my commitments, as I simply wasn't sure I could deliver. Quite simply, the bottom had fallen out of my career. Getting through office hours took every ounce of energy I had left. No one expected me to be at the office, but in order to heal myself I needed to feel some semblance of normalcy in my life (Runowicz 1995). "

Part of an individual's concept of self is derived from the various roles he or she engages in, such as work. A great deal of personal gratification is obtained through the achievement, the social recognition and the social interactions provided at and by work. Any forced retirement due to illness severely threatens self-image, self-worth and self-respect, which can produce considerable psychological distress. On the other hand, employment is not always particularly satisfying for some people. Some jobs can be so stressful or time-consuming that they detract from life's quality by intruding on other areas (Fallowfield 1990).

Multiple losses associated with the diagnosis of cancer often lead to loss of autonomy. Patients may lose their job, physical independence and social role. Older patients may have to give up their home. This enforced loss of role can often lead to boredom, with the resulting problems thereof.

When a person cannot cope with household duties and depends on others for the routine necessities of life such as shopping, cooking and cleaning, they may experience a fundamental role loss with a concomitant loss of self-esteem.

Role changes take place when the person with cancer is physically limited, so that the partner is forced to take over the patient's previous role and responsibilities. A few patients complain that their partners make little or no allowance for their illness, and expect them to carry on as before (Barraclough 1994).

1.13 PAIN

One of the worst aspects of cancer pain is that it's a constant reminder of the disease and of death. Many fear that the pain will become unbearable before death, and those of us involved in support networks have seen these fears proven true (Jacox 1994). Most generally, suffering can be defined as the state of severe distress associated with events that threaten the intactness of the person. The suffering of patients with terminal cancer can often be relieved by demonstrating that their pain truly can be controlled (Jacox 1994).

In 1982, Marcia Angell wrote "Few things a physician does are more important than relieving pain. Yet, treatment of pain in hospital patients is regularly and systematically inadequate."

Personal control is undermined when cancer is diagnosed and is further reduced by ongoing pain, invasive or undignified procedures, treatment toxicities, hospitalisation and surgery. When pain reduces patients' options to exercise control, it diminishes psychological well being and makes them feel helpless and vulnerable (Jacox 1994).

TABLE 1: EFFECT OF CANCER PAIN ON QUALITY OF LIFE (Ferrell 1991):

Physical

Decreased functional capability.
Diminished strength, endurance.
Nausea, poor appetite.
Poor or interrupted sleep.

Psychological

Diminished leisure, enjoyment.
Increased anxiety, fear.
Depression, personal distress.
Difficulty concentrating.
Somatic preoccupation.
Loss of control.

Social

Diminished social relationships.
Decreased sexual function, affection.
Altered appearance.
Increased caregiver burden.

Spiritual

Increased suffering.
Altered meaning.
Reevaluation of religious beliefs.

Avoidance of pain is one of man's most basic drives and one of the primary reasons for seeking medical help. Chronic pain severely restricts a person's ability to function and enjoy life and poses considerable psychological, social and economic stresses. Pain is a very individual, subjective experience, ameliorated or enhanced by such things such as culture, conditioning, attention and emotional state. Chronic pain is often a diminishing, humiliating, even frightening experience for the patient and tends to supersede all other sensations. One of the most feared consequences of cancer is uncontrolled pain. The appearance of pain in a cancer patient usually indicates progression of disease, but it must be remembered that pain perception is very subjective. Pain can mask depression and can be the result of excessive anxiety (Fallowfield 1990).

Cancer is a major health problem, with one in every ten deaths globally attributable to cancer. In 1984 more than three and a half million people suffered from cancer pain daily (WHO 1986). However, only a fraction of cancer patients in pain, receive adequate treatment for their pain. The necessary technology exists to alleviate this health problem. It has been demonstrated that cancer pain can be controlled in over 85% of terminal cancer patients by the rational use of drugs. An "analgesic pain killing ladder", developed by the World Health Organisation, provides a clear plan of action for health care services (Stjernswärd 1986).

The WHO analgesic ladder:

Non-opioids	paracetamol and aspirin.
Mild opioids	codeine.
Strong opioids	morphine.

When a drug does not work, a stronger, rather than a different one is prescribed.
Drugs are given round the clock rather than as required.

Skevington (1998) assessed quality of life, using a new, multidimensional, multilingual, generic profile designed for cross-cultural use in health care, i.e. the WHOQOL. In this instrument, pain and discomfort is one of 29 areas of quality of life. These areas or facets are grouped into six domains. It was found that pain and discomfort made a significant impact on perceptions of general quality of life related to health. The presence of pain also affected perceptions of five of the six domains of quality of life. The only domain that was unaffected, was the domain of spirituality, religion and personal beliefs. When quality of life is assessed, negative feelings are more closely associated with reports of pain and discomfort than any other facet.

Quality of life surrounding pain and discomfort consists of seven facets (Skevington 1998):
The availability of social care
Activities of daily living
Sleep
Spirituality, religion and personal beliefs
Mobility
Positive mood
Dependence on medication

These are the criteria against which the success of pain treatments may be evaluated. As predicted, those who were pain-free had a significantly better quality of life than those who were in pain. A longer duration of pain is associated with increasingly poorer quality of life. Intense affective pain is particularly detrimental to a good quality of life (Skevington 1998).

Pain control merits high priority for two reasons. First, unrelieved pain causes unnecessary suffering. Because pain diminishes activity, appetite and sleep, it can further weaken already debilitated patients. The psychological effect of cancer pain can be devastating. Patients with cancer often lose hope when pain emerges, believing that pain heralds the inexorable progress of a feared, destructive and fatal disease. Chronic unrelieved pain can lead patients to reject active treatment programs, and when their pain is severe or they are depressed, to consider or commit suicide. Besides mitigating suffering, pain control is important because, even when the underlying disease process is stable, uncontrolled pain prevents patients from working productively, enjoying recreation, or taking pleasure in their usual role in the family and society. Pain control therefore merits a high priority not only for those with advanced disease, but also for the patient whose condition is stable and whose life expectancy is long (Jacox 1994).

1.14 FATIGUE

After treatment it's common to feel exhausted and spent. No one comes through an ordeal as traumatic as cancer and jumps right back into life. Every survivor experiences feelings of uncertainty and depression about the future. Although the exact cause for chronic fatigue hasn't been elucidated, some believe it is brought about by the additional energy the body must expend on repairing injured cells. Another possibility is that bone marrow suppression is responsible (Runowicz 1995).

Recent multidimensional conceptualisations of fatigue in cancer patients suggest that fatigue is a subjective experience with significant physical (e.g. weakness), behavioural (e.g. alterations in sleep patterns and activity level), cognitive and affective (e.g. mood disturbance) components (Piper 1989).

Although fatigue is the most common symptom reported by cancer patients and has serious adverse effects on quality of life, it remains poorly understood. It is a subjective sensation often described by patients as a feeling of tiredness, lethargy or malaise. Cancer-related fatigue also has been characterised as asthenia (lack of strength). Cancer-related fatigue is probably multifactorial, with physical and psychological components. Fatigue is often distressing and can have serious adverse effects on quality of life. Fatigue may affect decisions to continue treatment or the ability of a patient to tolerate various forms of therapy. It can also significantly interfere with patient self-care abilities (Volgelzang 1997).

A survey was designed to characterise the epidemiology of cancer-related fatigue from the perspectives of the patient, primary caregiver and oncologist. More than three quarters of patients (78%) experienced fatigue (defined as a feeling of debilitating tiredness or loss of energy) during the course of their disease and treatment. Thirty-two percent experienced fatigue daily and 32% reported that fatigue significantly affected their daily routines. Caregivers reported observing fatigue in 86% of the index patients and oncologists perceived that 76% of their patients experienced fatigue. Although oncologists believed that pain adversely affected their patients to a greater degree than fatigue, patients felt that fatigue adversely affected their daily lives more than pain. Most oncologists believed fatigue is overlooked or undertreated and most patients considered fatigue a symptom to be endured. Fifty percent of patients did not discuss treatment options with their oncologists and only 27% reported that their oncologists recommended any treatment for fatigue. When used, treatments for fatigue were generally perceived by patients and caregivers to be successful. These data confirm the high prevalence and adverse impact of cancer-related fatigue, although it is seldom discussed and infrequently treated. For patients and oncologists, improving the quality of life of cancer patients requires a heightened awareness of fatigue, a better understanding of its impact and improved communication and familiarity with interventions that can reduce its debilitating effects (Volgelzang 1997).

Uncontrolled studies have reported that fatigue is a common symptom among patients with advanced cancer. It is also a frequent complaint among the general population. The aim of the study of Stone and co-workers (1999) was to determine the prevalence of fatigue among palliative care inpatients in comparison with a control group of age and sex-matched volunteers without cancer. In addition the correlates of fatigue were investigated. The prevalence of "severe subjective fatigue" (defined as fatigue greater than that experienced by 95% of the control group) was found to be 75%. Patients were malnourished, had diminished muscle function, and were suffering from a number of physical and mental symptoms. The severity of fatigue was unrelated to age, sex, diagnosis, presence or site of metastases, anaemia, dose of opioid or steroid, any of the hematological or biochemical indices (except urea), nutritional status, voluntary muscle function or mood. A multivariate analysis found that fatigue severity was significantly associated with pain and dyspnoea scores in the patients and with the symptoms of anxiety and depression in the controls. It was concluded that subjective fatigue is both prevalent and severe among patients with advanced cancer. The causes of this symptom remain obscure (Stone 1999).

Studies of on-treatment fatigue in cancer patients have shown that fatigue is often experienced during and shortly following cancer treatment. Information about off-treatment fatigue in cancer patients is much less common. Andrykowski (1998) examined the extent of after-treatment fatigue following treatment for breast cancer. Women with breast cancer and age-matched women with benign breast problems, completed a set of fatigue questionnaires at an initial assessment (28 months post treatment) and a 4-month follow-up assessment. The breast cancer group reported more fatigue, more weakness and less vitality relative to the benign breast problem group at both assessments. No relationship was found in the breast cancer group between fatigue and extent of treatment or time since treatment completion. Elucidation of the psychobiological processes underlying this symptom and development of clinical management strategies remain challenging.

1.15 SOCIAL RELATIONSHIPS

Social support appears to be an important resource for those suffering from chronic disease. It may lower the likelihood of illness initially. Social support does reliably speed recovery from illness and it reduces risk of mortality. Self-reports of good social relationships and positive adjustment to chronic disease are consistently found in the literature for cancer (Taylor 1990).

Social support may also reduce the distress that accompanies chronic illness. Fewer illness-related problems among chronically ill populations have been documented for those with high levels of social support. Social support also appears to affect health habits and in particular promotes adherence to medical regimens (Taylor 1990).

Chronic disease can itself adversely affect potential social support resources. For example, the stressful event of cancer creates fear and aversion in family and friends, but also creates a simultaneous awareness of the need to provide support. These tensions may produce a variety of adverse outcomes, such as physically avoiding the patient, avoiding open communication about the disease, minimising its impact or demonstrating forced cheerfulness. Under such conditions, the availability of effective social support may be reduced (Taylor 1990).

Distant relationships with friends and acquaintances appear to be more adversely affected in these ways than intimate relationships. However, intimate others, may themselves be highly distressed by the loved one's condition and be ineffective in providing support because their own support needs are unmet (Taylor 1990).

1.15.1 THE SOCIAL DOMAIN

A decline in social activities takes place after the diagnosis of breast cancer. Patients sometimes isolate themselves because of shyness, fear of rejection, or because their body and self-image has been negatively affected. However, it does appear that the reaction is limited and of a short duration for most patients. The first three months post mastectomy seem to be the most critical and psychological healing has taken place for most patients by this time.

In many circumstances the woman's own family and friends play a key role in helping her adjust to her mastectomy and to her illness. The relationship that we have with others meets a number of our general psychological needs. They provide a sense of identity, acceptance, and emotional security; they increase our feelings of self-worth and self-esteem; and, in time of stress, they can be a source of information, practical advice and general emotional support. Studies of people's reaction to various kinds of crises have consistently shown that they are better able to withstand these where they have attachments with others and an absence of this social support can make them more vulnerable to life stress at both physical and psychological levels. Social contacts per se can be a mixed blessing in the context of illness. It is the quality rather than the availability of relationships with others that counts. Furthermore, even positive and apparently supportive behaviours can have negative effects. The help and sympathy of others, no matter how well intended, can threaten autonomy, encourage dependency and confirm the patient's view of herself as ill or damaged (Ray 1985).

There is evidence from anthropological work that fear of abandonment during illness is not misplaced, nor is it always indicative of neurosis or paranoia. Cancer and AIDS sufferers are often worried that they will be abandoned. There are few occasions in life when the love and support of friends and family is more important than when ill, especially if the sufferer has chronic, progressive or terminal disease (Fallowfield 1990).

Mastectomy does not physically impose any limitations on a woman's social life, but the woman may become more withdrawn if she feels embarrassed by the fact of others knowing about her operation, even if it is accepted that the difference is not outwardly noticeable. She may feel that her image and identity has changed in their eyes, the image of her body and her identity as a woman, and that they are treating her differently. Others' behaviour may indeed change. People often respond with ambivalence to illness and disfigurement, avoiding the victim or treating her with pity or false cheerfulness and this can provide a very real incentive for social withdrawal (Dunkel-Schetter 1982).

Family and friends need to know that having cancer and being on chemotherapy can cause disturbances in relationships in the outside world. In a study by Ringler (1983), the patients reported that it was often useful to play down the seriousness of the disease or to keep it a secret altogether in order to avoid certain problems with other people. The most important of these problems were:

- Being treated, as if having cancer were the only important thing about them.
- Upsetting other people or scaring them away.
- Becoming subjected to the idle curiosity of mere acquaintances.

It may help to be aware in advance that the responses of the outside world to one's having cancer are often not only not helpful, but also actually a cause of additional difficulty and emotional upset.

"We meet so many other cancer patients at the hospital. We make friends, drawn by our similar situations. We lose new friends too. Suddenly one day they are not there any more. Death becomes real. We share one another's ups and downs, elation and despair (Weitsz 1995)."

In general, good social support can provide a buffer against the adverse psychological impact of stressful events such as developing cancer (Barraclough 1994). The benefits of social support have generally been grouped into three categories:

- Tangible assistance.
- Information.
- Emotional support.

1.15.2 THE FAMILY

Stable support from family and friends, together with the ability to participate in social activities, are immensely important contributory factors to quality of life. Provision for family needs should form part of any good cancer treatment service. Problems may arise between couples – communication barriers, sexual dysfunction, role changes and mood disorders in the partner. The husband may feel helpless and terrified of losing his partner.

In a study by Ringler (1983) patients reported that their families helped them with the disease and treatment in many different ways. Many patients also reported that their families also treated them differently now than they had before the cancer and the chemotherapy. Most of these changes were improvements, but a number of patients said they were very bothered because their families had become overprotective, both physically and psychologically. Those patients who said their families were overprotective had higher emotional distress than other patients.

A woman's relationship with her husband is an important factor in determining how well she adjusts to her mastectomy. A supportive husband can help a woman to cope with life stress in general. In a study of depression among women it was found that in many of the cases identified, the person had faced a stressful life event in the previous nine months, for example a threat to a relationship, an illness, or a major material loss. However an important factor in determining whether or not such an event actually led to an affective disorder was the presence or absence of a confiding relationship with a husband or boyfriend. With such a relationship, it seemed that women were less vulnerable and were protected against the psychological effects of loss and disappointment. It is important to note that it was the confiding nature of the relationship that was important and not just the existence of a husband or boyfriend. Marital status alone did not correlate with adjustment to breast cancer (Brown 1978).

The husband's attitudes toward his wife's illness and mastectomy and the stability of the marital relationship are crucial in determining eventual adjustment. There is thus a case for involving husbands in any counselling that is offered (Ray 1985).

In metastatic patients there appears to be a convergence between the amount of social support wanted – which was determined by the number of side effects and the extent of disease disability – and the adequacy of that support. The prediction that better family support would be associated with less difficulty and distress was not confirmed. In metastatic patients, results were in the opposite direction from the prediction, perhaps because patients who get the best support were patients who had more advanced disease, which may result in distress and difficulty which are relatively intractable (Ringler 1983).

If patients are disabled because of the disease and treatment, this creates a situation, which requires care and tact on both sides. The family has to avoid insulting the patient by coddling and on the other hand, avoid leaving the patient with not enough support. The patient must be ready to protest if too much support is forthcoming, to accept that help is needed with good grace, and to ask for more without shame (Ringler 1983).

Both patients and families need to allow themselves to face and experience the upset that goes with the disease – anger, fear, grief, guilt, regret – and to share these with each other to the extent that it is comfortable. Patients, soon after their diagnosis discover that they need to work to minimise their difficulties and normalise their situation. Patients and families need to be careful that their relationships do not become invalidated by overprotectiveness or too much unreal niceness (Ringler 1983).

When unhappy relationships, social deprivation, and poor mental and physical health have been present for years, the diagnosis of cancer in a family member may precipitate complete chaos.

Communication problems can be most acute in happy families, where talking about cancer and the possibility of dying, is most likely to cause pain. When the communication needs of the two partners are different, such couples are adding to each other's distress.

Patients with stable personalities, a satisfying past life and strong support from their families and friends, generally adjust more readily to terminal illness, than those whose former existence was of a troubled kind. The prospect of death may, however, be especially difficult for those who have a great deal to lose by dying, such as young people who have not yet achieved their full potential, or those utterly unaccustomed to the "sick role" (Barraclough 1994).

The husband has to cope with his feelings of loss: the disbelief and denial of his wife's diagnosis, the rage and confusion during her treatment, the anxiety and fear of watching her suffer. A husband's pain can be especially difficult, because in listening to his wife's groans and ministering to her needs, now one acknowledges his feelings. It is always: "How is your wife? How is she doing?" His own fears of being left behind are important and he too needs comfort and support during his wife's illness.

The husband's positive role must be emphasised and he must be involved in all stages of his partner's disease. The husband often feels guilt himself, but he needs to be reassured about it and urged to demonstrate his affection and to seek intimacy with his wife. In the majority of cases with adequate reassurance it is found that the stress of mastectomy may establish additional bonds of affection and mutual support that will further cement a marriage. Without a husband or significant partner, the mastectomy patient is particularly vulnerable and these women, together with those that have pre-existing psychological problems, need to be carefully watched for the detection of serious psychological morbidity that needs professional intervention (Baum 1988).

Happily married patients benefit from their husband's support in withstanding the stresses of their illness, but they also have more to lose if they do not survive.

In a study by Wilson & Morse (1991) the husbands became more attentive, compassionate and considerate. They no longer took their wives for granted. Although sexual relations decreased, husbands continued to experience intense emotions of affection, gratitude and love for their wives. The husbands maintained self-control at all times so that disruption to the household would be minimal despite their wives' mood swings, physical illness and mental apathy. It must be borne in mind that this is a select group who agreed to participate in this trial. There is obviously a wide spectrum of spousal behaviour from the caring types mentioned above, to the immature, selfish husband who further detracts from his ill wife's quality of life.

Wilson & Morse (1991) found that husbands feel obligated to be loyal, protective and supportive, to assume responsibility for commitment to the household and to assist their wives in fighting the disease. The commitment made at the onset of treatment tends to deny the option to leave the relationship during the current program of chemotherapy. Husbands who left the relationship usually did so after the disease was in remission.

In the study of Wilson & Morse (1991) the husband remained focused on his wife and on his own needs. They describe the process of buffering, which has two major components: First is the "doer role" where the husband waits upon his wife by meeting her physical needs, following her instructions for completion of household chores, and taking care of children. The other component is the "protector and advocacy role" where the husband acts as an intermediary among his sick wife, their friends and relatives.

Anger is sometimes more marked in relatives than in patients themselves. Encourage the redirection of anger, when married couples seem to be taking out on each other their shared anger about the illness. Re-channeling energy elsewhere, towards for example exercise, music, creative activity or cancer-related charity, is sometimes an excellent strategy (Barraclough 1994).

Although they describe it as an important domain, Bernhard and co-workers (1997) did not include "partnership" in their Quality of Life Core Questionnaire (see Addendum1, Chapter 2), because they considered it to be less relevant in comparisons of treatment related endpoints. Similarly, "sexual functioning" was not included due to feasibility problems in particular cultures and age groups.

Children often have a difficult time adjusting. It's hard for them to know how to cope, especially if their mother or grandmother returns home looking and acting sicker than when she left. They need reassurance that their loved one is back and ready to take care of them. But a survivor may feel too drained to take care of anyone other than herself. As a result, children may start acting out their fears and worries, finding it hard to concentrate at school or get along with other kids. They may be more reckless when they play, or they may worry obsessively about getting sick themselves. Their marks may drop or even improve as they throw themselves into their work as an escape. Any of these changes can occur when a child feels scared or worried and the best a mother can do is encourage her children to share their feelings, no matter how painful or hurtful they may be (see Addendum 6) (Runowicz 1995).

Depending on the patient's level of fatigue and other side effects, she might not be able to handle the concurrent roles of wife and mother, disciplinarian and homemaker, wage earner, mediator and friend. All the usual patterns may disappear and roles may be reversed. It may take extra care and attention to get family roles straightened out (Runowicz 1995).

1.15.3 SEXUAL RELATIONSHIPS

The breast should not be considered as a mere appendage of lactation, of no further use once the phase of childbearing is complete. The breast also has a role in sexual attraction, the maintenance of self-esteem, and body image, all of which may vary in importance with marital status, age and current fashion in dress (Baum 1988).

Marital and sexual problems are a general result of the stress of breast cancer and the treatment thereof. Especially younger mastectomy patients' sexual relationships are affected. It has also been shown that it is unlikely that a patient whose sexual relationship deteriorates in the first three months after mastectomy, will be unable to return to her previous level of functioning. Sexual problems were found despite the fact that most patients received emotional support and understanding from their spouses (Fourie 1996).

Most women are concerned at the time of mastectomy with what their husbands' reactions will be. They report that husbands can often be reassuring, persuading them of their continued love in spite of an altered appearance, or minimising the negative effects of the disfigurement by comparing if with the alternative of a progressive illness. Some women try to protect both their own and their husband's feelings by hiding the scar, and not allowing themselves to be seen naked, and there are some couples where the woman's changed appearance is not openly mentioned between them. The woman and her husband must evolve a way of dealing with the disfigurement, a way that takes into account the sensibilities and desires of each, although one partner may take more of the initiative or establish greater control in deciding this (Ray 1985).

In instances when the couple's sex life is adversely affected by the loss of the breast, this may be because of the wife's feelings, the husband's feelings, or both. Sometimes a woman experiences a loss of sex drive, or a "blocking" because of negative feelings about her own body (Ray 1985).

Several authors have pointed to the importance of the existing state of the marriage in determining sexual adjustment postoperatively. A warm and supportive relationship can withstand the strain of mastectomy and may even be further strengthened by the challenge it presents. On the other hand, when there is a lack of communication and support within a marriage, mastectomy adds to the tension and may trigger a further deterioration in the sexual relationship where it was initially problematic (Ray 1985).

According to Derogatis (1980) the issue of sexuality is central rather than subordinate in women's appreciation of the impact of cancer and greatly affects their fear of the disease, the delay in time in seeking a diagnosis and the course of their response to treatment. It is important to recognise that in a very important sense gynaecological and breast cancers and the surgical interventions employed to treat them, are unique: they are different from other forms of the disease in that they posses the potential to devastate the patient by imposing a unique threat to her self concept and psychological integration. This occurs through the destructive impact of the disease on the patient's body image and sexual identity. The loss of a breast through cancer represents both a severe body image trauma and a serious blow to self-esteem.

Patients with a history of stable adjustment prior to disease, as well as those who are well-informed and have developed constructive attitude postures are likely to do better, just as women who are older and possess a balanced or androgynous gender role definition appear less psychologically devastated by the disease.

After cancer many woman begin to doubt their sexuality and their appeal. Suddenly they find themselves wondering if they are still "whole" women. Physical deformities: the loss of a breast, scars post-surgery, radiation scarring – often cause enormous questions of sexual self-worth and the importance our culture places upon physical appearance and body image. A survivor wants to return to a healthy and active sex life and to accept her body postcancer, but she might suddenly begin wondering, "Does my partner still want me without my breast? Do I think I'm sexy?" (Runowicz 1995).

Instead of speaking openly about these fears and concerns, many couples hide behind a wall of silence. Often husbands are hesitant to initiate sex, afraid that contact may further hurt or damage his partner in some way. The wife, who may already be wondering how desirable she is, will take this hesitation as justification that she is somehow damaged or unappealing. By not discussing their feelings, a woman and her partner may find themselves embroiled in a vicious cycle of misunderstanding, potentially placing their marriage or relationship in serious jeopardy (Runowicz 1995).

According to Wilson & Morse (1991) an additional stressor for the couple was the lack of sexual relations because husbands feared causing their wives psychological or physical pain.

Breast cancer patients are the most frequent cancer survivors in primary care practise. The multimodal treatment of breast cancer improves survival outcome, but it also causes prolonged periods of medical intervention with associated physical and emotional sequelae. There are multiple predisposing factors to sexual dysfunction in breast cancer patients, including pre-existing sexual problems and normal age-related changes in sexual functioning. Physiologic changes caused by chemotherapy and hormone therapy also play an important role. Induction of premature menopause can result in an estrogen-deficiency state that can cause hot flushes, poor vaginal lubrication and urinary symptoms, which may contribute to sexual dysfunction. Older patients also experience these problems as a result of the discontinuation of hormone-replacement therapy at the time of breast cancer diagnosis. Tamoxifen can exacerbate these symptoms. Psychologic reactions to cancer can also give rise to sexual dysfunction in certain patients (Ganz 1998).

Major sexual problems can occur as a result of both physical impairment and emotional traumas. Anxiety that any attempts at sexual activity will fail or be rejected by a partner can have a devastating impact on an individual's quality of life. Even if full intercourse is no longer possible, most people still enjoy the warmth and satisfaction of affectionate cuddling, kissing and intimate non-coital caressing. For most individuals, sick or well, touching is a basic human need, confirming that they are loved and wanted. Those people denied physical intimacy and tenderness, due to mutilating surgery and chronic or life-threatening disease, are extremely vulnerable to depression. The partner of the patient might also need support and help to explore new ways of expressing love and gaining sexual gratification (Fallowfield 1990).

Several factors contribute to sexual problems:

- Physical changes.
- Body image changes. Weight changes, hair loss, mastectomy etc. often inhibit sexual activity for psychological reasons. The patient feels unattractive even physically repellent and the partner often has similar feelings about the spouse.
- Relationship changes. The healthy partner refrains from making sexual overtures, out of concern for the sick person, who sees this as rejection and feels even more unattractive.
- Mistaken beliefs. For example that cancer can be transmitted to a sexual partner or that intercourse will harm the patient, may inhibit sexual activity.

Weitsz (1995) saw her partner becoming physically unattractive, but found that the spiritual aspect of their relationship deepened considerably. Her love deepened and matured: "Tenderness is indescribable. We are inextricably intertwined and interdependent. We talk deeply and philosophically about life, death and life after death. We talk about us. It gives us a sense of peace."

Breast reconstruction has generally been found to contribute to an improvement in sexual functioning (Lerman 1984). It has been concluded that adaptation to breast cancer does not correlate with the type of surgery (mastectomy or lumpectomy), but rather to the subjective satisfaction with the breast, body image as a whole and the individual's specific coping mechanisms. Patients undergoing chemotherapy have also reported a negative impact on their sexual relationships.

Health professionals need to be aware of the magnitude of sexual problems generated by cancer. Next, they should be appreciate how meaningful their efforts may be in enhancing the quality of life available to cancer patients and their significant others. Health care providers should evaluate and discuss sexual concerns with their patients as a matter of routine. Bullard et al. (1980) found that 63% of patients would have liked more information regarding the effects of cancer on their sexuality. Of particular interest is that for so-called "single" patients, 84% expressed interest in an educational program on intimacy and sexuality for persons with cancer.

Knowledge of the sexual consequences of cancer has some definite implications for the therapy of cancer. The disease is occurring in a whole person and we must attend to all the needs of that person, not just the lesion. Similarly, we need to broaden our concerns about the cancer patient to include the spouses, lovers, children, friends and relatives of cancer patients. It is clear that the disease affects a social network and the health professional can often do more to benefit the patient by attending also to the effects of the illness on the "significant others". To fail to do so may mean that the psychological impact of the illness might be much more disabling than it need be. If we are genuinely concerned with improving the quality of life of cancer victims, we need to extend our efforts beyond the disease and beyond the patient (Golden 1980).

Morris and co-workers (1977) found that sexual difficulties were most often reported by women of peri-menopausal status.

Special problems are involved for the woman who is neither married nor in a stable relationship. She may feel that a sexual relationship is no longer a possibility for the future and that no man would now find her acceptable. The fact of having had a mastectomy may discourage her from even embarking on any new relationship, because of the embarrassment that would be involved in first telling her partner and the fear that he would then reject her (Ray 1985).

"Maybe it hurts to kiss, knowing that death will soon separate us. I have such a touch hunger – not for sex, but for tender intimacy. Maybe separation needs to be gradual – it's a practise run for the real thing. I feel my role changing to that of mothering and caring. It is a massive adjustment as we have always treasured our sexuality and had a fun-filled marriage. Suddenly all this is a thing of the past and I feel cheated" (Weitsz 1995).

1.16 PHYSICAL APPEARANCE

According to Maguire (1985) at least one in every five mastectomy patients will develop body image problems. Of these one tenth will be serious in that they will feel less feminine and less attractive. It was found that body image and self-image would not be affected directly after mastectomy but that it will occur after a few months.

There have been conflicting reports about the advantages in terms of breast reconstruction in the literature. In general it has been shown that patients opting for breast reconstruction have a much better body image than patients who do not have a reconstruction. Some reports claim that the incidence of lowered body image post mastectomy is in fact very low.

Of importance however is that there is a very strong link between body image problems and the development of affective disorders and sexual problems. A negative body image after mastectomy is significantly correlated with weak sexual adjustment (Fourie 1996).

As chemotherapy progressed, a change in physical appearance became obvious and was a constant reminder of the impact of the illness. Husbands did not perceive hair loss due to chemotherapy to be as frightening as it was to their wives, even if hair loss occurred over the entire body. Some used humour to comfort and counteract their wives' humiliation and fear of feeling "neutered". As their wives became increasingly drawn and fatigued, social events were curtailed (Wilson & Morse, 1991).

1.17 FINANCIAL CONSIDERATIONS

The smooth transition back to the workplace is not always possible. Employment discrimination can rear its ugly head in a number of ways. One can be fired or demoted from an existing job, have her benefits reduced or eliminated, not get hired for a new position, or be shunned by co-workers. Closely tied to employment is access to insurance coverage (Leigh 1992).

The cost of the treatment of cancer can be prohibitive. Surgery and hospitalisation are expensive and many of the latest chemotherapy regimens are also highly priced. High-tech procedures like CAT-scans and MRI-scans are priced at over a thousand rand per test. Even something as ordinary as a blood test costs a few hundred rand per test and has to be repeated often during chemotherapy. Add to this the fact that long distances often have to be travelled to the major oncology centre and that patients often have to pay for accommodation during lengthy treatments. In addition, people often lose their job or have to give it up. Patients may lose their medical insurance and other insurance may also be curtailed or denied. Financial worries can add additional stress and detract from an already impaired quality of life.

Cancer confers a substantial physical and financial burden on those who are afflicted. These hardships are increasingly borne by a growing elderly population (Stafford 1997).

Wilson & Morse (1991) found that financial difficulties, with patients no longer working, drained energy.

1.18 ATTITUDE AND DISPOSITION

Cancer patients are often characterised as being negative in their attitudes toward themselves. They have been described as self-critical and self-sacrificing. It has been suggested that they are relatively low in neuroticism and emotional responsivity, but also that they show little anger and hostility. Such findings would in many circumstances be interpreted as an indication of good adjustment and emotional stability, but in this context they are more often regarded as resulting from poor emotional discharge, the assumption being that anxiety and anger are experienced but not expressed. Indeed, high levels of denial and repression have been documented in cancer patients. Perhaps the most frequently cited correlates of the disease are a clustering of negative mood states, all relating to depression. It is many centuries since Galen (second century AD) first made the claim of an association between melancholia and cancer, and current descriptions of the cancer patient still refer to despair and hopelessness (Ray 1985).

Psychosocial and spiritual factors influence a broad spectrum of medical and surgical disorders. The adverse effects of stress have been most clearly documented in cardiovascular disease. In cancer, unresolved questions include the following: Do emotional factors have a causal role in either initiating or promoting a malignant process, and can they possibly accelerate the dissemination of cancer? The literature, which consists of anecdotes, case-control methods, and randomised trials, is inconsistent and beset with major methodological problems. Psychosocial interventions can be life enhancing in sharp contrast to the guilt-ridden programs of some alternative practitioners. A social support system and an element of spirituality and religion seem to be the most consistent predictors of quality of life and possible survival among patients with advanced malignant disease (Creagan 1997).

One factor that might influence the impact of an event is a person's resources for coping. An event might have the same significance for two people in terms of the way it is evaluated and the readjustment needed, but one may be able to make the adjustment more easily than another. The person's capacity to master life changes will be an important variable when predicting the psychological and physical disturbance that will result. A "hardy" personality has feelings of commitment, control and challenge as factors determining resistance to stress and consequent illness vulnerability (Ray 1985).

With these last qualifications, the influence of personality is implicitly recognised as a causal factor in illness, mediating the impact of events. The person's own values and resources determine the way in which events are perceived and the ease with which adjustments are made, and vulnerability is thus determined by the interaction of external events and these internal factors. The theoretical construct that provides a unifying theme for this interaction is that of stress. Stress may be defined as a characteristic of a situation in which the demands placed on an organism is greater than the physical, psychological and social resources that are available to meet these. In any given situation stress can be primarily attributed to either the nature of these demands or to the resource capacity of the person, or to both in conjunction. Stress has emotional consequences but also physical ones. It has been suggested that the influence of physical agents is generally mediated by psychological factors. Neuroendocrine and other physiological changes associated with stress can provide the link between stress and the susceptibility to illness. Stress might not in itself produce illness, but could bring about conditions under which illnesses could be easily established, as the ability to adapt becomes generally exhausted. Stress could affect the immunological response via the central nervous system and endocrine systems, increasing the person's vulnerability and thus altering the balance between the person and any particular disease agents to which she is exposed
(Ray 1985).

The General Adaptation Syndrome describes the sequence of distinct stages in the response to stress (Selye 1956):

- The first stage is that of alarm or emergency, during which there is a general increase in the activity of the pituitary-adrenocortical system.
- There follows a second stage of resistance, when the effects of the stress are successfully countered, but resistance to other stimuli may be decreased.

- Finally if the stress is maintained, there will be a breakdown in the process of adaptation as resources are exhausted and resistance fails.

In metastatic patients, the extent of using adjunctive methods of coping with the disease was correlated with other aspects of coping – how active patients were both in coping with side effects and in seeking information about test results. The use of more disease coping methods was also associated with lowered difficulty in metastatic patients (Ringler 1983).

There is in conclusion, a distinct possibility of a convergence between two areas of research hitherto unrelated: one being the influence of personality and stress on disease and the other being immunologic and endocrine studies. All disease is multifactorial – involving genetic, hormonal, neurochemical, immunological and emotional factors. The interactions between these are difficult to disentangle and the mediating mechanisms suggested are at present speculative and hypothetical. The study of these relationships is however, attracting increasing interest and offers the prospect of a novel perspective on an understanding of disease (Ray 1985).

1.19 THE INFLUENCE OF AGE

1.19.1 THE INFLUENCE OF AGE ON PROGNOSIS

Young women with early stage breast cancer do significantly worse when compared to older women in terms of relapse-free survival, cause-specific survival, distant metastasis and breast and regional node recurrence. However, the adverse effects of young age on outcome appears to be limited to node-negative patients. These findings suggest that node-negative early stage breast cancer in younger women is a more aggressive disease, with an increased risk for all patterns of failure and a decreased survival (Fowble 1994).

1.19.2 THE INFLUENCE OF AGE ON QUALITY OF LIFE

Age is another well-documented factor that has a strong influence in shaping a woman's response to potential traumas developing post mastectomy. Obviously the passage of time has no moderating effect; however, the events taking place in that time do. With childbearing and rearing accomplished and a successful marital relationship to sustain her, a woman has already accomplished a number of very significant life milestones in our society. She is in general, less apt to be devastated by a cancer that may rob her of her capacity to reproduce and/or render her less desirable as a sexual or marital partner (Derogatis 1980). Younger women make a poorer adjustment to mastectomy and are more devastated by losing a breast.

Some researchers have suggested that the loss of the breast causes greater problems for premenopausal than postmenopausal women. Others have argued that this problem can only be resolved in the individual case, with the significance of both the illness and the loss of the breast being determined by their specific meaning within the context of that person's life style, attitudes and values (Ray 1985).

Intuitively and according to developmental theory, younger patients should be more angry and resentful about their illness because they are less likely to have come to terms with the certainty of death. Correspondingly, any psychological benefits of the illness, such as increased appreciation of life, should be more prominent at a younger age (Salmon 1996).

In a study where quality of life was assessed in the adjuvant situation, several symptoms were found to be age-related. The younger chemotherapy group tended to rate a higher frequency of treatment-related symptoms than the younger radiotherapy group. A possible explanation is that the chemotherapy resulted in a chemical castration in many of these patients. In the postmenopausal subgroup the chemotherapy patients perceived less symptoms than the radiotherapy patients. These patterns may be explained by a tendency to push chemotherapy harder for the younger than the older patients (Berglund 1991).

It was found that patients who believed they were more responsible for treatment decisions reported higher levels of quality of life. Patients who were more active in participating in treatment decisions were younger, more educated and perceived their physicians as making more of an effort to facilitate patient involvement (Street 1997).

Controversy about whether cancer has an independent impact on patient quality of life led the authors (Stafford 1997) to evaluate the effects of cancer on a range of quality of life and health care utilisation measures within an elderly population:

In the United States, for individuals age 65 years and older, 2% were diagnosed with cancer annually, compared with 0,2% of those younger than 65 years. Cancer was reported by 17% of the elderly. Individuals with cancer reported poorer health, more limitations of the activities of daily living (ADLs) and the instrumental activities of daily living (IADLs) and greater health care utilisation than individuals without cancer. For individuals with cancer, difficulty walking (38%) and getting out of a chair (21%) were the most commonly reported ADL limitations, whereas difficulty completing heavy housework (34%) and shopping (17%) were the most common IADL limitations (Stafford 1997).

Self-esteem is one of the key elements of the psychological dimension. Self-esteem is developed and maintained through social interaction. The social dimension involves satisfaction with family life and friendships. Social relations are an important resource for elderly women. Because social relationships can change, self-esteem is also liable to change. Since ageing is accompanied by negative social changes, the self-esteem of older people is vulnerable (Rijken 1995).

The view that elderly women are liable to receive less than appropriate therapy has been supported by a study from seven US hospitals. Local therapy, even when co-morbidity is taken into account, was less radical than would have been the case in younger patients (Forrest 1994).

1.20 ETHNICITY

In South Africa, the black population has traditionally been a disadvantaged one. It is an uneducated and mostly very poor population. Black people are often ignorant of the signs and symptoms of cancer and the implications thereof. The prevailing attitude in black cultures is not to have a mastectomy and rather to visit traditional healers than western medical doctors. The result is that black women tend to present very late and with disseminated disease at the major oncology centres, so that their prognosis is bleak.

Increasingly, the quality of life of women diagnosed with breast carcinoma is being studied. However, there is little information regarding long term survivors among ethnic minority women. The purpose of Ashing-Giwa and co-workers' (1999) study was to describe the quality of life of long-term breast carcinoma survivors and to examine the role of ethnicity in influencing their well being. The survey instruments included standard measures of quality of life: the RAND SF-36 Health Perceptions Scale, the Cancer Rehabilitation and Evaluation Survey-Short Form (CARES-SF), the Ladder of Life and new items. It was found that differences in quality of life outcomes were attributable to socio-economic and life-burden factors and not to ethnicity.

1.21 SOCIOECONOMIC FACTORS

Epidemiological observations have fostered our understanding of the risks of developing breast cancer within a population. Female gender, increasing age, aspects of the menstrual history, family history and personal history of breast cancer are increasingly well-documented factors that contribute to the risk of developing this disease. Of the additional factors that possibly contribute to breast cancer risk, socio-economic status is one of the most influential. The exact manner in which this factor contributes to breast cancer risk is not fully understood. One possible explanation holds that women of higher socio-economic status delay having children until later in life than women of lower socio-economic status, thereby increasing their age at first pregnancy, a well known factor that increases breast cancer risk. Race and socio-economic status are directly related to breast cancer incidence in countries such as the United States, England and South-Africa where the population is diverse, racial discrimination is endemic and segments of the population are forced to live in conditions of poverty despite great national wealth (Henderson 1994).

Once diagnosed with breast cancer, consideration should be given in all patients as to socio-economic factors affecting survival. Nutritional status should be investigated and counselling offered with the goal of reducing relative body weight, improving overall nutritional status and eliminating or at least controlling comorbid factors such as alcohol and drug dependency (Pace 1994).

1.22 SURVIVORSHIP

Quality of survival is in the eye of the beholder. If the beholder is a physician, the factors defining quality survival are likely to be biomedical in nature, have scientific parameters and be measurable. If the beholder is a social worker or psychologist, these factors encompass psychosocial components and are humanistic in nature. If the beholder is a nurse, there tends to be a greater capacity to blend biomedical and psychosocial factors. And if the beholder is a patient, the factors defining quality of survival include all of the above, along with personal, social and cultural values. While the science of survival attempts to understand the disease itself, the art of survival attempts to understand the human experience of that disease (Leigh 1992).

Survivorship is a new concept in relation to cancer and has yet to undergo rigorous conceptual development. It has been described as the act of living on: a dynamic concept with no artificial boundaries. Survivorship has also been viewed as a continual, ongoing process rather than as a stage or component of survival. It is the experience of living with, through or beyond cancer. Survivorship extends far beyond physical recovery. Survivorship is about the quality of our lives with or without cancer, about healing the visible and invisible wounds and about feeling satisfied that we have made the right choices and are doing the best we can (Leigh 1992).

As the idea of cure becomes a reality for millions of survivors, many pay a high price to overcome remaining problems. Successful treatment is such a cause for celebration that it usually overshadows concerns about chronic or delayed sequelae. The importance of continued medical follow-up couldn't be overemphasised, since survivors are at increased risk for recurrence, other malignancies and complications of therapy. Besides the anxiety about cancer recurrence, numerous other emotional, psychological and social obstacles may impede recovery. Examples of such obstacles include fear of death or abandonment, a sense of isolation, changes in relationships, feelings of vulnerability and emotional lability, depression, changes in body image, sexual dysfunction and post-traumatic stress disorder. As many of these are adjustment problems or situational disorders and not hard-core psychopathology, help is usually available if the survivor is willing to explore solutions (Leigh 1992).

Even if we cannot change our destiny, we can change the way we react to it. There is no meaning to cancer – it is simply cancer. Meaning comes from the individual interpretations of the disease and the treatments (Leigh 1992).

1.23 RECURRENCE

Perhaps the most difficult phase for a woman to cope with is the recognition of treatment failure by the appearance of local or distant metastases. If one then adds to the woman's psychological trauma, treatment such as removal of ovaries and cytotoxic chemotherapy, one might predict that the load would be too great and the majority of women would "crack up" completely (Baum 1988).

Although now feeling "better equipped" about what to expect, nevertheless, the feeling of devastation and loss of control, that husbands experienced, persisted. Metastases were feared because it meant, "game over" (Wilson & Morse, 1991).

The patient who experiences a recurrence of cancer needs to be closely monitored for signs of psychological morbidity. The palliative aims of therapy at this stage, where cure is definitely not an option should be at the forefront of treatment planning. It is very important to break bad news in an empathetic way and this is a time-point where extensive attention to the patient and her family's informational needs must be paid.

1.24 DEATH

There comes a time eventually when the clinician wishes to withhold further active therapy and recognises that the expectation of life is now limited to months rather than years. Terminal care is either organised in the patient's local community or instituted at the oncology centre. The help of the social worker, hospice, cancer association and family and friends is enlisted. Symptoms are addressed, in particular pain control, but any active procedures are avoided.

According to Wilson & Morse (1991) death was a topic which was never discussed between spouses.

"Grieving starts before death. It starts while you are awaiting the final onslaught. One is often told that grief encompasses different emotions, and this is certainly true. It should be stressed however, that not everyone experiences these emotions in the same way or even in the same sequence. Certainly, elements of shock, denial, anger, grief, despair, gradual acceptance and an acquisition of a future perspective are part of the process. The nuances differ with each case. One of the problems with handling grief is the fact that it is often accompanied by anger" (Weitsz 1995).

Accounts of life-span emotional development maintain that the normal challenges of adulthood – and especially the approach of death in later life – stimulate a change in values. According to Erickson (1986), the final stage of adult psychosocial development revolves around a conflict between "integrity" (a sense of completeness and fulfilment) and "despair" (fear of death and regret at lost opportunity). Levinson (1990) identifies confrontation with one's mortality as an important developmental task, from which greater fulfilment can emerge.

Hinton (1999) assessed the awareness and acceptance of dying in a sample of cancer patients. Depression was linked with greater awareness in relatives but not in patients. Patients were more anxious if death seemed probable rather than certain or no more than possible. Acceptance usually increased, with 51% of patients and 69% of relatives becoming nearly/fully accepting. Relatives accepted more if patients were over 70 years of age, weak, unable to concentrate or had a quality of life index (QLI) below five, but patients were more accepting if female and if the QLI was above five. Pain did not increase acceptance. Acceptance was described in terms of death's inevitability, faith and spiritual values, life's diminishing rewards, completing life, final benefits, humour, sharing etc. Individuals often used more than one concept.

Impressive gains in the survival of some patients with malignant diseases have primarily reflected the availability of multimodality programs among others, for subsets of patients with regional breast cancer. Most patients with advanced solid tumours, however, will die of their disease. Sophisticated psychosocial investigations of patients with advanced cancer have targeted several areas in which clinicians can positively influence quality of life. Families often "cascade through an avalanche " of emotional upheavals as patients struggle with the sequelae of their illness. After a patient dies, clinicians should be familiar with some generally recognised patterns of behaviour that are indicative of a normal mourning process. This knowledge may help clinicians be aware of situations that might necessitate intervention of other professionals, either medical or pastoral. Attention to psychosocial events is an integral part of a comprehensive oncologic program to facilitate patients and families to live in an atmosphere of peace and dignity (Creagan 1993).

1.25 INFORMATION

1.25.1 GENERAL

"The more I knew, the more secure I felt, even if the news was bad. Ignorance frightens me; knowledge soothes me. The worst part is not knowing…definitely the worst part is not knowing" (Wilbur 1991).

While highly stressed and vulnerable, patients are frequently bombarded with information. Much of the information is in medical language and is difficult, if not impossible to understand: informed consents, treatment protocols and potential side effects. The physician often acts as gatekeeper and controls the type and amount of information delivered most of which is medical. Information must be presented in such a way that it can be understood and effectively used and medical information must be integrated with the values and life goals of each patient (Leigh 1992).

The diagnosis of cancer can be seen as an "informational" crisis. The patient brings to bear on her own personal situation all that she knows or thinks she knows about the disease and its implications. She is recognizing her own mortality, revising assumptions and expectations that she has previously held about the course of her life, and confronting the uncertainty and ambivalences generally associated with the illness. For most, a key element of the informational crisis of cancer is that they do not know what the outcome will be. They do not know whether their previous assumptions and expectations for health and longevity are valid or invalid. Thus the patient has to come to terms not so much with death as with the unpredictability of the future and with the ambiguity of her current status (Ray 1985).

Previously, the diagnosis of cancer was concealed from patients. This was because cancer carries so many stigmas and implies such a grim prognosis. Nowadays in the Western world almost all cancer patients are told what is wrong. Many patients continue to feel that they have been kept in the dark about the details of their illness and perceive various shortfalls in communication with their doctors. This may not be entirely the doctors' fault because, during emotionally charged interviews, patients often forget what questions they wanted to ask, or dare not ask them, or fail to take in what they are told. The flourishing of organizations to inform and support cancer patients, attest to the hunger for information felt by many patients (Barraclough 1994).

It is important to move away from the current reticence about discussing breast cancer towards more openness with appropriate support (Williamson, 1996). Luker (1996) found that lack of time and misconceptions about what patients most want to know hinder staff from being as helpful as they would wish. At least questions should be answered: being "fobbed off" or not answered increase patients' stress (Swindon 1995). Patients should be given all the pertinent information, so that the implications of treatment for the quality and practicalities of life during treatment are clear. This should be done in language that is clear and understood by the patients. They should not have to discover that choosing one treatment rather than another has trapped them into unexpected consequences (Alderson 1994). Pickering (1995) advocates nurse counselors for practical advice and emotional support, whereas Alderson (1994) found that some patients find complementary therapies useful.

Alderson (1994) found that patients thought that all options should be discussed with them, including the treatments' long term implications, benefits and risks. Most patients wanted detailed information about their cancer, most thought they should be told about uncertainties that exist, and most wanted to share decision making with their doctors.

Pickering (1995) found that treatment could sometimes be better organized. Diagnoses should be made and imparted as quickly as possible. Then the patient should have a few days to consider all the options. Access to good information is mandatory. He also found that continuity of care and follow up should be improved. The number of inexperienced and new personnel that a patient meets should be limited.

It is imperative that bad news be broken in a sensitive and compassionate way, as is elucidated by Weitsz (1995): "Don't they teach them in medical school to break the news gently, or at least compassionately?" The nursing staff leaves us well alone. I guess they don't like confronting patients and their families when the death sentence has just been passed.

According to Ault (1998) the key to educating patients is to be supportive and empathetic. It is important that women with breast cancer receive encouragement and support early on in their experience. The more factual and timely the information that women have, the better their ability is to make the right choice for themselves and their families. The realization that the information must be repeated frequently also allows women more time to contemplate the treatment options that have been offered. Finding out what the patient and family members already know or what they remember from the previous clinic visit is always a good place to start when helping them with treatment decisions. Allow the patient to make her own decisions and then respect her choices. Remind her that her decisions for treatment should be based on what is best for her and not on someone else's experiences. With knowledge comes power and with power comes control – control over her life, her disease and her treatment.

When a woman is diagnosed with breast cancer, she often faces a complex series of decisions about her treatment (Monson 1998). Firstly, she may be presented with several choices about the treatment of her breast:

- Breast conservation with lumpectomy and radiation therapy, or mastectomy with the option of reconstructive surgery.
- An axillary node dissection may be discussed along with surgical options. This is an important consideration because most of the long-term side effects – lymphedema, numbness and pain – are due to the axillary node dissection.
- The new sentinel node technique may help prevent unnecessary axillary lymph node removal and its associated morbidity. If the sentinel node is negative, axillary node dissection can be avoided.

Decisions about systemic treatment (Monson 1998):

- It is generally accepted that women with positive lymph nodes will benefit from systemic treatment.
- There is however, a wide range of outcomes for women with negative lymph nodes.
- Systemic treatment may involve chemotherapy, hormonal therapy or both. Factors that are taken in to account when determining adjuvant therapy include estrogen receptor status, involvement of lymph nodes, patient age, menopausal status and general health.
- Systemic treatment for advanced disease is planned according to the extent and severity of the disease. For patients who do not have visceral involvement, as well as elderly patients, where co-morbid disease is often problematic, hormonal therapy is normally the first choice. The same factors that influence decision making for adjuvant therapy also apply. In addition the site of metastases, might influence the choice of treatment. For example tamoxifen works very well for bone metastases and the addition of a bisphosphonate has been proven to reduce complications that arise as a direct result of bony metastases. The treatment of choice for brain metastases is radiotherapy and corticosteroids.

What information is important to women making these decisions and what influences them to choose one option over another? The patient's physician will explain treatment options and their expected outcomes – both the benefits and the risks. After this consultation, however, the patient often feels unprepared to make important decisions about treatment, for a variety of reasons. The four basic principles of medical ethics – beneficence, non-maleficence, autonomy and equity – are important to consider when we offer patients choices about their breast cancer treatment.

Several studies show that there are psychological benefits to participating in the choice of surgical treatment. Women, who were offered a choice, tended to have less anxiety and depression post surgery, regardless of the surgery chosen. The woman's partner may also experience these benefits. Being given a choice may heighten anxiety for some patients. Other patients are not given a choice at all for a variety of reasons including race and educational status. In not giving patients a choice, the ethical principle of equity is violated.

Decision-making preferences regarding treatment (Monson, 1998):

Active

1. I prefer to make the final choice about which treatment I will receive.
2. I prefer to make the final choice after seriously considering my doctor's opinion.

Collaborative

3. I prefer that my doctor and I share responsibility for deciding which treatment is best for me.

Passive

4. I prefer that my doctor make the final decision about which treatment is used, but considers my opinion.
5. I prefer to leave all decisions up to my doctor.

Each person has a general preference. This tends to be influenced by age, gender and educational level. Preferences may also be culturally influenced. The more life-threatening the situation, the more passive a role is preferred. Cancer patients who play a more active role want more detailed information regarding their diagnosis and treatment. Given the variability of preferences, individual assessment of whether or not a woman prefers to participate in decisions about her treatment remains the best clinical approach.

When a woman is initially diagnosed with breast cancer, she typically feels overwhelmed due to the abundance of treatment options, new words and concepts, and sense of urgency often placed on the situation. It is important to provide each patient with the access to the information she needs to make her decisions. In some states in the USA, it is mandatory to provide patients with written information (Monson 1998). The ability to recall information conveyed during the stressful time of breast cancer diagnosis has been shown to be fair to poor (Hughes 1993).

The physician, nursing staff and trained breast cancer survivors should all be utilized to provide the patient with information. These different experts all contribute very different aspects of breast cancer management to the patient. The fact that women have been given information does not guarantee that they understand it. Patients should be asked to repeat information, to ascertain that they have fully understood it. Any misconceptions should be clarified.

For most women, the diagnosis of breast cancer comes as a shock – they didn't have any symptoms, were busy with their lives, then suddenly everything changed. The same stresses which make information recall difficult in this situation can also make it difficult for women to solve problems and overcome potential barriers to the treatment plan they prefer. The information that she receives may provide her with a list of pros and cons for different options, but still leave her confused about what those pros and cons mean to her. Values clarification, a technique used to explore the personal value placed on each issue involved in the decision, can be helpful. For example, she may face the choice of chemotherapy in a situation where less than 10% of those who receive the treatment will live longer because of it. Value clarification can help a woman explore the very personal decision about whether a small survival benefit at any cost is more consistent with her values, or whether a better quality of life with a slightly increased risk of death, is her preference (Monson 1998).

Numerous psychological factors influence the choice of breast cancer treatment. The most obvious factors are related to body image concerns and fears of deformity, mutilation and loss of femininity. Decision-making at the time of breast cancer diagnosis has a profound effect on quality of life and survival. Several psychosocial interventions may facilitate adjustment to breast cancer, promote adherence to medical treatment, and affect the overall course of the disease. Patients should be encouraged to build a supportive network and attend local breast cancer support groups. Spouses and other family members can also benefit from the positive affirmation offered in these programs (Monson 1998).

Patients seem to have a strong wish to know what's going on. This was shown by the accuracy of metastatic patients in judging their therapy's success and also by the fact that patients are always looking for information and using it to make inferences about what the disease is doing (Ringler 1983).

The diagnosis of breast cancer marks a significant transition from health to chronic illness. Informational needs and decision making styles of patients and their families, may change across the continuum of the illness, making ongoing assessment and tailored interventions necessary (Monson 1998).

Patients sometimes have difficulty in deciding whether the treatment would really be of benefit to them, but feel that advice and counseling are non-existent.

A few patients complain that they have been told too much. This often reflects tactlessness or poor timing in the way that information was given. It could also be that complete stark truthfulness is seen as essential and patients are not allowed to use denial as a mental defense (Barraclough 1994). Patients should be given ample opportunity to question the situation but unwanted information should not be forced upon them.

Breaking bad news, can seem a daunting task. It may be helpful to remember that most patients find uncertainty (often accompanied by anxiety and morbid fantasies), harder to bear than knowing the facts (Barraclough 1994).

Husbands noted that their ability to cope with their wives' condition was dependent upon the kind of information obtained. Receiving a poor diagnosis was preferable to "being (left) in the dark" and fearing the worst (Wilson 1991).

Wilson (1991) found that health care professionals rarely gave husbands information. The men hoped to hear something positive. Anger at the system, at the lack of compassion of health care providers and at having to wait for test results, strained their ability to cope. For example, being forced to wait up to five days for test results was common. It was demeaning when scans were not shown to the couple, particularly when wives who used visualisation to understand their disease, needed to see the scans. Requesting information or phoning the physician was often unsuccessful.

1.25.2 GENETIC COUNSELLING

Many crucial problems are associated with the diagnosis of inherited cancer susceptibility. One of the most important is related to the psychosocial consequences of the knowledge by the patients and their relatives of their own genetic status. In a study by Freyer and co-workers (1999), patients completed the Hospital Anxiety and Depression Scale (HADS) and the Subjective Quality of Life Profile (SQLP). A high level of frustration and latent dissatisfaction related either to the management of the genetic information given by the clinicians and its psychosocial consequences or simply to the knowledge of the genetic risk factor, which was found. Further studies on the individual consequences of genetic testing, how information should be imparted and when psychotherapeutic interventions should be commenced, are needed to ensure the quality of pre-symptomatic genetic testing in this field of oncology.

1.25.3 PATIENT GROUP EDUCATION

Patient group education is an evidence-based and powerful intervention for supporting and guiding patients toward an understanding of the cancer experience. An education program for patients and families, entitled Learning to Live with Cancer, has been developed and evaluated in a Swedish research project and implemented clinically. The program is a core model with a structure that allows flexibility in addressing learning needs. It has grown into a pan-European program through "training the trainers" courses and is now available in many countries. This has taken the project into a new phase, since Europe is characterised not only by consisting of many different countries, but also by showing cultural diversity and variety in ethnical norms. The aim of this phase was to assess the presence of core-model divergences conditioned by cultural values and norms, and if present, to investigate adjustments proposed to increase the relevance of the program to best suit patients' learning needs in different cultures. A questionnaire was distributed to former participants in "training the trainers" courses. The findings indicate that only minor divergences are present and that the core model thus has the potential to meet the learning needs of cancer patients in many cultures (Grahn 1999).

1.26 RESOURCES IN GAUTENG: THE CANCER ASSOCIATION OF SOUTH-AFRICA

1.26.1 VISION

To be a world-class community-driven organisation in cancer control.

1.26.2 MISSION

It is the aim of the cancer association of South African to fight cancer and its consequences in partnership with all South African communities and relevant stakeholders by providing direction for and supporting the following cancer control components:

- Health promotion through prevention and early detection.
- Patient service facilitation.
- Research to enhance the above.

1.26.3 SERVICES RENDERED BY CANSA

- Community based home care service where the family is trained as the primary unit of care and then is equipped to take care of the patient.
- An advisory information service.
- Support groups for cancer patients / families.
- 8 Interim homes in the larger cities for out of town patients who receive treatment in the larger centra. Accommodation, meals and where possible, transport is available.
- Medical equipment, wigs and prostheses.
- Health promotion for early diagnosis and to combat cancer through advocacy and lobbying for a healthy environment, as well as the distribution of educational material, educational talks and exhibitions.
- Financial support for cancer research.

1.26.4 REACH FOR RECOVERY

Reach for Recovery is a group of volunteers who try to convey a message of hope to patients who have recently undergone a mastectomy. The aim of this group is to utilise selected trained volunteers to visit pre- and post-mastectomy patients with the aim of giving support and practical advice. The volunteers are women who have personally undergone a mastectomy and are therefore guiding other patients on the ground of their personal experience.

1.27 MANAGEMENT OF SIDE EFFECTS

Presently, all methods of cancer treatment harm healthy tissue, while trying to exterminate the cancer cells (Knapp 1995). Unpleasant side effects are major contributors to the overall distress of cancer patients.

One aspect of clinic procedure, which could be improved, is the preparation of the patient for treatment side effects. Although preparation is generally quite good for the more common side effects, there were some side effects – pain in the joints or limbs, tearing of eyes, nose bleeds and mouth sores – for which preparation is inadequate (Ringler 1983).

Hemopoetic toxicity is often very serious and can be life threatening in cases where septic shock develops. Low white cell counts lead to increased risk of infection while thrombocytopenia can cause bleeding episodes and anemia leads to fatigue. Nausea and vomiting are probably the most general and also the most feared side effects of chemotherapy. With the new $5HT_3$ antagonists, the management of nausea and vomiting has become much more effective. Alopecia, athralgia, myalgia, fatigue, phlebitis, mucositis, altered taste, weight loss and diarrhea are often problematic. Neuropathy is not only extremely unpleasant and painful, but is sometimes a permanent side effect. Impairment of cardiac function can be permanent, debilitating or even life threatening. Anaphylaxis and allergies may occur as well as problems associated with a suppressed immune system.

In a study by Ringler (1983) it was found that adjuvant patients are most bothered by nausea, which is clearly a treatment side effect, while metastatic patients are most bothered by tiredness and weakness, which may be caused by either the disease or the treatment. This suggests that metastatic patients focus attention more on the disease and its effects, making them less attentive than adjuvant patients to the treatment and its side effects.

Measures to minimize nausea and vomiting (Barraclough 1994):

- Minimize waiting time before treatment.
- Minimize patients' bad expectations. Patients who have seen others being sick or who are told to expect terrible nausea and vomiting, are more likely to suffer badly during their own treatment.
- Give supportive counseling and ample opportunities to discuss anxieties.
- Distract attention from cues: sucking mints to mask hospital smells and tastes, listening to music or relaxation tapes, performing mental tasks.

Sohara and coworkers studied 59 patients with hepatocellular carcinoma to determine the incidence of nausea and vomiting and the antiemetic effect of ondansetron. They found that when arterial chemo-embolization was performed, antiemetic treatment for approximately three days was necessary to improve patients' quality of life to an acceptable level.

1.28 SUPPORTIVE CARE

The interest of the scientific community in the supportive care of cancer patients has constantly increased during the last few years. In fact, adequate supportive care has been demonstrated to improve the survival of cancer patients as well as their quality of life by preventing or reducing the severity of side effects induced by cancer chemotherapy and relieving the symptoms due to the neoplastic disease itself (Ballatori 1993).

By supportive care is meant any medication or intervention that can prevent or ameliorate side effects and disease symptoms, or any other aid to improve the quality of life of the patient. This includes the management of hematological and non-hematological toxicity. Examples of non-hematological toxicity include: mucositis, extavasation, mutagenicity, neuro-, nephro-, cardio-, pulmonary-, gastrointestinal- and endocrinologic-toxicity. The term supportive care also includes psychological support for cancer patients and their families. A self-help group is an additional form of supportive care that can be extremely beneficial (see 1.8 resources in Gauteng).

Counseling activity range across a broad spectrum, from the qualities and skills necessary for communicating effectively at one end through to specialist professional help at the other. The abilities of doctors to help their patients to understand and cope effectively with their problems and facilitating changes that may be necessary to bring these about, are intrinsic to good communication. Patients rated emotional support from senior doctors at least as highly as that from their family and more important than any other source. One effect of acquiring these skills is that doctors are then able to identify patients who may be in need of the specialist help provided by those with professional training and expertise. Studies show that between one quarter and one third of all cancer patients have significant psychological distress and that the majority accepts counseling if offered (Sweetenham 1997).

Many agents used as therapy for cancer cause unwanted effects on the bone marrow. The net results of these agents are immune defects and peripheral blood cytopenias. The marrow has considerable capacity for recovery, and this can be exploited to therapeutic gain by using chemotherapy (with or without myeloid growth factors) to mobilize early haemopoetic cells into the peripheral blood; these can be used as rescue following further high-dose therapy (Clark 1997).

The periods of bone marrow suppression following chemotherapy leave patients open to serious and often life-threatening infectious complications. Therefore broad-spectrum empirical antibiotic therapy should be initiated when a neutropenic patient presents with fever. This concept has dramatically improved survival and quality of life in patients undergoing chemotherapy. It is suggested that only those patients whose cancer chemotherapy regimens are anticipated to result in a greater than 40% incidence of febrile neutropenia should have adjunctive cytokine treatments. The importance of using these costly agents rationally and judiciously cannot be overly emphasized (Freifeld 1997).

Untreated anemia is common among cancer patients. Both the cancer and treatment with chemotherapy can suppress the normal endogenous erythropoietic response to anemia, necessitating transfusions. In placebo-controlled phase III studies, administration of recombinant human erythropoietin (epoetin alpha) increased hemoglobin levels and decreased transfusion requirements in patients undergoing cancer chemotherapy. In these studies, an increase in self-perceived energy level, functional status and overall quality of life was noted in the subset of patients in whom hematocrit levels increased by ≥6%. Before and after the phase IV study, where all patients received epoetin alpha, each patient completed a linear analog self-assessment scale designed to measure energy level, daily activity, and overall quality of life. There was a progressive and significant increase in hemoglobin concentrations, decreasing the need for transfusions. The entire patient population demonstrated a statistically significant increase in mean scores for energy level, daily activity and overall quality of life, regardless of tumor response. The magnitude of the increase in these scores correlated with the magnitude of the increase in hemoglobin concentrations. These findings suggest that in cancer patients undergoing chemotherapy, the tradition of leaving anemia untreated may compromise the patients' ability to function and their quality of life (Glaspy 1997).

It is however still currently uncertain whether erythropoietin therapy really improves the quality of life of cancer patients, but some studies have shown decreased transfusion requirements in cancer patients.

The use of bisphosphonates (e.g. pamidronate) is an important supportive measure for patients with bone metastases. Pain, surgery, radiotherapy and hospitalizations can be reduced by bisphosphonate use.

Selective aspects of quality of life during supportive pamidronate treatment were assessed in breast cancer patients with osteolytic metastases. 144 patients were randomized to a pamidronate group (n = 76) or a control group (n = 68). A questionnaire specifically designed for this trial, measuring four domains, namely mobility impairment, bone pain, fatigue and gastrointestinal toxicity was administered at 3-monthly intervals. The analysis focused on changes in these quality of life domains over time. The median follow-up for both groups was 18 months. Mobility impairment and bone pain were significantly less in the pamidronate group as compared with the control group, due primarily to a rapid improvement shortly after pamidronate treatment. Thereafter, a gradual increase in there symptoms was noted in both groups. Gastrointestinal complaints and fatigue levels were similar over time in these two groups, suggesting that these symptoms are more dependent on disease-related events and cytotoxic treatment than on pamidronate treatment. The results indicate that reduced skeletal morbidity in breast cancer patients during pamidronate treatment is associated with an improvement in selective aspects of quality of life (Holten-Verzantvoort 1991).

1.29 ADDITIONAL STRATEGIES

Other strategies that promote a sense of well being and increased control over one's life include stress management, good nutrition and exercise. Some researchers suggest that each of these strategies may decrease the risk of breast cancer or its recurrence:

- Managing stress: includes techniques such as visualization, meditation and progressive relaxation.
- Dietary recommendations: a healthy low-fat diet comprised of an abundance of fresh fruits, vegetables, grains and very little animal fat.
- Exercise promotes emotional well being.

Nonpharmacologic interventions to reduce emotional distress and control symptoms can also be undertaken, including psychotherapy, coping skills training, patient education programs, relaxation training and exercise programs.

1.29.1 PSYCHOSOCIAL INTERVENTION

The following quotation was found in an oncology textbook in the section on standard medical care for breast cancer patients: Once the diagnosis of breast cancer is established, the patient's psychosocial adaptation skills should be evaluated. A baseline profile may help guide therapy and skilled intervention and counseling should be available to help the patient with emotional problems that may arise throughout the course of therapy (Fisher 1994). However the question arises: In how many oncology centers is this really an integral part of the standard of care?

Psychotherapeutic interventions, such as crisis intervention, brief psychotherapy, family therapy and group therapy, have been shown to reduce emotional distress in patients. Patient education programs, many of which include coping skill training, can increase knowledge about the disease, reduce anxiety, increase patient's feelings of purpose and meaning in life, reduce pain and depression, improve coping and increase confidence in the ability to manage pain (Taylor 1990).

There is a long and painful catalogue of psychological morbidity associated with breast disease. It is one of the privileges of dealing with these patients to recognize the incredible natural resources for coping that exist amongst the majority of women. But quality of care can be improved to reduce the stresses involved. The mere recognition of the psychological sequelae by husbands and by all professional groups caring for the women and a sensitive handling of the patient at each stage can go a long way to alleviating some of the stress (Baum 1988).

The Reach for Recovery Program consists of trained volunteers who have had a mastectomy themselves (see 1.8). In the USA specialist nurses known as Mastectomy Counselors, have been recruited into many breast clinics. These strategies should be scientifically evaluated as natural coping mechanisms do exist in the majority of women. Counselors are more reliable at detecting early evidence of psychological morbidity than clinic doctors so that patients can be referred on for medical or psychotherapeutic intervention.

Hammerlid and coworkers (1999) performed two studies of psychosocial intervention in head and neck cancer patients at different stages of their disease. The first study concerned long-term group psychological therapy for patients with newly diagnosed head and neck cancer. Quality of life was measures longitudinally for 1 year and compared with that of a control group. The second study comprised a short-term psycho-educational program 1year after treatment for head and neck cancer. Quality of life assessments were made repeatedly from diagnosis until 1 month after the intervention. The quality of life of the therapy group improved more than that of a control group in most areas measured during the study year, in particular psychiatric morbidity, social functioning and global quality of life. The results indicate benefits from the therapy, although the therapy group scored worse than the control group at diagnosis. These pilot studies suggest that head and neck cancer patients can benefit from different psychosocial interventions.

Criteria to consider when deciding which patients need psychosocial intervention (Ray 1985):

- Not all patients want additional support. Those who refuse help may not be restricted to those who adjust well by themselves and adjust without intervention. Refusers tended to be avoiders or deniers with respect to their illness, and the former strategy at least is one that is associated with poor adjustment. No patient can be pressured into taking part in a program and self-selection is thus one criterion that must be taken into account.
- Traditionally, only patients whose distress is noticed and judged to be of unusual degree are given special help. This routine detection of need misses many patients whose problems then remain unresolved.
- With the specialist nurse model, all patients can be provided with some support and this alone might benefit patients if the nurse has the requisite counseling skills. Patients who fail to adjust are then referred for more intensive care, and it seems from evidence to date that it is the nurse's capacity to monitor all patients and more reliably detect problems that reduces psychological morbidity.
- An alternative would be to provide an active intervention for all patients, recognizing that all patients meet with some problems in adjusting and that the process of adjustment can be facilitated even in patients who would cope reasonably well alone. A further advantage of this approach is its preventive nature. If a person has to wait until significant problems develop before intervention, maladaptive methods of coping may by then have become engrained and be difficult to modify. The cost effectiveness of this approach must be taken into account as it has a high cost in terms of resources.
- Finally, questionnaires or interviews can be used as soon as possible after diagnosis to predict patients at high risk and support can be offered to these people only. This option is also preventive in nature but it does assume that the greatest overall benefit is achieved by focusing resources upon those who are the most disturbed.

1.29.2 THE ROLE OF PHYSIOTHERAPY

In the United States of America, breast cancer patients were among the first cancer patients referred to physical therapists in the early to mid-1970's. Physical therapists can provide the cancer patient with improved function, increased comfort, and an acceptable cosmetic effect, resulting in restoration of the patient's self-esteem and body image (Adcock 1990).

Breast cancer patients can present with changes directly related to their cancer or resulting from their therapy. Some of these are ameliorable to physiotherapy. These deficits include upper extremity mobility, skin breakdown, neuropathic changes, postural changes and secondary edema. Since the majority of breast cancers do require some type of surgical intervention, the physical therapist plays a critical role in the area of preventive medicine. Therapists have the opportunity to provide treatment as well as to educate patients. If the patients understand that early intervention may prevent further problems and complications, they may be more compliant and actively participate in their care.

After surgery, the arm on the affected side must be slightly abducted and flexed at the shoulder and the distal aspect of the extremity elevated and supported. This position will inhibit post-surgical edema. The patient should be encouraged to actively move the hand, wrist, forearm and elbow. Patients should be educated about the increased danger of infection in the affected arm and that this will pose a threat throughout the rest of their life (see Table 2 and Addendum 8).

TABLE 2: PATIENT FORM LISTING SIGNS OF INFECTION (ADCOCK 1990)

Call your doctor or therapist if there are changes in your arms

COLOR – redness, streaking or blotching

TEXTURE – arm is softer, harder, skin is rough or indented

TEMPERATURE – arm feels warmer than the other extremity

SIZE - arm feels full or heavy
- clothing or jewelry do not fit as well

- increased circumferal measurements of 2/8 inch for more than 3 consecutive days

Treatment of decreased mobility of the upper extremity, particularly at the shoulder girdle, is easily correctable by an exercise program. If the tissue is not supple, it can be corrected by a deep friction massage using a steroid in a petroleum base. This type of massage breaks down adhesions, increases circulation and conditions the skin.

Tissue massage, as described above will enhance the integrity of the skin. Those patients who have wounds caused by delayed healing due to radiation therapy, ulcerated chest walls due to advanced disease, erythemas or moist exfoliations will require instructions in skin care. Also, a large number of patients may develop herpes zoster on the affected side. General skin care instructions include cleansing the skin with tepid water and no soap, patting the area dry, wearing loose, non-binding clothing, discontinue use of skin creams or lotions and avoiding direct exposure to the sun. If the patients have moist desquamation, application of cornstarch and topical steroids is helpful. Those patients who have extensive skin breakdown or advanced disease may benefit from cleansing the area followed by moist to dry dressing using water and hydrogen peroxide or saline solution. Analgesics may decrease their discomfort. Patients with herpes primarily benefit from medication. Cool compresses and steroid cream may make them more comfortable and promote healing of lesions.

Physiotherapy is also important for patients with neuropathic and postural changes, where early intervention can prevent chronic problems developing. For patients with persistent long-term neuropathic changes with severe disability, protective measures such as the use of a sling must be employed.

The incidence of edema has been decreasing with the advent of less radical surgical intervention. It remains however, a troubling problem for 30 to 40 percent of patients. Massage, exercise, elevation and compression can be used independently or in conjunction with one another (Adcock 1990).

1.29.3 NUTRITIONAL SUPPORT OF THE CANCER PATIENT

Malnutrition is a common problem in cancer patients that results in a devastating quality of life, economic and survival issues. "Cancer cachexia " refers to a complex, multifactorial syndrome characterized by anorexia or the spontaneous and unintended loss of appetite, generalized host tissue wasting, skeletal muscle atrophy, immune dysfunction and a variety of metabolic alterations. The malnourished cancer patient responds poorly to therapeutic interventions, such as chemotherapy, radiotherapy and surgery, with increased morbidity and mortality compared with well-nourished patients.

Many studies have reported the prevalence of malnutrition in cancer patients. In a multicenter cooperative study of more than 3000 cancer patients, it was reported that substantial weight loss was found in more than 50% of patients. Weight loss was identified in 40% of breast cancer patients. Cancer-induced malnutrition involves systemic and metabolic derangements (Rivadeneira 1998).

Evidence shows that losing weight and focusing on better nutrition and exercise may significantly decrease the chance of getting cancer. Scientists now suspect that as much as 80 percent of all cancers may be related to environment and to things we eat, drink and smoke (see Addenda 3, 4 and 5 for useful advice on eating correctly).

1.29.4 EXERCISE

Experimental studies in animals and epidemiological studies in human populations support an inverse association between exercise and the development of cancer. The proposed biological mechanism for the physical activity-cancer association includes exercise's effect on immune function, transit time of digestion, hormones and body fat. Additionally exercise may be beneficial in the treatment of cancer through mood elevation, decreased loss of lean tissue and increased quality of life (Oliveria 1997).

Dimeo and coworkers (1999) found that aerobic exercise could reduce fatigue and improve psychologic distress in cancer patients undergoing chemotherapy. A group of patients followed an exercise program during hospitalization for chemotherapy and a control group did not. Psychologic distress was assessed at hospital admission and discharge with the Profile of Mood States and Symptom Check List 90. By the time of hospital discharge, fatigue and somatic complaints had increased significantly in the control group but not in the exercising group. Furthermore, by the time of hospital discharge, the training group had a significant improvement in several scores of psychologic distress (obsessive-compulsive traits, fear, interpersonal sensitivity and phobic anxiety) and this outcome was not observed in the control group.

1.29.5 CYTOPROTECTIVE AGENTS

Dose-limiting toxicity secondary to anti-neoplastic chemotherapy is principally due to the inability of the drugs to differentiate between normal and malignant cells. This results in the damage of normal tissues, as well as the desired antitumor effect. Toxicity may be acute, as in cisplatin-induced nephrotoxicity or alkylating agent myelotoxicity and haemorrhagic cystitis, or cumalative, as in anthracyclin-related cardiac toxicity or cisplatin neurotoxicity. The consequences of this often include serious adverse effects and the inability to deliver adequate dose-intensive therapy against the cancer. Chemoprotective agents have been developed to provide site-specific protection against normal tissue toxicity, without compromising antitumor activity. Several chemoprotective agents have recently been developed, including dexrazoxane (ICRF-187), amifostine (ethiofos; WR-2721), mesna and ORG-2766. Initial results confirm their promise as selective protective agents. However, further randomized trials are required to identify their optimal role when used alone or in combination with other toxicity modifiers, including haematopoietic growth factors, with the ultimate aim being adequate dose escalation of chemotherapy to overcome tumor resistance (Lewis 1994).

Amifostine, a new cytoprotective agent has no significant effect on oncolytic efficacy, but side effect profiles improved for febrile neutropenia, neurotoxicity and nephrotoxcicity in a study by Longo (1999). Amifostine's greatest disadvantage, is its' high cost.

1.29.6 ALTERNATIVE THERAPIES

Many patients with advanced cancers that are incurable with conventional treatment seek alternative methods of treatment. Practitioners of alternative medicine claim that the non-toxic natural therapies may result in cures and prolongation of life and undoubtedly give a better quality of life.

Interest in the use of complementary therapies as a means of helping patients cope with their illnesses and improve their quality of life is growing among the general public and health care professionals. Some cancer patients seek such therapies to help reduce anxiety and to enhance hope (Wilkinson 1996).

In a study of alternative medicine among women with newly diagnosed early-stage breast cancer, Burstein (1999) found that women who initiated the use of alternative medicine after surgery reported a worse quality of life than women who had never used alternative medicine. Mental health scores were similar at base line among women who decided to use alternative medicine and those who did not. But three months after surgery the use of alternative medicine was independently associated with depression, fear of recurrence of cancer, lower scores for mental health and sexual satisfaction, and more physical symptoms as well as symptoms of greater intensity. All women reported improving quality of life one year after surgery.

Research by Gotay (1999) investigated complementary and alternative medicine use by cancer patients in Hawaii. Thirty-six percent of patients use complementary and alternative medicine, most commonly religious/spiritual therapy and herbal treatments. Complementary and alternative medicine use was linked with younger age, female gender, Catholic religion and more education.

Verhoef (1999) surveyed the extent of alternative therapy use in a cohort of brain tumor patients. Twenty-four percent of patients used alternative therapies and often more than one therapy at the same time. Motivation for use of these therapies was influenced by the desire for patient-focused treatment and a perceived need to take charge. Alternative therapy users were younger and more likely to be on sick or disability leave, to come in for repeat visits and to have conventional treatments. Users tended to have a lower quality of life with respect to physical well being, functional well being, disease specific and additional concerns. No major side effects or tumor responses were seen with alternative therapies. It was concluded that the use of alternative therapy in brain tumor patients is common and may reflect unmet patient needs with respect to their cancer care within the current model of health care delivery.

Massage is one complementary therapy that is now used in many cancer centers in the United Kingdom. It is time-consuming in terms of training and staff time, and there is little research to justify its use in terms of cost-effectiveness and benefits for patients. However, massage has been demonstrated to be physically and psychologically beneficial in a general hospital setting (Wilkinson 1996).

Cassileth (1991) compared survival and quality of life of patients with end-stage cancer treated at a prominent unorthodox cancer clinic and matched controls that received only conventional treatment. The study was not randomized, as patients who received the alternative therapy were self-selecting. This is clearly a limitation of the study. The study found no difference in survival between the two groups but the quality of life scores were consistently better among patients treated with conventional therapy, despite the fact that a greater proportion of these patients had received chemotherapy with the attendant side effects. The study suggests that the assumption that alternative therapies necessarily enhance the quality of life is not valid.

The value of alternative therapies can only be established meaningfully in the context of controlled clinical trials. Otherwise patients who do not have scientific training are at the mercy of people who are often only trying to make money out of unproved therapies.

Many factors contribute towards quality of life in patients with cancer, including quality of symptom control. Symptom control may be related to the effectiveness of therapy, social functioning, the degree of emotional support and the extent to which the patient feels hopeful and optimistic. Maximum symptom control is the first priority in trying to improve quality of life. It is nonsense to focus on emotional support when someone has uncontrollable pain or vomiting. One of the main argument in favour of patients with advanced incurable cancer seeing cancer specialists is the availability of expertise in symptom control which may be lacking in non-specialist centers (Slevin 1992).

1.29.7 RELAXATION TRAINING

Relaxation training is a widely used, promising nonpharmacological intervention with the chronically ill. Relaxation training decreases anxiety and nausea from chemotherapy and decreases pain (Taylor 1990). Systematic desensitization and relaxation training can help reduce anticipatory nausea and vomiting and other adverse reactions to chemotherapy.

1.30 SPIRITUALITY

In nursing practice, emphasis has increasingly been placed on giving care to the whole person. This is usually said to involve looking at a person's physiological, psychological, social and spiritual needs. In palliative care, concern with spirituality is all the more pertinent since terminal illness raises many questions about the meaning and nature of existence. However, research suggests that nurses have difficulty in recognising and assessing spiritual needs (Turner 1996).

Part of the difficulty may lie in our definitions and understanding of the concept of spirituality and the failure to distinguish it from religion. For some, the notion of "spirit" relates to the inner part, the real person that is not limited by physical or external phenomena. For others, it is concerned with belief in a transcendent realm, or with a relationship with a higher being. Spirituality thus involves a search for meaning, whereas religion is most often concerned with systems of faith and worship (Turner 1996).

One way of looking at spirituality is in terms of the concepts of "being" and "doing". Doing may be viewed as those aspects of human life that are worldly and short-lived, whereas being may be seen as a more permanent state, which remains after doing has ended. A person's being is particularly active when doing is in decline or has ceased altogether, as in chronic and incurable illness. At such times it enables the human personality to continue to grow and to be enriched (Turner 1996).

Our difficulty in recognising the important contribution of spirituality to a person's well being may in part result from a Western world view that tends to value scientific and material thinking and doing, to the exclusion of being. A young man, dying from advanced cancer, was admitted for terminal care. The issue he faced was how to discover that his value lay not just in doing, but in being; that his wife and family loved him for who he was rather than for what he did for them. Failure to discover meaning in relationships and to transcend the realm of purely material things is, for many, a source of intense spiritual pain (Turner 1996).

How do we discover our meaning in being? Fundamentally we are physical, psychological and spiritual beings who have biological needs and an innate drive for love, security, identity and acceptance. Most of the time we find these needs met in our relationships and our jobs. But when somebody is dying all these things change. What was once significant seems less so and what previously seemed unimportant may take on an increased meaning. One of the strengths of the early hospice movement was that it successfully combined a scientific approach to symptom control with an emphasis on the spiritual dimension, often referred to as "being with" or "being there". In its simplest sense this describes the notion of hospitality, that is providing someone with a safe place from which to begin to make sense of their predicament. At its highest it denotes the idea of using "the whole of ourselves to relate to our fellow human beings who are in trouble". We need to value relationships and the intangible qualities of caring, as well as the more quantitative aspects of care (Turner 1996).

A rediscovery of spiritual care has never been more needed, even if it is only to make sense of the constant predicament faced by those health care professionals who struggle to adopt a whole-person approach with limited time and resources and little or no education in the whole area of spirituality. It is time for spiritual care to come fully on to the agenda (Turner 1996).

1.31 SOCIAL SUPPORT GROUPS

Social support groups represent another social support resource for the chronically ill. Potentially, such groups can satisfy needs for social support that have been unmet by family members and caregivers. Alternatively, such support groups may be viewed as an additional source of support provided by those going through the event. Chronically ill patients report a variety of positive as well as negative experiences from such contacts. On the positive side, fellow patients were reported to be especially helpful when they acted as good role models on whom patients could pattern their own coping efforts or when they functioned as role models by surviving over the long term (Taylor 1990).

Generally, beneficial effects have been found as a result of social support group interventions. Self-help groups may help victims cope with the stigma associated with certain disorders, such as cancer. Unfortunately support groups reach only a relatively small proportion of chronically ill patients. Moreover, support groups appear to appeal disproportionately to well-educated, middle-class white females. The potential for self-help groups to be a general resource for the chronically ill has yet to be realised (Taylor 1990).

Family members and significant others who are going through stressful events with the patient could receive guidance in the most effective ways to provide social support and in the well-intended actions they should avoid because these actually make a stressful situation worse. In some cases even the simple provision of information may be supportive (Taylor 1990).

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ADDENDUM 1: TIPS FOR COPING DURING THE FIRST FEW MONTHS AFTER TREATMENT (RUNOWICZ 1995)

- *Be good to yourself.* Instead of trying to do everything for others, take some time off for yourself. Read a good book, have a manicure, take in a movie, or visit a new shop or art exhibit. Indulging yourself isn't selfish, it's good medicine for the mind.
- *Learn to say no.* You're in control of your life, and politely refusing to do something isn't rude, it's your right.
- *Pace yourself.* Not everything has to get done right away. If you're feeling overwhelmed, divide your list of tasks into manageable parts and prioritize them, being sure to delegate some of the work to others.
- *Take a walk.* It's the best kind of exercise to start with after treatment and will help clear your mind of tension and anxiety. Speak to your doctor about when you can resume normal activity.
- *Talk about your concerns.* Spoken out loud, worries have a way of seeming smaller and less overwhelming. If you don't have a friend or family member to chat with, call your doctor and ask her advice.
- *Pick your battles.* Not every skirmish is worth winning, not every argument worth fighting over.
- *Look at the positive side.* Nothing in life is ever perfect, not even before cancer entered your life. So think about all you've achieved, and be proud of it.
- *Get enough sleep.* Feeling tired is your body's warning signal that it needs to rest and replenish its energies.
- *Laugh at yourself.* If your hair has just started to grow back, think of how goofy you look. When you're feeling down, it's important to find something – no matter how self-deprecating – to giggle about and give yourself a lift.
- *Help someone else.* Whether its picking up a quart of milk for the neighbor or testing your daughter for a geography test, reaching out to others can help you feel stronger and more in control of your own life.
- *Try something new.* Taking on new hobbies and learning new skills can bolster your self-image and make you feel better about your life that lies ahead.

ADDENDUM 2: STAY ALERT (RUNOWICZ 1995)

At first it's hard not to react to every ache and pain as a sign of recurrent cancer. I tell my patients to make me a list and ask them to include even their slightest symptoms. More often than not, I end up reassuring them that it's nothing. But it helps when they write down their concerns, listing *all* the symptoms that they may be worried about. Often, when they come in, they're a bit befuddled and intimidated to be seeing the doctor. Sometimes they'll forget what it is that they wanted to discuss.

Between visits to your doctor, watch for any of the following problems:

- Changes in your breast or in your scar area such as lumps, thickening, redness, or swelling.
- Pain in your breast, shoulder, hips, lower back, abdomen or pelvis.
- Lumps in neck, under arms, in groin, or in breasts that could signal lymph node involvement.
- Persistent indigestion or gas.
- Nausea, vomiting, diarrhea or heartburn that lasts for several days.
- Bloating or a feeling of fullness after a light meal.
- Irregular vaginal bleeding.
- Backache.
- Nagging cough or hoarseness.
- Fever.
- Loss of appetite or sudden, unexplained weight loss or gain.
- Dizziness, blurred vision, severe or frequent headaches, or trouble walking.

ADDENDUM 3: TIPS TO CUT THE FAT (RUNOWICZ 1995)

Did you know that 60% of all cancers in women might be related to what they eat? Numerous studies show that eating too much fat may increase a woman's chances of getting cancers of the colon, breast and endometrium. Every woman secretes a hormone from the adrenal gland called androstenedione. As part of the body's normal metabolic function, this hormone is converted to a weak form of estrogen in the fat cells. The more fat you eat and the more weight you carry, the more fat cells you have and the more estrogen builds up. Excess estrogen stimulates the development of uterine and breast tissue, which may cause some cancers to grow. Limiting the fat in your diet may reduce your cancer risk.

- Keep an honest food diary for two weeks. You will find out what (and how much) you eat. Identifying bad food habits is the first step toward changing them.
- Eat leaner cuts of meat, low-fat or no-fat dairy products, more seafood and fewer fried foods.
- Trim all visible fat from meats before and after cooking; remove skin from poultry before cooking.
- Use nonstick pans for sautéing. Instead of oil, use chicken broth or spray lightly with vegetable oil.
- Use fruit preserves or unsweetened applesauce in baking instead of butter or margarine.
- Boil, grill, bake, poach or steam foods instead of pan-frying or deep-frying. Use a rack to allow fat to drip into a pan. Baste with wine, lemon juice or orange juice. Do not use fatty drippings. Self-basting poultry can be high in saturated fat, so read the label first before you buy it.
- Instead of mayonnaise or sour cream, mix one-third low-fat yogurt with two-thirds low-fat cottage cheese.
- Substitute low-fat yogurt, skim milk or buttermilk for cream in gravies and dressings. Yogurt will not separate when heated if you add one teaspoon of cornstarch per cup of yogurt.
- Use low-fat recipes. Look for cookbooks that list calorie and percent of fat per serving in their recipes to help you eat the healthy way.
- Learn to use spice instead of fat to flavor your foods.

- Eat more fruits, vegetables and whole grains. The National Cancer Institute recommends that you eat at least five or more servings of fruits and vegetables a day to reduce risk of developing colon and other cancers.
- Limit red meats and cheese. Instead use more poultry, fish, beans and grains for sources of protein in your diet.
- Shop for low-fat or no-fat alternatives.
- Resist that second helping. Your brain needs twenty minutes to register that you are full.
- Don't try to be perfect. Your eating habits took a long time to develop and will take some time to change as well. If you try to cut out everything, you'll end up feeling deprived and risk one high-fat binge after another. When you eat a high-fat meal just try to balance it with low-fat foods the rest of the day. Keep low-fat, low-calorie nibbles on hand to cope with hunger pangs and cravings.

ADDENDUM 4: SWITCHING FROM HIGH-FAT FOODS TO LOW-FAT ALTERNATIVES (RUNOWICZ 1995)

Instead of This	Try This
Ice cream	Nonfat frozen yogurt or sorbet
Butter	Unsweetened fruit preserves
Cream soups	Gazpacho, minestrone and consommé
Sour cream dip	Salsa
Potato chips	Pretzels
Iced cake or doughnuts	Angel food cake
Brownies	Gingersnaps, fig bars
Croissants	Plain bagel or whole-wheat roll
Salami, Bologna	Turkey, roasted lean ham
Oil-packed tuna	Water-packed tuna
French-fries	Roasted or baked potato
Sour cream	Yogurt or low-fat cottage cheese
Corn chips	Air-popped corn
Cheddar cheese	Part-skim mozzarella
One whole egg	One or two egg whites
Ham and cheese omelet	Vegetable and egg white omelet
Fruit-flavored yogurt	Nonfat yogurt with sliced fresh fruit
Olives	Pickles
Whole milk	Skim milk

ADDENDUM 5: TAKING CARE OF YOUR HEALTH: DIET NUTRITION AND LIFESTYLE (RUNOWICZ 1995)

- Too much fat may promote cancer.
- The need for fiber – eat five half-cup servings of fruits and vegetables per day.
- Limit your amount of animal protein – rather eat complex carbohydrates and vegetable protein like beans, rice or soy products like tofu or tempeh.
- Drink alcohol rarely, if at all – maximum one to two glasses of wine or one shot of hard liquor per day.
- What about supplements? – there is still too much confounding data to recommend taking beta–carotene, vitamin E and vitamin C to prevent cancer. The advice is rather to eat lots of fresh fruits and vegetables.
- The need for calcium – the recommended daily allowance for premenopausal women is 800 milligrams daily and for postmenopausal women, 1500 milligrams daily.
- The need for exercise – to reap the full benefit of a low-fat, high-fiber diet, it's important to add regular physical activity. Regular exercise can stimulate the immune system, reduce your risk for chronic diseases and degenerative conditions like coronary heart disease, diabetes, osteoathritis and osteoporosis. It also lessens depression. Twenty minutes of fast walking, biking or jazz dancing two or three times a week.
- Smoking – If you're a cancer survivor and still continue to smoke, you might as well put a gun to your head and fire: sooner or later it will kill you. Evidence shows that tobacco eventually kills close to 25% of those who use it.
- Unprotected sun exposure – these days getting a tan isn't healthy, it's downright dangerous. A history of sunburn and a family background are two main risk factors for malignant melanoma, a deadly form of skin cancer that strikes thousands of women each year. Use a sun-protection factor of at least 15 and limit time out of doors. Regular self-examinations are an important part of early detection. Most skin moles are harmless, but ask yourself these questions: Has it changed in size, thickness, shape or texture? Does it have an irregular border? Is it bigger than a pencil eraser? Is any new mole translucent, tan, brown, black or multicolored? Is it painful, itchy, bleeding or does not heal? Notify your oncologist.

- Food additives and meal preparation – some cooking methods, such as high-temperature grilling, smoking, salt-curing and pickling, can produce possible cancer-causing substances in foods.
- Alternative cancer regimens like shark cartilage, raw juice therapy, shiitake mushroom tea, kinesiology – at present none of these unorthodox methods have been proven.

ADDENDUM 6: REASSURING YOUR CHILD ABOUT CANCER (RUNOWICZ 1995)

- Having cancer doesn't necessarily mean a person will die from it.
- Nothing you did or didn't do caused mommy to get cancer.
- Nothing you thought or said caused the cancer to grow.
- Cancer isn't contagious – you can't catch it from someone else.
- Because your mom or grandmother has cancer doesn't always mean you or someone else in your family will get it too.
- The way you behave can't change the fact that your mom had cancer or that your family is upset.
- It's important to continue with school and outside activities.
- There are others to talk to besides your parents about your fears.

ADDENDUM 7: THE MONTHLY BREAST SELF-EXAMINATION (RUNOWICZ 1995)

When it comes to breast cancer, early detection can make all the difference. That's why it's essential you examine your breasts every month using these guidelines:

- *In the shower,* with fingers flat, gently slide your hands over every part of both breasts, checking for any lump, hard knot or thickening.
- *Lying down,* place a pillow under your right shoulder and put your right hand behind your head. Using your left hand, with fingers flat, press gently in a small circular motion, starting at the outermost top edge of your breast and spiraling toward the nipple. Repeat with the left breast. Then check your underarm area – which is also, breast tissue – using the same circular motion.
- *Before a mirror,* with arms at your sides, then with arms raised overhead, check for changes in the size, shape and contour of each breast. Look for swelling, dimpling or changes in skin texture. Gently squeeze both nipples and look for any discharge.
- *Report any changes* immediately to your doctor. Only about one in ten lumps that premenopausal women report to doctors turns out to be malignant. But your best defense against breast cancer is to know for sure.

Make it a habit to check your breasts thoroughly at least once a month. The examination should be done the week following your menstrual period or the first day of the month if you are no longer menstruating.

ADDENDUM 8: SPECIAL INSTRUCTIONS FOR HAND AND ARM CARE (ADCOCK 1990)

1. AVOID CUTS, SCRATCHES AND IRRITATION
    - use cuticle cream instead of scissors
    - wear heavy gloves and long sleeves when gardening and avoid thorns
    - use rubber gloves for washing dishes and cleaning
2. DO NOT HAVE INJECTIONS OR VACCINATIONS IN THE AFFECTED ARM - ASK TO HAVE THEM ON THE OTHER SIDE
3. AVOID WASPS, BEES AND OTHER INSECTS
    - call the doctor if you get a wasp or bee sting
    - use insect repellant if you are going to be exposed to insects
4. AVOID BURNS
    - if you smoke, hold your cigarette in the other hand
    - always use a padded glove when reaching into the oven
    - avoid sunburn – use protective sun lotion and tan gradually – if possible, cover your affected arm when in the sun (with long sleeves or a towel)
5. AVOID BINDING OR SQUEEZING YOUR ARM
    - do not have blood pressure taken on the affected side
    - wear loose jewelry (wrist watch, bracelets and rings)
    - wear loose sleeves
    - do not carry your handbag on the affected shoulder or in the affected hand; carry it on the other side
6. AVOID UNDERARM IRRITATION
    - talk to your doctor and/or therapist before shaving your underarm
    - ask your doctor and/or therapists advice about deodorant – do not use any product which causes rash or other irritation
7. AVOID STRAINING YOUR ARM
    - let others carry heavy objects
    - do not move furniture
    - ask your therapist's advice about strenuous activities you want to do
8. TAKE EXTRA CARE OF YOUR HAND AND ARM
    - use lanolin cream on your hand and arm several times a day

- in case of minor breaks in the skin (insect bites or scrapes), wash the affected area and cover it with a bandage
- burns or cuts should be seen immediately by a doctor and/or therapist, an antibiotic is usually needed
- call your doctor or therapist promptly if any sign of infection occurs

CHAPTER 2: THE DIFFERENT METHODS TO MEASURE QUALITY OF LIFE

2.1 INTRODUCTION

In 1991 Stjernswärd wrote: A consensus needs to be drawn on a scientifically valid and reliable method for estimating quality of life (QOL); it should be practical and realistic to use, and with minor modifications, applicable cross-culturally. Can the experts agree on such a method soon? Up to now, few quality of life studies has led to changes in clinical practice.

Despite the widespread acceptance of quality of life as the ideal guideline in health care and thus in clinical research, serious conceptual and methodological problems continue to plague the area. Quality of life has become a key concept in the medical community. The health care provider's treatment and the effect that it has on the patient are two very different perspectives. Connecting these two perspectives is a task for which the quality of life concept is very well suited, in that it comprises both objective and subjective aspects: The personal, subjective experience of one's own life, as well as the more objective assessment of external factors that influence its quality (Ventegodt 1992).

Research designed to measure quality of life, however suffers from various problems relating to theory and method. The lack of theoretical foundation is a cardinal problem. Without an overarching theory of quality of life to guide the design of instruments, it is difficult to determine what to measure and how. Related to this is the problem of validation. Instruments are typically checked only by observation-to-observation cross checks and rarely by reference to theory, let alone to the experience of the respondents: Do they feel their quality of life is gauged correctly by the instrument (Ventegod 1992)?

Historically, the difficulty in assessing more multidimensional, cancer-specific quality of life has been hallmarked by the inability to reach consensus about what dimensions are of importance. This lack of definition has stymied the development of new, more disease-specific, domain-appropriate instruments.

The heterogeneity of QOL instruments and the enthusiasm of arguments advanced in support of each are an indication of incompletely resolved tensions between the requirements of psychometric comprehensiveness and orthodoxy on the one hand and brevity and practicality on the other. Studies that try to compare and cross-validate the various instruments provide a potential means to reduce the confusion.

There is no gold standard for the measurement of quality of life. In this chapter the hypotheses on which quality of life investigations are based and the requirements for the tests with which investigators seek to prove and expand their theories will be discussed. The basis for every hypothesis is a working definition of "Quality of Life" and a survey of such definitions is presented. The multitude of quality of life instruments will also be investigated as to their strengths and weaknesses to demonstrate the applicability of each test. At the end of the chapter a selection of scales and symptom indexes are included for the benefit of students in this field. I have included all the instruments that I encountered, without any specific preferences.

2.2 A THEORETICAL FRAMEWORK FOR QUALITY OF LIFE:

1. It can only be described and assessed by the individual.
2. It must take many aspects of life into account.
3. It must be related to individual aims and goals.
4. Improvement is related to the ability to identify and achieve these goals.
5. Illness and treatment modify these goals.
6. The goals must be realistic.
7. Action is required to narrow the potential gap. This may be by the patient alone or with the help of others.
8. The gap between the expectation and the reality may be the driving force for some individuals.
9. As each goal is achieved new ones are identified, opening the gap again. It is a constantly changing picture (Calman 1984).

According to Barofsky (1986) there are three current approaches to quality of life assessment:

1. Understanding the assessment as a reflection of a judgment process. Judgement-based quality of life assessments investigate how and why a person makes a particular judgement.
2. Population-based assessments (technically the most advanced).
3. Psychosocial assessments (the most prevalent) are concerned with how an individual copes and adjusts. These types of assessments were derived from psychiatric and psychological concepts.

Schipper (1986) identifies four important methodological issues:

1. What is the definition of quality of life and what are its components?
2. Who should measure quality of life?
3. When do you measure quality of life and how do you analyze the data? Quality of life is a continuum and should not be measured at one point in time.
4. How do you ensure that what you are measuring is the quality of life you define?
5. The following criterion should be added: The actual measurement should be done in a uniform and controlled way. The patient should have a private area, the questionnaire should be filled in before being seen by the doctor and the patient should not be influenced by anyone during this time.

Essential minimum criteria for the development of quality of life measures (Schipper 1986):

1. Indices should be disease specific.
2. The index must be functionally oriented.
3. Designed for patient self-administration.
4. Questions should be generally applicable.
   Easy to interpret and exhibit consistent interpretation.
   Few enough questions so that high compliance is maintained.
5. Should be repeatable.
6. Sensitive across the range of clinical practice.
7. Must be validated in the following areas: face, construct, sensitivity, and freedom from social desirability bias and discriminatory function.

According to Ballatori (1993) there is agreement on the following points:

1. We need to measure quality of life of cancer patients and its variations, possibly in relation to the clinical evolution of the disease and to the treatments administered to the patients.
2. We must use measurement scales, such as linear visual analogue scales (VAS) or categorical scales (scores). The former seem preferable to categorical scales from the point of view of analysis of data (they have associated continuous variables instead of the discreteness of categorical scales), although more difficult for the patients to complete.
3. We need multidimensional measurements, as quality of life involves different aspects of the cancer patient's life, such as feeling, psychological condition, social relationships, patient's relationship with his or her disease and treatment toxicity.
4. The patient must perform the evaluation; no other person can have an exact perception of the patient's quality of life, perceptions, and so on.
5. Results of the evaluation must be expressed in a very simple way, so as to use them easily in statistical analysis in combination with survival data, treatment response and therapy toxicity.
6. Any new questionnaire should be tested for reproducibility and validity. Many of the available questionnaires do not meet the above-mentioned criteria and therefore the results of studies on quality of life which employ them are open to criticism.

2.3 CONCEPTUAL FRAMEWORK FOR QUALITY OF LIFE STUDIES

The conceptual arguments relating to the use of categories or domains to measure quality of life have been established previously through the RAND Health Insurance Experiment and are used extensively in measures (e.g. SF36, Nottingham Health Profile, FACT and EORTC QLQ-C30, see addenda). Essentially health is described as a series of discrete yet overlapping areas known as dimensions or domains. The standard approach to measurement of "functioning" in each domain is that a series of questions are developed, which probe that particular area of health. Statistical reliability can be demonstrated by using analyses such as Cronbach's alpha or factor analysis to demonstrate that the questions within the domain correlate with one another and differ between domains (Jenney 1998).

In comparative clinical trials, the *difference* in quality of life between treatments is of primary interest. There are global indicators of well being and functioning (e.g. physical well being) as well as more specific indicators of symptoms of disease and treatment (e.g. appetite).

In large-scale cross-cultural clinical trials, a detailed assessment of numerous aspects of quality of life may be neither appropriate nor feasible. Given that the purpose of such trials is to compare treatment regimens with regard to patients' overall quality of life, not to determine specific reactions associated with a specific drug, global measures are appropriate to assess outcome. Different regimens may have different side effects and effects may vary among various subgroups of patients. The relative importance attached to side effects has been shown to be influenced by patient factors such as age, gender, diagnosis and treatment (Coates 1983a).

Responses on global measures assessed with single items are expected to reflect the summation of the individual meaning and importance of various factors for each patient. Although less precise for specific treatment effects, these measures may be sensitive to the wide spectrum of reactions seen in patients on and off treatment and will detect these changes on single dimensions, allowing for comparison across treatments (Bernhard 1997).

There are two further reasons to include global in addition to specific measures in clinical trials (Hürney 1995). First the perception of a particular aspect and its relative importance (i.e. weight) may vary not only among individuals but also within individuals over time and across different situations (e.g. on or off treatment). Second the measures must be cross-culturally equivalent to the degree that treatment effects can reliably be studied across cultural groups (Bernhard 1996). There may be cultural variation in perception of disease and treatment sequelae and therefore specific aspects may be perceived differently across the multiple cultural and social class groups typically involved in international clinical trials. Because global scales are less affected by this problem, for treatment comparisons across different cultural groups they are an alternative to the predefined weighting system of multi-item scales (Bernhard 1997).

Measures of specific disease and treatment-related symptoms are a useful complement to global outcome measures of well being and functioning. Studying the association between the specific and global measures over time and in relation to the biomedical variables can give insight into the underlying interactions over the different phases of disease and treatment (Bernhard 1997).

Quality of life research within the cancer population must address the separate issues created by both the broad cancer diagnosis and the specific disease presentation. Both aspects contribute to the actual function and quality of life of patients. The former has primarily psychosocial repercussions that concern mortality, social stigma/stereotype and having a long-term, often incurable illness. The latter involves the clinical, functional and psychosocial sequelae of the actual disease course and treatment (Parsons 1998).

2.4 TYPES OF QUALITY OF LIFE STUDIES

Quality of life studies in cancer research can be categorized into three types (de Haes 1985):

1. Discrimination: Comparisons between different groups of cancer patients.
2. Comparisons of cancer patients with controls.
3. Descriptive studies.

There are two basic approaches to measurement of health-related quality of life: Each has advantages and disadvantages. The use of a disease-specific measure allows detailed assessment of symptoms and concerns that are pertinent to a particular group of patients without the measure becoming too cumbersome. The principle aim of this approach is to increase the responsiveness of the measure by including only important aspects of health related quality of life that are relevant to the patients being studied. Such measures do not allow easy comparison between groups of patients (Jenney 1998).

Conversely, generic measures (measures designed for use with any illness group) allow comparisons between groups and peers. Although generic measures may lack sensitivity for some aspects of functioning for individual groups of patients, they provide the only objective means for comparisons between groups, allowing assessment of the impact of the disease and its treatments. The disadvantage of such measures is that they may not focus adequately on particular areas of concern for different groups of patients (Jenney 1998).

A Multitude of methods measuring quality of life has been reported in the literature. Some are simple enough to use in most clinical situations, while many methods are complicated, time-consuming and require the services of psychologists over a long period of time. It appears that many of the current measures of quality of life were designed to investigate relatively specific and perhaps minor nuances in the quality of care. Often, results of such measures are not appropriate in other clinical situations and certain advancements in therapeutic approaches can invalidate the findings based on these measures (Stjernsward 1996).

Butow (1991) compared the PACIS (perceived adjustment to chronic illness scale), 3 one-item LASA (linear analogue self-assessment) scales, the GLQ-8 (general health questionnaire), Bf-S (befindlichkeitsskala von Zerssen), FLIC (functional living index: cancer), HAD (hospital anxiety and depression scale) and the POMS (profile of mood state). He found that, in general, correlations between new and established measures were good, indicating convergent and concurrent validity. The choice of a QOL scale for a particular study depends on the patient groups, the treatments involved and on the available resources. Butows' comparative study favored the use of brief, simple scales. By doing this, the range of situations in which assessment of QOL is feasible is enlarged considerably.

Many different assessment instruments are available. Some measure just one domain and others provide a more global assessment. Alternative methods involve letting patients themselves choose a personal list of items that are important to them (Barraclough 1994).

Health *per se* is difficult to define because of its multidimensional nature. Many indexes exist but they are either based on very general definitions of health that equate health with quality of life or they focus narrowly on some form of illness (Spitzer 1981). Many workers try to measure life's quality, but they use only one or a few aspects that they consider most relevant to the condition of their own primary interest.

Various "domains" can be measured: psychological, social, sexual, occupational, physical, spiritual, satisfaction with care etc. Trying to measure all of these domains is over-ambitious, but measuring just one aspect is a crude approximation. Additionally assessment instruments have to be quick and simple if they are to be given to large numbers of patients (Fallowfield 1990).

2.5 DEFINING QUALITY OF LIFE

Quality of life is difficult to define. Its meaning depends, at least in part, on the context in which it is used. Within the context of health and medical outcome assessments, the impact of health on the quality of life of the individual, is mostly what the observer wishes to measure. This is termed "health-related quality of life". It is useful in that it emphasizes the impact of health on the much broader concept of quality of life but also acknowledges that issues beyond physical functioning are assessed (Jenny 1998). From a psychometric point of view, quality of life is a multidimensional construct that encompasses physical, mental, social, emotional and behavioral components of well being and functioning (Bullinger 1995).

An important aspect of the definition of quality of life is the personal perspective; essentially, one is attempting to assess the uniquely subjective perception of how individual patients feel about their health status and/or nonmedical aspects of their lives (Gill 1994).

It has become fashionable to equate health – defined comprehensively – with quality of life. However, quality of life, as traditionally defined, is a much broader concept than health. In addition to health, quality of life encompasses standard of living, the quality of housing and the neighborhood in which one lives, job satisfaction and many other factors. While health used to be defined primarily in terms of death and the extent of morbidity, the emerging conceptualization of health is far broader. It encompasses how well people function in everyday life, emotional well being and personal evaluations of health in general. To distinguish the new conceptualization from the old, the term "quality of life" has been adopted (Ware 1991).

The World Health Organization (WHO) defined health as a "state of complete physical, mental and social well being and not merely the absence of disease or infirmity". Thus there are clear precedents for the dimensionality of health and specifically for the distinction between physical and mental health. The second criterion for evaluating a health status measure is the range of health levels that are defined. Scales that restrict the range of measurement, other considerations being equal, are inferior to scales that do not (Ware 1991).

Should we emphasize disease-specific or generic measures? Generic scales assess concepts that are relevant to everyone. They are not specific to any age, disease or treatment group. Generic measures focus on such basic human values as the ability to function in everyday life and emotional well being. Generic health consists of three categories namely, physical functioning, mental health and general health. In general, specific measures do not allow for broad comparisons (Feeny 1998). According to Ware (1991), the ideal is to use both generic and disease-specific measures and to analyze them together.

In addressing quality of life in a clinical trial context, it is useful to have both a general definition and an operational definition that guides the measurement of the construct. Most general definitions include physical, mental and social well being. In clinical trials, it was recommended by Moinpour and coworkers (1989) that quality of life be operationally defined with respect to health care and the treatment of disease, i.e. how physical, mental and social well-being are affected by medical intervention. For example, the measurement of physical mobility and the ability to perform a job would be relevant items to measure in a cancer clinical trial. Items that are affected by a number of factors that are mostly unrelated to medical care should not be included, for example job satisfaction.

Quality of life can be measured with a single global instrument that encompasses the three components of the WHO definition, for example the Spitzer Scale, the Functional Living Index-Cancer (FLIC) or Selby's LASA (see 2.8 and 2.9). Use of a global measure allows comparison across a wide variety of trials. The single global measure can also be supplemented with disease-specific and treatment-specific items for that trial. The problem is the lack of a single, global instrument that researchers accept as applicable to measurement of quality of life across many different cancer trials (Moinpour 1989).

Other investigators have described quality of life with a larger number of dimensions: Aaronsen (1986, 1987 & 1988b) recommend that 12 components be included in the assessment of quality of life in clinical trials: pain and pain relief, fatigue and malaise, psychological distress, nausea and vomiting, physical functioning, symptoms and side-effects, body image, sexual functioning, social functioning, memory and concentration, economic disruption and global quality of life.

Conceptually, quality of life is a somewhat vague term. Trying to define it explicitly, so that objective measurement would be possible, is a complicated issue. Fallowfield (1990) adopted a broad approach because certain aspects of quality of life are (at the moment) immeasurable, but nevertheless very important. Campbell (1976a) conducted important research on the components of quality of life and their relationships to one another. The quality of life investigated was however, not health-related. The types of domains that the investigations focused on were: housing, employment, standard of living, marriage etc.

Many researchers and theorists with an interest in the field of quality of life conceptualize it as a multidimensional concept that encompasses all aspects of physical, social and psychological function (Aaronsen 1988a, Cella 1990, Schipper 1985, Knapp 1993). Ware (1984) emphasizes the importance of disease impact on quality of life. He proposes a hierarchy of impacts beginning with the physiological impact of the disease, extending to influences on personal functioning, psychologic distress, general health perceptions and social role functioning. This implies that the interpretation of outcomes of medical treatment by physiological measurement alone, ignore much greater components of disease impact.

The quality of life construct is defined as the individual's subjective assessment of all areas of physical, emotional and social functioning (Calman 1987, Cella 1990).

The need to evaluate subjective morbidity and the impact of both an intervention and disease on a patient's lifestyle is becoming increasingly recognized, this approach has become to be known as measuring quality of life (Bernheim 1987, Holland 1984 & Van Dam 1984).

Quality of life is a frequently used term in the medical literature. The question is: "Does non-health related quality of life, differ from health-related quality of life and if so, how do these concepts differ?" (Bergner 1989). Despite the appeal of material possessions, one of the primary requisites to the enjoyment of a high quality of life is good health (Fallowfield 1990).

The subjective nature of quality of life is illustrated by a patient's insightful comment. She indicated that her quality of life had greatly improved during the preceding week, explaining, "Nothing that is happening to me has improved. In fact, physically I am feeling worse. What is different *is how I am taking it"*. Clearly the subjective nature of quality of life means that it will vary greatly from person to person and even for a given individual over time in the same objective circumstances (Cohen 1996).

Cohen and coworkers (1996) defined quality of life as subjective well being. They reasoned that a single global question asking a person to rate his/her overall quality of life is perhaps the most valid measure, in that it most closely represents what that individual means by quality of life, but such a scale fails to identify the factors contributing to the assessment. To provide the best care possible, health care workers would need to know what contributed to the person's decision to rate his/her quality of life as high or low.

Most health status and quality of life measures have included the three dimensions of health according to the World Health Organization's definition: The World Health Organization (1946) defines health as physical, psychological and social well being. People with a life-threatening illness, however, define health as a sense of personal integrity and wholeness (Kagawa-Singer 1993) encompassing physical, mental/emotional and spiritual domains (Fryback 1993). Cassel's comments regarding the suffering of persons are relevant to this latter definition of health:

- Our intactness as persons, our coherence and integrity, come not from the intactness of the body, but from the wholeness of the web of relationships with self and others (Cassel 1991).

- Suffering occurs when an impending destruction of the person is perceived; it continues until the threat of disintegration has passed or until the integrity of the person can be restored in some other manner (Cassel 1982).
- Meaning and transcendence offer two additional ways by which the suffering associated with destruction of a part of personhood is ameliorated (Cassell 1982).

Existential concerns are of great importance to people with a life-threatening illness (Fryback 1993) but this domain is not included in most of the quality of life measures. The existential domain (Yalom 1980) includes concerns regarding:

- Death - existential obliteration.
- Freedom - the absence of external structure.
- Isolation - the unbridgeable gap separating self from all else.
- Meaning - the dilemma of meaning-seeking creatures who recognize the possibility of a cosmos without meaning.

If our quality of life measures are to account for important determinants of quality of life such as "how am I taking it" we will need to include measures relating to coping and existential well being, which place the person's interpretation of his/her objective circumstances in the context of his/her world view. Salmon and colleagues (1996) began to do this with their Life Evaluation Questionnaire (LEQ).

Ventegod (1992) defines quality of life as follows: Quality of life resides in the full expression of life's potentials.

Good health is one of the most important requisites to the enjoyment of a high quality of life. Fallowfield (1990) grouped the factors that contribute to quality of life in four core or primary domains as follows:

TABLE 1: DOMAINS OF QUALITY OF LIFE (FALLOWFIELD 1990)

Core domains	Typical items
1. Psychological	Depression
	Anxiety
	Adjustment to illness
2. Social	Personal and sexual relationships
	Engagement in social and leisure activities
3. Occupational	Ability and desire to carry out paid employment
	Ability to cope with household duties
4. Physical	Pain
	Mobility
	Sleep
	Appetite and nausea
	Sexual functioning

Environmental quality, including the quality of community life, may be relevant outcomes especially for health promotion interventions. Dupuis (1988) proposes that quality of life is enhanced as the distance between attained and desired goals diminish. This definition is the same as the definition of Calman (1984): Quality of life therefore, measures the difference, at a particular moment in time, between the hopes and expectations of the individual and that individual's present experiences. These definitions are useful because they set operational limits to quality of life and define quality of life as an internally measured parameter, for which no absolute bounds can be set.

Quality of life is frequently not defined in reports of clinical trials that have appeared. In some instances, quality of life is defined as a level on a measure, for example the Karnofsky Performance Status. Each investigation that purports to investigate quality of life actually examines a very narrow and specific set of factors. Quality of life domains suggested as relevant outcomes of health and medical care are listed in Table 2 (Bergner 1989).

TABLE 2: SUGGESTED DOMAINS OF QUALITY OF LIFE (BERGNER 1989)

- Symptoms
- Functional status
    - Self care
    - Mobility
    - Physical activity
- Role activities
    - Work
    - Household management
- Social functioning
    - Personal interactions
    - Intimacy
    - Community interactions
- Emotional status
    - Anxiety
    - Stress
    - Depression
    - Locus of control
    - Spiritual well-being
- Cognition
- Sleep and rest
- Energy and vitality
- Health perceptions
- General life satisfaction

Some researchers consider quality of life as a risk factor or cause of illness as well as an outcome of medical care (Bergner 1989). Thus, someone who leads a stressful life is seen as a high risk for heart disease. The stress is thought of as quality of life.

There also exists considerable debate as to whether a concept such as universal quality of life exists. Are parameters of quality of life constant across cultures or are certain components seen in one culture and not in another? (Schipper 1986).

2.6 REQUIREMENTS OF QUALITY OF LIFE MEASURES FOR CLINICAL PRACTICE (CONSTRUCT)

- Comprehensive, so that all aspects of health status are included.
- A method for answering the questions that does not involve the clinician.
- Reliable.
- Quick to complete.
- Easy to understand.

The following basic requirements of tests and measurements must be met: reliability, validity and standardization (Fallowfield 1990). If data is available, responsiveness to change over time is also important.

2.6.1 RELIABILITY

One of the most important criteria for determining whether a test has been constructed properly is to examine its reliability. The important question is: "Does this test measure accurately and consistently what it is meant to be measuring?" Many kinds of chance factors in a person's life can influence their score on any self-rating questionnaire. The test developer must be able to indicate how inaccurate any score is likely to be as a result of these chance factors. Sensible interpretations of test scores can only be made if something is known about the test's reliability. This is extremely important when health status is changing over the course of treatment or with disease progression. The *reliability coefficient* of a test is needed to ascertain whether an improvement or deterioration in a patient's quality of life score is due to the therapy been given or due to chance factors.

The *reliability coefficient* can be calculated in different ways:

1. Split-test reliability

Two versions of the same test are given to the sample population. The sample population having been matched for age, social characteristics, sex or disease state. If only one form is available, the test is split into two equal parts and both parts are given to the same individuals in the target population. If the two test scores are similar for the group, then it is likely that the test is consistent and reliable. Perfect reliability would produce a correlation coefficient of 1.00, but coefficients of approximately 0.90 are indicative of a good test.

2. Test-retest reliability

The sample population is given the same test on two different occasions and the correlation coefficient between both scores is calculated. The timing between administrations of the test is very important. A too short time difference will enable respondents to recall their previous answers and reliability may be overestimated. If the time interval is too long, changes in the patient (disease progression etc.) could cause a change in the test score, which could lead to an underestimation of the tests' actual reliability.

3. Standard error of measurement

The standard error provides an estimate of the range of variation in a patient's score if he or she was repeatedly to take the same test on an infinite number of occasions. Therefore it is possible to compute the "zonal" range of inaccuracy on either side of an obtained score.

Reliability is less important than validity. If a test is unreliable the validity will also be low. Any valid test is reliable by definition. However, an instrument can be extremely reliable but not valid. There are quality of life measures, which "reliably" measure only a limited aspect of quality of life. Those that deal only with physical functioning might well suggest that quality of life is very good. For example, following surgery for bowel cancer, a man might have a perfectly functioning colostomy and no sign of metastatic spread of the disease. This would result in a high and reliable score on health performance scales such as Karnofsky (1947). That same patient, however, might be deeply anxious about recurrent disease, severely depressed about impotence and loss of attractiveness to his sexual partner; he might also have stopped working due to fears of odour or leakage from the bag and given up a sporting activity such as swimming. It hardly requires a test to show that such a person has suffered a considerable decline in his quality of life, which is not reflected by an indice that only examines physical functioning. Indices that only measure physical functioning are clearly invalid measures of quality of life.

2.6.2 VALIDITY

Validity is the extent to which a test measures what it should measure. Validity is more difficult to assess than reliability and often involves extensive analysis of many different correlations between measures. There are four main types of validity: face, content, criterion and construct.

Face validity

Do the items in the test, on a subjective evaluation, ask questions relevant to the purpose of the test? For example, in a test measuring memory function following brain injury, one might expect to find questions concerning the name of the current Prime Minister or the capital of France, but such questions are totally invalid in a quality of life scale.

Content validity

How comprehensively were the important constructs of interest covered? For example, in a quality of life questionnaire for use in cancer patients receiving chemotherapy, one might expect to find many items dealing with the potential side effects of treatment.

Traditionally, the way to establish which items should be included in an instrument to ensure good content validity, is to interview typical patients and ask them very open-ended questions to determine the important areas of concern. The problems most frequently cited by patients should then be incorporated into the questionnaire.

Criterion validity

Criterion validity must be studied if a test is designed as a predictive measure. Correlating the test item scores with an established measure and establishing a validity coefficient establishes the criterion validity. These coefficients are usually much lower than those demanded for reliability. Validity coefficients as low as 0.30 are often quite acceptable.

One might predict for example, that high anxiety pre-operatively would correlate with excessive demands for analgesics for pain relief post-operatively. Thus, if the object of the study was to use a psychological test to screen patients who might find their anxiety alleviated by good counseling, it would first be necessary to establish the criterion validity of the test – that is, do highly anxious people, according to the new measure, require more pain relief than those who are not anxious?

Construct validity

Construct validation is an analysis of the meaning of test scores in terms of psychological concepts or "constructs" (Cronbach & Meehl 1955). Every test is to some degree impure and very rarely does it measure exactly what its name implies. Yet the test cannot be interpreted until we know what factors determine scores.

The interpretation of a test is built up very gradually and probably is never complete. As knowledge develops, we arrive at a more complete listing of the influences that affect the test score and at some estimate of the strength of each influence. At present the interpretation of even the best–established psychological tests fall short of the ideal – this, because theories of ability and personality are incomplete and hazy (Cronbach 1970).

Whereas predictive validity is examined in a single experiment, construct validity is established through a long-continued interplay between observation, reasoning and imagination (Cronbach 1970).

The user of the test wants to know how the test can be interpreted and how confidently. The manual should indicate what interpretation the author advises and should summarize the available evidence from all types of studies relevant to this interpretation. If the user wishes to make some other interpretation, he must examine all the evidence on the test in the light of his own theory (Cronbach 1970).

There are three parts to construct validation:

- Suggest what constructs might account for test performance. This is an act of imagination based on observation or logical study of the test.
- Derive testable hypotheses from the theory surrounding the construct. This is a purely logical operation.
- Carry out an empirical study to test one hypothesis after another (Cronbach 1970).

Specificity

Specificity is the proportion of true negatives that are correctly identified by the test (Altman 1991).

Sensitivity

The sensitivity score of an instrument tells us about the accuracy of the measure in picking up changes in a patient's quality of life, due to things such as disease progression or remission and psychological status. Sensitivity is the proportion of true positives that are correctly identified by the test (Altman 1991). Sensitivity is calculated as follows:

Number of true cases ÷ number of true cases plus false negative scores

2.6.3 NORMS AND STANDARDIZATION

When evaluating tests and interpreting their scores, we have to consider, in addition to reliability and validity, the way in which the various scores are being expressed. A numerical score tells us very little about a patient's quality of life, unless we have further information about the scores which most people of a similar age, sex, social class, educational background or disease state would have in similar circumstances. In *standardized* tests, scores are derived or transformed in a manner, which permits the individual scores to be compared with group norms.

When dealing with global scores from tests purporting to measure quality of life, it is very important to know more about the mean and standard deviations from it, in order to analyze the data satisfactorily. Transformations of raw scores into standard deviation-units allow psychologists or persons who know anything about normal distribution curves to see immediately how far above or below average an individual lies. This enables comparisons to be made which are not possible with the raw scores alone (Fallowfield 1990).
More detailed information about these issues are to be found in: Cronbach (1970), Anastasi (1976), Nachmias (1981) and Nunnally (1978).

2.7 THINGS TO CONSIDER WHEN CHOOSING A TEST (FALLOWFIELD 1990):

1. Is it valid and reliable?
2. Are norms available?
3. Is it suitable for the target population?
4. Are the questions easy to read and understand?
5. Is scoring complex or easy?
6. Is the layout of the questionnaire clear?
7. What is the format of the questions?
8. Is it comprehensive but as brief as possible?
9. Does it ask socially loaded questions?
10. Who will complete the questions – the doctor or the patient?

Inclusion of a global quality of life measure is highly recommended if resources permit, because it is important that overall patient distress be measured (Troidal 1987).

Specific instruments for measuring quality of life in cancer patients have been developed, but these sometimes fail to focus adequately on the special problems of a particular cancer, or on the consequence of a particular mode of therapy. There are two main types of instruments to choose from:

- Linear Analogue Self-Assessment (LASA) scales.

LASA scales (or VAS/Visual Analogue Scales) use lines usually ten centimeters long. The length of the line represents the continuum of an experience and the patient marks the line at the point, which corresponds to her perception of that experience. The ends of the lines represent the extremes, from best to worst, of the experience under consideration. LASA scales are easy for patients to complete, but difficult to score.

- Categorical Scales.

Categorical Scales are pre-coded and therefore quick and simple to complete and score. Patients are asked to tick a labeled box, or number, corresponding to their perception of the item in question. A Likert Scale results from the addition of the numerical scores from items of subsets within a rating scale to form a single score.

The categorical scale is more feasible than the visual or linear analogue scale (VAS/LASA) for most large-scale clinical trial research. In theory, the VAS/LASA, by providing a greater range of response choices, is more reliable, valid and responsive to change over time than categorical scales, but comparisons of the two types of scales have not shown this to be the case. The VAS/LASA approach is sometimes difficult for patients to understand and processing is more labor intensive (Selby 1987).

2.8 LINEAR ANALOGUE SELF-ASSESSMENT (LASA) SCALES

LASA scales, also known in social sciences as Visual Analogue Scales (VAS) have been used since early in this century (McCormack 1988). These measures have been widely applied in psychosocial medicine, particularly in pain research. At the beginning of quality of life research in oncology, they were introduced as endpoints in cancer clinical trials by Priestman and Baum (1976).

LASA scales can discriminate between endocrine and cytotoxic treatment and between responders and non-responders to treatment of advanced breast cancer (Baum 1980). Coates confirmed the relationship between LASA scales, performance status and treatment side effects for various cancer sites (1983b & 1990). LASA scales have frequently been used in psycho-oncology, although primarily not as clinical trial endpoints, with the exception of trials in patients with metastatic breast cancer (Coates 1987, Tannock 1988, Fraser 1993b).

Further support for the validity of these scales (including physical well-being, mood and appetite scales used in the International Breast Cancer Study Group form (see Addendum 9) was provided by a trial in metastatic breast cancer, where responsiveness to treatment, discrimination between different chemotherapy regimens (Coates 1987) and significant independent prognostic value for survival (Coates 1992b) was demonstrated.

The LASA methodology, which was first applied in metastatic disease where patients are frequently symptomatic and disease control by effective cytotoxic therapy may more likely produce a measurable effect on QOL, has also been shown to be of clinical relevance in the adjuvant setting, where cytotoxic therapy has a measurable but transient effect (Bernhard 1997).

2.8.1 THE FUNCTIONAL LIVING INDEX: CANCER (FLIC)

Schipper and coworkers developed the FLIC in 1984. It is a good example of a graded linear analogue scale. The 22-item self-report scale (see Addendum 3) has been validated on 837 cancer patients in Canada. The scales are numeric Likert scales, with response options ranging from 1 to 7. The FLIC is a global, cancer-specific, multidimensional quality of life instrument. It measures the following domains: physical, emotional, functional and social/family wellbeing. Items on symptoms and confidence in prescribed treatment (relationship with physician) are also included. There are doubts as to whether or not it has sufficient items for each dimension to accurately detect significant changes in quality of life over a period of time. An example of a study using the FLIC is the analysis of EST 4983: Assessment of quality of life for metastatic lung cancer patients (Finkelstein 1987). This was a pioneering study for the Eastern Coast Oncology Group (ECOG) for the use of quality of life parameters in clinical trials.

Each response on the FLIC is scored to the nearest whole integer. Scores on each of the 22 items, ranges from 1 to 7. For some FLIC question scores, higher scores consistently represent a higher quality of life. Analysis is based on the total score, which is the sum of all the items after they have been recorded.

2.8.2 THE LINEAR ANALOGUE SELF-ASSESMENT SCALE OF PRIESTMAN AND BAUM

Priestman and Baum (1976) measured subjective effects of treatment for advanced cancer of the breast by summing single-dimensional scales (see Addendum 8). This is a self-assessment questionnaire and was developed in the visual analogue scale format. Priestman and Baum developed their test to measure the impact of breast cancer and its treatment on quality of life. Table 3 shows examples of the different categories in which patients produce self-ratings for four main areas:

TABLE 3: THE DIFFERENT CATEGORIES OF PRIESTMAN AND BAUM'S LASA

- The symptoms and effects of disease and treatment.
- Psychological problems.
- Physical indices.
- Personal relationships.

The Priestman and Baum test has been use to compare the quality of life of patients receiving either chemotherapy or endocrine therapy for breast cancer and appears to have good sensitivity and reliability. The same criticisms and limitations that apply to all visual analogue scale tests also apply to this one.

2.8.3 SELBY'S LASA

This scale was specifically designed for use in clinical trials for cancer sufferers. Most of the 32 items (see Addendum 10) were derived from the Sickness Impact Profile (see Addendum 14). Good reliability coefficients and satisfactory discrimination between clinically distinct groups of patients have been documented (Selby 1984).

2.8.4 THE GENERAL LIFE QUESTIONNAIRE (GLQ):

Coates (1992) chose a linear analogue self-assessment (LASA) format because of its simplicity, patient acceptance, reliability and established validity. He developed a quality of life measure based on patients' own ranking of side effects and non-physical problems (see table 4).

TABLE 4: GLQ-8 DESIGN: ITEM TITLES AND CORRELATED SYMPTOMS

Feeling anxious or depressed. Feeling low and miserable; affects family; feeling of having to have unwanted treatment; cannot concentrate; affects work/home duties; feeling anxious or tense.

Feeling sick (nausea or vomiting). Nausea; vomiting.

Numbness or pins and needles. Pins and needles in fingers or toes; numbness in fingers or toes; hot flashes.

Loss of hair. Constipation; diarrhea; hair loss; length of time treatment takes; trouble finding a parking spot.

Tiredness. Constantly tired; giddiness on standing up; sore throat; shortness of breath; difficulty sleeping; general aches and pains.

Appetite or sense of taste. Taste change; weight loss; weight gain; appetite loss; easy bruising; increased thirst; increased appetite.

Sexual interest or ability. Loss of sexual feeling; loss of sexual ability.

Thought of actually having treatment. Dry skin; thought of coming for treatment; having to have a needle.

2.8.5 THE QUALITY OF LIFE CORE QUESTIONNAIRE:

The International Breast Cancer Study Group (IBCSG) developed and tested the Quality of Life Core Questionnaire (see Addendum 9). It takes the form of a Linear Analogue Self-assessment or LASA scale. It differs from other breast cancer and cancer specific questionnaires in respect to conceptual, methodological and practical issues. The restriction to a few key indicators is in contrast to other study settings where quality of life must be assessed more comprehensively, as, for example, in health surveys. This form is therefore neither a generic substitute for other QOL instruments, nor a "definitive" measure of QOL, but a tool designed for a specific purpose (Bernhard 1997).

The IBCSG questionnaire uses global measures based on single-item-direct patient estimation instead of numerical summation of various specific items. In contrast to the classical psychometric approach a global single-item measure is expected to be less valid because different individuals may to a certain extent interpret it in different ways. However, given that global health measures reflect the disease and treatment-related issues that are salient for each individual patient, they are an appropriate endpoint, especially for treatment comparisons in repeated measurement designs where each patient is compared with herself. Indicators of specific symptoms or side effects, such as hot flashes, have more obvious face validity (Bernhard 1997).

2.9 CATEGORICAL SCALES

2.9.1 MEASURES BASED ON PHYSICAL ASPECTS

When people become ill, one of the very first aspects to be influenced is their physical functioning. Clinical researchers have used systematic measures of functional status for more that 50 years (Bergner 1989). The first measures were developed to assess the baseline performance status of a patient. Functional status assessments are routinely used to determine patient eligibility for clinical trials and to aid treatment decisions. WHO or Karnofsky performance status indices are routinely used in the cancer clinic to decide whether or not to administer chemotherapy.

The distinguishing characteristics of the WHO and Karnofsky Performance Status measures are:

- They are brief.
- A physician completes them on the basis of observation and history of a patient.

The ECOG and Karnofsky performance status measures were developed by physicians to systematize the collection and recording of information that was thought to be relevant for the diagnosis and treatment of patients. Rigorous development and testing was not done and the reliability is poor (Hutchinson 1979, Mor 1984). This severely limits the use of these measures for monitoring patient progress and assessing outcome.

TABLE 5: THE WHO PERFORMANCE STATUS SCALE

GRADE	DESCRIPTION	KARNOVSKY
0	Fully active, able to carry on all pre-disease performance without restriction.	90 – 100
1	Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature.	70 – 80
2	Ambulatory and capable of all self care, but unable to carry out any work activities. Up and about more than 50% of waking hours.	50 – 60
3	Capable of only limited self care, confined to bed or chair more than 50 % of waking hours.	30 – 40
4	Completely disabled. Can not carry on any self-care. Totally confined to bed or chair.	10 – 20

The Karnofsky Performance Status (KPS):

This index was already published in 1948 for use in cancer research and is based on an interpretation of quality of life in terms of physical ability (Karnofsky 1948). It is one of the most frequently cited "quality of life" measures found in the medical literature. Frequency of usage is, however, no indication of appropriateness. Karnofsky and

Burchenal actually developed the performance scale as a means of determining nursing requirements in a ward. The Karnofsky performance status is a useful method to determine physical functioning and has been shown to correlate well with survival, but it is a very crude method for assessing quality of life. The most important difficulty is that the physician fills it in and that it makes no assessment of a patient's psychosocial status.

Clark and Fallowfield (1986) point out some absurdities of the scale, in particular the assumption that a patient with a low score due to immobility is considered to have a poor quality of life and that a patient with a higher score necessarily has a better quality of life. Additionally, all observation scales have the problem that they involve an entirely subjective evaluation made by a clinician. Bias inevitably arises and there are studies to show unacceptable variability between raters. The strength of both the Karnofsky and WHO performance status scales is their simplicity and the fact that a useful assessment of physical function can be made without complicated and time-consuming tests. The fact that clinical decisions about the treatment of cancer patients are made on a daily basis as a result of these two indices, show their usefulness in the oncology field.

TABLE 6: THE KARNOFSKY INDEX

100	Normal, no complaints, no evidence of disease.
90	Able to carry on normal activity, minor signs or symptoms of disease.
80	Normal activity with effort, some signs or symptoms of disease.
70	Cares for self, but unable to carry on normal activity or do work.
60	Requires occasional assistance but is able to care for most of personal needs.
50	Requires considerable assistance and frequent medical care.
40	Disabled; requires special care and assistance.
30	Severely disabled; hospitalization is indicated although death is not imminent.
20	Very ill, hospitalization and active supportive care necessary.
10	Moribund.
0	Dead.

Other functional status measures are the Index of Activities of Daily Living (ADL; Katz 1976), the Sickness Impact Profile (SIPS; Bergner 1981), the Cancer Inventory of Problem

Situations (CIPS; Schag 1983) and the Barthel Index (Mahoney 1965), which assess performance of activities of daily living. These measures assess activities such as walking, eating and dressing. They are not meant to be used for designated conditions and have been developed with some attention to reliability of measurement, validity and scoring. The patient or someone completes these measures, without the doctor's involvement.

Patrick (1973) measured the perceived social values of defined functional levels of health. Hochberg (1979) determined the physical function of glioblastoma patients. Grogono and Woodgate (1971) developed a 10-item scale focussing mainly on physical function. Kaplan (1979) created a health index with two components: level of well being and prognosis, the latter being the probability of attaining a level of well being by a certain time.

The problem with unifunctional measures of quality of life is that they may provide a very distorted outcome evaluation (Schipper 1986). Functional status measures miss much that is important in quality of life, because less that one third of patients who have a serious chronic illness have measurable limitations in personal or role functioning. Moreover, functional status measures do not adequately assess mental health (Ware 1984).

The Katz Index: Activities of Daily Living (1963):

Its primary use was in the assessment of functional status of elderly patients in long-term care settings. The Katz index measures basic socio-biological functions (see Addendum 4). Nurses or doctors rate patients on six items: bathing, dressing, toileting, mobility, continence and feeding. It is a good example of a scale created for a variety of diagnoses, but is not very valid as a quality of life measure.

Patients are rated as either dependent or independent for each item and then graded from A to G on the basis of these judgements. As with the Karnofsky performance status, high grades on the Activities of Daily Living do correlate well with survival (Katz 1970). The Katz index has been shown to be of prognostic value in determining the long-term course of adaptation in stroke victims or patients with hip fractures. A major problem limiting the scale's usefulness is its inability to discriminate well between differences in functioning at the upper end of the scale, as about 80% of the elderly do not experience functional limitations.

This scale has good validity and reliability and is helpful in measuring the functional status of elderly, institutionalized patients, but the application of the scale in general population studies of quality of life is not appropriate.

2.9.2 MEASURES BASED ON PSYCHOLOGICAL/EMOTIONAL FACTORS

An apparently mobile, well-functioning and physically fit person may be experiencing debilitating emotions and consequently an extremely poor quality of life. It is therefore of paramount importance to include a thorough evaluation of the patient's mood in any good quality of life instrument. A selection of measures measuring the emotional wellbeing of people will be discussed.

Post mastectomy depression and loss of self-esteem was assessed by Worden and Weisman (1977) using several instruments restricted to emotional factors.

The befindlichkeitsskala von Zerssen (Bf-S):

The Bf-S is a specific and precise standard scale. This 28-item, one-dimensional adjective checklist is very sensitive to anxiety and especially depression. It was initially developed by von Zersssen for serial assessments of mood in longitudinal psychopharmacological studies and has become a standard measure for mood alterations in different clinical settings. It has been validated in German and French-speaking populations and used in cancer patients (Hürney 1992).

The profile of mood states (POMS) of Pollock (1979) and McNair (1981):

Asking them to rate how applicable 65 different mood descriptions are to them assesses individuals' current emotional state. Patients may choose responses ranging from "not at all" to "extremely". Good specificity has been shown for the POMS. The Profile of Mood States contains six different subscales (see Addendum 15):

Tension	
Anger	
Depression	:SUBSCALES OF POMS
Vigor	
Fatigue	
Confusion	

The hospital anxiety and depression scale (HAD):

Developed by Zigmond and Snaith (1983) specifically for use with physically ill populations. There are two subscales namely, anxiety and depression, but items of a somatic nature, for example fatigue, which could also be attributed to physical disease as much as mood disturbance, are not included (see Addendum 16).

There are fourteen items, half for each of the two subscales, and the items are rated on a four-point scale. The Hospital Anxiety and Depression Scale has the advantage that it is very easy and quick to administer, complete and score. It takes about two minutes to complete and two minutes to score. It has been shown to be sensitive and specific and has been translated into many languages. Its validity has been confirmed in many studies. A score of 7 or less implies normality, 8 to 10 is borderline and 11 or more suggests significant anxiety or depression.

The perceived adjustment to chronic illness scale (PACIS):

The Perceived Adjustment to Chronic Illness Scale (PACIS) is a global indicator designed to capture the patient's view of her effort to cope with illness. In a study by Hürney (1993) a large proportion of PACIS variance was explained by disease and treatment burden suggesting that this indicator does reflect psychological adjustment.

The Rand Mental Health Inventory (MHI):

The Mental Health Inventory is a validated, 38-item instrument designed to assess psychological state.

2.9.3 MEASURES BASED ON SOCIAL FUNCTION

There is increasing evidence that social support may predict survival in breast cancer patients (Maunsell 1995, Hürney 1993). Social relationships influence subjective evaluation of quality of life. Social functioning and social support however, have been reported to be the most problematic areas for investigators to measure. Investigators must be aware that the construct for social functioning is a powerful one with respect to explaining variance in the measurement of quality of life (McMillen 1989).

The social support questionnaire (SSQ6):

A promising brief instrument for measurement of social functioning is the six-item Social Support Questionnaire (SSQ6). Validation however, was carried out with college students instead of patients and there was a ceiling effect regarding social support (McMillen 1989).

2.9.4 MEASURES BASED ON SYMPTOMS

Westaby (1979) focussed on symptoms, drug use and work capability in patients who have had surgery for coronary artery disease.

The Brief Fatigue Inventory (BFI) Mendoza 1999

Several scales have been created to measure fatigue, but many are too long and difficult for very ill patients to complete. The Brief Fatigue Inventory was developed for the rapid assessment of fatigue severity. The BFI was shown to be an internally stable (reliable) measure that tapped a single dimension, best interpreted as severity of fatigue. It has been correlated highly with similar measures.

The McGill/Melzack Pain Questionnaire (MPQ)

Chronic, unremitting pain imposes a severe deleterious effect on quality of life. Consequently, a satisfactory pain inventory, despite its apparent specificity, does constitute an important element of quality of life assessment. The McGill Pain Questionnaire (MPQ), a systematic and objective measure of pain, was developed in 1971 (Melzack). It was the most widely used pain inventory in clinical practice and research. It was however, possibly, superseded by the Brief Pain Inventory in the late 1990's. The MPQ comprises groups of adjectives, some of which are shown in Addendum 5, and these rank values are scored to provide a pain rating index. Melzack (1975) has shown the MPQ to be highly reliable and valid, even with patients as young as 12 years old. Many questionnaires using Visual Analogue Scales have been developed using items adapted from the MPQ to assess pain.

The Memorial Pain Assessment Card (MPAC):

The MPAC is a validated instrument designed to assess pain intensity and pain relief. It includes three 100 mm visual analog scales (VAS) for pain intensity, pain relief and mood and an eight-item categorical verbal rating scale (VRS).

The Memorial Symptom Assessment Scale (MSAS) and Global Distress Index (GDI):

The Memorial Symptom Assessment Scale is a 32-item, patient-rated instrument that was developed at the Memorial Sloan-Kettering Cancer Center. It assesses 26 symptoms in terms of three dimensions – frequency, intensity and distress – and six symptoms in terms of two dimensions – intensity and distress. Each symptom characteristic is scored reflecting frequency, intensity and distress.

TABLE 7: SCORING FOR THE MEMORIAL SYMPTOM ASSESSMENT SCALE

Frequency	1= rarely	2= occasionally	3= frequently	4= almost constantly
Intensity	1= slight	2= moderate	3= severe	4= very severe
Distress	0= not at all			
	1= a little bit	2= somewhat	3= quite a bit	4= very much

Its validity and reliability have been confirmed in patients with solid tumors, including advanced breast, colon, prostate and ovarian carcinomas. The Memorial Symptom Assessment Scale- Global Distress Index (MSAS-GDI) is a ten-item subscale that reflects global symptom distress (Seidmann 1995).

The FACT fatigue and anemia scales (Yellen 1997)

Using the 28-item Functional Assessment of Cancer Therapy-General (FACT-G) questionnaire as a base, 20 additional questions related to the symptoms and concerns of patients with anemia were developed. Thirteen of these 20 questions dealt with fatigue, while the remaining 7 covered other concerns related to anemia. Using semi-structured interviews with 14 anemic oncology patients and 5 oncology experts, two instruments were produced: The FACT-Fatigue (FACT-F), consisting of the FACT-G plus 13 fatigue items, and the FACT-Anemia (FACT-An), consisting of the FACT-F plus 7 nonfatigue items.

The 41-item FACT-F and the 48-item FACT-An scores showed good stability and the fatigue subscales showed strong internal consistency. Convergent and discriminant validity testing revealed a significant positive relationship with other known measures of fatigue, a significant negative relationship with vigor, and a predicted lack of relationship with social desirability. The total scores of both scales differentiated patients by hemoglobin level and patient-rated performance status.

The FACT-F and the FACT-An are useful measures of quality of life in cancer treatment, adding more focus to the problems of fatigue and anemia. The Fatigue Subscale may also stand alone as a very brief, but reliable valid measure of fatigue.

2.9.5 MEASURES BASED ON SUBJECTIVE EFFECTS

Clinical observation, systematic research and popular anecdote indicate that, when confronted by death, people change the criteria by which they evaluate their lives. Questionnaires used routinely to assess quality of life in people with poor-prognosis cancer tend to be symptom-based and do not assess factors, which become important to patients when confronted by fatal illness, such as the meaning of life and the degree to which life has been enriched by the illness. Principal component analysis identified five dimensions:

- Clearer perception of the meaning of life.
- Freedom versus restriction of life.
- Resentment of the illness.
- Contentment with past and present life.
- Past and present social integration.

The life evaluation questionnaire (LEQ) of Salmon (1996):

Only the most symptom-oriented scales (freedom, resentment) correlated with the Rotterdam Symptom Checklist. Scale scores showed that younger patients were more resentful of their illness, but also gained a clearer perception of the meaning of life. The Life Evaluation Questionnaire (LEQ) developed by Salmon and coworkers (1996) can evaluate psychological needs of people with incurable cancer, which are neglected by existing instruments.

The Life Evaluation Questionnaire does not provide a complete assessment of a patient's psychological reaction to illness. References to illness-specific symptoms were excluded at the outset and anxiety and depression items were excluded on the basis of the analysis. The questionnaire focuses on patients' evaluation of the effect of their symptoms on their lives. More conventional scales, based on physical and emotional symptoms, should also be included if a complete assessment of quality of life is sought. The reliability values are high and indicate that the aspects of life evaluation that the Life Evaluation Questionnaire does measure are measured accurately.

The Life Evaluation Questionnaire should be useful to assess treatments targeted to adaptation to, and the meaning of, illness such as counseling and psychotherapy. The scale could also be used to identify areas of concern on which psychological treatments could focus. The questionnaire was also beneficial to many patients, who welcomed the opportunity to voice concerns, which they had not previously expressed.

2.9.6 MULTIDIMENSIONAL GENERIC MEASURES

Much of the early research relied on more generalized, health related, quality of life instruments that were developed for use within the general population. The benefits of using generalized instruments for a disease population are that the scores may be compared with the standardized norms of the general population. In this manner, differences between healthy and ill populations may be identified, clarifying domains that are affected by disease (Parsons 1989). However Najan and Levine (1981) have suggested that quality of life measures that are focused on disease or treatment can miss critical aspects of quality of life for a particular patient.

There is a strong interaction between physical condition and the psychological sphere of the patients: functional status is closely related to all social and psychological dimensions of life. Therefore, the questionnaire, though divided in sections, must regard the patient in his of her entirety (Ballatori 1993). The successful studies in the field view quality of life in functional terms and as a construct consisting of: vocational, physical, psychological and social function (Schipper 1986).

The Alameda County Human Population Laboratory:

The Alameda County Human Population Laboratory (Hochstim 1970, Breslow 1972) yields three separate scores for physical, mental and social health. It is comprehensive but lengthy.

The Cancer Rehabilitation Evaluation System-Short Form (CARES-SF):

The Cancer Rehabilitation Evaluation System was developed specifically to address illness-related dysfunction. For use in clinical trials, rather than for use in needs assessment, a shorter 59-item version, the CARES-SF was extracted from the 139-items CARES (see Addendum 2). The CARES-SF was tested for reliability and validity by te Velde and co-workers (1996). In general, the CARES-SF was found to be feasible. It required 11 minutes to complete (on average) and mostly could be filled out by the patients themselves without assistance. Problems were found from items related to sexuality or intimate relationships, which were sometimes considered to be too intrusive.

The General Health Questionnaire (GHQ):

Goldberg developed his questionnaire as a technique for the identification and assessment of non-psychotic psychiatric illness. The questionnaire is useful for identifying patients with affective neuroses, i.e. minor depressions, anxiety states and what was previously called "neurasthenics". Golberg's General Health Questionnaire comes in three different versions, containing 28, 30 or 60 items (Goldberg 1972). The 28-item test is most generally used and will be discussed. It has four sub-scales assessing depression, anxiety, social functioning and physical symptoms. Patients underline the response that is the closest to how they have been feeling about each of the 28 statements (see Addendum 11). Scoring is quick and simple and can be done either by using a Likert-type score of zero to three, or a bimodal response scale with "less" or "no more" than usual scoring zero and "rather" or "much more than usual" scoring one. This is a way of avoiding "end-users" or "middle users", that is the patients who always respond at the extremes of scales or always use the middle options.

The General Health Questionnaire has good reliability and has been validated against the Clinical Interview Schedule. Its also performs well against other psychiatric screening tests. Because it has been used in many different clinical settings and in community studies with large numbers of people, it is a useful instrument for quality of life assessment. Unfortunately it only assesses physical functioning and psychological status, so the whole spectrum of quality of life is not investigated.

The Integrative Quality of Life Theory (Ventegod 1998):

According to Ventegod there are seven criteria that a quality of life instrument must meet in order to become a scientifically sound construct:

1. A definition of quality of life.
2. An embedding philosophy of human life.
3. A theory that operationalizes this philosophy by deriving questions that are unambiguous, non-overlapping and jointly exhaustive and assigning relative weights to these questions.
4. Quantifiable response alternatives.
5. Technical checks (reproducibility, sensitivity, well- scaledness, etc.)
6. Validation through meaningfulness to investigators, respondents and users.
7. Aesthetic appeal of the questionnaire.

The integrative quality of life theory is a meta-theory that integrates six actual quality of life theories by organizing them from a subjective to an objective spectrum. The subjective quality of life items are quality of life as immediate, self-experienced well being; as satisfaction in life and as happiness ad modum Aristotle. According to Aristotle human happiness consists of living in conformity with nature. Objective quality of life concerns items such as: Does the respondent have a partner, children, a job, and hobbies?

The two remaining theories are about human nature: Maslow's theory about human needs and expanded by Aggems and a theory of human beings seen as striving to express life' potentials. Two additional theories blend the subjective and the objective ends of the spectrum: The temporal organization of life refers to the way in which life is divided between work, family and leisure. And spatial organization refers to the socio-spatial domains:

Subjective

1. Immediate self-experienced well being
2. Satisfaction
3. Happiness
4. Fulfillment of needs
5. Experience of objective temporal domains
6. Experience of objective spatial domains
7. Expression of life's potential
8. Objective factors

Objective

These theories are global: covering all aspects of an individual's life and not just one aspect thereof, and generic: applicable to all persons, not just those with a certain type of disease.

The McMasters Health Index (MHIQ):

The Health index from McMaster University (1977) measures the social, emotional and physical function of persons with a wide range of health problems. This instrument has been found to be reliable in a variety of clinical settings. The McMasters Health Index Questionnaire consists of 59 questions. The scores derived from the answers to these questions are added to give the three above mentioned indices as well as a global index of perceived quality of life.

The MOS Short-Form General Health Survey:

Ware suggested the measurement of physical and mental health, social and role functioning and general health perceptions. He and his coworkers developed the MOS Short-form General Health Survey to measure these five constructs plus pain (Stewart 1988).

The Nottingham Health Profile (NHP):

This health profile was developed in 1980 by Hunt and McEwen as a survey tool, but has been used increasingly in the United Kingdom to evaluate the outcome of medical interventions (Hunt 1985). Evidence for reliability and validity has been provided by an enormous amount of research.

In part one of the NHP (Addendum 6) the following problem areas are investigated: energy, pain, emotional reactions, sleep, social isolation and physical mobility. In part two (Addendum 7) seven statements are covered, concerning the areas of daily life that are often affected by ill-health: paid employment, jobs around the house, social life, personal relationships, sex life, hobbies and interests and holidays. Respondents must answer "yes" or "no" to statements such as "things are getting me down". The statements are weighted in order to reflect the relative importance or severity of each item. A high score is indicative of severe problems and the maximum score is 100 for part one and part two of the test respectively.

The Nottingham Health Profile discriminates well between healthy and physically ill people. Unfortunately it only focuses on negative aspects of health, so that patients cannot indicate well being accurately. Zero scores don't necessarily reflect the absence of problems and the test is insensitive to small but significant areas of distress. It is however, well-researched, acceptable, cheap and easy to score.

Psychosocial Adjustment to Illness Scale (PAIS) of Morrow (1978):

Morrow (1978) developed this impressive test which can be used to evaluate quality of life in a variety of patient populations (see Addendum 13). The Psychosocial Adjustment to Illness Scale was specifically developed to address illness-related dysfunction. The experience of the authors gained from studying the psychosocial impact of illness has resulted in an extremely comprehensive instrument. It was originally a semi-structured interview, administered by trained doctors, nurses, psychologists or social workers, but became available later as a self-report questionnaire. The test has 45 questions looking at a patient's global adjustment to illness in seven important areas affecting quality of life:

1. Health care orientation – their attitudes towards and expectations concerning physicians and treatments.
2. Vocational environment – satisfaction with job performance and adjustment to work.
3. Domestic environment – the impact of illness on family finances and communication.
4. Sexual relationships – effect illness has had on frequency, satisfaction and pleasure from sexual activity.
5. Extended family relationships – problems with extended family members since illness.
6. Social environment – the maintenance of interest in social activities.
7. Psychological distress – anxiety, depression and other sequelae.

The core domains according to Fallowfield (1990) that should be included in any adequate quality of life instrument are all found covered very well in the Psychosocial Adjustment to Illness Scale. It is unfortunately very long, taking patients about 30 minutes to complete and it is also difficult to score. Ratings for each question are made on a four-point scale. Scores are converted to standardized T-scores found in tables in the handbook, providing a PAIS total score, which can be compared to published norms. Unlike many other measures, norms are available for different patient populations, also for cancer patients. The test has good reliability coefficients and correlates well with other tests measuring psychological dimensions (has good criterion validity). This test measures the adjustment to the fact, that illness and its treatment, exerts an important influence on quality of life, especially in chronic diseases, extremely well.

The Sickness Impact Profile (SIP):

The Sickness Impact Profile (SIP), based on the concept of health-related dysfunction, is an outcome measure derived from quantitative estimates of changes in the behavior of respondents (see Addendum 14). It has 312 items in 14 categories and is therefore comprehensive but time-consuming (Bergner 1981). This is a widely used and well-known quality of life questionnaire.

The selected statements can be divided into independent categories: physical function and psychosocial function. The questions are answered with a "yes" or "no". All statements answered in the affirmative have their scale values added up to yield a percentage overall score. An overall score or scores for the two main dimensions can be computed. Validity and reliability have been proven and the questionnaire has been updated to improve it. Few quality of life instruments have undergone such extensive work on validation and reliability and it has therefore often been used to evaluate treatments. It is however, cumbersome and time-consuming both for extremely ill patients and for busy clinicians. These limitations make it unacceptable for routine use but it is an important instrument to consider for use in clinical trials.

The WHOQOL-100

The WHOQOL-100 (World Health Organization's Quality of Life questionnaire) was used in a two-part study by Tazaki (1998). The purpose of the study was to evaluate quality of life among cancer patients to see if any significant differences were seen in cancer stages, treatment status and prognosis. For the qualitative study, two focus groups were conducted by medical professionals to establish the applicability of the WHOQOL instrument in evaluating the quality of life of cancer patients, but most participants were negative about using a generic instrument such as WHOQOL. For the quantitative study, 197 cancer patients were analyzed, using the WHOQOL. There was high reliability and a high correlation between the psychological and environmental domains, the physical domain and the level of independence and social relations and the environment and between health conditions perceived by patients and quality of life scores. Differences by gender, treatments and cancer sites were also found to be significantly different at the 5% significance level. The results indicated that the WHOQOL core instrument was sensitive enough to evaluate the quality of life of cancer patients. It is however, very lengthy and time-consuming and a shorter version the WHOQOL-Bref. Consisting of 26 questions, is currently being developed.

2.9.7 MULTIDIMENSIONAL DISEASE-SPECIFIC MEASURES

Generalized tools are useful for the comparison of individuals to the general population. It may be inappropriate however, to assume that cancer patients exist within the same context as the general population. Cancer patients' lives are very different from those of normal individuals due to the enormous physical and emotional burdens that cancer survivors must endure. Thus, the significance and value of experiences/healthstates/compromise in functioning for the cancer patient may be markedly different from generalized population norms. The information gathered must be sensitive to differences within the disease population (Parsons 1998).

Several multi-dimensional, disease-specific questionnaires have been developed and validated specifically for use within the adult cancer population:

The Ability Index:

The Ability Index of Izsak and Medalie (1971): This index integrates 21 items covering physical, emotional, social and economic factors into a single score. It is modified for each type of cancer.

The Breast Cancer Chemotherapy Questionnaire (BCQ) of Levine 1988:

This questionnaire was developed for use as an outcome measure in clinical trials of adjuvant chemotherapy in women with stage II breast cancer. The BCQ consists of 30 questions that focus on loss of attractiveness, fatigue, physical symptoms, inconvenience, emotional distress and feelings of hope and support from others. The BCQ was validated by its correlation with other questionnaires. The BCQ correlated more strongly with global ratings of both physical and emotional function by the patients and their physicians than the other instruments (Spitzer, Karnofsky and Rand Physical & Emotional Health Status).

A comparison between the quality of life outcomes of patients in the two treatment groups in the period when one group had completed treatment and the other had not, showed that the BCQ and Karnofsky scale, were the only instruments able to demonstrate differences between the groups.

The BCQ was administered to the patient by a trained nurse-interviewer. The use of questionnaires administered by personal interview, as compared with those that are self-administered is controversial. Interviewer-administered questionnaires are more expensive to use and with such questionnaires it has been suggested that a patient may respond more favorably than truth in order to please the interviewer. On the other hand, the nurse in the study of Levine (1988) was occasionally able to identify particular treatment-related problems amenable to intervention, because of the personal interview.

The EORTC QLQ-C30:

The EORTC QLQ-C30 questionnaire is a multidimensional QOL scale for use with breast cancer patients (see Addendum 17). In 1986, the European Organization for Research and Treatment of Cancer (EORTC) initiated a research program to develop an integrated, modular approach for evaluating the quality of life of patients participating in international clinical trials.

The QLQ-C30 incorporates nine multi-item scales:

- Five functional scales: physical, role, cognitive, emotional and social.
- Three symptom scales: fatigue, pain and nausea & vomiting.
- A global health and quality of life scale.
- Several single-item symptom measures are also included.

During development and validation studies it was found that the average time required to complete the questionnaire was approximately 11 minutes. Most patients could complete the questionnaire on their own. The reliability and validity of the questionnaire were highly consistent across the three language-cultural groups studied. The results (Aaronsen 1993b) support the EORTC QLQ-C30 as a reliable and valid measure of the quality of life of cancer patients in multicultural clinical research settings.

Sprangers et al. (1996) constructed a breast cancer- specific quality of life questionnaire module to be used in conjunction with the EORTC QLQ-C30. The module, the QLQ-BR23, consists of 23 items covering symptoms and side effects related to different treatment modalities, body image, sexuality and future perspective. This module was tested in 170 Dutch, 168 Spanish and 158 American cancer patients at two points in time. Multitrait analysis confirmed the hypothesized structure of four of the five scales. Cronbach's alpha coefficients were, in general, lowest in Spain (range 0.46 to 0.94) and highest in the United States (range 0.70 to 0.91). On the basis of known-groups comparisons, selective scales distinguished clearly between patients differing in disease stage, previous surgery, performance status and treatment modality, according to expectation. Additionally, selective scales detected change over time as a function of changes in performance status and treatment-induced change.

The results supported the clinical and cross-cultural validity of the QLQ-BR23 as a supplementary questionnaire for assessing specific quality of life issues relevant to patients with breast cancer (Sprangers 1996).

The Functional Assessment of Cancer Scales (FACT):

The Functional Assessment of Cancer Therapy Scales is a modular approach to quality of life assessment. It includes a core instrument, the FACT-G (general), which can be used, for any type of cancer. Subscales or modules for specific subgroups of patients supplement the core instrument. FACT-B is the instrument for use with breast cancer patients. (Cella 1993).

The FACT-G is constructed out of the following domains: physical well being, family/social well being, relationship with doctor, emotional well being and functional well being. The FACT scale is reliable and has been validated. For a more detailed description of the FACT scale see Chapter 4. Updates of the FACT are available, but the questionnaire available at the time that the research was initiated, was used and a discussion is provided in chapter 4.

The Rotterdam Symptom Checklist (RSCL):

This instrument was developed by De Haes (1983) to measure the toxicity and impact of treatment for cancer on psychosocial functioning (see Addendum 12). Respondents rate different items on a four-point scale by ticking a box opposite the reply which comes closest to how they have been feeling over the previous three days. The two primary subscales measure physical and psychosocial dimensions by means of thirty questions.

Additional items for assessment of treatment or illness-related variables are often included for use with patients who have breast cancer.

Good sensitivity, validity and specificity for psychosocial items on the scale have been established. The test is very easy to understand, is well accepted by patients, simple to administer and quick to complete (five to ten minutes). Additionally, scoring is straightforward and easy to compute. It has been suggested that this scale does not adequately cover sexual or social dimensions of quality of life and additional physical items have been proposed for use with specific groups of cancer patients.

The Spitzer Scale or Quality of Life Index (QLI):

Spitzer and co-workers developed this scale in 1981 for use with cancer patients (see Addendum 18). It is a physician-scored scale but can also be scored by patients themselves. The test had to be quick to complete, simple to administer and more comprehensive than only testing for simple physical functioning. The five key areas that Spitzer identified were activity, daily living, perception of health, social support and outlook on life. These domains are rated on a three-point scale from naught to two, resulting in a maximum score of ten.

Good inter-rater reliability between physicians and good correlations between patients' self-ratings and those of their clinicians has been established. It had been validated on patient populations in Australia and Canada and discriminates well between patients with different illnesses and at different stages of disease. A limitation is the fact that the scale gives equal weighting to all items, which could be unrealistic. Specificity of problems is also not addressed adequately, because there are not enough items in each key area. The primary strength of this scale is its simplicity and speed.

This scale can be more accurately termed a quality of life measure than the Karnofsky of WHO performance status measures, because it assesses more than physical functioning, although the total score correlates more substantially with measures of physical functioning as opposed to psychosocial functioning (Spitzer 1981).

2.10 THE QUALITY OF TIME GAINED

Curing a cancer may be achieved with or without the loss of normal functions. The direct dimensions that can be measured according to these definitions are the years of life gained and the quality of the gained life years. These two dimensions, length and quality of life, can be expressed as quality adjusted life years (QALYs) or quality adjusted time without symptoms of disease and toxicity of treatment (Porzsolt 1993). In order to express benefits of adjuvant therapies for breast cancer that incorporate aspects of quality of life for treatment decision-making, Gelber (1993) has developed a quality-adjusted survival analysis, called Q-TWiST. This method involves determining the time without symptoms of the disease and toxicity of treatment (TWiST).

Porzsolt (1993) also advocates the use of QALYs (quality adjusted life years) and Q- TWiST (quality adjusted time without symptoms of disease and toxicity of treatment). For the palliative treatment of patients with incurable disease he finds the aforementioned two parameters to be more realistic goals to strive for than remission.

2.10.1 TwiST: TIME WITHOUT SYMPTOMS OR TOXICITY

A very important concept in the adjuvant setting is a global indicator of subjective health estimation, namely time without symptoms or toxicity (TwiST). A key goal in the International Breast Cancer Study Group (IBCSG) treatment evaluation is to link patient-rated quality of life and physician-rated toxicity to derive values to be used as weights in the Q-TwiST model. It partitions time from treatment to death into three periods: the toxicity of initial treatment (TOX), time without symptoms or toxicity (TwiST) and a post-recurrence period with disease symptoms (REL). Treatments are then compared by overall survival duration, subtracting some of the time spent in TOX and REL according to measures of utility (Bernhard 1997).

TwiST is however, largely a symptom measure. It does not fully evaluate the psychosocial dimensions typically included in quality of life evaluation (Schipper 1985).

A quality-adjusted survival (Q-TwiST) analysis of EORTC Trial 30853, comparing goserelin acetate and flutamide with bilateral orchiectomy in patients with metastatic prostate cancer, was performed by Rosendahl and coworkers (1999). Although orchiectomy had a survival benefit when quality-adjusted survival is not taken into account, orchiectomy translated into a disadvantaged quality of life in real terms. The Q-TwiST analysis resulted in a 5.2-month difference in favour of goserelin and flutamide. The Q-TwiST analysis showed that a subjective definition of health states reflects the differences in quality of life better than so called "hard" measures such as ordinary survival benefit.

One can plot the amount of quality-adjusted survival time associated with more and less intensively treated groups over time. This Q-TwiST gain function elegantly displays the future gains to be expected on average from an initial investment in toxic therapy (Coates 1993).

2.10.2 QUALITY ADJUSTED LIFE YEARS (QALYs)

Quality Adjusted Life Years (QALYs) is based on the principle that benefits of treatment are measured not only in years of survival gained, but also in their quality. Discussions about the economic impact of cancer clinical trials must therefore be based on three outcomes: survival, morbidity and the quality of life. If healthcare policy could potentially rely on quality of life research for decision making regarding resource allocation, that research had better be methodically sound. Quality of life is multidimensional in nature and includes at minimum, physical, social and emotional concepts. A scientifically tested quality of life instrument must be used in the way in which it was intended to be used. Quality of life research often provides a continuum of response relating a symptom, behavior or emotion to its impact on daily living. Adequate statistical analysis is therefore called for. Quality of life analysis is more frequently concerned with correlations, analysis of variance and more complex analysis that provide data on Quality Adjusted Life Years (QALYs) and Time Without Symptoms and Toxicity (TWIST) (Watkins Bruner 1995).

2.11 THE QUALITY OF QUALITY OF LIFE DATA

Cancer clinical trials are primarily designed to assess the effect of treatment on response and survival. There is, however, increasing recognition among investigators that a comprehensive understanding of the effect of cancer therapies requires consideration of patient quality of life (Klar 1998). Goodyear and Fraumeni (1996) reported that the number of publications concerned with patient quality of life doubles every three years.

A continuing challenge in all trials measuring quality of life is the timely completion of scheduled assessments. Low rates of compliance can compromise the interpretation of results particularly if compliance depends on patient characteristics (e.g. patient health). The baseline assessment is included to provide a benchmark against which later assessments can be compared. There are many possible explanations for low rates of compliance (e.g. patient was too ill, staff oversight).

During the assessment of quality of life of metastatic lung cancer patients it was found that the dropout rate was considerable (Finkelstein 1987).

2.12 METHODOLOGICAL CONSIDERATIONS

2.12.1 FACTORS ASSOCIATED WITH MISSING DATA

In a number of trials for the International Breast Cancer Study Group, Bernhard and coworkers (1997) found that the factors most highly associated with missing quality of life forms were institution and chemotherapy compliance. Patients who did not receive the full course of assigned chemotherapy had lower submission rates than those who did: the major reason for stopping therapy early was patient refusal.

Results of the assessment of QOL for metastatic lung cancer patients EST 4983 must be interpreted with caution, since there is a bias in the selection of patients who completed the QOL questionnaire over several months compared to those who only completed the initial and possibly one or two questionnaires during therapy. Both morbidity and mortality were selection factors. Further, it is possible that compliance was itself correlated with quality of life (Finkelstein 1987).

1.12.2 TIMING

The consideration of timing and clinical status is particularly germane to oncology research given the variability of the clinical course during and after cancer therapy. Patients' issues during therapy in the acute phase tend to be very different from their issues in the long term, reflecting the transition from acute concerns for mortality and treatment-induced morbidity to long-term concerns about normalcy and reintegration into normal functioning (Parsons 1998).

In the literature, the patient's response to chemotherapy is described primarily from the health professional's perspective. Most studies do not address inherent changes as the disease progresses. Although cancer is a disease of multiple stages, frequently data collection is based on one interview at a particular stage rather than many interviews done over time and during various stages of treatment. The one-shot approach ignores the changing nature of the disease progression. Thus there is a scarcity of longitudinal information regarding day-to-day management of chemotherapy for the patient (Wilson & Morse, 1991).

Individual patients can be surveyed at several points over time (longitudinal study), or a randomly distributed sample of the patients may be surveyed at one time as a snapshot of time across a population (cross-sectional study). The advantages of the cross-sectional snapshot often include access to a larger population and the ability to conduct the assessment in a relatively shorter research window. The most striking disadvantage is that patients will be in the treatment and/or recovery period at variable times. The interpretation of results from a cross-sectional study must be made judiciously, because it is so dependent on case mix. The longitudinal study allows for intra-reporter comparison across time as well as linkage to the clinical state (Parsons 1998).

The timing of the assessment is an important consideration for research. Studies may be cross sectional or longitudinal. Clearly, determining the timing of assessment is dependent on the overall purpose of the study and the availability of suitable measures. Chronic illness outcomes research, mandates longitudinal testing to capture the dynamics of an illness with multiple sequelae, spanning a range of time. Cross-sectional research facilitates the accumulation of larger numbers of subjects and is appropriate for the assessment of a finite outcome at a fixed point in time. Cross-sectional studies do not offer causative or comparative data (from baseline to endpoint) for an individual patient, but they can be used to establish general trends in the population (Parsons 1998).

In adjuvant trials for the International Breast Cancer Study Group (IBCSG), Bernhard (1997) found that for patients receiving tamoxifen alone, quality of life improved as time from surgery increased, but the start of tamoxifen had no effect. In contrast, for chemotherapy patients, appetite, physical well-being and, in premenopausal patients, coping were worse one to five days after the start of CMF (cyclophosphamide, methotrexate and fluorouracil), but chemotherapy had little effect on mood and emotional well-being.

In a phase III trial of a sixteen-week multidrug regimen versus cyclophosphamide, doxorubicin and fluorouracil (CAF) as adjuvant therapy for node-positive, receptor negative breast cancer, the timing of the questionnaire proved problematic: Quality of life at the time of the during-treatment evaluation was significantly lower with the 16-week regimen than with CAF. The greater reduction in quality of life with the 16-week regimen than CAF during treatment might reflect, in part, the timing of the during-treatment evaluations after the most recent treatment. The Breast Chemotherapy Questionnaire (BCQ) asks the patients about the previous 2 weeks. During this time the patients on the 16-week regimen had received weeks 11 and 12 of treatment, whereas patients who were on the CAF regimen had gone 2 weeks without treatment. The lower scores with the 16-week regimen than CAF might reflect the fact that the patients on the former had actually received treatment in the previous 2 weeks, whereas patients on the latter had had a 2-week break. This shows the difficulties with choosing the best time to evaluate quality of life: evaluation of quality of life on day 15 of a CAF cycle provides a better measure of CAF toxicity but fails to evaluate the effects of a 2-week break between treatment on quality of life (Fetting 1998).

2.12.3 IMPACT OF LANGUAGE AND CULTURAL GROUPS

In the studies that Bernhard and coworkers (1997) conducted for the International Breast Cancer Study Group (IBCSG), they found that language or cultural groups had the biggest effect on the variance of baseline quality of life scores than any socio- demographic or biomedical factor. The impact of language or cultural group also exceeded that of adjuvant treatment modalities in subsequent assessments. Patterns of scores were however, similar in the different language groups.

2.13 STATISTICAL CONSIDERATIONS

2.13.1 SELF-RATING VERSUS OBSERVER-RATED SCALES

Patient-based measures of quality of life should supplement physician judgements of treatment-related toxic effects routinely reported in most trials. Aaronsen and coworkers (1988a) distinguished between subjective response criteria as judged by observers and quality of life assessments provided by patients.

According to Fallowfield (1990) and Barraclough (1994) quality of life is by definition about the patient's own perceptions and it is therefore better to measure it with self-rating rather than observer-rating scales. In a large number of cases the doctors' ratings of the severity of patients' physical and psychological symptoms, do not agree with the patients' own ratings thereof. In comparing the correlation of the patient's and the doctor's evaluations of the patient, Ballatori (1993) found that physicians are not able to judge a patient's psychological condition reliably. Maguire and coworkers (1999) found that the rate of false positive reporting by carers was high. In their study thirteen of the 59 patients were suffering from an affective disorder. This had been recognized by the general practitioner in only five cases and six patients who had a normal mood were wrongly diagnosed as being depressed. It was concluded that it is unreliable to rely on carers' proxy reports of the symptoms experienced by patients and that more accurate personal assessments are needed where possible. It is likely that this will only be achieved by ensuring that those health professionals involved in palliative care have training in the relevant assessment skills.

The aim of a study by Sneeuw (1998) was to examine whether significant others can provide useful proxy information on health-related quality of life. The level and pattern of agreement between patient and proxy ratings of the EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire), the reliability and validity of both types of information and the influence of several factors on the extent of agreement, was assessed. Quality of life ratings were obtained for 307 and 224 patient-proxy pairs (at baseline and at follow-up respectively). Agreement was moderate to good. Multi-trait multi-method analysis showed good convergence and discrimination of specific quality of life domains. Comparison of mean scores revealed a small but systematic bias between patient and proxy ratings. The maximum level of disagreement was found at intermediate levels of quality of life, with smaller discrepancies noted for patients with either a relatively poor or good quality of life. Both patient and proxy ratings were reliable and responsive to changes over time. Several characteristics of the patients and their significant others were found to be associated with the level of agreement, but explained less than 15% of the variance in patient-proxy differences. It was found that significant others as proxy respondents of cancer patients' quality of life where this is necessary, is a viable method.

Aaronsen (1990), Campbell (1976b), Cohen (1992) and Guyatt (1993) all state that quality of life is a subjective evaluation rather than an objective reality and so can only be assessed with reliability by the person whose quality of life is being evaluated. Brunelli (1998) found that the percentages of agreement between patients' ratings and proxy-ratings were higher for physical than for psychological and cognitive symptoms and that there was a greater agreement on the absence rather than the presence of a problem. Their results suggest that caution is needed in the use of health-care workers as alternative sources of information regarding patients' quality of life.

Sneeuw and coworkers (1997) used the COOP / Wonca charts to investigate the value of caregiver ratings in evaluating quality of life in patients with cancer. One important starting point in quality of life research is that the assessment is essentially subjective, with the patient being the primary source of information on his or her quality of life. There are several reasons why it is important to study the value of proxy quality of life ratings provided by the patient's caregivers at home (family or close companions) and in the clinic (physicians or nurses).

Firstly it might be useful in helping to resolve the problem of poor compliance rates in the collection of self-report quality of life data that has been encountered frequently in cancer clinical trials. Patient loss to follow-up is often related to patients' poor health (i.e. it is non-random). Unfortunately, it is precisely at this point of disease progression or acute symptom experience that we are intensely interested in assessing changes in the quality of life. Unacceptable levels of missing data, especially if it is non-randomly missing data, may lead to substantial bias in the analysis of quality of life data. Secondly, proxy judgements of patients' quality of life can and often does play a role, at least implicitly, in decisions regarding treatment and patient care. Especially in oncology, where many patients are treated with palliative rather than curative intent, quality of life considerations may weigh heavily in delivering the most adequate patient care. It is therefore important to understand the extent to which caregivers can assess accurately the patients' level of functioning and well being.

The accuracy of proxy ratings is usually assessed by examining the extent to which proxy ratings correspond to those of the patient's self-assessment. A lot of heterogeneity in research methodology and a diversity of results characterize the literature in this field. In spite of this, the prevailing opinion is that the capacity of caregivers to accurately rate the patients' quality of life is limited.

Sneeuw's investigation (1997) found close agreement between patient and caregiver ratings. Relative to the patients, the physicians were more efficient in detecting changes over time in physical fitness and overall health, but less so in relation to social function and pain.

2.13.2 THE USE OF SUMMARY MEASURES AND STATISTICS

Assessment of health related quality of life has become an important endpoint in many clinical trials of cancer therapy. Most of these studies entail multiple quality of life scales that are assessed repeatedly over time. As a result, the problem of multiple comparisons is a primary analytical challenge with these trials. The use of summary measures and statistics both reduces the number of hypotheses tested and facilitates the interpretation of trial results where the primary question is "Does the overall quality of life differ between treatment arms?" (Fairclough 1997).

2.14 AUTOMATED COLLECTION OF QUALITY OF LIFE DATA

Velikova and coworkers (1999) assessed alternative automated methods of collecting data on quality of life in cancer patients. After initial evaluation of a range of technologies, they compared computer touch-screen questionnaires with paper questionnaires. Cancer patients completed the European Organization for Research and Treatment of Cancer Quality of life questionnaire (EORTC QLQ-C30) and the Hospital Anxiety and Depression Scale (HADS) on paper and on a touch-screen. The quality of the data collected with the touch-screen was good, with no missed responses. It was concluded that computer touch-screen quality of life questionnaires were well accepted by cancer patients, with good quality and reliability.

2.15 CLINICAL BENEFIT RESPONSE

Although the ultimate aim of treating the cancer patient is cure, in most metastatic solid tumors this, unfortunately, can only infrequently be achieved with chemotherapy. However, potential benefits such as palliation of symptoms or prolongation of survival, are other reasons for using chemotherapy for solid tumors. The evaluation of some of these benefits is problematic (Verweij 1996).

For many diseases, objective regression of disease is not appropriately reflected in a prolongation of survival. The justification for nevertheless administering chemotherapy in these cases is that most medical oncologists believe that objective tumor regression also results in a decrease of tumor-related symptoms. Therefore, additional tools for properly investigating the palliation of symptoms are of importance. For many years quality of life assessment with all of its limitations, has been used for this purpose (Verweij 1996).

Rothenberg (1996) uses a new "clinical benefit response" method in a phase II trial of gemcitabine in patients with refractory pancreatic cancer. Despite the fact that objective tumor regression was scarcely mentioned, the authors report that a considerable number of patients benefited from treatment in other respects. The use of clinical benefit response as an endpoint of phase II studies is new and very interesting, but the data must be interpreted carefully.

TABLE 8: DEFINITION OF CLINICAL BENEFIT RESPONSE (Rothenberg 1996)

≥ 50% reduction in pain intensity
≥ 50% reduction in analgesic consumption
≥ 20% improvement in the Karnofsky performance scale that was sustained for ≥ 4 consecutive weeks
≥ 7% weight gain

The first two parameters are considered together and the other two as independent factors.
If one of the factors is judged to be negative the patient is a non-responder.
If only one of the factors is positive and all of the others are stable, the patient is a responder.

Reduction in pain has a subjective element. Recording of daily analgesic consumption is dependent on patient compliance and patients sometimes misinform their physicians. Even the Karnofsky performance score can be awarded very subjectively.

The potential clinical gain should be balanced against the potential negative effects of chemotherapy, namely the side effects. Accurate reporting of side effects is another difficult issue. This is another reason for being cautious in evaluating assessment tools with a subjective element.

Clinical benefit response may well become a very important and relatively simple tool for measuring the effects of chemotherapy. Randomized studies are required and comparisons with quality of life measurements should be performed (Verweij 1996).

2.16 CLINICAL FINDINGS

2.16.1 RESULTS OF ADJUVANT TRIALS

Results of the international breast cancer study group trials (IBCSG) VI and VII were analyzed for biomedical and sociodemographic factors that impact on baseline quality of life (QOL) scores. Among premenopausal patients, those with poor prognostic factors showed a tendency to report worse QOL, with estrogen receptor status as an independent predictor for mood. Older postmenopausal patients reported better emotional well being, mood and less effort to cope compared with younger premenopausal patients. Co-morbidity, type of surgery, treatment assignment and sociodemographic factors showed a statistically significant impact in postmenopausal patients only (Bernhard 1997).

There was an impressive improvement of all QOL scores with time, which reflects patients' adaptation to disease and treatment in the adjuvant setting. QOL scores at time points when patients were assigned to receive CMF (cyclophosphamide, methotrexate and fluorouracil) therapy were systematically lower, although the difference diminished over time. Overall, chemotherapy has a measurable adverse effect on patients' QOL, but this is transient and minor compared to patients' adaptation following diagnosis and surgery. (Bernhard 1997).

In trial IX patients undergoing chemotherapy (CMF) reported worse physical well-being and mood and more effort to cope with their disease (perceived adjustment to chronic illness scale PACIS) than patients receiving endocrine therapy only. There were no treatment differences in social support at any of the time points
(Bernhard 1997).

Recurrence had a major impact on QOL. There was a significant drop in all QOL scores between the pre- and post-recurrence assessments, with the post-recurrence scores approaching the scores recorded at baseline. Recurrence was perceived as a major event and the drop to baseline scores reflects a significant loss of patients' adaptation (Bernhard 1997).

The indicators of symptoms/side effects showed different profiles of changes over time, reflecting the different side effects of chemotherapy, endocrine therapy and surgery. In addition, the relative impact of the various specific indicators on physical wellbeing changed over time, suggesting that a global multi-item scale using weights, which are constant across time, may not be optimal. The strong association between physical wellbeing and mood under chemotherapy (Bernhard 1997) emphasized the overall emotional burden of cytotoxic side effects.

2.17 ANALYSIS

Researchers should have a basic understanding of elementary statistics, as the adequate analysis of quality of life data is extremely important. The sorts of analyses applied depend mainly on the purpose of the study.

Single-item scores or looking at variables within key domains which appear to be causing difficulty is sufficient if the aim is to use the information to tailor therapy for the individual or to apply appropriate ameliorative interventions when necessary.

Comparison of group "means" between patients receiving different therapies is more problematic and the difficulties are compounded when the total number of patients in each group is small. Patients with extreme scores can skew the results of overall quality of life for the majority of the other patients.

Pooling of all scores from different sections or domains of the questionnaire is also problematic. Patients with low scores in one area can be compensated by high scores in other areas, with a resultant confounding of the results.

Within the context of generic instruments, there are two theoretical approaches to measurement and presentation of the scores obtained: health profiles and summary scores. The former allows more detailed assessments within domains and is therefore more responsive to change. Subscale or domain scores can be provided that allows identification of specific areas of functioning that may be impaired. They may be essential for assessment of interventions that are designed to improve specific aspects of health-related quality of life (Jenney 1998).

A single summary score, or health index, may also be used that reflects overall health-related quality of life. All of the items in the instrument are summed to provide an overall score. Such scores are useful for population comparisons and in cost-benefit analyses. However, they do not provide details of specific areas of impairment of health-related quality of life (Jenney 1989).

Utility measures provide a single summary score of health related quality of life but also takes into account the preferences of individuals of different health states. They reflect both the health status of the individual and the value that the individual puts upon that health state (Jenney 1998).

2.18 CONCLUSION

There are currently many good tests available for quality of life measurement. These can help doctors determine the impact of their therapies on more that just the physical and functional aspects of their patients' lives. Failure to attempt to monitor quality of life is not good medical practice, nor is it good science.

TABLE 9: COMPARISON OF SOME QUALITY OF LIFE INSTRUMENTS

INSTRUMENT	DOMAIN	ADVANTAGES	DISADVANTAGES
Ability Index: Izsak & Medalie	E M P R	Modified for different cancer types	Single score
Alameda County Human Population Laboratory	E P R	Comprehensive	Generic & too long
BCQ: Breast Cancer Chemotherapy Questionnaire: Levine	E I P R S	Specifically for adjuvant stage II breast Valid & responsive	Not global Interviewer administered
BFI: Brief Fatigue Inventory: Mendoza	S	Reliable, brief, self-report	Measures a single dimension
Bf-S: Befindlichkeitsskala von Zerssen	E	Sensitive to anxiety & depression. Valid.	Not validated for English patients
BPI: Brief pain Inventory	S		Measures only one domain
CARES-SF Cancer Rehabilitation Evaluation System-Short Form: te Velde	C D E F H I P R S	Reliable & valid. Quick to complete. For patient self-assessment & clinical trials.	Lack of disease-specific questions
COOP/WONCA charts	E F H P Q R S	Sensitive to changes over time. Brief. Caregivers or patients complete it	Generic
EORTC QLQ-C30	C E F P R S	Reliable & valid. Categorical. Applicable across cultures Disease specific modules available Translations available in 24 languages Responsive to changes in patients' health status over time	Certain cultures may have problems with sexual items
FACT Functional Assessment of Cancer Therapy	D E F P R S	Reliable & valid Applicable across cultures Disease specific modules available Translations available Sensitive to change	Certain cultures may have problems with sexual items
FLIC: Functional Living Index Cancer: Shipper	D E F P S R	Quick self-report graded valid LASA test Cancer specific & multidimensional	? Sensitivity, single score. Labor intensive. Not for large-scale clinical trials research.
GHQ: General Health Questionnaire: Goldberg	E S R	Easy to score, reliable & valid	Does not cover all domains adequately
GLQ-8: General Life Questionnaire: Coates	E S R	Simplicity, patient acceptance, reliability & validity	Does not cover all domains adequately Same disadvantages as other LASA scales See Priestman & Baum
Grogono & Woodgate	P	Sensitive & specific. Translations	Poor reliability
HAD: Hospital Anxiety & Depression Scale	E	Quick and easy to use and score	Measures only one domain
IQL: Integrative Quality of Life: Ventegodt	M	Valid and reliable	Very long and difficult to score
Kaplan	P	Measures level of well-being & prognosis	Uni-dimensional and generic
Karnofsky Performance Status	F	Quick & useful to determine physical functioning Widely used	Measures only one domain Entirely subjective evaluation made by a clinician

LEQ: Life Evaluation Questionnaire Salmon	E	Evaluates psychological needs very well Helps patients to voice their concerns	Measures only one domain
Katz Index: Activities of Daily Living	F	Applicable for a variety of diagnoses Correlates well with survival Has prognostic value	Not valid for quality of life measurement Focus is on severe disability: thus inappropriate for most outpatient purposes
McMaster Health Index Questionnaire MHIQ	E P R	Global, good psychometric properties, Categorical, brief and patient rated.	Reliability not as high as the Nottingham Health Profile.
MOS Short-form General Health Survey: Ware 36 item & 20 item versions	E H P R S	Reliable, convergent & discriminant validity. Norms available	Generic
MPQ: McGill/Melzack Pain Questionnaire	S	Reliable, specific & valid	Measures only one domain
NHP: Nottingham Health Profile Part 1 has 38 items	E P R S	Good psychometric properties & easy to score. Patient reported & categorical.	Well being cannot be indicated Accurately
PACIS: Perceived Adjustment to Chronic Illness Scale: Hürney	E	Reflects psychological adjustment Global	Generic
PAIS: Psychological Adjustment to Illness Scale	E D F H R S	Comprehensive & reliable Norms available. Has a global measure. Good criterion validity	Difficult to score and very long (46 items). Lack of disease-specific questions
POMS: Profile of Mood States – Brief	E	Patient self-report. Brief. Categorical. Acceptable psychometric properties.	Measures only one domain
Priestman & Baum: LASA	E F P R S	Sensitive, specific & reliable Self-assessment	Time-consuming to score Scores may not relate well to the specific domain Discrimination may not be "real" Meaning of changes in scores is Obscure
QOL Core Questionnaire of the IBCSG LASA scale	E H P R S	Global single-item measure. Treatment comparisons of the same patient	Restricted to a few domains LASA Interpretation of questions
Rand Personal Functioning Index (21 items)	F P	Patient self-report. Brief. Categorical. Acceptable psychometric properties.	Not comprehensive enough
RSCL: Rotterdam Symptom Checklist: de Haes	E F P R S	Sensitive, specific, valid & easy to understand. Quick to complete & easy to score	? Availability of norms Sexual and social dimensions are possibly inadequate
Selby's LASA	E F R S	Reliable, valid & breast cancer specific. Self or observer scored. Quick	As for Priestman & Baum
Spitzer's QLI-Index	E F H P R	Brief, reliable, valid Physician or patient scored Measure of mostly physical functioning	Response variation on social functioning was minimal. Very low composite scores (0-3) were rarely obtained.

SIP: Sickness Impact Profile: Bergner	E F R S	Widely used, valid & reliable	Single score and / or 12 categories Cumbersome & time-consuming (136 questions). Not disease-specific
SSQ6 Social Support Questionnaire	R	Promising and brief (six items)	Validation done with college students Does not discriminate among patients with high scores. One domain
WHO Performance Status	F	Quick & useful to determine physical functioning Widely used	Measures only one domain Entirely subjective evaluation made by a clinician
WHOQOL-100	E F P R S	Reliable, specific & sensitive, with high construct validity WHOQOL-Bref Is being tested (26 items)	Generic instrument & too long Some vague questions

KEY:

C	cognitive	D	relationship with doctor
E	emotional	F	functional
H	health	I	inconvenience
M	meta-theory	P	physical
Q	quality of life	R	relationships
S	symptoms		

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ADDENDUM 1: BREAST CHEMOTHERAPY QUESTIONNAIRE

(BCQ LEVINE 1988) (Seven-point scale, initial questionnaire)

This questionnaire is designed for women who are receiving or have in the past received chemotherapy for breast cancer. I will be asking you about how you have been feeling, physically and emotionally, during the last 2 weeks. The questions I will ask you, focus on some of the problems and some of the feelings that may be experienced by women who have been given chemotherapy for breast cancer. The table below states the possible numbered responses for each color card. In the second table, there is a column in which you must show your response number to each question (for which the color card to be used is indicated). For example, for question number one, a blue card is to be used. If your response to question number one is "some of the time", you must enter number 4 into the appropriate space.

BLUE CARD	YELLOW CARD	GRAY CARD	GREEN CARD
1. All of the time	1. None of the time	1. A great deal of trouble or inconvenience	1. A great deal of trouble
2. Most of the time	2. A little of the time	2. A lot of trouble or inconvenience	2. A lot of trouble
3. A good bit of the time	3. Some of the time	3. A fair bit of trouble or inconvenience	3. A fair bit of trouble
4. Some of the time	4. A good bit of the time	4. Some trouble or inconvenience	4. Some trouble
5. A little of the time	5. Most of the time	5. A little trouble or inconvenience	5. A little trouble
6. Hardly any of the time	6. Almost all of the time	6. Hardly any trouble or inconvenience	6. Hardly any trouble
7. None of the time	7. All of the time	7. No trouble or inconvenience	7. No trouble

QUESTION	CARD	RE-SPONSE
1. How often during the past 2 weeks have you felt worried or upset as a result of thinning or loss of your hair?	Blue	
2. How often during the past 2 weeks have you felt optimistic or positive regarding the future?	Yellow	
3. How often during the past 2 weeks have you felt that your fingers were numb or falling	Blue	

asleep?		
4. How much trouble or inconvenience have you had during the last 2 weeks as a result of having to come or stay at the clinic or hospital for medical care?	Gray	
5. How often during the last 2 weeks have you felt low in energy?	Blue	
6. In general, how often during the last 2 weeks have you felt tearful or down in the dumps?	Blue	
7. How much trouble have you had in the last 2 weeks as a result of feeling nauseated?	Green	
8. How often during the last 2 weeks have you been troubled or upset as a result of feeling unattractive?	Blue	
9. How much of the time during the last 2 weeks have you felt the future looks hopeful and promising?	Yellow	
10. How often during the last 2 weeks have you had trouble getting a good night's sleep?	Blue	
11. How much trouble or inconvenience have you had during the last 2 weeks as a result of waiting to see a physician while visiting the clinic or hospital?	Gray	
12. How often during the last 2 weeks have you felt tired of fatigued while hurrying?	Blue	
13. In general, how often during the last 2 weeks have you felt worried or tense?	Blue	
14. How often during the last 2 weeks have you had an upset stomach?	Blue	
15. How often during the last 2 weeks have you felt uncomfortable or embarrassed as a result of thinning or loss of your hair?	Blue	
16. How much help and support have you received from people outside your family during the last 2 weeks?	Yellow	
17. How often during the last 2 weeks did you have the sensation that you smelled of chemicals?	Blue	
18. How much trouble or inconvenience have you had during the last 2 weeks as a result of sitting in the waiting room at the clinic or hospital?	Gray	
19. How often during the last 2 weeks have you had problems with fatigue or tiredness which interfered with your housework?	Blue	
20. In general, how often during the last 2 weeks have you felt frustrated or irritable?	Blue	
21. How much of the time during the last 2 weeks have you been troubled by increased production of gas?	Blue	
22. How often during the last 2 weeks have you been sad or tearful as a result of thinning or loss of your hair?	Blue	
23. How often during the last 2 weeks have you felt good about yourself?	Yellow	
24. How much of the time during the last 2 weeks have you felt drowsy during the day?	Blue	
25. How much trouble or inconvenience have you had during the last 2 weeks as a result of waiting for treatment at the clinic or hospital?	Gray	
26. How much of the time during the last 2 weeks have you had problems with fatigue or tiredness which limited your usual social activities?	Blue	
27. How much of the time during the last 2 weeks would you say that your family has been worried about you and about your health?	Blue	
28. How much of the time during the last 2 weeks have you been troubled by constipation?	Blue	
29. How much trouble or distress have you had as a result of pain, soreness, or sores in your mouth, during the last 2 weeks?	Green	

30. How much of the time during the last 2 weeks have you been troubled by burning, watery or sore eyes?	Blue	

ADDENDUM 2: ITEM CONTENT OF THE CARES-SF (TE VELDE 1996)

The response categories for all items are expressed in terms of perceived applicability, with response choices ranging: Not At All, A Little, A Fair Amount, Much, Very Much.

1. I have difficulty bending or lifting.
2. I do not have the energy I used to.
3. I have difficulty doing household chores.
4. I have difficulty bathing, brushing my teeth, or grooming myself.
5. I have difficulty planning activities because of the cancer or its treatments.
6. I cannot gain weight.
7. I find food unappealing.
8. I find that cancer or its treatments interfere with my ability to work.
9. I frequently have pain.
10. I find that my clothes do not fit.
11. I find that doctors don't explain what they are doing to me.
12. I have difficulty asking doctors questions.
13. I have difficulty understanding what the doctors tell me about the cancer or its treatments.
14. I would like to have more control over what the doctors do to me.
15. I am uncomfortable with the changes in my body.
16. I frequently feel anxious.
17. I have difficulty sleeping.
18. I have difficulty concentrating.
19. I have difficulty asking friends and relatives to do things for me.
20. I have difficulty telling my friends or relatives about the cancer.
21. I find that my friends or relatives tell me I'm looking well when I'm not.
22. I find that my friends or relatives do not visit often enough.
23. I find that my friends or relatives have difficulty talking with me about my illness.
24. I become nervous when I'm waiting to see the doctor.
25. I become nervous when I get my blood drawn.
26. I worry about whether the cancer is progressing.
27. I worry about not being able to care for myself.
28. I do not feel sexually attractive.
29. I am not interested in having sex.

30. I sometimes don't follow my doctor's instructions.

31. I have financial problems.

32. I have insurance problems.

33. I have difficulty with transportation to and from my medical appointments and/or other places.

34. I am gaining too much weight.

35. I have frequent episodes of diarrhea.

36. I have times when I do not have control of my bladder.

Do you have children?

37. I have difficulty helping my children cope with my illness.

Are you working or have you been employed during the last month?

38. I have difficulty talking to the people who work with me about the cancer.

39. I have difficulty asking for time off from work for medical treatments.

40. I am worried about being fired.

Did you look for work during the past month?

41. I have difficulty finding a new job since I have had cancer.

Have you attempted sexual intercourse since your cancer diagnosis?

42. I find that the frequency of sexual intercourse has decreased.

Are you married or in a significant relationship?

43. My partner and I have difficulty talking about our feelings.

44. My partner and I have difficulty talking about our wills and financial arrangements.

45. I do not feel like embracing, kissing, or caressing my partner.

46. My partner and I are not getting along as well as we usually do.

47. My partner spends too much time taking care of me.

48. I have difficulty asking my partner to take care of me.

Are you single and not in a significant relationship?

49. I have difficulty initiating contact with potential dates.

50. I have difficulty telling a date about the cancer or its treatments.

Have you had chemotherapy treatments in the last month?

51. I become nervous when I get chemotherapy.

52. I become nauseated during and/or before chemotherapy.

53. I feel nauseated after I receive chemotherapy.

54. I vomit after chemotherapy.

55. I have other side effects after chemotherapy.

Have you had radiation therapy treatments in the last month?

56. I get nervous when I get radiation treatments.

57. I feel nauseous or vomit after my radiation treatments.

Do you have an ostomy?

58. I have problems with ostomy care and maintenance.

Do you have a prosthesis?

59. I have difficulty with my prosthetic device (artificial limb, breast prosthesis, etc.).

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ADDENDUM 3:FUNCTIONAL LIVING INDEX: CANCER (FLIC) SCHIPPER 1984

PLEASE INDICATE WITH AN X YOUR RATING

1. Most people experience some feeling of depression at times. Rate how often you feel these feelings.

1	2	3	4	5	6	7
never						continually

2. How well are you coping with your everyday stress?

1	2	3	4	5	6	7
not well						very well

3. How much time do you spend thinking about your illness?

1	2	3	4	5	6	7
constantly						never

4. Rate your ability to maintain your usual recreation or leisure activities.

1	2	3	4	5	6	7
able						unable

5. Has nausea affected your daily functioning?

1	2	3	4	5	6	7
not at all						a great deal

6. How well do you feel today?

1	2	3	4	5	6	7
extremely poor						extremely well

7. Do you feel well enough to make a meal or do minor household repairs today?

1	2	3	4	5	6	7
very able						not able

8. Rate the degree to which your cancer has imposed a hardship on those closest to you in the past weeks.

1	2	3	4	5	6	7
no hardship						tremendous hardship

9. Rate how often you feel discouraged about your life.

1	2	3	4	5	6	7
always						never

10. Rate your satisfaction with your work and your jobs around the house in the past month.

1	2	3	4	5	6	7
very dissatisfied						very satisfied

11. How uncomfortable do you feel today?

1	2	3	4	5	6	7
not at all						very uncomfortable

12. Rate in your opinion, how disruptive your cancer has been to those closest to you in the past 2 weeks.

1	2	3	4	5	6	7
totally disruptive						no disruption

13. How much is pain or discomfort interfering with your daily activities?

1	2	3	4	5	6	7
not at all						a great deal

14. Rate the degree to which your cancer has imposed a hardship on you (personally) in the past 2 weeks.

1	2	3	4	5	6	7
tremendous hardship						no hardship

15. How much of your usual household tasks are you able to complete?

1	2	3	4	5	6	7
all						none

16. Rate how willing you were to see and spend time with those closest to you, in the past 2 weeks.

1	2	3	4	5	6	7
unwilling						very willing

17. How much nausea have you had in the past 2 weeks?

1	2	3	4	5	6	7
none						a great deal

18. Rate the degree to which you are frightened of the future.

1	2	3	4	5	6	7
constantly terrified						not afraid

19. Rate how willing you were to see and spend time with friends, in the past 2 weeks.

1	2	3	4	5	6	7
unwilling						very willing

20. How much of your pain or discomfort over the past 2 weeks was related to your cancer?

1	2	3	4	5	6	7
none						all

21. Rate your confidence in your prescribed course of treatment.

1	2	3	4	5	6	7
no confidence						very confident

22. How well do you appear today?

1	2	3	4	5	6	7
extremely poor						extremely well

Please check to see if you have completed all questions. Thank you for your valuable assistance in this project.

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ADDENDUM 4: SOME DEFINITIONS AND GRADES FOR THE KATZ INDEX OF ACTIVITIES OF DAILY LIVING (KATZ, 1963)

Index of Independence in Activities of Daily Living

The index of independence in activities of daily living is based on an evaluation of the functional independence or dependence of patients in bathing, dressing, going to the toilet, transferring, continence, and feeding. Specific definitions of functional independence and dependence appear below the index.

A Independent in feeding, continence, transferring, going to toilet, and bathing.
B Independent in all but one of these functions.
C Independent in all but bathing, and one additional function.
D Independent in all but bathing, dressing and one additional function.
E Independent in all but bathing, dressing, going to toilet, and one additional function
F Independent in all but bathing, dressing, going to toilet, transferring, and one additional function.
G Dependent in all six functions.
Other Dependent in at least two functions, but not classifiable as C, D, E, or F.

Independence means without supervision, direction, or active personal assistance, except as specifically noted below. This is based on actual status and not on ability. A patient who refuses to perform a function is considered as not performing the function, even though he is deemed able.

Eg bathing (sponge, shower or tub)

Independent: assistance only in bathing a single part (as back or disabled extremity) or bathes self completely.

Dependent: assistance in bathing more than one part of body: assistance in getting in or out of tub or does not bathe self.

ADDENDUM 5: McGILL PAIN QUESTIONNAIRE (MELZACK, 1971)

What does pain feel like?

Tell which words best describe your present pain

Use only a single word in each appropriate group the one that applies best

Indicate answer with (▯)

1		**2**		**3**		**4**	
1. flickering		1. jumping		1. pricking		1. sharp	
2. quivering		2. flashing		2. boring		2. cutting	
3. pulsing		3. shooting		3. drilling		3. lacerating	
4. throbbing				4. stabbing			
5. beating				5. lancinating			
6. pounding							
5		**6**		**7**		**8**	
1. pinching		1. tugging		1. hot		1. tingling	
2. pressing		2. pulling		2. burning		2. itchy	
3. gnawing		3. wrenching		3. scalding		3. smarting	
4. cramping				4. searing		4. stinging	
5. crushing							
9		**10**		**11**		**12**	
1. dull		1. tender		1. tiring		1. sickening	
2. sore		2. taut		2. exhausting		2. suffocating	
3. hurting		3. rasping					
4. aching		4. splitting					
5. heavy							
13		**14**		**15**		**16**	
1. fearful		1. punishing		1. wretched		1. annoying	
2. frightful		2. grueling		2. blinding		2. troublesome	
3. terrifying		3. cruel				3. miserable	
		4. vicious				4. intense	
		5. killing				5. unbearable	
17		**18**		**19**		**20**	
1. spreading		1. tight		1. cool		1. nagging	
2. radiating		2. numb		2. cold		2. nauseating	
3. penetrating		3. drawing		3. freezing		3. agonizing	

4. piercing		4. squeezing				4. dreadful	
		5. tearing				5. torturing	

ADDENDUM 6: NOTTINGHAM HEALTH PROFILE (HUNT 1980)

(Some items from Part 1)

Listed below are some problems people may have in their daily life.

Look down the list and put a tick in the box under "yes" for any problem you have at the moment.

Tick the box under "no" for any problem you do not have.

Please answer every question. If you are not sure whether to say yes or no, tick whichever answer you think is more true at the moment.

	YES	NO
I'm tired all the time		
I have pain at night		
Things are getting me down		
	YES	NO
I have unbearable pain		
I take tablets to help me sleep		
I've forgotten what it's like to enjoy myself		
	YES	NO
I'm feeling on edge		
I find it painful to change position		
I feel lonely		
	YES	NO
I can only walk about indoors		
I find it hard to bend		
Everything is an effort		

ADDENDUM 7: NOTTINGHAM HEALTH PROFILE (HUNT, 1980)

(Part 2)

Now we would like you to think about the activities in your life which may be affected by health problems.

In the list below, tick "yes" for each activity in your life which is being affected by your state of health. Tick "no" for each activity which is not being affected, or which does not apply to you.

Is your present state of health causing problems with your...	YES	NO
JOB OF WORK (That is, paid employment)		
LOOKING AFTER THE HOME (Examples: cleaning and cooking, repairs, odd jobs round the home, etc.)		
SOCIAL LIFE (Examples: going out, seeing friends, going to the pub, etc.)		
HOME LIFE (That is: relationships with other people in your home)		
SEX LIFE		
INTERESTS AND HOBBIES (Examples: sports, arts and crafts, do-it-yourself, etc.)		
HOLIDAYS (Examples: summer or winter holidays, weekends away, etc.)		

ADDENDUM 8: SOME ITEMS FROM PRIESTMAN AND BAUM'S LASA (PRIESTMAN 1976)

DIFFICULTY WITH SLEEP

Most nights ____| Never

FEELING OF WELL BEING

Very bad ____| Very good

RELATIONSHIP WITH PARTNER

Impossible ____| Excellent

RELATIONSHIP WITH OTHER PEOPLE

Impossible ____| Excellent

SEXUAL RELATIONSHIPS

Total loss ____| Better than ever

DECISION MAKING

Impossible ____| Excellent

ABILITY TO PERFORM HOUSEWORK

Impossible ____| Better than ever

ADDENDUM 9: QUALITY OF LIFE CORE QUESTIONNAIRE (BERNHARD, 1997)

International Breast cancer Trials VI, VII, VIII, IX, 10–93 to 14-93
Quality of Life Core Questionnaire

Patient instructions:

We would like to know how strongly you are affected by your illness and treatment. Please answer all of the following questions by **placing a vertical mark on the line** depending on how you assess yourself.

For example: Have you had trouble sleeping?

None ____________________________|______ A lot

This mark would indicate considerable sleeping difficulties since your last assessment.

Your information will be treated as strictly confidential. Thank you for replying!

Please turn over for the questionnaire

How have you been within the last two weeks?

Physical Well Being Good ______________________________ Lousy

Mood Happy ______________________________ Miserable

Tiredness None ______________________________ A lot

Appetite Good ______________________________ None

Hot Flushes None ______________________________ A lot

Feeling sick (nausea and vomiting) None ______________________________ A lot

How much effort does it cost you to cope with your illness?

No effort at all ______________________________ A great deal of effort

Do you feel supported by the people close to you?

Very much ______________________________ Not at all

Does the operation restrict the use of your arm?

Not at all ______________________________ A lot

Imagine that you would have to live the rest of your life in your current condition. Please indicate, on the line below, how you would rate a life in your current condition between perfect health and worst health.

Make a vertical mark according to your estimate.

Perfect health ______________________________ Worst health

Please check that all questions are answered. Thank you!

ADDENDUM 10: PART OF SELBY'S LASA (1984)

Please score how you *feel* each of these aspects of your life was affected by *the state of your health,* during *today* (24 hours)

☐ ***Depression***

extremely ____________________________________ not depressed at all
depressed

☐ ***Appearance of your body***

extremely ____________________________________ completely satisfactory
dissatisfied for me at my age
(because of the state of my health,
disease or treatment)

☐ ***Family relationships and marriage/cohabitation***

extremely ____________________________________ normal family
bad relationships life for me
because of the state
of my health

☐ ***Housework***

no housework ____________________________________ normal house-hold
because of the duties for me
state of my health

☐ ***Eating* (increased or decreased)**

COMPLETE (a) or (b)

(a)

not eating ____________________________________ normal eating
for me

(b)

greatly ____________________________________ normal eating
increased eating for me

ADDENDUM 11: THE GENERAL HEALTH QUESTIONNAIRE (GHQ 28) PART A – (DAVID GOLDBERG, 1972)

Please read this carefully:

We should like to know if you have had any medical complaints and how your health has been in general, *over the past few weeks*. Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL questions.

Thank you very much for your co-operation.

Have you recently:

	Better than usual	Same as usual	Worse than usual	Much worse than usual
A2 been feeling in need of a good tonic?	Not at all	No more than usual	Rather more than usual	Much more than usual
A3 been feeling run down and out of sorts?	Not at all	No more than usual	Rather more than usual	Much more than usual
A4 felt that you are ill?	Not at all	No more than usual	Rather more than usual	Much more than usual
A5 been getting any pains in your head?	Not at all	No more than usual	Rather more than usual	Much more than usual
A6 been getting a feeling of tightness or pressure in your head?	Not at all	No more than usual	Rather more than usual	Much more than usual
A7 been having hot or cold spells?	Not at all	No more than usual	Rather more than usual	Much more than usual

ADDENDUM 12:ITEMS IN THE ROTTERDAM SYMPTOM CHECKLIST (RSCL) (DE HAES, 1983)

Name____________________________ Title ______________________ Date of Birth______________________

Date ______________________________ Occupation ________________________ Hospital ______________

In this questionnaire you will be asked about your symptoms.

Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling during the last three days.

Please turn over for: Section 1

ROTTERDAM SYMPTOM CHECKLIST

1. Lack of appetite		**2. Irritability**		**3. Worry about my health**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	
4.Tiredness		**5. Worrying**		**6. Sore muscles**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	
7. Depressed		**8. Lack of energy**		**9. Pain**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	
10. Nervousness		**11. Nausea**		**12. Feel desperate about the future**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	
13. Difficulty in falling asleep		**14. Headache**		**15. Vomiting**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	
16. Feeling self-conscious		**17. Dizziness**		**18. Lack of sexual interest**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	
19. Feel lonely		**20. Dissatisfied with my appearance**		**21. Feel tense**	
Not at all		Not at all		Not at all	
A little		A little		A little	
Somewhat		Somewhat		Somewhat	
Very much		Very much		Very much	

ADDENDUM 13: SOME ITEM FROM SECTION VI OF THE PAIS – SOCIAL ENVIRONMENT (MORROW, 1978)

(1) INDIVIDUAL LEISURE INTEREST

Are you still as interested in your leisure time activities and hobbies as you were prior to your illness (i.e. watching TV, sewing, bicycling, etc.)?

[ ] 0 = same level of interest as previously
[ ] 1 = slightly less interest than before
[ ] 2 = significantly less interest than before
[ ] 3 = little or no interest remaining

(2) INDIVIDUAL LEISURE ACTIVITIES

How about actual participation? Are you still actively involved in doing those activities?

[ ] 0 = participation remains unchanged
[ ] 1 = participation reduced slightly
[ ] 2 = participation reduced significantly
[ ] 3 = little or no participation at present

(3) FAMILY LEISURE INTEREST

Are you as interested in leisure time activities with your family (i.e. playing cards and games, taking trips, going swimming, etc.) as you were prior to your illness?

[ ] 0 = same level of interest as previously
[ ] 1 = slightly less interest than before
[ ] 2 = significantly less interest than before
[ ] 3 = little or no interest remaining

ADDENDUM 14: SOME ITEMS OF THE SICKNESS IMPACT PROFILE (BERGNER, 1976)

Dimension	**Category Items Describing Behavior Related to:**	**Selected Items**
Independent categories	Sleep and rest	I sit during much of the day I sleep or nap during the day
	Eating	I am eating no food at all, nutrition is taken through tubes or intravenous fluids I am eating special or different food
I. Physical	Ambulation	I walk shorter distances or stop to rest often I do not walk at all
II. Psychosocial	Body care and movement	I do not bathe myself at all, but am bathed by someone else I am very clumsy in body movements
	Social interaction	I am doing fewer social activities with groups of people I isolate myself as much as I can from the rest of the family
	Emotional behavior	I laugh or cry suddenly I act irritable and impatient with myself for example, talk badly about myself swear at myself, blame myself for things that happen

ADDENDUM 15: PART OF THE PROFILE OF MOOD STATES (POMS) (McNAIR, 1981)

Below is a list of words that describe feelings people have. Please read each one carefully. Then fill in ONE circle under the answer to the right which best describes HOW YOU HAVE BEEN FEELING DURING THE PAST WEEK INCLUDING TODAY.

	Not at all	A little	Moderately	Quite a bit	Extremely		Not at all	A little	Moderately	Quite a bit	Extremely
1. Friendly	(0)	(1)	(2)	(3)	(4)	21. Hopeless............	(0)	(1)	(2)	(3)	(4)
2. Tense	(0)	(1)	(2)	(3)	(4)	22. Relaxed...............	(0)	(1)	(2)	(3)	(4)
3. Angry	(0)	(1)	(2)	(3)	(4)	23. Unworthy............	(0)	(1)	(2)	(3)	(4)
4. Worn out	(0)	(1)	(3)	(3)	(4)	24. Spiteful..........	(0)	(1)	(2)	(3)	(4)
5. Unhappy	(0)	(1)	(2)	(3)	(4)	25. Sympathetic.........	(0)	(1)	(2)	(3)	(4)
6. Clear-headed ...	(0)	(1)	(2)	(3)	(4)	26. Uneasy...............	(0)	(1)	(2)	(3)	(4)
7. Lively	(0)	(1)	(2)	(3)	(4)	27. Restless...............	(0)	(1)	(2)	(3)	(4)
8. Confused	(0)	(1)	(2)	(3)	(4)	28. Unable to concentrate	(0)	(1)	(2)	(3)	(4)
9. Sorry for things done	(0)	(1)	(2)	(3)	(4)	29. Fatigued...............	(0)	(1)	(2)	(3)	(4)
10. Shaky	(0)	(1)	(2)	(3)	(4)	30. Helpful	(0)	(1)	(2)	(3)	(4)
11. Listless	(0)	(1)	(2)	(3)	(4)	31. Annoyed	(0)	(1)	(2)	(3)	(4)
12. Peeved	(0)	(1)	(2)	(3)	(4)	32. Discouraged	(0)	(1)	(2)	(3)	(4)
13. Considerate	(0)	(1)	(2)	(3)	(4)	33. Resentful	(0)	(1)	(2)	(3)	(4)
14. Sad	(0)	(1)	(2)	(3)	(4)	34. Nervous	(0)	(1)	(2)	(3)	(4)
15. Active	(0)	(1)	(2)	(3)	(4)	35. Lonely	(0)	(1)	(2)	(3)	(4)
16. On edge	(0)	(1)	(2)	(3)	(4)	36. Miserable	(0)	(1)	(2)	(3)	(4)
17. Grouchy	(0)	(1)	(2)	(3)	(4)	37. Muddled	(0)	(1)	(2)	(3)	(4)
18. Blue	(0)	(1)	(2)	(3)	(4)	38. Cheerful	(0)	(1)	(2)	(3)	(4)
19. Energetic	(0)	(1)	(2)	(3)	(4)	39. Bitter	(0)	(1)	(2)	(3)	(4)
20. Panicky	(0)	(1)	(2)	(3)	(4)	40. Exhausted	(0)	(1)	(2)	(3)	(4)

ADDENDUM 16: THE HOSPITAL ANXIETY AND DEPRESSION SCALE (HAD SCALE) ZIGMOND, 1983

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he will be able to help you more. This questionnaire is designed to help your doctor to know how you feel. Read each item and place a firm tick in the box opposite the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought-out response.

I feel tense or 'wound' up:			**I feel as if I am slowed down:**		
I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**		
I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**		
I can laugh and see the funny side of things			**I feel restless as if I have to be on the move**		
Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**		
I feel cheerful:			**I get sudden feelings of panic:**		
I can sit at ease and feel relaxed:			**I can enjoy a good book, radio or TV program:**		

ADDENDUM 17: EORTC QLQ-C30 (AARONSEN, 1993) AND QLQ-BR23 (SPRANGERS, 1996)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials : ____________________
Your birthdate (day, month, year) : ____________________
Today's date (day, month, year) : ____________________

		No	**Yes**
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase ?	1	2
2.	Do you have any trouble taking a long walk?	1	2
3.	Do you have any trouble taking a short walk outside the house?	1	2
4.	Do you have to stay in a bed or a chair for most of the day?	1	2
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2
6.	Are you limited in any way in doing either you work or doing household jobs?	1	2
7.	Are you completely unable to work at a job or to do household jobs?	1	2

During the past week:

		Not at all	**A Little**	**Quite a bit**	**Very much**
8	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4
16.	Have you been constipated?	1	2	3	4

Please go on to the next page

During the past week:

	Not at all	A Little	Quite a bit	Very much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Were you limited in doing either your work or other daily activities?	1	2	3	4
27. Were you limited in pursuing your hobbies or other daily activities?	1	2	3	4
28. Has your physical condition or medical treatment interfered with your **family** life?	1	2	3	4
29. Has your physical condition or medical treatment interfered with your **social** activities?	1	2	3	4
30. Has your physical condition or medical caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

31. How would you rate your overall **physical condition** during the past week?

1 2 3 4 5 6 7

Very poor Excellent

32. How would you rate your overall **health** during the past week?

1 2 3 4 5 6 7

Very poor Excellent

33. How would you rate your overall **quality of life** during the past week?

1 2 3 4 5 6 7

Very poor Excellent

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EORTC QLQ-BR23

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

During the past week:

	Not at all	**A Little**	**Quite a bit**	**Very much**
34. Did you have a dry mouth?	1	2	3	4
35. Did food and drink taste different than usual?	1	2	3	4
36. Were your eyes painful, irritated or watery?	1	2	3	4
37. Have you lost any hair?	1	2	3	4
38. Answer this question only if you had any hair loss: Were you upset by the loss of you hair?	1	2	3	4
39. Did you feel ill or unwell?	1	2	3	4
40. Did you have hot flushes?	1	2	3	4
41. Did you have headaches?	1	2	3	4
42. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
43. Have you been feeling less feminine as a result of your disease or treatment?	1	2	3	4
44. Did you find it difficult to look at yourself naked?	1	2	3	4
45. Have you been dissatisfied with your body?	1	2	3	4
46. Were you worried about your health in the future?	1	2	3	4

During the past <u>four</u> weeks:

	Not at all	**A Little**	**Quite a bit**	**Very Much**
47. To what extent were you interested in sex?	1	2	3	4
48. To what extent were you sexually active? (with or without intercourse)	1	2	3	4
49. Answer this question only if you have been sexually active: To what extent was sex enjoyable for you?	1	2	3	4

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Version 1.0

ADDENDUM 18: QUALITY OF LIFE INDEX (SPITZER 1981)

ACTIVITY	**During the last week, the patient** • Has been working or studying full time, or nearly so, in usual occupation; or managing own household; or participating in unpaid or voluntary activities, whether retired or not……………………………………………2 • Has been working or studying in usual occupation or managing own household or participating in unpaid or voluntary activities; but requiring major assistance or a significant reduction in hours worked or a sheltered situation or was on sick leave……..1 • Has not been working or studying in any capacity and not managing own household…..0
DAILY LIVING	**During the last week, the patient** • Has been self-reliant in eating, washing, toiletting and dressing; using public transport or driving own car ……………………………………..2 • Has been requiring assistance (another person or special equipment) for daily activities and transport but performing light tasks……………………………1 • Has not been managing personal care nor light tasks and/or not leaving own home or institution at all……………………………………..0
HEALTH	**During the last week, the patient** • Has been appearing to feel well or reporting feeling 'great' most of the time……………2 • Has been lacking energy or not feeling entirely 'up to par' more than just occasionally.. 1 • Has been feeling very ill or 'lousy', seeming weak and washed out most of the time or was unconscious……………………………………0
SUPPORT	**During the last week, the patient** • The patient has been having good relationships with others and receiving strong support from **at least one** family member and/or friend……………………..2 • Support received or perceived has been limited from family and friends and/or by the patient's condition…………………………………1 • Support from family and friends occurred infrequently or only when absolutely necessary or patient was unconscious…………………………………0
OUTLOOK	**During the last week, the patient** • Has usually been appearing calm and positive in outlook, accepting and in control of personal circumstances, including surroundings…………………………2 • Has sometimes been troubled because not fully in control of personal circumstances or has been having periods of obvious anxiety or depression……………………1 • Has been seriously confused or very frightened or consistently anxious and depressed or unconscious…………………………………… 0

CHAPTER 3: WHY IS IT NECESSARY TO EVALUATE QUALITY OF LIFE?

3.1 INTRODUCTION

One of the motivations for the assessment of quality of life is the increased attention to cancer control research at the National Cancer Institute (NCI) of America and at many, if not all of the cooperative research groups.

Quality of life is an emerging science of particular relevance to clinical cancer research. The availability of reliable quality of life measures may profoundly alter the clinical trials process. However, lack of rigor in the evaluation of such indices and uncritical interpretation of results may seriously compromise the credibility of the concept (Schipper 1985). In addition the assessment of quality of life is a complex issue.

Over the years, much research has been done in the field of quality of life, but its impact on the handling and treatment of cancer patients has been either non-existent or minimal. This is patently clear when scanning reports of clinical research in the medical literature (Stjernswärd 1986). But the diagnosis and management of cancer can have a major impact on every aspect of patients' quality of life (Ozyilkan 1998).

Cancer is frequently treated as a chronic disease, necessitating numerous periods of treatment and continual surveillance. Side–effects of chemotherapy and radiotherapy may require additional medical interventions, as will the symptoms of progressive disease such as pain and debilitation. Every factor that is fundamental to overall quality of life is at significant risk of compromise (Garfinkel 1991).

Anticancer treatments used to be evaluated mainly in terms of length of survival, with a disregard for the quality of survival. Now, partially because some chemotherapy regimens have such unpleasant side-effects, systemic measures of quality of life are being introduced, in clinical trials and in everyday clinical practice (Fallowfield 1990). Coates (1992) states that a balance must be found between the good and the harm that a given treatment is likely to achieve. Breast cancer is a common cancer for which chemotherapy is effective but toxic and which causes controversy that might be lessened by more frequent use of appropriate quality of life assessment. With the current emphasis on "quality of life", new treatment techniques should try to minimize side effects as well as achieving better rates of cancer cure (Barraclough 1994).

The need to measure quality of life in the clinical setting is especially important in studies where survival advantages on various treatment arms may be minimal. Performance status and measures of pain provide important information, but an additional valuable dimension is measured by the patient's assessment of their functional and psychological status (Finkelstein 1987).

The true potential of a quality of life assessment is in its capacity to contribute to the design of a treatment regimen or to monitor clinical practice (Barofsky 1986).

3.2 THE METAMORPHOSIS IN MEDICAL CARE

A dichotomy has developed in the last fifty years: treatments have become much more powerful and life support systems have been developed that enable far more toxic treatments to be given, than could previously be considered. Thus the situation of "better " scientific medicine capable of replacing neoplastic bone marrow versus humanistic medicine, more in tune with patients' feelings and aspirations has developed. The validity of quality of life studies is intensified, because they represent a measure closer to the ultimate outcome measure in clinical medicine: the ability of a patient with an illness to carry on living a life of functional and philosophic meaning (Schipper 1986).

3.3 PROBLEMS AND ISSUES FOR FURTHER INVESTIGATION

3.3.1 GENERAL PROBLEMS

According to Bergner 1989 four broad problems arise from examination of the clinical research that assesses quality of life or health:

1. Conceptualization of the construct. The terms quality of life, health status and functional status are often used interchangeably and without specific definition. Each investigator must think about his or her own study, the study population, and the intervention and decide what should be assessed.
2. The need for and value of a "gold standard" for measuring health status. There is however, no gold standard. Health status, like intelligence, is a complex attribute that requires a multidimensional measure at the very least. The choice of an intelligence test for a particular situation is based on that situation.
3. The clinical significance and sensitivity of the measures. Intelligence tests do have an important advantage over measures of health status or quality of life. They have been used often enough, so that the meaning of a particular score is understood. The clinical importance of score differences in health status are still unclear, and the meaning of any particular score on a health status measure does not produce a mental picture of a real patient. There is also considerable uncertainty about the sensitivity of the measures to changes within the same person or sensitivity to differences between people.
4. Practical problems of administration.
    - Questionnaires can be self-administered or conducted as an interview. We do not know much about the equivalence of these methods, nor about the effect of the place in which the questionnaire is completed.
    - Questionnaires may be inappropriate for some segments of the population, such as illiterate people, people who are not proficient in the English language or people of different cultures to the cultural group that the questionnaire was developed and tested on.

3.3.2 NON-COMPLIANCE

Hopwood and coworkers (1998) conducted a survey to find out how quality of life questionnaires were being administered, with the aim of standardizing procedures and improving compliance. Logistical problems included unavailability of staff or lack of questionnaires (organizational) and patient-related problems (patient was too ill, or had difficulty reading or left before completing the form). Patient refusals were an uncommon reason for non-compliance and patients were considered to be generally in favour of quality of life assessment. Measures to improve these problems include publishing guidelines for quality of life administration and information leaflets for patients together with staff training.

Seidman et al. (1995) studied quality of life in patients with metastatic breast cancer receiving paclitaxel and granulocyte colony stimulating factor (G-CSF) in a phase II trial. They found that the difficulties encountered with longitudinal data collection in a medically ill population further complicated efforts to obtain comprehensive information and introduced a dropout bias. Although methods may be employed to enhance patient compliance, difficulties unique to patients with metastatic breast cancer, such as removal from study because of disease progression and noncompliance as a result of high levels of symptom distress, may be unavoidable.

3.4 ASPECTS OF IMPORTANCE TO THE PATIENT

Studies have shown that patients are primarily concerned with non-physical matters, whereas studies designed by clinicians and most quality of life measures consider mostly physical signs (Schipper 1986, Coates 1983).

In addition to their role in clinical trials, there is a need to identify, on an individual basis, issues that may adversely affect the patient's quality of life. Ideally an instrument could be used effectively in both situations and allow reassessment of any intervention designed to improve quality of life. One reason for attempting to understand and measure quality of life is to provide for the increasing demand for informed choice for patients. (Jenney 1998).

Physicians are often unaware of important changes in their patient's physical and emotional functioning. A physician may easily spend years writing "doing well" in the notes of a patient who has become progressively more crippled before his eyes. Thus standardized information on functional ability may be useful in clinical care as well as in research. The value of such information has been shown for geriatric inpatient evaluation units, but has been harder to show for other kinds of care (Deyo 1991).

3.5 UNWANTED EFFECTS OF TREATMENT

"I knew I had cancer. They advised an operation and I declined, not because of heroism but because it did not agree with my view on life and death. I had no alternative. They should have taken out my bladder, irradiated me, and the whole incident would give me a 35% chance of survival, mutilated and for a limited time. We are all going to die. Some of us very soon, others much later. My experience is: we live a better life as it is, namely, for a limited time. Then it hardly matters how long the life prolongation lasts, when all is lost in eternity" (Stjernswärd 1986).

Unfortunately the majority of medical treatments and interventions do not only have purported beneficial effects, but also have unwanted and unpleasant side effects. The therapy may affect aspects of a person's life that are not strictly medical. It may not be pleasant to become bald and nauseous. The consequences of treatment and treatment-related side-effects may affect all of the patient's life. Therefore, a quality of life assessment should be performed (Bergner 1989).

3.6 BENEFICIAL EFFECTS OF TREATMENT

Researchers are not only interested in the unintended adverse effects of treatment but also the unintended beneficial effects (Bergner 1989).

Cancer is feared as a life-threatening disease that conveys a threat of intractable pain, hopelessness and wasting away before death occurs (Klagsbrum, 1983). Although advanced and successful forms of cancer treatment such as chemotherapy are available many adverse and unrelenting side effects must be endured. Precious little is known about the coping strategies of those undergoing chemotherapy. Understanding these experiences would provide health professionals with valuable insights into ways families cope, thus enhancing their quality of life (Wilson & Morse, 1991).

Drug companies and manufacturers of medical devices are also consumers of quality of life and health status assessments. One reason is that proof of benefits of new drugs must be established, especially when they may be more costly. If a new drug is shown to have quality of life benefits, this is also a very useful marketing advantage (Bergner 1989).

Unfortunately, most of the drug company studies are not published or are published long after they are completed because they deal with new products or new uses for old products. Two examples can be instructive. One is the auranofin trial sponsored by Smith, Kline and French (Bomardier 1981) and the other is the trial of captopril sponsored by Squibb (Croog 1986). Both trials were designed with a primary focus on variables that are neither medical nor physiologic. The auranofin trial's objectives were to study the costs and benefits of auranofin and uses existing multidimensional measures of health status and illness-related symptoms. The captopril trial examined specific aspects of quality of life with specific and independent measures that assessed depression, distress, fatigue, impotence, cognition, etc. The measures were a mixture of existing measures, modifications of existing measures and new measures developed specifically for this trial. Outcomes of therapy were presented for each measure with no attempt at integration or aggregation (Bergner 1989).

3.7 QUALITY OF LIFE EVALUATION AS AN INTEGRAL PART OF CLINICAL TRIALS

It is now generally agreed that quality of life should be measured as an integral component of most cancer clinical trials, particularly where treatments are given with palliative intent. However, this is easier said than done. Time is short in busy cancer clinics and with increasing emphasis on trials including large numbers of patients carried out mainly in district general hospitals the logistics are formidable (Slevin 1992). There has been an increasing recognition of the need to incorporate assessment of quality of life into clinical trials. A joint working group of the Food and Drug Administration and the National Cancer Institute has recommended that end points in clinical trials should include an assessment of quality of life (Jenney 1998). The clinical usefulness of comparative (randomized) trials would be greatly enhanced if results were also expressed in terms of quality of life (Bernheim 1987).

Quality of life studies have been used to describe follow-up to a single treatment modality, such as bone marrow transplantation or in randomized clinical trials. Depending on the goals of the study and the suitability of the instruments selected, comparisons can be made within the study population by clinically relevant sub-groupings or can be made with normative data from the general population to describe deviations in global or domain-specific assessments (Parsons 1998).

One of the most important objectives of all clinical research in oncology is to improve care of patients with malignant disease. The benefits of a cancer treatment regimen should outweigh its cost in patient suffering. By adding quality of life end points to the traditional end points of overall survival, disease-free survival and tumor response, medical researchers can make more informed decisions about risk-benefit trade-offs (Moinpour 1989).

Classic examples of how quality of life measurement can inform physicians and improve medical practice are found in the trials by Sugarbaker et al. (1982) and Hicks and coworkers (1985). The reporting of unexpected treatment impacts on quality of life variables led to changes in procedures for radiotherapy and surgical and physical therapy for patients with soft tissue sarcoma. These changes were associated with improved patient functioning.

Improved quality of life as a result of cancer treatment is highly valued by patients and physicians and is deemed an important criterion for approval of new agents and by extension, new combinations of agents – by the Food and Drug Administration (Dreicher 1998).

A study by Glimelius et al. (1989) provides valuable insight into the relation between disease control and quality of life. Chemotherapy for patients with advanced colorectal cancer is given with palliative intent. In a study of less toxic single agent 5-fluorouracil versus a more toxic combination arm of 5-fluorouracil plus methotrexate and leucovorin rescue, the patients on the combination arm had a greater response rate. Despite the increased toxicity, 55% of the patients given combination chemotherapy rated themselves as having an improved quality of life compared with only 9% of the single agent group. This suggests that the intensive chemotherapy was superior as a palliative treatment in this patient population.

A study by Kaasa and coworkers (1988) again suggests that side effects were not the major determinants of quality of life. The overall improvement in quality of life in both groups (radiotherapy or chemotherapy for non-small cell lung cancer), despite a response in only a minority, suggests that the benefits may be related to the optimism and support provided by close medical supervision.

The key policies recommended by the South Western Oncology Group (SWOG) for inclusion of quality of life endpoints in certain trials are:

- Begin assessment of quality of life in specific types of phase III protocols.
- Always measure physical functioning, emotional functioning, symptoms (general and protocol specific) and global quality of life separately.
- Include measures of social functioning and additional protocol specific measures if resources permit.
- Use patients-based questionnaires with psychometric properties that have been documented in published studies (McMillen 1989).

A most important aspect of a phase III study is the quality of the patient's survival. It seems nonsensical to apply a therapy which detracts from the quality of survival while causing objective tumor response. The patient only appreciates the toxicity of the therapy, if he is deriving a significant improvement in function as a result of the treatment. In this respect the evaluation of the quality of survival and subjective improvements is important during these studies, but as yet they (these factors) cannot be used as objective response criteria (Jones 1988).

3.7.1 THE ADJUVANT SETTING

In adjuvant therapy and even more in preventative interventions, the woman who undertakes more or less toxic treatment does so in the hope of future gain. In neither case does the patient have discernable disease at the time that therapy is used; thus any morbidity incurred can be compensated only by delay of disease or death. Where alternative strategies for the pursuit of such benefits are being compared, it is important to measure the impact of each on quality of life (Coates 1993).

In order to improve assessment of the cost-benefit balance in a trial comparing adjuvant therapies of differing intensity and duration, it was considered as important to measure quality of life related aspects prospectively. Serial quality of life assessments were obtained every three months for 2 years from patients with operable breast cancer in two ongoing International Breast Cancer Study Group (IBCSG) randomized clinical trials of adjuvant treatment. The quality of life assessments included patient-derived perceived coping (PACIS, personal adjustment to chronic illness scale), well being (Bf-S, Befindlichkeitsskala von Zerrssen), mood, physical well being and appetite (LASA, linear analogue self assessments). The analysis of serial assessments for 265 patients with each of the first four assessments completed showed that all measures improved with increasing time from study entry; that the degrees of improvement for the four major language groups were similar; and that measures were sensitive to treatment difference. Hürny et al. (1992) concluded that the measurement of quality of life related aspects in a multicultural clinical trial are feasible and possibly relevant for the evaluation of treatment results.

The research efforts to evaluate quality of life and improve survival with breast cancer adjuvant therapy have proceeded largely independently of one another. Patients rely heavily on their physician to weigh the potential benefits and risks of therapy alternatives and provide clear treatment recommendations. Since physicians play the central role in the evaluation of adjuvant therapy, quality of life must assess a concept relevant to physicians if it is to be clinically useful (Fetting 1988).

An important next step in quality of life research is what Levine et al (1988) call the "responsiveness" of quality of life measures. One aspect of this effort is to determine how well quality of life measures distinguishes among regimens in an adjuvant trial. The researchers demonstrated that their measure distinguished between patients who had completed and patients who were still receiving adjuvant therapy. But physicians do not need a test to tell them that quality of life is reduced in patients on adjuvant chemotherapy compared to those who have completed treatment. A litmus test for these measures will be how well they discriminate among regimens not so obviously different (Fetting 1988).

The first and most important finding is that adjuvant therapy improves disease-free survival in patients with stage I breast cancer. This is promising but the majority of stage I patients never develop a recurrence. Until better methods predicting recurrence or diagnosing micro metastatic disease are developed, the majority of stage I patients will be treated needlessly. The impact on these patients is of major concern (Fetting 1988).

Secondly, one real possibility is that the more intense regimens being developed for future adjuvant therapy may prove only marginally better than current therapies. Regimens with such modest survival benefits will be more compelling if it can be documented that the impact of therapy on patients is not significantly more detrimental than that with standard regimens. To date the impact of treatment has been inferred from survival and toxicity data. Survival data says nothing about the quality of survival. Toxicity evaluations describe the type, frequency, severity and duration of toxicity but do not describe personal and/or social consequences (Fetting 1988).

An intergroup trial was conducted to compare an investigational 16-week regimen with a standard CAF-regimen (cyclophosphamide, doxorubicin and fluorouracil). The 16-week regimen features greater doxorubicin and fluorouracil dose-intensity than CAF and improved scheduling of anti-metabolites with sequential methotrexate and fluorouracil, as well as infusional fluorouracil. This trial was given as adjuvant therapy for node-positive, receptor-negative breast cancer patients in the adjuvant setting.

Breast cancer outcomes included recurrence as well as disease-free overall survival. Toxicity was evaluated by the Common Toxicity Criteria. Treatment related quality of life was assessed by the Breast Chemotherapy Questionnaire (BCQ) before, during and 4 months after treatment in 163 patients. During treatment, quality of life declined significantly more with the 16-week regimen than CAF, but by 4 months post-treatment, there was no difference.

The 16-week regimen produced marginally better breast cancer outcomes than CAF with similar toxicity but a greater reduction in during-treatment quality of life. It was concluded that the 16-week regimen should not be used instead of a standard-dose regimen without careful consideration of its pros and cons (Fetting 1998).

Late effects of adjuvant treatment on perceived health and quality of life were assessed through a questionnaire mailed to 448 premenopausal and postmenopausal breast cancer patients, free from recurrence 2-10 years after primary therapy. The patients had been randomized to postoperative radiotherapy or adjuvant chemotherapy as adjuncts to primary surgery. The differences between the two treatments were generally small. However, the radiotherapy patients had significantly greater problems with decreased stamina, symptoms related to the operation scar and anxiety. The chemotherapy patients had significantly more problems with smell aversion. Activity level inside and outside the home, anxiousness and depressive symptoms were similar in both groups. The chemotherapy group scored their overall quality of life higher than the radiotherapy patients (Berglund 1991).

Gelber et al. (1991) looked at a large randomized trial comparing a single cycle of preoperative adjuvant chemotherapy with six cycles of conventionally timed chemotherapy. The quality of life would be expected to be significantly worse with the longer, more intensive chemotherapy but at five year follow up the patients who had received the longer therapy had better five year survival than those who received a single preoperative cycle. The quality of life was evaluated by using Q-twist, which looks at the quality adjusted time without symptoms. Despite the greater initial toxicity with the more intensive and longer chemotherapy these patients had a longer freedom from disease and less time with the problems of recurrent disease and its treatment. There was thus an improvement in both quantity and quality of life for patients who received the more intensive therapy.

3.7.2 THE METASTATIC SETTING

End points related to quality of life have only recently been incorporated into clinical trials. Their use in randomized, controlled (phase III) studies is increasing and is providing valuable comparative data. The potential utility of such measurements in single-arm efficacy (phase II) trials has received less attention but possibly provides the means to explore the interactions among quality of life, tumor response and treatment toxicity. Additionally, a baseline quality of life assessment often is a predictor of survival in patients with advanced breast cancer (Seidman 1995).

Seidman (1995) studied quality of life in a phase II trial of paclitaxel and G-CSF (granulocyte-colony stimulating factor) for the treatment of metastatic breast cancer. They found the information provided by quality of life measures to be quite useful, but caution that it must be recognized that interpretation of subjective data in a single-arm, open-label trial is inherently problematic. The sample size available for evaluation in most phase II trials is small, and results may not be generalizable. Furthermore, patients eligible to receive a promising new agent may experience feelings of optimism and well being not related to the treatment itself.

In the Seidman (1995) study favorable response was associated with improved quality of life. The improved symptoms and other quality of life parameters in patients with partial tumor response suggest an acceptable balance between the antitumor effect and drug-related morbidity. For patients with progression of disease it is difficult to ascertain the relative contribution of drug-related toxicity and disease progression to the decline in quality of life scores.

Priestman and Baum carried out one of the earliest studies looking at the effect of treatment on quality of life in advanced breast cancer in the mid-1970s. This study used linear analogue self-assessment scales to compare subjective responses in a trial of patients with advanced breast cancer randomized to endocrine or cytotoxic treatment. The higher response rate in patients receiving cytotoxic chemotherapy correlated with a better overall quality of life than that found in patients receiving endocrine therapy despite the higher incidence of side effects with cytotoxic chemotherapy (Slevin 1992).

Another trial in advanced breast cancer was conducted by the Australian/New Zealand breast cancer trial group, which randomized patients to receive either continuous or intermittent combination chemotherapy. In patients receiving intermittent therapy, treatment was stopped after three cycles if the disease did not progress. If the disease later progressed the treatment was given for a further three cycles (Coates 1987).

The other arm of the study received continuous chemotherapy. The results of this study were counterintuitive. Overall quality of life, response to treatment and time to ultimate treatment failure all favored continuous therapy. Patients receiving intermittent therapy possibly had increased anxiety when they were not having treatment. However, the changes in quality of life were also found to be significant independent predictors of survival. This suggested that the quality of life reflected the state of the metastatic disease and that the increased side effects of chemotherapy were outweighed by the benefit the patients received from having better disease control (Coates 1987).

Metastatic breast cancer is rarely curable with standard chemotherapy. Since a significant portion of patients with operable breast cancer are candidates for adjuvant chemotherapy with cyclophosphamide/methotrexate/fluorouracil (CMF) or cyclophosphamide/doxorubicin/fluorouracil (CAF) or similar regimens, many patients with advanced breast cancer will have already been exposed to the drugs most commonly used to treat advanced disease, rendering them less likely to respond to such treatment a second time. The identification of active new drugs or drug combinations, therefore, is urgently needed (Perez 1996).

The optimal dose for megestrol acetate could be determined with additional support from quality of life date. Patients with stage IV breast cancer were randomly selected to receive either 160, 800 or 1600 mg of megestrol acetate daily. This medication is used as second-line hormonal therapy for advanced breast cancer. Quality of life was assessed at trial entry and at 1 and 3 months during treatment. At 3 months, women treated with 160 mg per day reported less severe side effects, better physical functioning, less psychologic distress and improvements in quality of life compared with those treated with 1600 mg daily. Patients who received 800 mg daily fell between the low- and high-dose arms in intensity of drug side effects, but responded similarly to those in the 160 mg group in terms of physical functioning, psychologic distress and overall quality of life. Thus the 160 mg daily dose may be optimal, achieving maximal treatment effects with fewer side effects and better quality of life (Stefaneck 1994).

A phase II trial evaluating the efficacy of the paclitaxel/carboplatin combination, along with an evaluation of thrombopoietin levels and quality of life (using the FACT-B instrument), was initiated in 1996. Results from this trial will help document the role of the paxlitaxel/carboplatin combination in the treatment of women with breast cancer (Perez 1996).

The result of the analysis of QOL for metastatic lung cancer patients EST 4983 showed that the variables which are highly correlated with a higher quality of life are good performance status and being male (Finkelstein 1987). Pain, race, education, marital status and living arrangements did not show any association with the QOL score after accounting for performance status and sex. The type of therapy and whether it was single agent or combination therapy also did not show any association with the QOL score. This is also true for treatment complications.

Measurements of functional status are important for the assessment of lung cancer therapies, and minimally, this can be achieved by assessment of changes in pain, performance status, and weight, which are made at each cycle of therapy. Patient-reported assessment of quality of life may also be important. However, the results of EST 4983 did not conclusively show the value of the QOL instrument, because of poor patient compliance.

Results of a phase II study for the treatment of ovarian cancer show that quality of life as measured, based on the score from the FACT-O, improved over time with a statistical significant difference from baseline detected during therapy and at the end of therapy ($p<0.01$). The purpose of the study was to evaluate an outpatient Taxol and Carboplatin regimen for patients with suboptimally debulked ovarian cancer. The specific objectives of the study were to evaluate the objective response rate and toxicity, to evaluate the progression-free interval and overall survival, and to describe changes in quality of life over time, in patients receiving Taxol plus Carboplatin. The minimal toxicity of the regimen is reflected in the high percentage of patients that completed therapy. The objective response rate was 72 %, the median duration of response was 11 months and the median overall survival was 30 months for patients with measurable disease. The favorable outcome of this trial is further supported by the improvement of quality of life that was demonstrated (Weller 1998).

The use of megestrol acetate in the treatment of weight loss in gastrointestinal cancer patients has been disappointing. The aim of the study by McMillan et al. (1999) was to compare the combination of megestrol acetate and placebo with megestrol acetate and ibuprofen in the treatment of weight loss in such patients. Quality of life was assessed with the European Organization for Research and Treatment of Cancer's EuroQol-EQ-5D and EORTC QLQ-C30. It was found that the combination of megestrol acetate and ibuprofen appeared to reverse weight loss and appeared to improve quality of life in this patient group.

Many of the published results on palliative treatments demonstrate effects on remission or time to progression but no effects on the function of the tumour which result in decreased survival and impairs quality of life. If there are only marginal effects on duration of survival, which is in fact true for most palliative treatments, it is essential to demonstrate that our clinical interventions improve the quality of the patients' remaining life (Porzsolt 1993).

TABLE 1: CHEMOTHERAPY AND QUALITY OF LIFE (SLEVIN 1992)

- More effective therapy is usually associated with better quality of life.
- More intensive therapy is therefore not always associated with lower quality of life.
- Side effects may be less important than control of disease.
- Patients may report improved quality of life despite showing no objective response. This could be related to
    - minimal tumor shrinkage giving relief of symptoms
    - increased medical attention
    - provision of hope
    -

3.8 QUALITY OF LIFE AS A PROGNOSTIC FACTOR

Baseline quality of life assessment may provide prognostic information distinct from that obtained through standard prognostic indicators alone. Seidman et al. (1995) found that the combination of two factors - extent of disease and baseline quality of life assessment – predicted survival more accurately than either used separately.

During quality of life (QOL) validation studies, it was noted that changes in some QOL scores were significantly associated with prognosis (Coates 1987, Coates 1988). Quality of life data can be analyzed to investigate the relationships between measured aspects of QOL and survival duration (Coates 1992). Baseline QOL scores recorded at the time of randomization were used as predictors of survival starting from that time. All baseline QOL scores except those for pain were significant predictors of overall survival. In a multivariate model, simultaneous allowances were made for significant non-QOL prognostic factors (performance status, liver metastases, brain metastases and node metastases).

Additionally Coates (1992) found that the tumor response category was clearly related to change in QOL scores, during the first three cycles of chemotherapy. Scores for physical well-being, mood, appetite, and the uniscale and QOL index all improved significantly in the group as a whole and in patients achieving a response, but there was no significant change among non-responders.

The association that Coates (1992) observed in his study between survival and scores in simple, practical measures of QOL (5 linear analog self-assessment scales for patients and the Spitzer scale completed by the physician) provides an additional powerful argument for including such measures in clinical trials and routine practice of oncology.

The prognostic value for survival of the Quality of Life Core Questionnaire of the International Breast Cancer Study Group was demonstrated in various cancer sites. Among the scales previously described as predictive were single item linear analogue self-assessment (LASA) scales for physical well being and overall quality of life. The independent prognostic information carried by such measures was again shown in patients with advanced malignancy who filled in the European Organization for Research and Treatment of Cancer (EORTC) questionnaire QLQ-C30. Single-item scores for global health status and QOL remained independently prognostic after controlling for performance status and age, and, among solid tumor patients, metastatic site. This association was also present for the social functioning scale but not for the other functional and symptom measures (Bernhard 1997).

Several studies have recently reported on the importance of quality of life in predicting the survival of patients with lung carcinoma. To confirm these reports, the relationship between survival and quality of life, as measured by the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire and Duke-UNC Social

Support Scale, was examined within a group of patients with advanced non-small cell lung carcinoma treated in a randomized clinical trial. Patients completed the questionnaires at baseline. The Cox proportional hazards model was used to determine the incremental contribution quality of life provided in predicting survival beyond the effect of known clinical prognostic variables. It was found that this study did not confirm the prognostic importance of overall quality of life. Rather, after adjustments for significant clinical factors, a patient-provided pain report had the greatest prognostic importance (Herndon 1999).

3.9 TO IMPROVE STANDARDS OF CARE

In clinical experience, quality of life assessment in cancer patients may be a supportive intervention by itself, increasing awareness of quality of life issues in both patients and staff (Bernhard 1995).

Because a large part of medical care is directed at managing chronic diseases, wider availability of quality of life information would enhance our ability to assess quality of care and to compare alternative management strategies (Deyo 1991).

3.9.1 SURGERY

For breast cancer

The approach with regard to surgery of breast cancer has undergone a metamorphosis in the last thirty years. The view that breast cancer can be treated as a regional disease solely by aggressive surgical techniques has been proven incorrect. A shift has taken place from the routine performance of a radical mastectomy, to modified radical mastectomy, to segmental mastectomy or lumpectomy. Now even the routine practice of axillary dissections, is being challenged by the concept of sentinel node biopsies (Ganz 1999).

Mastectomy still prevails as the key treatment for early breast cancer, so little is as yet known of the psychological effects of conservative surgery. There is controversy in the literature over the beneficial effects on quality of life that lumpectomy patients experience versus those experienced by mastectomy patients. Some researchers claim that there is a benefit for lumpectomy patients and others find that there is no benefit. It is imperative that clinical trials focusing on the outcomes of different procedures on survival should include rigorous measures of psychological outcome alongside other variables. It has to be borne in mind that lumpectomy patients require radiotherapy and this can also cause psychological problems.

The body image of women is clearly more affected by mastectomy than by breast conserving treatment even several years after treatment. Sneeuw et al. (1992) examined the relationship between cosmetic and functional results of breast conserving therapy and psychosocial functioning in a sample of 76 patients with early stage breast cancer. Psychological functioning was measured with the 28-item version of the General Health Questionnaire (GHQ see chapter 2 Addendum 11). High levels of psychological distress, disturbance of body image (concerns about disfigurement and loss of femininity) and decreased sexual functioning were noted in approximately one-quarter of the study sample. About half the patients expressed concerns with disease recurrence and their future health. Psychosocial problems were only modestly associated with treatment-related cosmetic and functional outcomes, as determined by clinical ratings and objective assessments. The patient's own ratings of breast cosmesis and arm functioning exhibited somewhat higher correlations with self-reported psychosocial functioning. In particular, a significant association was noted between the patient's ratings of overall cosmesis and arm edema and their body image. The association between cosmetic and functional results and self-reported psychosocial health was strongest among those patients younger in age and treated longer ago. The patient's own assessments of cosmetic and functional outcomes should therefore be used as the primary source of information.

Dr. Maguire cites a number of articles that indicate fewer body image problems with lumpectomy than with mastectomy. Some of these lumpectomy patients however, experienced increased anxiety due to excessive fear of recurrence of their cancer (this anxiety may have been due to inadequate preoperative counseling). The foregoing seems to be the main evidence supporting Dr. Maguire's thesis that "breast conservation does not reduce psychological morbidity." In our own patients we found that the lumpectomy patients had significantly less loss of feelings of attractiveness and femininity than the mastectomy patients. Additionally, lumpectomy patients rated their husbands' sexual behavior as having been enhanced after surgery whereas the mastectomy patients felt that their husbands' sexual behavior showed a decline. We also compared the two treatment groups with regard to the frequency of severe sexual dysfunction; this was almost three times as common in the mastectomy group as in the lumpectomy group (Wise 1994).

Axillary lymph node dissection (ALND) has been a standard procedure in the management of breast cancer. In a patient with a clinically negative axilla, ALND is performed primarily for staging purposes, to guide adjuvant treatment. Recently, the routine use of ALND has been questioned because the results of the procedure may not change the choice of adjuvant systemic therapy and/or the survival benefit of a change in adjuvant therapy would be small. Parmigiani and coworkers (1999) constructed a decision model to quantify the benefits of ALND for patients eligible for breast-conserving therapy. The largest benefits from ALND are seen in estrogen receptor (ER) positive women with small primary tumors who might not be candidates for adjuvant chemotherapy if their lymph nodes test negative. Virtually no benefit is found in ER negative women, almost all of whom would receive adjuvant chemotherapy. When adjusted for quality of life, ALND may have an overall negative impact. In general the benefits of ALND increase with the expected severity of adjuvant therapy on quality of life. This model quantifies the benefits of ALND and assists decision making by patients and physicians.

Velanovich and Szymanski (1999) attempted to define the incidence and effect of postoperative lymphedema on quality of life in breast cancer patients. They used the SF-36, a generic instrument, measuring eight domains of quality of life (see chapter 2 and addendum 2). Patients were divided into three groups: breast surgery without axillary lymph node dissection (ALND), breast surgery with ALND but no lymphedema and breast surgery with ALND and lymphedema. Patients in the "without ALND" and "no lymphedema" groups had similar scores in all domains of the SF-36. However, patients in the "positive lymphedema" group had significantly lower scores in the domains of role-emotional and bodily pain. Although lymphedema occurred in only 8.3% of patients, it produced demonstrable diminutions in quality of life. Therefore, efforts to reduce the incidence of lymphedema, such as sentinel lymph node biopsy or selective ALND, are to the benefit of breast cancer patients.

One of the most vexing late effects of axillary-node dissection is lymphedema of the arm. Though rarely life threatening, it is one of the most troublesome and feared consequences of breast-cancer surgery. Among women who have undergone radical mastectomy, up to 60 percent have lymphedema. The frequency is about 30 percent in women treated with modified radical mastectomy or breast-conserving surgery. For women who also receive radiation to the axillary area, the rate of lymphedema is higher (Loprinzi 1999).

Lymphedema is an important problem for women who survive breast cancer because it is unsightly, painful, restricts arm movement, increases the risk of infection and the swelling can be psychologically distressing. The management of lymphedema is also difficult.

Loprinzi (1999) used a prospective, double blind, randomised, and crossover design study, to see whether coumarin was effective in reducing lymphedema. The outcome of treatment was evaluated by detailed measurements of arm volume and a questionnaire completed by each patient. A lack of efficacy was demonstrated and we are also alerted to the potentially serious hepatotoxic effects of the drug.

For other kinds of cancer

Quality of life evaluation is one of the parameters used by surgeons to evaluate new surgical approaches in gastric cancer. Considering quality of life, endoscopic mucosal resection or laparoscopic wedge resection is the best front-line therapy for several mucosal cancers. It was found that evaluation of all information concerning tumor stage, location, histologic type, expected survival and quality of life after resection, is of paramount importance for the surgeons planning future approaches (Roukos 1999).

An assessment of the long-term results of surgery for temporal bone paragangliomas, with special consideration of the patients' ability to cope with the functional deficits was performed by Briner et al. (1999). The otologic extradural approach allowed complete tumor removal in 83% of patients, with minimal perioperative morbidity. Seventy-five percent of the patients regained their preoperative quality of life and 97% returned to their previous occupation in 1 to 2 years.

The ileoanal pull-through procedure is gaining increasing favor and use in surgical treatment of children with ulcerative colitis and familial adenomatous polyposis. Participants completed the standardized Medical Outcome Study Short Form-36 (SF-36), which has well-established normative values (see chapter 2 and addendum 2). The study group was not statistically different from age-appropriate population normal values on all assessable scales of physical and mental health in the SF-36 survey including physical functioning, role limitations-physical, bodily pain, general health, vitality, social functioning, role limitations-emotional and mental health. The surgical scar was the sole negative factor of significance. It was concluded that the ileoanal pull-through procedure is an excellent surgical option for children with ulcerative colitis or familial adenomatous polyposis and it produced minimal, if any, adverse effects on their long-term quality of life (Shamberger 1999).

During recent years considerable interest has been focused on quality of life as an additional therapeutic outcome measure in the surgical treatment of gastric carcinoma. However, the long-term consequences of gastrectomy and the impact of quality of life of different reconstructive techniques are still a matter of controversy. To broaden the criteria for choice of treatment, Svedlund and co-workers (1999) conducted a prospective randomized clinical trial to determine the impact of various gastrectomy procedures on quality of life during a 5-year follow-up period. Consecutive patients eligible for curative gastric cancer surgery were randomized to have either total or subtotal gastrectomy or a jejunal S-shaped pouch as a gastric substitute after total gastrectomy. Assessments of quality of life were made on seven occasions during a 5-year period. Survival rates were similar in all treatment groups. Patients who had a total gastrectomy continued to suffer from alimentary symptoms, during the entire follow-up period. However, patients who underwent subtotal gastrectomy had a significantly better outcome. Patients given a gastric substitute after gastrectomy improved with the passage of time and had an even better outcome in the long run. It was concluded that patients' quality of life must be taken into consideration in order to optimize the rehabilitation after gastrectomy.

Esper and coworkers (1999) conducted a descriptive comparative study to evaluate the quality of life experience in patients who are receiving treatment for advanced prostate cancer. The relationship between response to the treatment and quality of life was investigated. Patients, who demonstrated response to therapy based on declining prostate specific antigen levels, demonstrated a significant increase in their quality of life scores compared to those patients who were not responding to treatment. Although significant differences in survival at this stage of prostate cancer, in patients who receive therapeutic treatment versus those who do not, have yet to be demonstrated, there appears to be a benefit in quality of life for those patients who respond to therapy. This data supports the use of quality of life measurements in patients undergoing treatment for advanced prostate cancer. This information can be used in discussions with patients who are facing treatment decisions and who are concerned about the impact of treatment on their overall quality of life.

Hillmann and coworkers (1999) performed a study to determine whether there is a difference, with regard to functional outcome and quality of life, between endoproshetic replacement and rotationplasty for the treatment of malignant tumors of the distal past of the femur or the proximal part of the tibia. Quality of life was measured with the European Organization for Research and Treatment questionnaire (see chapter 2 and addendum 17). A scale developed by the Muscoloskeletal Tumor Society was used to evaluate functional results. There was no statistical difference in functional scores between the two methods of treatment. Quality of life was significantly higher for hobbies and other daily activities for patients who had had a rotationplasty, who also experienced less pain restricting their daily activities. Despite good functional and quality of life results, the cosmetic appearance may be the most serious disadvantage of rotationplasty.

The quality of life of elderly patients (performance status 0 to 2) with advanced non-small cell lung cancer was explored in a randomized trial that compared vinorelbine treatment with supportive care alone. Quality of life was evaluated with the European Organization for Research and Treatment of Cancer questionnaires QLQ-C30 (see chapter 2 and addendum 17) and QLQ-LC13. Vinorelbine-treated patients scored better than control patients on quality of life functioning scales, and they reported fewer lung cancer-related symptoms but reported worse toxicity-related symptoms. It was concluded that vinorelbine improves survival of elderly (70 years and older) patients with advanced non-small cell lung cancer and possibly improves overall quality of life (Anonymous 1999).

Cruickshanks et al. (1999) attempted to determine whether quality of life differs between patients with choroidal melanoma treated with enucleation and those treated with radiation therapy. Quality of life was assessed using the Medical Outcome Study Short Form 36 (see chapter 2 and addendum 2) and the National Eye Institute Visual Function Questionnaire and by the Time-Tradeoff interview method. After adjusting for factors that could exhibit an influence, there were few differences in any of the quality of life measures by treatment status. It was concluded that choice of treatment for choroidal melanoma does not seem to be associated with large differences in quality of life during long-term follow up.

In a prospective multicenter trial, patients with metastatic colorectal cancer who had failed 5-fluorouracil therapy were randomized to receive either best supportive care plus treatment with irinotecan or best supportive care alone. Overall survival, the primary end point of the study, was significantly improved in patients receiving the irinotecan treatment. Appreciable deterioration in global quality of life (50% from baseline) occurred significantly later in the irinotecan-treated patients than in the controls. Additionally, for quality of life analyses of all symptoms, except diarrhea, mean scores were significantly in favor of patients assigned to the irinotecan treatment than for those assigned to best supportive care alone. This is the first time that the benefit of second-line chemotherapy has been demonstrated by a randomized controlled trial in advanced colorectal cancer (Cunningham 1999).

In a study by Van Cutsem (1999) patients with non-bulky metastatic colorectal cancer who had failed first-line 5-flurouracil therapy were randomized to receive second-line treatment with either irinotecan or a high-dose infusional 5-fluorouracil regimen. Patients treated with irinotecan survived significantly longer than those treated with infusional 5-fluorouracil. Overall, mean global quality of life scores were similar in the two arms of the study throughout the period of treatment and follow-up, demonstrating that the more effective disease control achieved by irinotecan at least maintains quality of life. Indeed, deterioration of quality of life (defined as > 50% decrease from baseline score) occurred significantly later in irinotecan-treated patients. In light of these data, irinotecan should be considered the reference treatment for patients with 5-fluorouracil refractory advanced colorectal cancer.

Considered during the past as a terminal condition, peritoneal carcinomatosis was approached during the last two decades as a curable disease. The introduction of cytoreductive surgery or peritonectomy in the treatment of peritoneal neoplastic diseases drastically changed the natural history of peritoneal carcinomatosis. Another technique that showed an important impact on disease control is intraperitoneal hyperthermic perfusion, one of the most fascinating treatments of peritoneal carcinomatosis, that results in an impressive increase in overall survival and quality of life in treated patients. In addition, the morbidity of intraperitoneal hyperthermic perfusion is low (Deraco 1999).

Chronic low-frequency electrical stimulation can safely transform fatiguing muscle into fatigue-resistant muscle. This fundamental discovery was used to reconstruct the anal sphincter after abdominoperineal resection for cancer. Rouanet and coworkers (1999) investigated the oncologic, functional and quality of life results of a cohort of patients who underwent the procedure. It was found to be an oncologically safe procedure and functional results improved with time. Technical progress is necessary to improve the quality of life of patients.

3.9.2 RADIOTHERAPY

Marks and coworkers (1999) assessed the cost-effectiveness of postmastectomy local-regional radiation therapy for patients with breast cancer with regard to local-regional relapse and Quality Adjusted Life Years (QALYs). Radiotherapy reduces the risk of local-regional relapse by 67%. Absolute improvements in 10-year overall survival due to radiotherapy are assumed to vary between 1 and 12%. The cost per Quality Adjusted Life Years gained at 10 years is \$10 000 to \$110 000 for survival benefits $\geq 3\%$, which compares favorably to that of other accepted medical procedures.

3.9.3 CHEMOTHERAPY

A treatment arena with potential for quality of life assessment is experimentation with granulocyte macrophage colony stimulating factors (GM-CSF) or granulocyte colony stimulating factors (G-CSF). This therapy stimulates the bone marrow to accelerate its production of granulocyte progenitors, thereby permitting high-dose cytotoxic therapy.

Neutropenia and life-threatening sepsis can be treated with the colony stimulating factors. Evaluation of the trade-off between a greater potential for cure with a higher dose of the primary drug versus the impact of the toxic effects of GM-CSF and G-CSF on patient quality of life requires feedback from the patients regarding effects of all aspects of treatment (McMillen 1989).

Advanced metastatic non-small lung cancer that has progressed on initial cisplatin-based therapy has a poor prognosis. For these patients twenty-four hour infusions of paclitaxel as second-line therapy have shown minimal activity. Prolonged infusions of paclitaxel have shown activity in breast cancer patients who have failed short infusions of paclitaxel. In this study patients with refractory non-small cell lung cancer were treated with 96-hour paclitaxel infusions. Quality of life assessments using the Factual Assessment of Cancer Therapy – Lung questionnaire were performed at baseline and with each treatment cycle. In conclusion, although no objective responses were seen, disease stabilization occurred in 31% of patients. Overall toxicity was tolerable with no major negative impact on quality of life in those patients receiving two or more cycles of treatment (Socinski 1999).

Surgical resection offers the best chance for cure for early stage non-small cell lung cancer, but the 5-year survival rates are only moderate, with systemic relapse being the major cause of death. Pre-operative chemotherapy has shown promise. A feasibility study was performed in patients with early stage (IB, II, IIIA) resectable non-small cell lung cancer; randomized either to three cycles of chemotherapy (mitomycin-C, vinblastine & cisplatin = MVP) followed by surgery or to surgery alone. Fifty-five percent achieved objective tumor response and a further 27% minor tumor shrinkage; no patients had progressive disease. No severe (WHO grade III-IV) toxicities occurred. No significant deterioration in quality of life was detected during chemotherapy. It was thus found that pre-operative MVP chemotherapy is feasible in early stage non-small cell lung cancer (de Boer 1999).

Lilleby et al. (1999) assessed morbidity, side effects and quality of life in patients treated for localized prostate cancer with curative aim. 154 Patients had undergone definitive radiotherapy and 108 patients had had a radical prostatectomy. At least 1 year after treatment the patients completed several questionnaires assessing quality of life: The European Organization for Research and Treatment of Cancer Questionnaire

(EORTC QLQ-C30), selected questions from the Psychosocial Adjustment to Illness Scale PAIS (to assess sexuality) and certain disease specific questionnaires. Despite malignancy and/or treatment-related morbidity, quality of life was comparable in both groups with respectively 9% radiation and 6% prostatectomy patients reporting moderately or severely impaired quality of life. In the mutivariate analysis physical function, emotional function and fatigue were significantly correlated with quality of life. It was found that in spite of considerable malignancy and/treatment-related morbidity, quality of life was good or only slightly impaired in the majority of patients who presented with stable disease >1 year after definitive radiotherapy or radical prostatectomy with no difference as compared to the age-matched normal population.

3.10 AS AN AID IN CLINICAL DESCISION MAKING

If survival statistics do not seem to be significantly different for several treatment procedures then one must seriously consider issues related to self-esteem and quality of life as major determinants in decisions about choice of treatment; bearing in mind a desire to conserve body integrity and sexual prowess without compromising chances for cancer cure (Schain 1980).

In the area of primary prevention it is important that quality of life investigations in cancer not only focus on the relatively small differences in quality of life between therapeutic approaches, but also consider differences in quality of life between cancer patients and individuals free of disease. Cost effectiveness is becoming increasingly important as resources are diminishing. Many countries are considering cost-effectiveness in developing national strategies to control cancer. Comparisons are being made between the extent of cancer control that can be purchased with fixed resources: prevention versus early detection versus therapy (Stjernswärd 1986). In post-apartheid South Africa, where the emphasis has shifted to favor primary medical care and resources are limited, cost-effectiveness is also at a premium in the health services.

Stjernswärd (1986) asks: "What is the difference in quality of life for patients whose cancer is detected early and easily excised as opposed to patients who present themselves at health centers with disease in an advanced stage, where there is high morbidity with treatment, and in many cases, where only palliative therapy can be offered?"

Physicians often bear the responsibility to choose which management strategy is in the patient's best interest and must be informed about the impact of all different options on quality of life (Bernheim 1987). Incorporation of quality of life criteria has become increasingly accepted in clinical trials that test the efficacy of experimental cancer therapies. With this information, physicians and patients can approach decision-making about various treatments with a fuller understanding of their ramifications (Priestman 1976).

A landmark study, where the results of quality of life data were used to improve the quality of life of patients, is the study of Sugarbaker (1982). The study found that radiotherapy for soft-tissue sarcoma was impairing the mobility and sexual functioning of the patients. The patients' quality of life responses led to their treatment being optimized. As a result of this, a great improvement has occurred in the functional outcome of the patients. These results have provoked changes in radiotherapy, surgical procedures and physical therapy for soft-tissue sarcoma patients.

Quality of life assessments can therefore improve medical outcomes and lead to improvements in medical care (Barofsky 1986).

Quality of life information is of crucial importance in optimizing cost-benefit balances in clinical decision making (Coates 1992).

Metastatic breast cancer is not curable, but it is perhaps the most common cancer situation in which reasonable effective systemic therapy is available. Endocrine treatment is generally preferred initially, if the patient does not have dire disease, because of significantly less toxicity. Coates (1992) found that at least in some situations, the use of cytotoxic chemotherapy results in a net improvement in quality of life and that more therapy may be better than less. A similar conclusion was reached in a Canadian trial in metastatic breast cancer, one in which a reduced dosage of chemotherapy was associated with inferior objective and subjective outcomes (Tannock 1988).

Decision making in health care depends on accurate and appropriate assessment of the current status of the patient and of the impact of available therapeutic options on both the progress of the disease and the wellbeing of the patient. The net effect on the patient depends on the balance between the good the treatment may do in controlling the disease and the harm it may do by way of side effects. This balance is struck explicitly or implicitly whenever a decision is made to give or withhold a treatment. Tumor response can be categorized by means of the standard tools for tumor response. Assessment of the effect of a treatment on the tumor, in terms of response, is thus made routinely, although these tumor measurement tools are far from perfect (Coates 1992a).

The responsiveness of quality of life instruments becomes important in this context. One aspect of this effort is to determine how well quality of life measures distinguish between different regimens. A litmus test for quality of life measures will be how well they discriminate among regimens not so obviously different (Levine 1988).

QOL tools now available for assessing the impact of therapy on patients are solidly established and robust. The latest QOL instruments are arguably more directly relevant to the evaluation of the ultimate goals of therapy and demonstrably more valuable than either response or performance status in assessing prognosis. Now that simple practical scales are available, there is a strong case for their introduction into routine clinical practice. This would ensure that the level of treatment chosen is in the best interests of the patient (Coates 1992a).

In patients with ovarian cancer, quality of life is defined by the severity of the disease. In early stage disease, patients focus on the long-term effects of therapy, whereas in late-stage disease, symptom management is paramount. The chemotherapeutic agents used to combat ovarian cancer have a wide range of adverse effects, the management of which is key to ensuring a patient's quality of life. The Functional Assessment of Cancer Therapy questionnaire for ovarian cancer (FACT-O) is a short questionnaire grouped by logical categories that can be completed by most patients without assistance within 5 minutes. Furthermore, the FACT-O allows patients to weigh each category of questions based on the categories' perceived importance to the quality of the patients' lives. These two factors allow the FACT-O to be used to institute management decisions on the level of both the individual patients and the institution (Fish 1999).

3.11 TO HELP FORMULATE HEALTH POLICY

3.11.1 GENERAL

The availability of reliable quality of life assessment methods would be very important as a tool to help convince health policy makers to set the right priorities in cancer care and to establish proper resource allocation. Results from valid quality of life measures could lead to important changes in cancer control policy in several situations: from primary prevention, early diagnosis, screening and therapy, to pain relief and care of the dying (Stjernsward 1986).

The overwhelming majority of resources for cancer are allocated to finding a cure. For most cancer patients, however, no curative treatment exists. The quality of life in these patients would be better if they had access to palliative care from the start. The WHO global cancer control program is based on the concept that enough knowledge exists today about cancer to take effective action that will significantly reduce cancer morbidity and mortality worldwide, if properly implemented. There is an urgent need for rethinking. Global resources are limited as well as unequally distributed and it is not realistic to expect them to increase in the near future. Setting the right priorities and strategies in a systematic way to gain maximum benefit from available resources, preferably through well-conceived cancer control programs, has become mandatory. Without doing so, there can be little impact on cancer, especially in the less developed countries (Stjernswärd 1991).

A number of countries are now beginning to consider cost-effectiveness in developing national strategies to control cancer. Comparisons are being made between the extent of cancer control that can be purchased with fixed resources: prevention vs. early detection vs. therapy vs. palliative care. Quality of life comparisons should be made between people without cancer and those with it and early-stage versus advanced-stage cancer patients. Unfortunately, the majority of the world's cancer patients fall into the large group where no effective therapy exists and only palliative treatments can be offered. There is a need for quality of life studies to investigate the appropriateness of palliative care, rather than the administration of therapies that are known to be ineffective and are often given simply because the physician feels that he must provide some therapy for every patient. Such studies could provide the physicians and the patients with a suitable basis for making the most appropriate treatment decisions (Stjernswärd 1991).

Results from reliable and valid quality of life measures could lead to important changes in cancer control policy (Stjernswärd 1991).

Health status measures may be used to formulate health policy by providing information about the health status of populations, to evaluate innovations in health service delivery (e.g. shortened length of hospital stay) and in clinical research to evaluate new therapies. Ultimately the measures are intended to help improve the care and health of individuals (Bergner 1989).

Intensive care (ICU) is increasingly being used in the management of cancer patients. It is important that a disproportionate share of special care resources is not expended on the futile care of terminally ill patients. A requirement for mechanical ventilation has been stated to affect survival in cancer patients. In a study by Kongsgaard and Meidell (1999) the ICU mortality in oncologic patients was 63%. Their results indicate that this treatment modality should not generally be restricted in critically ill cancer patients. The quality of life of the patients who survived should be of interest to those involved in further medical and ethical decisions concerning the level of care in the ICU.

Women with HIV infection have a higher risk for cervical squamous intaepithelial lesions than do women without HIV infection and the optimal regimen for cervical cancer screening in these women is uncertain. Goldie and co-workers (1999) assessed the net health consequences, costs and cost-effectiveness of various screening strategies for cervical neoplasia and cancer in HIV-infected women. They measured quality-adjusted life years (QALYs), lifetime costs and incremental cost-effectiveness. They found that in HIV-infected women, cervical cancer screening with annual PAP smears after two negative smears obtained 6 months apart offers quality-adjusted life expectancy benefits at a cost comparable to that of other clinical preventive interventions.

3.11.2 QUALITY ADJUSTED LIFE YEAR (QALY)

Although quality of life is often measured, interpretation of these outcomes in relation to mortality is difficult. Survival analysis places each individual in one of two categories: alive or dead. Among those alive, all individuals are considered equivalent. Thus, a patient confined to bed with severe symptoms is scored the same as someone who is active and asymptomatic. A General Health Policy Model is proposed as a solution to this problem. The model adjusts life expectancy for diminished quality of life, which is measures using a standardized instrument known as the Quality of Well-Being (QWB) scale. The model expresses the effect of treatment in a unit known as a Well-Year or Quality Adjusted Life Year (QALY). These units integrate side effects and benefits of treatment by combining into a single number, mortality, morbidity and duration of each health state. Similar methods, such as Q-TWiST, have been proposed for use in cancer clinical trials. However Q-TwiST is a subset of the more general model and carries limitations for cross-disease comparisons. The general health outcome model can be of considerable value for analyzing the costs, risks and benefits of cancer therapies (Kaplan 1993).

3.11.2 QUALITY-ADJUSTED TIME WITHOUT SYMPTOMS AND TOXICITY (Q-TwiST)

The effectiveness of cancer treatments is often expressed in terms of disease-free survival or overall survival, relative risk reduction or odds ratios and the quality of life effects are often assessed separately from survival. Such end points and summary measures may be inadequate, however, for comparing two treatments in terms of their palliative effects because there is a trade-off between treatment toxicity and increased disease-free interval. Furthermore, this trade-off may depend on individual patient preferences and prognostic situations. Gelber (1993) describes a method for evaluating the effectiveness of cancer treatments in terms of palliation by simultaneously considering both quality and quantity of time following treatment so that therapeutic choice may be determined according to patient preferences on quality of life and prognostic situation. Gelber's method is an extension of the Quality-adjusted Time Without Symptoms and Toxicity (Q-TwiST) method for comparing treatment effectiveness in clinical trials of adjuvant therapies.

3.12 SCREENING

Screening has been shown to reduce cancer mortality. The possible negative effect on quality of life for screening approaches is overruled by the positive effect on survival. The negative effects on quality of life caused by screening methods not proven to be effective are a matter of concern (Stjernswärd 1986). Again cost-effectiveness within the framework of limited resources must be considered and quality of life studies can provide additional, valuable information as an aid to decision making about screening procedures.

3.13 QUALITY OF LIFE IN THE ADJUVANT SETTING

Adjuvant treatment for breast cancer may be associated with considerable early toxic side effects, while treatment benefits may accrue only after long follow-up periods. In order to improve assessment of the cost-benefit balance, the International Breast Cancer Study Group (IBCSG) is developing a model of treatment evaluation which incorporates the traditional endpoints (disease-free and overall survival), the toxicity and disease variables rated by physicians, but also "subjective" aspects of quality of life rated by patients (Bernhard 1997).

Because the survival benefit of adjuvant treatment so far achieved is modest, it can best be studied in large-scale randomized clinical trials. To assess the impact of adjuvant therapy in this particular setting, a quality of life measurement approach must meet the following criteria (Bernhard 1997):

1. It has to be applicable within clinical routine, taking into account the complex logistics of large-scale and especially international trials. This means that the measures must be simple, focussing on the specific trial endpoints.
2. The measures need to meet the standard psychometric criteria of reliability and validity. The measures need to be especially responsive to differences among a variety of adjuvant treatment regimens and to changes in the course of the disease.
3. In many cases these trials involve multiple cultures and countries. The measures therefore need to be cross-culturally equivalent.

In comparative clinical trials, the *difference* in quality of life between treatments is of primary interest.

3.14 PALLIATIVE CARE

In the palliative care setting a precise definition of the goals of treatment is likely to result in clinical interventions which are economical, more tailored to the patients' needs, and which could lead to an improvement of the relationship between patients and physicians and may even influence the validation of medical services (Porzsolt 1993). The development of strategies requires the definition of goals. Weak strategy leads to poor adherence to protocols and poor compliance. Both non-adherence and non-compliance are significant problems in oncology (Schleifer 1991).

Definitive curative therapy certainly overrides most quality of life questions. However, quality of life becomes important if there is more than one curative therapeutic strategy or if the therapy is not always curative. A major problem in global cancer control is that the majority of patients are found with an advanced stage of disease at the time of diagnosis. Most clinical trials today compare the quantity of survival, not the quality of survival. Mostly the only aspects of quality of life that are reported by investigators, are toxicities and complications (Stjernswäard 1986).

In the palliative care setting, quality of life and health status are the primary outcomes of the treatment. The interventions mostly have substantial impact on everyday functioning and sense of well being.

Even when the cancer is too advanced to be cured, palliative treatment can often achieve worthwhile results. The following aims may be attained by palliative treatment:

- Symptom relief.
- Preventing future symptoms, which may develop.
- The prolongation of life.

Palliative treatments should not be worse than the symptoms they are intended to control. Doses should be kept at the lowest effective level, to minimize side-effects, and regimes kept simple to avoid repeated treatment sessions (Barraclough, 1994).

3.15 SYMPTOM PALLIATION

The assessment of symptom palliation is an essential component of many treatment comparisons in clinical trials, but Stephens et al. (1999) found no consensus as to its precise definition. They attempted to define and analyze symptom palliation in cancer clinical trials. Their findings emphasize the need for caution in interpreting results and the importance of working towards a standard definition of symptom palliation. The current lack of specified criteria makes analysis and interpretation of trial results difficult and comparison across trials impossible. A standard definition for use in the analysis of clinical trials is proposed, which takes into account aspects of onset, duration and degree of palliation, and symptom improvement, control and prevention.

3.16 ACTIVE SUPPORTIVE CARE

In the palliative setting, the very important question arises of whether to treat with aggressive therapy, or not. This is an area where quality of life studies can play a crucial role. Studies where treatment versus best supportive care are examined, must investigate the quality of life of the patients intensively, as might supply the supporting evidence in favor of a specific approach (Stjernswärd 1986).

How are a few months of life prolongation with therapy at high cost and side-effects to be evaluated, if during this time the patient has no enjoyment of life and may suffer pain, despair and isolation from her family? Given reliable documented information on what can be expected, either choosing aggressive treatment or active supportive care, physicians and patients could make this difficult decision on a more rational basis (Stjernswärd 1986).

3.17 QUALITY OF LIFE ON DIFFERENT TREATMENT REGIMENS

3.17.1 INTRODUCTION

QOL measures have been used mostly to compare treatments.

Multitudes of clinical trials are undertaken where the aim is to prove the superiority of one treatment regimen (or single agent) to another. Trials of this nature can only be interpreted meaningfully if quality of life evaluations are included in the primary study design.

Coates (1992) has used QOL measures to compare treatment strategies.

A study was designed to investigate the personal experience of patients with nonmetastatic breast cancer, who were treated with the concurrent administration of radiotherapy and chemotherapy (mitoxantrone and cyclophosphamide) in terms of side effects and quality of life. Quality of life was measures by the European Organisation for Research and Treatment of Cancer QLQ-C30 and pain was measures by a visual analogue scale (VAS). Multidimensional quality of life assessment showed that treatment mainly affects physical functioning and global quality of life. Multivariate analysis showed that the main determinants of quality of life at the end of treatment were fatigue, pain and loss of appetite experienced during treatment. The concurrent administration of chemotherapy and radiotherapy deteriorates patients' quality of life but in a proportion similar to sequential administration while presenting the advantage of a shorter duration of treatment (Macquart-Moulin, 1999). The incorporation of quality of life measures enables the people involved to undertake a more informed therapeutic decision-making analysis.

3.17.2 RADIOTHERAPY

Bone is a common site for metastatic carcinoma. Bone metastases occur in about half of advanced breast cancer patients. Pain is the usual presenting symptom, for which radiotherapy is undoubtedly an effective treatment. Although the value of palliative irradiation for bone pain has been recognised for over half a century, the optimum dose and fractionation schedules remain controversial. Gaze (1997) compared the efficacy, side effects and effect on quality of life of two commonly used radiotherapy schedules in the management of painful bone metastases. In a prospective trial patients were randomised to receive either a single 10 Gray treatment or a course of 22.5 Gray in five daily fractions for the relief of localised metastatic bone pain. There were no statistically significant differences in response rates or median duration of pain control. There were no differences between the groups in the effect of treatment on a variety of quality of life parameters.

3.17.3 CHEMORADIOTHERAPY

List and co-workers (1999) prospectively evaluated performance and quality of life in advanced stage head and neck cancer patients on a curative-intent, concomitant chemo-radiotherapy regimen aimed at improving loco-regional control, survival and quality of life. The regimen consisted of twice-daily radiation, fluorouracil, hydroxyurea and cisplatin. Patients were assessed before, during and at 3-month intervals after treatment with the Functional Assessment of Cancer Therapy – Head and Neck (FACT-HN) and patient-reported symptoms (McMaster University Head and Neck Radiotherapy Questionnaire). The data supports the feasibility of intense chemo-radiation as primary treatment for advanced head and neck cancer. Results confirm acute toxicity but indicate that many of the treatment-related performance and quality of life declines resolve by 12 months.

3.17.4 HORMONAL MANIPULATION

Sex hormone manipulation is commonly used in the treatment of breast cancer. Removal of ovaries, medication to block sex hormone function, or administration of hormones of the opposite sex, is among the procedures used. The psychological consequences of amenorrhoea, growth of body hair, and deepening of the voice in women are naturally distressing. Fortunately tamoxifen which is now the standard frontline treatment for hormone-dependant breast cancer is relatively free of such effects (Barraclough 1994).

Simons (1996) investigated the effects of medroxyprogesterone acetate on appetite, weight and quality of life in patients with advanced-stage, incurable, non-hormone-sensitive cancer. Patients were randomised between double-blind medroxyprogesterone acetate 500 mg twice daily or placebo. A beneficial effect of medroxyprogesterone acetate on appetite was observed. A mean weight gain was seen in the medroxyprogesterone group, versus an ongoing mean weight loss in the placebo group. This difference was statistically significant. During the study, several areas of quality of life (measured with the EORTC QLQ-C30) deteriorated in the total group of patients. With the exception of an improvement in appetite and possibly also a reduction in nausea and vomiting, no measurable beneficial effects of medroxyprogesterone acetate on quality of life could be demonstrated. It must be remembered that these are patients with end-stage cancer, where the cancer has already induced metabolic wasting of the patient and the opportunity for improving quality of life is very small. The side effect profile of medroxyprogesterone acetate was favourable: only a trend toward an increase in (usually mild) peripheral edema was observed.

In breast cancer patients, once the disease spreads, 70% of these patients will eventually develop clinically manifest bone metastases. Therefore, breast cancer patients with extraskeletal metastatic disease and patients with locally advanced disease are at high risk of suffering during their limited survival time, from impairment of their quality of life due to events of skeletal morbidity such as bone pain, pathological fractures and hypercalcaemia (van Holten-Verzantvoort 1996). In previous studies van Holten-Verzantvoort and others have shown that long-term supportive bisphosphonate treatment significantly reduces skeletal morbidity in patients with breast cancer and established bone disease (Elomaa 1983; Paterson 1993; van Holten-Verzantvoort 1987), and improves selective aspects of quality of life (van Holten-Verzantvoort 1991). Koeberle and co-workers (1999) demonstrated that bone pain could be effectively reduced by repeated pamidronate infusions in patients with advanced osteolytic bone disease.

Hortobagyi (1996) conducted a phase III clinical trial comparing pamidronate disodium to placebo in breast cancer patients with bone metastases. Quality of life was one of the important aspects of the trial. The Spitzer Scale (see chapter 2 and addendum 18), ECOG performance status, evaluation of bone pain and the use of analgesics were included in the analysis. Changes from baseline in these parameters were compared between groups by the Wilcoxon rank-sum test. There were no differences between the two groups in the use of analgesic drugs or quality of life scores. There was significantly less increase in bone pain and deterioration of performance status in the pamidronate group than in the placebo group. Pamidronate was well tolerated.

Toxicity of treatment is of great importance when palliation is the objective. In a study by van Holten-Verzantvoort (1996) the occurrence of nausea and vomiting, and stomatitis in one case, was attributed to pamidronate treatment resulting in withdrawal from the study. Primary gastrointestinal intolerance does occur, usually within weeks after the start of treatment. In contrast to these clinical findings, the quality of life survey did not detect a difference in the level of gastrointestinal complaints between pamidronate and control patients.

3.18 FOR OVERALL PATIENT BENEFIT

The identification of the effects of therapy on quality of life both in the short and long term may be of value. This is particularly relevant for the evaluation of long term survivors of cancer. Measurement of quality of life may also be of value even if cure is not possible. For example, the quality of life of a patient may be the most important end point in the context of palliative care (Jenney 1998).

During the development of the Life Evaluation Questionnaire (LEQ) a number of patients commented on the opportunity that it provided to express concerns that were normally unexpressed (Salmon1996).

Epstein et al. (1999) investigated quality of life and oral function following radiotherapy for head and neck cancer. They found that oral complications following radiotherapy for head and neck cancer are common and affect quality of life. Use of a general function scale such as the European Organization for the Research and Treatment of Cancer questionnaire (EORTC) with the addition of disease/site specific scales may provide useful data on outcome of therapy and upon the complications associated with therapy and impact upon the quality of life.

3.19 CONCLUSION

There are several important reasons why the quality of life of patients should be measured accurately in the medical field:

- The identification of problems that are particular to the specific field of medicine, so that these problems can be ameliorated.
- Quality of life assessments can be useful in making medical treatment decisions and it can be used as an outcome measure in clinical trials. It is important to demonstrate in cancer patients that the palliative treatment is not more harmful than the disease itself, particularly when survival rates are disappointing and the treatments are increasingly toxic.
- It can be usefully employed in the health policy field where standard units are used to compare the different impact of chronic diseases and to assess the cost-effectiveness of interventions. Reliable quality of life assessments are helpful in calculating the direct and indirect cost of illness.

Interest in the measurement of quality of life has dramatically increased over the last six years. The patients' perspective is increasingly being recognized as the most important component in medical treatment and care. However, the inadequacy of reporting quality of life data in the medical literature has been highlighted on numerous occasions recently. Problem areas that have been identified are:

- There is a lack of clarification as to what is being measured?
- Why is it being measured?
- Is the measure valid?

It is obviously desirable to have a standard approach and common measuring instruments. There are however, so many different measures to be found that it becomes almost impossible to make progress in the field. Many instruments have unknown psychometric properties and cannot usefully be compared to some of the more standard measures. Even for a well-known and often used instrument norms generally are non existent. It is therefore important not to develop new measures but to choose among the existing instruments with an eye to brevity and simplicity as well as established reliability and validity.

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CHAPTER 4: MATERIALS AND METHODS

4.1 INTRODUCTION

Metastatic breast cancer is almost always incurable with standard chemotherapy, utilized either as a single agent or in combination. No new combination of agents has shown significantly greater activity than a variety of Adriamycin-containing combinations first used in the mid - 1970's. Variations in dose and schedule have had little impact on long-term survival in patients with metastatic breast cancer.

It must also be borne in mind that the aim of treatment in the metastatic setting is palliative rather that curative. Therefore it becomes imperative to examine the impact of treatment for metastatic breast cancer on the overall quality of life of the patient.

This study provides an opportunity to address several important quality of life issues. It allows us to examine and compare the quality of life of patients receiving therapies that differ significantly in toxicity, i.e. chemotherapy, chemo-hormonal therapy or hormonal therapy. Treatments for any line of locally advanced or metastatic disease were included, whereas the current studies on quality of life only analyze specific time-spans, mostly of front-line treatment. Salvage therapy for metastatic breast cancer has been almost exclusively studies in small Phase II trials which have not evaluated quality of life (Petru 1987). The other very important aspect is the unique opportunity to compare the quality of life of different ethnic groups in South Africa. Quality of life comparisons will be drawn between white and black patients.

The quality of life measure to be used is the **F**unctional **A**ssessment **C**ancer **T**herapy–**B**reast Cancer (FACT-B) see Addendum 3. It is a multidimensional and disease specific instrument. The FACT-B has a 29 item generic core plus10 items that are specific for breast cancer patients. Patients rate all items on a 5-point rating scale ranging from "not at all" to "very much". The FACT-B provides a total QOL score as well as information about physical well being, social/family well being, relationship with the doctor, emotional well being, functional well being and disease-specific concerns. The FACT-B has been demonstrated to have sufficient reliability, validity and sensitivity to change over time.

The Functional Assessment of Cancer Therapy for breast cancer (FACT-B) scale was chosen as the measurement instrument for the study, because:

- The instrument has already been proven to have sound psychometric properties.
- Experience in its utilization had already been established through previous work with the FACT-B.
- FACT-B is a self-report measure that nearly all patients with a sixth grade reading level can quickly and easily complete without assistance.
- FACT-B is reliable and valid and appears responsive to changes in health status over time.
- Translations of FACT-B into Zulu, Pedi and Tswana, the three most common black languages in South Africa are available (Mullin 99).
- It is widely used worldwide in clinical research involving QOL issues.

4.2 OBJECTIVES

When a person is diagnosed with cancer, it necessarily has an impact on their quality of life. Additionally the treatment of cancer will change their quality of life. Differences in ethnicity will lead to the impact of disease and treatment to be different. This hypothesis will be tested by means of the following objectives:

1. Are there differences in quality of life at different time-points, i.e. before therapy, during therapy or after therapy?
2. Are there quality of life differences between patients receiving chemotherapy, hormonal therapy, chemo-hormonal therapy, radiotherapy or patients who are on observation?
3. Are there differences in the quality of life of different ethnic groups, with specific regard to the individual quality of life domains?

4.3 SELECTION OF PATIENTS

- Histologically confirmed Stage III B (inoperable) or Stage IV adenocarcinoma of the breast with manifestations of progressing regional or metastatic cancer (See Table 7: AJCC Staging of Breast Cancer).
- Female patients above 18 years of age.
- Within the frame of inoperable Stage III or IV disease, any patient is eligible, irrespective of treatment line, or treatment type.
- Patients with Stage III or IV disease in complete remission are eligible.
- Written informed consent obtained (See Addendum 2 for Model Informed Consent Document).

4.4 INTRODUCTION TO THE FACT SCALES

The **F**unctional **A**ssessment **C**ancer **T**herapy (FACT) scales have been under development since October 1987 (Cella 1987) and are copyrighted. Written permission for its use was obtained from:
Dr. David Cella, Rush–Presbytarian-St. Luke's Medical Center, Chicago, Illinois, USA.

The FACT scales are self-report measures of quality of life in people with cancer and HIV infection. Nearly all patients with a sixth grade reading level can easily complete them without assistance. There are currently twelve Cancer-specific scales (see table 1), eleven of which are disease-specific extensions of the 29-item general version (FACT-G) and include items relevant to that particular disease (Cella 1994). Versions of the FACT are listed below in Table 1:

TABLE 1: AVAILABILITY OF FACT CANCER-SPECIFIC SCALES

FACT-G	A General version of the scale which can be used with patients of any tumor type, and which constitutes the core of the following disease-specific scales:
FACT-B	For Breast cancer patients
FACT-BL	For BLadder cancer patients
FACT-Br	For Brain tumors
FACT-C	For Colorectal cancer patients
FACT-CNS	Cancer in the Central Nervous System
FACT-Cx	For Cervical (Cx) cancer
FACT-E	Esophageal cancer
FACT-H&N	For Head and Neck cancer patients
FACT-L	For Lung cancer patients
FACT-O	Ovarian cancer
FACT-P	Prostate cancer
FACT-Pa	Pancreatic cancer

There are 29 Likert-type items, which comprise 5 sub scales common across all seven measures (FACT-G). The number of items specific to the cancer site varies from 9 to 12 (see table 2).

One additional item at the end of each sub scale asks respondents to rate how much that particular aspect of life (e.g., physical well being, social/family well-being etc.) affects his or her quality of life. These ratings are made on a 0 - 10 scale where "0" corresponds with "not at all" and a "10" corresponds with "very much so". These items are currently experimental and may ultimately be used to weight sub-scale scores. For now, unweighted scores are used, so these particular items are nor used in either the sub-scale scores or in the overall quality of life score.

TABLE 2: THE SIX SUB-SCALES OF THE FACT QUESTIONNAIRES

1. Physical Well-being	7 items
2. Social/Family Well-being	7 items
3. Relationship with Doctor	2 items
4. Emotional Well-being	5 items (version 2) 6 items (version 3)
5. Functional Well-being	7 items
6. Additional concerns	9 items for FACT-B thus total items=37 for version 2 thus total items=38 for version 3

Format of version 3: The FACT-G is now comprised of 29 items due to the addition of one item to the Emotional Well-being subscale. However, this item is not scored in FACT version 3. All other items, including the additional 6 experimental items have been retained.

The FACT scales are designed for patient self-administration, but can also be administered as an interview. For self-administration, patients should be instructed to read the brief directions at the top of the page. After the patient's correct understanding has been confirmed, he/she should be encouraged to complete every item in order without skipping any, except where directed (e.g., item 15). For interview administration, it is helpful to have the patient hold a card on which the response options have been printed. Data is available from Dr. Cella as to the comparability of interview and written methods.

It is important that the questionnaire is administered before being influenced by any "news" that the physician may have and also before the administration of chemotherapy. The patient should also be alone in a room, or in the case of an interview, with only the interviewer present. This is because the presence of friends or family members could influence certain answers, especially on items such as "sex life".

When the FACT scale is administered as an interview, it is extremely important not to influence the patient in any way. The patient must know that there are no "right" or "wrong" answers and that participation or response to the questionnaire, will not influence the patient's treatment or management in any negative way.

The FACT-B was available to patients in any of the following languages:

FACT-B PEDI	(see Addendum 5).
FACT-B ZULU	(see Addendum 7).
FACT-B TSWANA	(see Addendum 6).
FACT-B ENGLISH	(see Addendum 3).
FACT-B AFRIKAANS	(see Addendum 4).

4.5 TRANSLATION PROCEDURE FOR THE FACT–B INTO AFRIKAANS

- Identification of source (original document). The FACT-G and one disease-specific subscale for breast cancer was identified as the original document to be translated into Afrikaans an indigenous South African language.
- All items were checked for redundancy so that the smallest possible number of items was translated.
- A list of all items was prepared for submission to the translators.
- Identification of bilingual translators.
- All translators were required to be native speakers of the target language (i.e. the language FACT was being translated into), and to be fluent in English.
- Forward translation by two independent persons.
- Translators were instructed to consider that the items on the FACT attempt to measure physical and psychological states of health and well being and that these states can be somewhat abstract. Therefore, translators were asked to focus on capturing the essential content (meaning) of the question rather than performing an exact (literal) translation.
- Translators were also instructed to use simple, straightforward language rather than to use phrasing that might be more precise but difficult for less educated patients to comprehend.
- The result of this was the creation of two separate forward translations of the FACT-B.
- The forward translations were reconciled and discrepancies were resolved.

- The most culturally relevant way of stating the translated questions was chosen and a reconciled version, which combined input from the two forward translations, was constructed.
- After deliberation the reconciled version was back translated.
- Investigator review. An independent bilingual health professional was asked to review the following documents to ensure consistency and cultural relevance:
    1. source document (original)
    2. reconciled forward translation and
    3. back translation.
- The investigator was asked to consider simple, straightforward translations of each item.
- It was stressed that all translations should be culturally meaningful to members of that particular culture. Special emphasis was placed on creating a document that could be applied to members of all educational levels.
- The reviewer had not seen the documents before.
- All reviewer comments were sent back to Pretoria Academic Hospital's Oncology Centre.
- Reconciliation of reviewer comments and the translated documents.
- Additional input from the reviewer along with the comparison of all documents permitted us to arrive at a final translation.
- Final check.
- The FACT-G and the disease-spesific subscale (for breast cancer) items were compiled in questionnaire form.
- The Afrikaans FACT-B was given to a few independent persons for final approval.
- Validation was performed during the final statistical analysis.

PERSONS INVOLVED WITH THE TRANSLATION

IJ Ueckermann MAPhil.
Tel: (H) 043-7484255

Dr. C Dicks MMed(Rad)
Tel: (W) 341 3502 (H) 329 0214

MS Mertz MSc.PHARM
Tel: (W) 3541399 (H) 6542320

4.6 TRAINING OF INTERVIEWERS

- As the majority of the black patients attending the Oncology Unit are currently illiterate, nursing staff of Pretoria Academic Hospital Department of Medical Oncology were approached to assist with the administration of the FACB-B as interviews. These were the FACT-B translations into the most prevalent ethnic languages found in South Africa, namely Pedi, Tswana and Zulu.
- Nurses who are fluent in each of these languages were identified and trained to administer the FACT-B.
- They were introduced to the concept of quality of life and the FACT-B. The important steps in the administration of a quality of life instrument as an interview was taught to them (as described in 4.4).
- During the course of the project, two more training sessions were held.
- When problems were encountered, the interviewere had to clarify the problem with the researcher.

4.7 SCORING OF THE FACT-B

The FACT-B scale description is given in table 3. Refer to table 4 for a FACT-G scoring guide. The scoring guide identifies those items, which must be reversed before being added to obtain subscale totals. Items are reversed by subtracting the response from "4". After reversing proper items, all subscale items are summed to a total, which is the subscale score (Cella 1994). The FACT-B score is obtained by adding the Additional concerns subscale total to the FACT-G total.

4.7.1 HANDLING MISSING ITEMS

If there are missing items, subscales can be prorated. This is done by multiplying the sum of the subscale by the number of items in the subscale, then dividing by the number of items actually answered. This can be done directly on the scoring guide (Table 4).

When there are missing data, prorating by subscale in this way is acceptable as long as more than 50% of the items were answered. The total score is then calculated as the sum of the unweighted subscale scores. The FACT scale is considered to be an acceptable indicator of patient quality of life as long as overall item response rate is greater than 80% (i.e. at least 23 of 28 FACT-G items completed). This is not to be confused with individual item response rate, which allows a subscale to be prorated for missing items if greater than 50% of items are answered (Cella 1994).

4.7.2 SCORING THE SPECIFIC FACT-B SCALE

The total score for the specific FACT Scales is the sum of the FACT-G (the first 5 subscales common to all scales) plus the "Additional Concerns" subscale. Again, over 50% of the items (i.e. 5 of 9 items) must be completed in order to consider the subscale valid.

For the "Additional Concerns" subscale (i.e. disease-specific questions), a scoring guide is incorporated at the end of table 4. The procedure for scoring is the same as described above for the FACT-G. By following this scoring guide and transcribing the FACT-G score, the two totals can be summed to derive the TOTAL FACT SCORE. The translated versions can be scored in exactly the same way (Cella 1994).

4.7.3 A NOTE ON SELECTING SCORES FOR ANALYSIS

These scoring templates allow one to obtain two different total scores in addition to each individual subscale score. The FACT-G total score provides a useful summary of overall quality of life across a diverse group of patients. The disease-specific questionnaire total scores (i.e. FACT-G plus disease-specific subscale score) may further refine the FACT-G summary score. However two alternative approaches are noteworthy: One is to seperately analyze the FACT-G total score and the disease-specific subscale score. Another is to select subscales of the FACT which are most likely to be changed by an intervention being tested. For example, the Physical, Functional and Disease-specific subscales would be most likely to change in a chemotherapy clinical trial. On the other hand, the Emotional or Social

Wellbeing subscale would be expected to change most when evaluating a psychosocial intervention (Cella 1994).

TABLE 3: FACT-B SCALE DESCRIPTION

FACT-B scale	Number of items	Highest possible score
	28 general 9 specific (6 experimental)	37 x 4 = 148

TABLE 4: FACT-G SCORING GUIDE (UNWEIGHTED) INCORPORATING THE ADDITIONAL CONCERNS OF THE FACT-B

1. Record answers in "item response" column.
2. Perform reversals as indicated to obtain "item scores".
3. Multiply the sum of the item scores by the number of items in the subscale, then divide by the number of items answered. This produces the subscale score.
4. Add subscale scores to derive total score.

Subscale	**Item Number**	**Reverse?**	**Item Response**		**Item Score**	
Physical Well Being	1	4 -		=		
	2	4 -		=		
	3	4 -		=		
	4	4 -		=		
	5	4 -		=		
	6	4 -		=		
	7	4 -		=		
			Sum Item Scores	→	[___]	x 7 ÷ [___] = [___]
			Enter number of items answered			______ ↑
Social/ Family Well Being	9	4 -		=		
	10	0+		=		
	11	0+		=		
	12	0+		=		
	13	4 -		=		
	14	0+		=		
	15	0+		=		
			Sum Item Scores	→	[___]	x 7 ÷ [___] = [___]
			Enter number of items answered			______ ↑
Relationship With Doctor	17	0+		=		
	18	0+		=		
			Sum Item Scores	→	[___]	______ → [___]

Continued on the next page

Subscale	Item Number	Reverse?	Item Response		Item Score	
Emotional Well Being	20	4 -		=		
	21	0+		=		
	22	4 -		=		
	23	4 -		=		
	24	4 -		=		

Sum Item Scores ➔ [___] x 5 ÷ [___] =[___]

Enter number of items answered__________ 🡅

Functional Well Being	27	0+		=		
	28	0+		=		
	29	0+		=		
	30	0+		=		
	31	0+		=		
	32	0+		=		
	33	0+		=		

Sum Item Scores ➔ [___] x 7 ÷ [___] =[___]

Enter number of items answered__________ 🡅

Sum of SUBSCALE Scores = FACT-G TOTAL SCORE ➔ [___]

Subscale	Item Number	Reverse?	Item Response		Item Score	
Additional subscale	35	4 -		=		
	36	4 -		=		
	37	4 -		=		
	38	0+		=		
	39	4 -		=		
	40	4 -		=		
	41	4 -		=		
	42	4 -		=		
	43	0+		=		

Sum Item Scores ➔ [___] x 9 ÷ [___] =[___]

Enter number of items answered__________ 🡅

Enter FACT-G score ➔ [___]

Add to get TOTAL FACT-B SCORE ➔ [___]

4.8 METHOD FOR COLLECTION OF THE FACT-B

- Eligible patients were identified by screening.
- Patients were approached and the study was introduced to them.
- Informed consent was signed.
- The FACT-B was explained to the patient and the patient was given the option to either complete the questionnaire on her own or alternately the questionnaire was administered as an interview.
- The FACT-B was completed in a quiet area, before the physician had seen the patient. The patient was on her own, as family memebers of friends might have influenced her responses.
- If the Fact-B was conducted as an interview as is the case for illiterate patients, great care was taken not to influence the patient's answers in any way.
- The completed FACT-B was checked for missing items or items with more than one response and the patient was asked to clarify her answers.
- Follow-up administrations of the FACT-B were scheduled. The FACT-B was given to the patients at basline, during treatment (as close as possible to day 1 week 16 when maximum toxicity and response would be expected) and after treatment.
- The baseline database for each patient was completed with the aid of all the relevant clinical and demographic information. This included the Hospital classification, which is an indication of the patient's financial status (see Addendum 8). Baseline sociodemographic data was entered into an Exel spreadsheet.

4.9 VALIDATION OF THE FACT-B TRANSLATIONS

English speaking patients completed the original FACT-B that had previously been validated for North American breast cancer patients (Brady 1997). The validity of the FACT-B for South-African patients, where cultural differences might influence the composition of the FACT-B, was calculated. This was even more important because of the cultural diversity that was found in the sample group, namely Pedi, Zulu, Tswana, Afrikaans and English patients. An analysis was done using the STATA Release 6 (1999) statistical package, to validate the FACT-B for the South-African breast cancer population.

Initial validations were done for the tranlations of the FACT-B (Mullin 1999) that were already available in the three most common indigenous black languages, namely Pedi, Tswana and Zulu. Chrohnbach's alpha was calculated for each separate domain and for the total FACT-B score. An alpha value of 0.7 or higher suffices and is indicative of modest reliability.The alpha values that were obtained, were compared to the validations of Mullin (1999). Mullin's validations were for a "mixed" cancer group and specifically for the FACT-G core questionnaire. Validation for the Afrikaans FACT-B was done in the same manner, but comparisons could not be made, because no other validated Afrikaans questionnaire exists currently.

The number of breast cancer patients for each validation sample were as follows:

Afrikaans	64
Zulu	63
Pedi	62
Tswana	64

For the final analysis group (N=100) alpha values were generated separately for each of the questionnaire items for the white patients, the black patients and the group as a whole. This was done for FACT-B questionnaires completed before and during treatment.

4.10 STATISTICAL CONSIDERATIONS FOR THE ANALYSIS OF THE PILOT PROJECT

During August to November 1998 an interim analysis of the data collected by means of the FACT-B instrument was performed. The rationale for the interim analysis was twofold:

1. To establish norms for the statistical procedures.
2. To ascertain if there were any gross shortcomings in the quality of the data which might still be ameliorated.

4.10.1 PRELIMINARY REMARKS ABOUT GENERAL METHODOLOGY

A two-factor analysis of variance with repeated measure was deemed to be a suitable analytical method for the objectives set out in 4.2. The Null hypothesis for the following potential effects was tested by this method:

- Main effect A (effect of the treatment method with regard to racial groups): "There are general differences in QOL score, between the distinct treatment types for individual racial groups."
- Main effect B (timing effect): "There are general differences in the QOL scores at different time points."
- Interchange between A and B: "QOL differences for distinct treatment types found between different race groups, are dependent on timing. Simultaneously, different QOL scores at distinct timings are dependent on the treatment type (while taking the effect of race into consideration)."

Besides the 2-factor analysis of variance, which took the progress information into consideration, a one-factor analysis of variance was calculated at each time point. This type of variance analysis is less powerful but it is also less restrictive on the available amount of evaluable data.

4.10.2 DEPENDENT VARIABLES AND GROUP VARIABLES

For all the analyses the dependent variable was the Quality of Life (QOL) calculated as set out in 4.7. For each questionnaire there are 7 possible scales being measured:

1. Total QOL score
2. Physical well-being
3. Social/family well-being
4. Relationship with doctor
5. Emotional well-being
6. Functional well-being and
7. Additional concerns pertaining to breast cancer

The group variable for the analysis of the complex of questions 1 and 2 is the type of treatment. The group variable for the analysis of the complex of questions 1 and 3 is racial group.

4.11 SELECTION OF CASES FOR THE FINAL ANALYSIS

Because of the reasons discussed in Chapter 6, it was decided to select only the following cases for the final analysis:

- Patients receiving chemotherapy.
- Patients receiving either frontline, secondline or thirdline treatment.
- Patients who had completed a baseline, and at least one FACT-B questionnaire during treatment. The "during" treatment FACT-B was scheduled for day one week 16.
- If there was more than one questionnaire completed during treatment, the questionnaire that co-incided, or was closest to day one week 16, was chosen.
- The number of patients in the pilot sudy was 200 and 100 of these were included in the final analysis.

4.12 STATISTICAL CONSIDERATIONS FOR THE FINAL ANALYSIS

The objectives were re-formulated as follows:

1. Are there differences in quality of life during treatment between the different races?
2. What are the reasons for the differences in quality of life as they relate to the different race groups?
3. Are there changes in quality of life before treatment versus during treatment?

Multiple regression analyses were used for both the total score as well as the individual domains:

- Baseline quality of life was the only quality of life score included in the predictors.
- Time 2 (during treatment) was the dependent variable.
- Time 1 was the baseline measure.

- Predictors were race, time 1 or 2, performance status, disease stage, actual age, educational status, marital status, time elapsed between baseline and the "during" questionnaire,

  co-morbid disease and baseline quality of life scores. Living arrangement was not included, because there was less than 25% of patients living alone in each race group.

The analyses reported are:

1. Summary statistics – total sample and by race.
2. Chronbach's alpha was calculated for each construct and for the total score the final analysis group, for each construct, both at baseline and during treatment. Alpha assesses the reliability of a summative rating scale composed of the items in the construct. Modest reliability of 0.7 or higher suffices.
3. Hotelling's T-square was employed to assess whether race groups differed with respect to the observation vector (dphys, dsoc, ddoc, demot, dfunct, dadd), and races were found not to differ (in absence of covariates).
4. Dphys is defined as the difference between the physical well being score during treatment and physical well being score at baseline. The definitions for the social well being score, the relationship with the doctor, the emotional, functional, additional concerns and total scores were similar. Comparisons of races with respect to dphys through dadd initially without a covariate (model has poor R-square), then with baseline totals i.e. phys through add as cofactor (R-square improved markedly) and then finally by adding age, performance status, stage, education, time between the two questionnaires, marital status and concomitant medication (R-square improved slightly). It was suspected that race and education will be confounded but eliminating education did not improve the results and it was therefore not deleted.
5. Kaplan-Meier survival curves were drawn for the two different race groups and the chi square was calculated.

TABLE 5: LEGEND FOR THE PREDICTORS USED IN THE REGRESSION ANALYSIS

PREDICTOR	LEGEND	N IN EACH CATEGORY
Race	0= white	50%
	1= black	50%
Disease status	Stage 3	25%
	Stage 4	75%
Educational status	0= less than grade 12	55%
	1= grade 12 or higher	45%
Marital status	0= single/married	82%
	1= divorced/widowed	18%
Co-morbid disease	0= none	72%
	1= has co-morbid disease	28%

Living arrangement was not included in the analysis because there was less than 5% of patients living alone.

4.13 GENERAL ONCOLOGY PRINCIPLES UTILIZED IN THE STUDY

A number of general oncology principles were used throughout the study:

ECOG performance status: see Table 6.

AJCC staging of breast cancer (Beahrs 1992): see Table 7.

Declaration of Helsinky: see Addendum 1.

TABLE 6: ECOG PERFORMANCE STATUS WITH CORRESPONDING KARNOFSKY SCORE

GRADE	DESCRIPTION	KARNOFSKY
0	Fully active, able to carry on all pre-disease performance without restriction	90 – 100
1	Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature	70 – 80
2	Ambulatory and capable of all self care, but unable to carry out any work activities. Up and about more than 50% of waking hours	50 – 60
3	Capable of only limited self care, confined to bed or chair more than 50 % of waking hours	30 – 40
4	Completely disabled. Can not carry on any self-care. Totally confined to bed or chair	10 – 20

TABLE 7: AJCC STAGING OF BREAST CANCER (Beahrs 1992)

TNM DEFINITIONS

Primary Tumor

Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraductal carcinoma, lobular carcinoma in situ, or Paget's disease of the nipple with no tumor
T1	Tumor 2 cm or less in greatest dimension
T1a	0.5 cm or smaller
T1b	More than 0.5 cm, but not more than 1 cm in greatest dimension
T1c	More than 1 cm, but not more than 2 cm in greatest dimension
T2	Tumor more than 2 cm but not more than 5 cm in greatest dimension
T3	Tumor more than 5 cm in greatest dimension
T4	Tumor of any size with direct extension to chest wall or skin
T4a	Extension to chest wall
T4b	Edema (including peau d' orange), ulceration of the skin of the breast or satellite skin nodules confined to the same breast
T4c	Both (T4a and T4b)
T4d	Inflammatory carcinoma

Regional Lymph Node Involvement (Clinical)

Nx	Regional lymph nodes cannot be assessed (e.g. previously removed)
N0	No regional lymph node metastasis
N1	Metastasis to movable ipsilateral axillary node(s)
N2	Metastasis to ipsilateral axillary lymph node(s) fixed to one another or to other structures
N3	Metastases to ipsilateral internal mammary lymph node(s)

Distant metastases

Mx	Presence of distant metastases cannot be assessed
M0	No distant metastasis
M1	Distant metastasis (including metastases to ipsilateral supraclavicular node(s)

STAGE GROUPING

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage IIA	T0, N1, M0
	T1, N1, M0
	T2, N0, M0
Stage IIB	T2, N1, M0
	T3, N0, M0
Stage IIIA	T0, N2, M0
	T1, N2, M0
	T2, N2, M0
	T3, N1, M0
	T3, N2, M0
Stage IIIB	T4, any N, M0
	Any T, N3, M0
Stage IV	Any T, any N, M1

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ADDENDUM 1: DECLARATION OF HELSINKI

Recommendations guiding physicians in biomedical
Research involving human subjects

Adopted by the 18th world Medical Assembly,
Helsinki, Finland, June 1964
amended by the 29th World Medical Assembly,
Tokyo, Japan, October 1975
and
The 35th World medical Assembly,
Venice, Italy, October 1983
and
The 41th World Medical Assembly, Hong-Kong, September 1989

INTRODUCTION:

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient".

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding or the etiology and pathogenesis of disease.

In current medical practice most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research.

Medical progress is based on research that ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research that may affect the environment, and the welfare of animals used for research must be respected.

Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

I. BASIC PRINCIPLES

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor provided and this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent

medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in the Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely given informed consent, preferably in writing.
10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case a physician who is not engaged in the

investigation and who is completely independent of this official relationship should obtain the informed consent.

11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE

(Clinical research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, re-establishing health or alleviating suffering.
2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient – including those of a control group, if any – should be assured of the best-proven diagnostic and therapeutic method.
4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent Committee (1,2).
6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

(Non-clinical biomedical research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illness.
3. The investigator or the investigating team should discontinue the research if in his/her or their judgement it may, if continued, be harmful to the individual,

In research on man, the interest of science and society should never take precedence over considerations related to the wellbeing of the subject.

ADDENDUM 2: PROPOSED INFORMED CONSENT FOR PATIENTS EVALUATED WITH THE FACT-B

QUALITY OF LIFE IN PATIENTS WITH METASTATIC BREAST CANCER

I ____________________ willingly agree to participate in this study which has been explained to me by ____________________ . Participation in this study is voluntary. No compensation for participation will be given. I understand that I am free to withdraw my consent to participate in this program at any time without prejudice to my subsequent care. If I do not take part in or withdraw from the study, I will continue to receive the best possible care.

PURPOSE OF THE STUDY

It has been explained to me that I have locally advanced or metastatic breast cancer. Investigation into my quality of life will be done to determine which factors influence quality of life and to what extent these factors influence quality of life.

DESCRIPTION OF PROCEDURES

A socio demographic form inquiring about facts such as marital status and income will be filled in at the start. Thereafter the Functional Assessment of Cancer Therapy (FACT) for Breast cancer (FACT-B) will be explained to me. It takes about 10 minutes to fill in the form. The FACT-B will be completed at certain clinic visits. If I cannot read, the questionnaire will be administered as an interview.

RISKS AND DISCOMFORTS

I will be reminded of unpleasant aspects of my disease or life. Additionally some of the questions are of a personal nature. I may choose to refuse to answer certain questions.

Continued on the next page

BENEFITS

There is no clearcut benefit at this time. The knowledge gained from the study may however be used directly to improve the quality of life of patients with breast cancer.

I have read all of the above, asked questions, received answers concerning aspects that I did not understand, and I willingly give my consent to participate in this program. Upon signing this form, I will receive a copy.

PATIENT SIGNATURE DATE

WITNESS DATE

PHYSICIAN OR DATA MANAGER DATE

ADDENDUM 3: FACT-B (VERSION 3) ENGLISH

Below is a list of statements that other people with your illness have said are important.

By circling one number per line, please indicate how true each statement has been for you <u>during the past 7 days.</u>

PHYSICAL WELL-BEING

	not at all	a little bit	somewhat	quite a bit	very much
1. I have a lack of energy	0	1	2	3	4
2. I have nausea	0	1	2	3	4
3. Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
4. I have pain	0	1	2	3	4
5. I am bothered by side-effects of treatment	0	1	2	3	4
6. I feel sick	0	1	2	3	4
7. I am forced to spend time in bed	0	1	2	3	4
8. Looking at the above 7 questions, how much would you say your **PHYSICAL WELL-BEING** affects your quality of life?	(circle one number) **0 1 2 3 4 5 6 7 8 9 10** **not at all very much so**				

SOCIAL/FAMILY WELL-BEING

	not at all	a little bit	somewhat	quite a bit	very much
9. I feel distant from my friends	0	1	2	3	4
10. I get emotional support from my family	0	1	2	3	4
11. I get support from my friends and neighbors	0	1	2	3	4
12. My family has accepted my illness	0	1	2	3	4
13. Family communication about my illness is poor	0	1	2	3	4
14. I feel close to my partner (or the person who is my main support)	0	1	2	3	4
15. Have you been sexually active during the past year? No______ Yes______ If yes: I am satisfied with my sex life	0	1	2	3	4
16. Looking at the above 7 questions, how much would you say your **SOCIAL/FAMILY WELL-BEING** affects your quality of life?	(circle one number) **0 1 2 3 4 5 6 7 8 9 10** **not at all very much so**				

RELATIONSHIP WITH DOCTOR

	not at all	a little bit	Somewhat	quite a bit	very much
17. I have confidence in my doctor(s)	0	1	2	3	4
18. My doctor is available to answer my questions	0	1	2	3	4
19. Looking at the above 2 questions, how much would you say your **RELATIONSHIP WITH THE DOCTOR** affects your quality of life?	(circle one number) **0 1 2 3 4 5 6 7 8 9 10** **not at all** **very much so**				

EMOTIONAL WELL-BEING

	not at all	a little bit	Somewhat	quite a bit	very much
20. I feel sad	0	1	2	3	4
21. I am proud of how I'm coping with my illness	0	1	2	3	4
22. I am losing hope in the fight against my illness	0	1	2	3	4
23. I feel nervous	0	1	2	3	4
24. I worry about dying	0	1	2	3	4
25. I worry that my condition will get worse	0	1	2	3	4
26. Looking at the above 6 questions, how much would you say your **EMOTIONAL WELL-BEING** affects your quality of life?	(circle one number) **0 1 2 3 4 5 6 7 8 9 10** **not at all** **very much so**				

FUNCTIONAL WELL-BEING

	not at all	a little bit	somewhat	quite a bit	very much
27. I am able to work (include work in the home)	0	1	2	3	4
28. My work (include work in home) is fulfilling	0	1	2	3	4
29. I am able to enjoy life	0	1	2	3	4
30. I have accepted my illness	0	1	2	3	4
31. I am sleeping well	0	1	2	3	4
32. I am enjoying the things I usually do for fun	0	1	2	3	4
33. I am content with the quality of my life right now	0	1	2	3	4
34. Looking at the above 7 questions, how much would you say your **FUNCTIONAL WELL-BEING** affects your quality of life?	(circle one number) **0 1 2 3 4 5 6 7 8 9 10** **not at all** **very much so**				

ADDITIONAL CONCERNS

	not at all	a little bit	somewhat	quite a bit	very much
35. I have been short of breath	0	1	2	3	4
36. I am self-conscious about the way I dress	0	1	2	3	4
37. My arms are swollen and tender	0	1	2	3	4
38. I feel sexually attractive	0	1	2	3	4
39. I have been bothered by hair loss	0	1	2	3	4
40. I worry about the risk of cancer in other family members	0	1	2	3	4
41. I worry about the effect of stress on my illness	0	1	2	3	4
42. I am bothered by a change in weight	0	1	2	3	4
43. I am able to feel like a woman	0	1	2	3	4
44. Looking at the above 9 questions, how much would you say your **ADDITIONAL CONCERNS** affects your quality of life?	(circle one number) **0 1 2 3 4 5 6 7 8 9 10** **not at all** **very much so**				

ADDENDUM 4: FACT-B (WEERGAWE 3) AFRIKAANS

Instruksies: Die lys stellings hieronder dui aan wat vir ander persone/pasiënte met u siektetoestand belangrik is. **Dui asseblief aan hoe waar u elke stelling gedurende die afgelope 7 dae gevind het, deur die toepaslike nommer by elkeen van die stellings te merk.**

FISIESE WELSTAND

	glad nie	bietjie	gemiddeld	taamlik baie	geweldig
1. Ek ly aan energieverlies	0	1	2	3	4
2. Ek is naar	0	1	2	3	4
3. Weens my fisiese toestand vind ek dit moeilik om aan my gesin se behoeftes te voldoen	0	1	2	3	4
4. Ek verduur pyn	0	1	2	3	4
5. Newe-effekte van die behandeling tas my aan	0	1	2	3	4
6. Ek voel siek	0	1	2	3	4
7. Ek word gedwing om tyd in die bed deur te bring	0	1	2	3	4
8. As u die voorafgaande 7 vrae indringend beskou, in watter mate beïnvloed u **FISIESE WELSTAND** u lewenskwaliteit ?	(omkring een nommer) **0 1 2 3 4 5 6 7 8 9 10** **glad nie** **geweldig baie**				

SOSIALE WELSTAND

	glad nie	bietjie	gemiddeld	taamlik baie	geweldig
9. Ek voel afgesonder van my vriende	0	1	2	3	4
10. Ek kry emosionele ondersteuning van my familie	0	1	2	3	4
11. My vriende en bure ondersteun my	0	1	2	3	4
12. My familie het my siekte aanvaar	0	1	2	3	4
13. Gesinskommunikasie oor my siekte is swak	0	1	2	3	4
14. Ek voel na aan my lewensmaat (of die persoon wat my hoof-ondersteuner is)	0	1	2	3	4
15. Was u seksueel aktief gedurende die afgelope jaar? Nee______ Ja______ indien ja: Ek is tevrede met my sekslewe	0	1	2	3	4
16. As u die voorafgaande 7 vrae indringend beskou, in watter mate beïnvloed u **SOSIALE WELSTAND** u lewenskwaliteit ?	(omkring een nommer) **0 1 2 3 4 5 6 7 8 9 10** **glad nie** **geweldig baie**				

VERHOUDING MET U GENEESHEER

	glad nie	bietjie	Gemiddeld	taamlik baie	Geweldig
17. Ek het vertroue in my dokter(s)	0	1	2	3	4
18. My dokter is beskikbaar om my vrae te beantwoord	0	1	2	3	4
19. As u die voorafgaande 2 vrae indringend beskou, in watter mate beïnvloed u **VERHOUDING MET U GENEESHEER** u lewenskwaliteit ?	(omkring een nommer) **0 1 2 3 4 5 6 7 8 9 10** **glad nie geweldig baie**				

EMOSIONELE WELSTAND

	glad nie	bietjie	gemiddeld	taamlik baie	geweldig
20. Ek voel hartseer	0	1	2	3	4
21. Ek is trots op die wyse waarop ek my siekte baasraak	0	1	2	3	4
22. Ek voel negatief oor my kanse op herstel	0	1	2	3	4
23. Ek voel senuweeagtig	0	1	2	3	4
24. Ek bekommer my oor die dood	0	1	2	3	4
25. Ek bekommer my daaroor dat my toestand kan versleg	0	1	2	3	4
26. As u die voorafgaande 6 vrae indringend beskou, in watter mate beïnvloed u **EMOSIONELE WELSTAND** u lewenskwaliteit ?	(omkring een nommer) **0 1 2 3 4 5 6 7 8 9 10** **glad nie geweldig baie**				

FUNKSIONELE WELSTAND

	glad nie	bietjie	gemiddeld	taamlik baie	Geweldig
27. Ek kan werk (insluitend huiswerk)	0	1	2	3	4
28. My werk (insluitend huiswerk) is vervullend	0	1	2	3	4
29. Ek is in staat om genot uit die lewe te put	0	1	2	3	4
30. Ek aanvaar my siekte	0	1	2	3	4
31. Ek slaap goed	0	1	2	3	4
32. Ek geniet my normale ontspanningsaktiwiteite	0	1	2	3	4
33. Ek is tevrede met my huidige lewenskwaliteit	0	1	2	3	4
34. As u die voorafgaande 7 vrae indringend beskou, in watter mate beïnvloed u **FUNKSIONELE WELSTAND** u lewenskwaliteit ?	(omkring een nommer) **0 1 2 3 4 5 6 7 8 9 10** **glad nie geweldig baie**				

ADDISIONELE BEKOMMERNISSE

	glad nie	bietjie	gemiddeld	taamlik baie	Geweldig
35. Ek is kortasem	0	1	2	3	4
36. Ek is selfbewus oor die wyse waarop ek aantrek	0	1	2	3	4
37. My arms is geswel en seer	0	1	2	3	4
38. Ek voel seksueel aantreklik	0	1	2	3	4
39. Ek ondervind haarverlies	0	1	2	3	4
40. Ek is bekommerd oor die risiko van kanker in ander gesinslede	0	1	2	3	4
41. Ek is bekommerd oor die effek van stres op my siekte	0	1	2	3	4
42. Gewigsverlies is 'n bron van kommer	0	1	2	3	4
43. Ek voel volkome vroulik	0	1	2	3	4
44. As u die voorafgaande 9 vrae indringend beskou, in watter mate beïnvloed u **ADDISIONELE BEKOMMERNISSE** u lewenskwaliteit ?	(omkring een nommer) **0 1 2 3 4 5 6 7 8 9 10** **glad nie** **geweldig baie**				

ADDENDUM 5: FACT-B (VERSION 3) PEDI / NORTH SOTHO

Ka fase go na le lenaneo la dipego leo batho ba bangwe ba go swarwa ke bolwetši bja go swana le bja gago ba rego di bohlokwa. ka go thalela sediko nomorong e tee mothalading o tee bontšha ka fao pego ye nngwe le ye nngwe e nepagetšeng malebana le ka fao o bego o le ka gona mo lebakeng la matšatši a šupa a a fetilego

PABALELO MMELENG

	le ga-nnyane	gannyane	bokao-nenyana	bokoane	bokoan-kudu
1. Ga ke na maatla	0	1	2	3	4
2. Ke tlabatlaba dibete	0	1	2	3	4
3. Ka baka la go se phiphsine mmeleng, ke šitwa go phethagatša dinyaka kwa tša ba lapa la ka	0	1	2	3	4
4. Ke na le sehlabi	0	1	2	3	4
5. Ke tshwenywa ke ditlamorago tša ka morago ga kalafo	0	1	2	3	4
6. Ke ikwa ke lwala	0	1	2	3	4
7. Ke gapeletšega go dula lebakanyana ka malaong	0	1	2	3	4
8. Ge o lebeletše dipotšišo tša ka godimo tše 7 pabalelo mmeleng wa gago e ama bjang khwaliti ya bophelo bja gago?	(thalela sediko nomorong e tee) **0 1 2 3 4 5 6 7 8 9 10** **le gannyane kudukudu**				

PABALELO YA LEAGO / LAPA

	le ga-nnyane	gannyane	bokao-nenyana	bokoane	bokoan-kudu
9. Ke lewa ke boduto	0	1	2	3	4
10. Ke hwetša thekgo moyeng go tšwa go ba lapa la ka	0	1	2	3	4
11. Ke hwetša thekgo moyeng go tšwa go bagwera le go baagišani	0	1	2	3	4
12. Ba lapa ba amogetše bolwetši bja ka	0	1	2	3	4
13. Kgokagano ya ba lapa ka ga bolwetši bja ka ga e kgotsofatše	0	1	2	3	4
14. Ke ikwa ke le kgauswi le molekane wa ka (goba motho wo a nthekgilego kudu)	0	1	2	3	4
15. Tumo ya gago ya tša leratano e be e le ya mahlahla ngwageng wa go feta? Aowa ____ Ee____ Ge eba ee: Ke kgotsofatšwa ke bophelo bja ka bja leratano	0	1	2	3	4
16. Ge o lebeletše dipotšišo tša ka godimo tše 7 kamano yagago go ba lelapa le leago ya leago la lapa e ama bjang khwaliti ya bophelo bja gago?	(thalela sediko nomorong e tee) **0 1 2 3 4 5 6 7 8 9 10** **le gannyane kudukudu**				

TSWALANO LE NGAKA

	le gannyane	Gannyane	bokaonenyana	bokoane	bokoankudu
17. Ke tshepa ngaka (dingaka) ya ka	0	1	2	3	4
18. Ngaka e gona go araba dipotšišo tša ka	0	1	2	3	4
19. Ge o lebeletše dipotšišo tše pedi tša ka godimo, tswalano le ngaka e ama bjang khwaliti ya bophelo bja gago?	(thalela sediko nomorong e tee) **0 1 2 3 4 5 6 7 8 9 10** **le gannyane kudukudu**				

PABALELO MOYENG

	le gannyane	gannyane	bokaonenyana	bokoane	bokoankudu
20. Ke kwa ke nyamile	0	1	2	3	4
21. Ke ikgogomoša ka mokgwa wo ke laolago bolwetši bjaka	0	1	2	3	4
22. Ke felelwa ke maatla go lwantšha bolwetši bja ka	0	1	2	3	4
23. Ke ikwa ke tšhogatšhoga	0	1	2	3	4
24. Ke ikwa ke tshweywa ke kakenyo ya lehu	0	1	2	3	4
25. Ke tšhošwa ke gore maemo a ka a tlaaba šoro go ya pele	0	1	2	3	4
26. Ge o lebeletše dipotšišo tše di tshelelago tša ka godimo, pabalelo moyeng e ama bjang khwaliti ya bophelo bja gago?	(thalela sediko nomorong e tee) **0 1 2 3 4 5 6 7 8 9 10** **le gannyane kudukudu**				

PABALELOTIRIšWA

	le gannyane	Gannyane	bokaonenyana	bokoane	bokoankudu
27. Ke kgona go šoma (go akaretšwa mošomo wa ka gae)	0	1	2	3	4
28. Mošomo wa ka (go akaretšwa mošomo wa ka gae) o a phethagatšwa	0	1	2	3	4
29. Ke ipshina ka bophelo	0	1	2	3	4
30. Ke amogetše bolwetši bja ka	0	1	2	3	4
31. Ke robala gabotse	0	1	2	3	4
32. Ke ipshina ka dilwana tšeo ke di dirago go ithabiša	0	1	2	3	4
33. Ke ikwa ke kgotsofala ka bophelo baka	0	1	2	3	4
34. Ge o lebeletše dipotšišo tše di šupago tša ka godimo, pabalelo tirišwa e ama bjang khwaliti ya bophelo bja gago?	(thalela sediko nomorong e tee) **0 1 2 3 4 5 6 7 8 9 10** **le gannyane kudukudu**				

TLALELETšO YA DIPOTšIšO

	le gannyane	gannyane	bokaonenyana	bokoane	bokoankudu
35. Ke be ke hlaelela moya	0	1	2	3	4
36. Ke hlokomela ka fao ke aparago ka gona	0	1	2	3	4
37. Matsogo a ka a rurugile goba a bohloko	0	1	2	3	4
38. Ke a ratega (ge ke na le molekane waka)	0	1	2	3	4
39. Ke tshwenywa ke go loba moriri	0	1	2	3	4
40. Ke hlobaetša ke kgonagalo ya go ba gona ga bolwetši bja kankere ka lapeng	0	1	2	3	4
41. Ke hlobaetšwa ke go tshwenye ga mogopolong ka ga sephetho sa bolwetsi bjaka	0	1	2	3	4
42. Ke hlobaetšwa phetogo ya boima bja ka	0	1	2	3	4
43. Ke ikwa ke le mosadi	0	1	2	3	4
44. Ge o lebeletše dipotšišo tše senyane tša ka godimo o bona tlaleletšo ya dikamego e ama bjang khwaliti ya bophelo bja gago?	(thalela sediko nomorong e tee) **0 1 2 3 4 5 6 7 8 9 10** **le gannyane** **kudukudu**				

ADDENDUM 6: FACT-B (VERSION 3) TSWANA

Fa tlase go tlhagelela dipolelwana tse batho ba bangwe ba ba nang le bolwetse jo bo tshwanang le jwa gago ba di kaileng e le tsa botlhokwa. Sekeletsa nomoro e le nngwe mo moleng mongwe le mongwe, go supa gore polelwana nngwe le nngwe ke boammaruri jang mo go wena, mo malatsing a a supa a a fetileng

BIOTEKANELO JWA MMELE

	le goka	go le gonnye-nyane	ka mokgwa o o rileng	go le thata	thata thata
1. Ke tlhoka maatla	0	1	2	3	4
2. Ke a sellega	0	1	2	3	4
3. Ke tlholwa ke go tlamela ba lolapa lwa me ka ntlha ya bokoa ba mmele wa me	0	1	2	3	4
4. Ke na le ditlhabi	0	1	2	3	4
5. Mmele o koafatsa ke kalofo - Mmele wa ka o koa kagofetse morago ga kalafo	0	1	2	3	4
6. Ke ikutlwa ke bobola / lwala	0	1	2	3	4
7. Ke patelesega go tlhola ke robetse	0	1	2	3	4
8. Fa o lebile dipotso tse supa 7 tse di fa godimo, o bona e kete **BOITEKANELO JWA MMELE** wa gago bo ama jang boleng jwa botshelo jwa gago?	(sekeletsa nomoro e le nngwe) **0 1 2 3 4 5 6 7 8 9 10** **Le goka** **Thatathata**				

BOTSALANO / BOITEKANELO JWA LOLAPA

	le goka	go le gonnye-nyane	ka mokgwa o o rileng	go le thata	thata thata
09. Ke ikutlwa ke sa tlhole ke na le nako le ditsala tsa me	0	1	2	3	4
10. Ke bona tshegetso go tswa go ba lolapa lwame	0	1	2	3	4
11. Ke bona tshegetso go tswa go ditsala le go baagisani bame	0	1	2	3	4
12. Ba lolapa lwa me ba amogetse bolwetse jwa me	0	1	2	3	4
13. Puisano ka ga bolwetsi jwame e bokoa go ba lolapa lwame	0	1	2	3	4
14. Ke ikutlwa ke le gaufi le molekane wa me (kgotsa motho yo o ntshegeditseng e le ruri)	0	1	2	3	4
15. A o ntse o robalana ngwageng o o fetileng? Nnyaya ____ Ee____ Fa o rile ee, re tlhalosetse o re : Ke kgotsofetse ka botshelo jwa me fa ke robalana	0	1	2	3	4
16. Fa o lebile dipotso tse supa 7 tse di fa godimo, o bona e kete **BOTSALANO / BOITEKANELO JWA LOLAPA** lwa gago bo ama jang boleng jwa botshelo jwa gago?	(sekeletsa nomoro e le nngwe) **0 1 2 3 4 5 6 7 8 9 10** **Le goka** **Thatathata**				

BOTSALANO JWA GAGO LE NGAKA YA GAGO

	le goka	go le gonnye-nyane	ka mokgwa o o rileng	go le thata	thata thata
17. Ke ikanya (di)ngaka ya me	0	1	2	3	4
18. Ngaka ya me e teng / gone go araba dipotso tsa me	0	1	2	3	4
19. Fa o leba dipotso tse pedi tse di fa godimo, a o ka kaya gore **BOTSALANO JWA GAGO LE NGAKA** ya gago bo ama botshelo jwa gago jang?	(sekeletsa nomoro e le nngwe) **0 1 2 3 4 5 6 7 8 9 10** **Le goka** **Thatathata**				

MAIKUTLO A A ITEKANETSENG

	le goka	go le gonnye-nyane	ka mokgwa o o rileng	go le thata	thata thata
20. Ke ikutlwa ke hutsafetse	0	1	2	3	4
21. Ke motlotlo ka mokgwa o ke tswelelang ka ga bolwetsi jwa me	0	1	2	3	4
22. Ke felelwa ke tshepo ya go fenya bolwetse jwa me	0	1	2	3	4
23. Ke a boifa	0	1	2	3	4
24. Ke tlhobaetswa ke go akanya ka go swa	0	1	2	3	4
25 Ke tshwenngwa ke phetogo ya seemo sa botshelo jwame	0	1	2	3	4
26. Fa o leba dipotso tse thataro 6 tse di fa godimo, o bona e kete botshelo jwa gago bo amiwa jang ke **MAIKUTLO A A ITEKANETSENG** ?	(sekeletsa nomoro e le nngwe) **0 1 2 3 4 5 6 7 8 9 10** **Le goka Thatathata**				

GO DIRA O ITEKANETSE

	le goka	go le gonnye-nyane	ka mokgwa o o rileng	go le thata	thata thata
27. Ke kgona go dira (ke akaretsa tiro ya kwa gae)	0	1	2	3	4
28. Tiro ya me (ke akaretsa le ya kwa gae) e a kgotsofatsa	0	1	2	3	4
29. Ke itumelela go dira dilo tse ka gale ke di dirang go itumedisa fela. Ke thabela go tshela	0	1	2	3	4
30. Ke amogetse bolwetse jwa me	0	1	2	3	4
31. Ke robala sentle	0	1	2	3	4
32. Ke thabela dilo tse ka gale de di dirang go itumedisa	0	1	2	3	4
33. Ke kgotsofadiwa ke boleng jwa botshelo jwa me mo nakong ya ga jaana	0	1	2	3	4
34. Fa o leba dipotso tse supa 7 tse di fa godimo, o bona e kete botshelo jwa gago bo amiwa ke **GO DIRA O ITEKANETSE** jang?	(sekeletsa nomoro e le nngwe) **0 1 2 3 4 5 6 7 8 9 10** **Le goka Thatathata**				

DILO DINGWE TSE DI NTSHWENYANG / NTLHOBAETSANG

	le goka	go le gonnye-nyane	ka mokgwa o o rileng	go le thata	thata thata
35. Ke felelwa ke mowa	0	1	2	3	4
36. Ke kelothlhoko gore ke apara jang	0	1	2	3	4
37. Matsogo a me a rurugile kgotsa a bonolo	0	1	2	3	4
38. Ke ikuthlwa ke ratwake banna	0	1	2	3	4
39. Ke tshwenngwa ke go felelwa ke moriri	0	1	2	3	4
40. Ke tshwenngwa ke tekeletso ya boletse jwa kankere mo lapeng lame	0	1	2	3	4
41. Ke tshwenngwa ke kakoretso ua bolweise jajo kankere mo lolopeng lome	0	1	2	3	4
42. Ke tshwenngwa ke moikutlo ka ntiha ya bolwetse jwa me	0	1	2	3	4
43. Ke kgona go ikutlwa jaaka mosadisadi	0	1	2	3	4
44. Fa o leba dipotso tse robongwe 9 tse di fa godimo, o bona e kete **DILO DINGWE TSE DI GO TSWHENYANG / TLHOBAETSANG** di ama jang boleng jwa botshelo jwa gago?	(sekeletsa nomoro e le nngwe) **0 1 2 3 4 5 6 7 8 9 10** **Le goka** **Thatathata**				

ADDENDUM 7: FACT-B (VERSION 3) ZULU

Ngezansi Kunohlu Iwenzinto abantu abagula njengawe abati zibalulekile, Ngokuzungeleza inombolo eyodwa emgqeni ngamunye, yisho ukuthi isitatimende ngasinye sibe yiqiniso kangakanani kuwe ezinsukwini eziyisikhombisa 7 ezedlule.

ISIMO SEMPILO

	aKwenzeki	Kuyenzeka kancane	Kuzenzeka Kwesinye Isikhathi	Kuvamile ukwenzeke	Kuyenzega kakhulu
1. Ngiphelelwa amandla	0	1	2	3	4
2. Kuthi mangibuyise	0	1	2	3	4
3. Ngenxa yesimo sempilo yami ngi nenkinga ukumelana nezidingo zomndeni wami	0	1	2	3	4
4. Nginezinhlungu	0	1	2	3	4
5. Ngikhathazwa okunye ukugula okubangwa imithi engilashwe ngayo	0	1	2	3	4
6. Ngiyagula	0	1	2	3	4
7. Ngiphoqelekile ukuchitha isikhathi sami embhedeni	0	1	2	3	4
8. Uma ubheka kulemibuzo eyisikhombisa 7 engenhla ungathi isimo sempilo yakho silithinta kanjani izinga lempilo yakho	(zungelezela inombolo eyodwa) **0 1 2 3 4 5 6 7 8 9 10** **Asilithinti Neze** **Silithinta Kakhulu**				

ISIMO SEZENHLAWAKAHLE YOMNDENI

	aKwenzeki	Kuyenzeka kancane	Kuzenzeka Kwesinye isikhathi	Kuvamile ukwenzeke	Kuyenzega Kakhulu
09. Ngizwa ngiqhelile kubangane bami	0	1	2	3	4
10. Ngithola ukwesekelwa ngokomoya ngabomndeni	0	1	2	3	4
11. Ngithola ukusekelwa ngekomoya ngabamgane nomakhelwane bami	0	1	2	3	4
12. Umndeni wami uyakwamukele ukugula kwami	0	1	2	3	4
13. Umndeni awusaxoxi kahle ngokugula kwami	0	1	2	3	4
14. Ngizizwa ngisondelene nomngane wami (noma lowomuntu ongisizayo kakhulu)	0	1	2	3	4
15. Ubuhlangane oconsini kulonyaka odlule Qha______ Yebo______ Uma kunjalo: Ngenelisekile Ngempilo yobulili bami	0	1	2	3	4
16. Uma ubheka lemibuzo eyisikhombisa 7 engenhla ungathi isimo sezenhlalakahle somndeni wakho silithinta kanjani izinga lempilo yakho?	(zungelezela inombolo eyodwa) **0 1 2 3 4 5 6 7 8 9 10** **Asilithinti Neze** **Silithinta Kakhulu**				

UBUDLELWANO BAKHO NODOKOTELA

	aKwenzeki	Kuyenzeka kancane	Kuzenzeka Kwesinye isikhathi	Kuvamile ukwenzeke	Kuyenzega kakhulu
17. Ngiyamethemba udokotela wami (odokotela bami)	0	1	2	3	4
18. Udoketela wami uyathembakala ukuphendula imibuzo yami	0	1	2	3	4
19. Uma ubheka lemibuzo emibili 2 engenhla ungathi uudlelwana bakho nodokotela bukuthinta kanjani izinga lempilo yakho?	(zungelezela inombolo eyodwa) **0 1 2 3 4 5 6 7 8 9 10** **Asilithinti Neze** **Silithinta Kakhulu**				

UKUPHATHEKA KAHLE EMOYENI

	aKwenzeki	Kuyenzeka kancane	Kuzenzeka Kwesinye isikhathi	Kuvamile ukwenzeke	Kuyenzega kakhulu
20. Ngikhathazekile	0	1	2	3	4
21. Ngiyaziqhenya ngendlela engikwazi ngayo ukumelana nesifo sami	0	1	2	3	4
22. Ngiphelelwa yithemba ekulweni nesifo sami	0	1	2	3	4
23. Nginovalo	0	1	2	3	4
24. Ngiyakhathazeka ngokugula kwami	0	1	2	3	4
25. Ngikhathazwa ukuthi isimo sokugula kwami singahle sibe sibi kakhulu	0	1	2	3	4
26. Uma ubheka lemibuzo eyisithupha engenhla 6 ungathi ukuphatheka kahle emoyeni kulithinta kanjani izinga lempilo yakho?	(zungelezela inombolo eyodwa) **0 1 2 3 4 5 6 7 8 9 10** **Asilithinti Neze** **Silithinta Kakhulu**				

UKUPHATHEKA KAHLE NGOKOMSEBEZI

	aKwenzeki	Kuyenzeka kancane	Kuzenzeka Kwesinye isikhathi	Kuvamile ukwenzeke	Kuyenzega kakhulu
27. Ngiyasebenza (ngisho nomsebenzi wasekhaya)	0	1	2	3	4
28. Umsebenzi wami ngisho nowasekhaya uyangenelisa	0	1	2	3	4
29. Ngiyakwazi ukuzijabulisa ngempilo yami	0	1	2	3	4
30. Sengikwamukele ukugula kwami	0	1	2	3	4
31. Ngilala kahle	0	1	2	3	4
32. Ngiyazijabulisa ngezinto engejwayele ukuzijabulisa ngazo	0	1	2	3	4
33. Ngenelisiwe yizinga lempilo yami	0	1	2	3	4
34. Uma ubheka lemibuzo eyisikhombisa 7 engenhla ungathi ukuphatheka kahle ngokomsebenzi owenza ngemihla kulithinta kanjani izinga lempilo yakho?	(zungelezela inombolo eyodwa) **0 1 2 3 4 5 6 7 8 9 10** **Asilithinti Neze** **Silithinta Kakhulu**				

OKUNYE OKUKUKHATHAZAYO

	aKwenzeki	Kuyenzeka kancane	Kuzenzeka Kwesinye isikhathi	Kuvamile ukwenzeke	Kuyenzega Kakhulu
35. Ngiphelelwa umoya	0	1	2	3	4
36. Ngiyakhathazeka (noma giyazenyaza) ngendlela engigquoka ngayo	0	1	2	3	4
37. Izingalo zami zivuvukele	0	1	2	3	4
38. Ngiyabukeka	0	1	2	3	4
39. Ngikhathazwa ukuqothuka kwezinwele	0	1	2	3	4
40. Ngikhathazwa ukuthi abanye bomndeni bangaba sengozini yesifo somdlavuza (cancer)	0	1	2	3	4
41. Ngikhathazwa imiphumela yokukhathazeka empil weni yami	0	1	2	3	4
42. Ngikhathazwa ukushintsha kwesisindo somzimba wami	0	1	2	3	4
43. Ngisakwazi ukuzizwa ngiwumuntu wesifazane	0	1	2	3	4
44. Uma ubheka lemibuzo engu 9 engenhla ungathi okunye okukukhathazayo kulithinta kanjani izinga lempilo yakho?	(zungelezela inombolo eyodwa) **0 1 2 3 4 5 6 7 8 9 10** **Asilithinti Neze** **Silithinta Kakhulu**				

ADDENDUM 8: HOSPITAL CLASSIFICATION

This addendum gives an indication of the patient's financial status.

CLASSIFICATION	INCOME SINGLE PERSON Annual	INCOME FOR FAMILY Annual	HAS TO PAY Per visit
02	Less than R10 000 or assets less than R50 000	Less than R18 000 or assets less than R90 000	R13
03	Less than R14 000 or assets less than R70 000	Less than R18 000 or assets less than R130 000	R26
04	Less than R21 000 or assets less than R105 000	Less than R35 000 or assets less than R175 000	R39
17	More than R21 000 or assets more than R105 000	More than R35 000 or assets more than R175 000	R55
67	Patient has a medical aid	Patient has a medical aid	R55 entrance and all tests to be paid by the medical aid
08	Patient has the military medial aid	Family has the military medical aid	All costs covered by the military medical fund
58	Pensioner has the military medial aid	Pensioner and family has the military medical aid	All costs covered by the military medical fund

CHAPTER 5: RESULTS

First the validations of the Zulu, Pedi, Tswana and Afrikaans translations of the FACT-B questionnaires will be presented. Then a short discussion of the results of the pilot project is given. A detailed description of the patient demographical data follows. The findings of the final analysis, including summary statistics, Hotelling's T-test, multivariate analysis and survival analysis are then given.

5.1 VALIDATION OF THE TRANSLATED QUESTIONNAIRES

Tables 1 and 2 list the Chronbach's reliability coefficients for the Pedi (N= 62), Tswana (N= 64), Zulu (N= 63) and Afrikaans (N= 64) translations. The values for the three black languages are compared to the findings of Mullin (1999). Table 3 lists the mean scores and standard deviations for each of the FACT subscales, the FACT-G scale and the FACT-B scale, that had been found for the Pedi, Tswana, Zulu and Afrikaans translated versions of the FACT-B. These means and standard deviations are then compared to and an English version that had been found in the literature (Cella 1993).

TABLE 1: RELIABILITY (CHRONBACH'S ALPHA) OF THE THREE AFRICAN LANGUAGE VERSIONS OF THE FUNCTIONAL ASSESSMENT OF CANCER THERAPY.

SCALE		**LANGUAGE**		
	VERIFICATION	**PEDI**	**TSWANA**	**ZULU**
Physical Well Being 7 items	Mertz	0.71	0.85	0.79
	Mullin	0.78	0.79	0.64
Social/Family Well Being, 7 items	Mertz	0.54	0.48	0.47
	Mullin	0.60	0.61	0.36
Relationship with Doctor 2 items	Mertz	0.83	0.85	0.46
	Mullin	0.80	0.92	0.86
Emotional Well Being 5 items are scored	Mertz	0.78	0.84	0.61
	Mullin	0.86	0.70	0.72
Functional Well Being 7 items	Mertz	0.86	0.84	0.86
	Mullin	0.92	0.82	0.80
Additional Concerns 9 items	Mertz	0.77	0.69	0.53
TOTAL FACT-B SCORE	Mertz	0.77	0.73	0.81

Compared with values determined by Mullin (1999)

TABLE 2: RELIABILITY (CHRONBACH'S ALPHA) OF THE AFRIKAANS VERSION OF THE FUNCTIONAL ASSESSMENT OF CANCER THERAPY.

SCALE		CHRONBACH'S ALPHA
Physical Well Being	(7 items)	0.87
Social/Family Well Being	(7 items)	0.65
Relationship with Doctor	(2 items)	0.58
Emotional Well Being	(5 items)	0.78
Functional Well Being	(7 items)	0.89
Additional Concerns	(9 items)	0.65
TOTAL FACT-B SCORE		0.82

TABLE 3: MEANS (M) AND STANDARD DEVIATIONS (SD) OF THE FACT-B SCALE FOR THE THREE AFRICAN LANGUAGES, AFRIKAANS AND THE ORIGINAL ENGLISH LANGUAGE VERSION

(CELLA et al 1993), (BRADY et al 1997)

Scale	Language									
	PEDI N=62		TSWANA N=64		ZULU N=63		AFRIKAANS N=64		ENGLISH N=466	
	M	SD	M	SD	M	SD	M	SD	M	SD
PWB	16.3	5.0	15.8	6.0	19.7	6.0	17.8	6.4	20.5	5.5
SWB	20.1	5.0	17.8	4.3	21.0	4.6	21.7	4.2	21.9	4.8
RWD	7.2	1.7	7.2	1.2	7.7	0.9	7.3	1.2	6.9	1.5
EWB	14.2	4.9	12.2	4.8	15.3	4.2	15.2	3.9	14.8	3.9
FWB	19.8	6.8	17.3	5.6	20.7	6.7	16.8	6.7	18.0	6.1
ADD	22.5	7.1	19.9	5.6	25.4	6.2	22.8	6.0	------	------
FACT G	77.5	17.3	70.1	15.9	84.3	17.0	78.9	17.8	82.0	15.9
FACT B	100.1	22.1	89.9	19.1	109.7	22.0	101.7	22.1	------	------

See KEY on next page

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KEY FOR TABLE 3:

PWB	physical well being	SWB	social well being
RWD	relationship with doctor	EWB	emotional well being
FWB	functional well being	ADD	additional concerns

5.2 ANALYSIS OF THE PILOT PROJECT

5.2.1 PATIENT POPULATION

Data for 200 patients who had completed at least one QOL questionnaire was analyzed.

5.2.2 MISSING DATA

This is an ubiquitous phenomenon is the field of quality of life research.
Some of the reasons for missing data are:

- Patients with a poor prognosis and rapidly progressing disease die before all evaluations can be completed.
- Some patients have early progression, so that at the time when the "during" QOL measurement is scheduled, treatment has to be changed and this time point has to be designated "after" treatment.
- Patient non-compliance, especially at time of disease progression, when the QOL evaluation becomes paramount.
- Staff non-compliance or oversight. This is a particularly vexing problem and the only factor that could be improved, resulting in less missing data.

5.2.3 SUMMARY OF THE MOST IMPORTANT FINDINGS

In table 4 the effect of different types of treatment on individual quality of life domains is shown. And in tables 5 and 6 the findings about race related differences in quality of life is detailed.

TABLE 4: FINDINGS ABOUT THE EFFECTS OF DIFFERENT TYPES OF TREATMENT ON QUALITY OF LIFE

TREATMENT	DOMAIN (P-value)	RESULTS
Hormonal vs. chemotherapy.	Functional well being P=0.044	Before, during and after treatment patients on **hormones** describe their condition as **worse.**
Any treatment.	Physical well being P=0.002	For any treatment patients describe their condition as **worse** during treatment.
Hormonal or chemotherapy.	Relationship with doctor P=0.044	Relationship with dr. is **worse** during therapy.
Hormonal or chemotherapy.	Emotional P=0.002 and functional P=0.019	Emotional and functional well-being is better during treatment than before.
Hormonal or chemotherapy.	Relationship with doctor P=0.027	Relationship with the doctor is **worse during treatment** than thereafter.
Chemotherapy	Additional concerns P=0.025	Patients on **chemotherapy are feeling worse after treatment** than before.

TABLE 5: COMPARISONS BETWEEN THE QUALITY OF LIFE OF THE DIFFERENT RACE GROUPS

RACE	DOMAIN	RESULTS
Black patients.	Physical well being P=0.043	All patients describe their physical well-being as deteriorating during treatment (chemo or hormonal), but **black** patients feel even worse than white patients.
Black patients.	Social and family well being P=0.000	The social and family well being of **black patients is worse**, than that of white patients during treatment (chemo or hormonal).
Black patients.	Physical well being P=0.018 Social and family well being P=0.000 Emotional well being P=0.016 Total score P=0.008	Already before treatment the quality of life of **black** patients is **worse** than that of white patients.
Black patients.	Physical well being P=0.013 Social and family well being P=0.000	During any treatment the physical and social/family well-being is worse for black patients.
Black patients.	Additional concerns P=0.041	After treatment (any treatment) additional concerns are worse for black patients

TABLE 6: COMPARISONS OF TOTAL FACT SCORES SHOWING THE EFFECT OF RACE MEASURED AT A SINGLE TIME POINT (BEFORE ANY TYPE OF TREATMENT)

DOMAIN	RACE	N	MEAN SCORE
PHYSICAL WELL BEING	White	57	21.19
	Black	70	18.77
SOCIAL/FAMILY WELL BEING	White	57	23.57
	Black	70	19.82
RELATIONSHIP WITH DOCTOR	White	57	7.71
	Black	70	7.55
EMOTIONAL WELL BEING	White	57	14.64
	Black	70	12.67
FUNCTIONAL WELL BEING	White	57	21.31
	Black	70	19.53
ADDITIONAL CONCERNS	White	57	23.75
	Black	70	23.98
TOTAL SCORES	White	57	111.73
	Black	70	102.11

5.3 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENT POPULATION

5.3.1 DATA

Demographic and clinical data for the patients are listed in tables 7 to 14. Seventeen of the patients also completed FACT-B questionnaires for either second- or thirdline treatment with chemotherapy. That is the reason why the final analysis was performed with 100 sets of data. Demographics are principally recorded for the actual number of patients (83) and only for the total number of data-sets (100) in cases where a characteristic (for example performance status or disease stage) could change for a subsequent treatment line.

Table 7 and figure 1 show the amount of patients in each ethnic group. Information also contained in table 7, separated into race groups is: patients who defaulted from treatment, participation in clinical trials, employment and marital status.

Table 8 details the menopausal status, number of metastases, receptor status, tumor grade and number of nodes at mastectomy for the different race groups. Figure 2 shows the age distribution curves for the patients, which is to be read in conjunction with the menopausal status of the patients. In table 9 treatment-related clinical characteristics for the white and black patients are given. This includes information such as "inoperable" at first diagnosis, which patients had had a mastectomy, radiotherapy, adjuvant chemotherapy and medication for depression and/or anxiety.

The hospital classification, which is indicative of financial status, is given for white and black patients in table 10. Table 11 shows the performance status, disease stage and educational level at the time of questionnaire completion. A finer distinction of educational level is given in table 13. The chemotherapy regimen received by the patients is expounded in table 12 as well as figure 3 and the medication for depression and/or anxiety in table 14.

TABLE 7: GENERAL DEMOGRAPHIC CHARACTERISTICS FOR THE PATIENT GROUP OF THE FINAL ANALYSIS

<table>
<tr><th colspan="3">CHARACTERISTIC</th><th colspan="3">N=83</th></tr>
<tr><td rowspan="5">ETHNICITY</td><td colspan="2">Afrikaans</td><td colspan="3">33</td></tr>
<tr><td colspan="2">English</td><td colspan="3">8</td></tr>
<tr><td colspan="2">Pedi</td><td colspan="3">16</td></tr>
<tr><td colspan="2">Tswana</td><td colspan="3">11</td></tr>
<tr><td colspan="2">Zulu</td><td colspan="3">15</td></tr>
<tr><td rowspan="3">DEFAULTED FROM TREATMENT</td><td colspan="2"></td><td colspan="2">YES</td><td>NO</td></tr>
<tr><td colspan="2">Whites</td><td colspan="2">4</td><td>37</td></tr>
<tr><td colspan="2">Blacks</td><td colspan="2">10</td><td>32</td></tr>
<tr><td rowspan="3">PARTICIPATED IN A STUDY</td><td colspan="2"></td><td>NO</td><td>YES</td><td>>ONE</td></tr>
<tr><td colspan="2">Whites</td><td>7</td><td>29</td><td>5</td></tr>
<tr><td colspan="2">Blacks</td><td>3</td><td>38</td><td>1</td></tr>
<tr><td rowspan="3">EMPLOYMENT</td><td></td><td>Employed</td><td>Un-employed</td><td>Home-Maker</td><td>Retired</td></tr>
<tr><td>Whites</td><td>12</td><td>2</td><td>16</td><td>11</td></tr>
<tr><td>Blacks</td><td>18</td><td>10</td><td>8</td><td>6</td></tr>
<tr><td>MARITAL STATUS</td><td></td><td>Single</td><td>Married</td><td>Divorced</td><td>Widowed</td></tr>
<tr><td></td><td>Whites</td><td>3</td><td>30</td><td>4</td><td>4</td></tr>
<tr><td></td><td>Blacks</td><td>25</td><td>13</td><td>2</td><td>2</td></tr>
</table>

TABLE 8: GENERAL CLINICAL CHARACTERISTICS FOR THE PATIENT GROUP OF THE FINAL ANALYSIS

CHARACTERISTIC		N=83		
MENOPAUSAL STATUS		**PRE-**	**POST-**	
	Whites (N=41)	14	27	
	Blacks (N=42)	21	21	
NUMBER OF METASTASES		**1**	**2**	**≥3**
	Whites	7	13	21
	Blacks	3	5	34
RECEPTOR STATUS		**negative**	**positive**	**unknown**
	Whites	12	13	16
	Blacks	13	13	16
TUMOR GRADE (if known)		**1**	**2**	**3**
	Whites	1	15	13
	Blacks	0	25	9
NUMBER OF NODES AT MASTECTOMY (if known)		**0**	**1-3**	**>3**
	Whites	11	9	8
	Blacks	4	0	5

TABLE 9: TREATMENT-RELATED CLINICAL CHARACTERISTICS FOR THE PATIENT GROUP OF THE FINAL ANALYSIS

CHARACTERISTIC		N=83	
INOPERABLE AT FIRST DIAGNOSIS	**Whites**	14	
	Blacks	36	
HAD SURGERY	**Whites**	28	
	Blacks	12	
HAD RADIOTHERAPY			
No radiotherapy at all	**Whites**	21	
	Blacks	25	
Post mastectomy (adjuvant)	**Whites**	3	
	Blacks	1	
For advanced disease only	**Whites**	13	
	Blacks	14	
As adjuvant & for advanced Disease	**Whites**	4	
	Blacks	2	
HAD ADJUVANT CHEMOTHERAPY	**Whites**	9	
	Blacks	0	
RECEIVED MEDICATION FOR DEPRESSION AND/OR ANXIETY		**NO**	**YES**
	Whites	14	27
	Blacks	31	11

TABLE 10: FINANCIAL STATUS OF PATIENTS ACCORDING TO THEIR HOSPITAL CLASSIFICATION

CLASSIFICATION	02	03	04	08	67	Misc.
Whites	9	3	2	1	7	8
Blacks	34	1	2	1	4	0

See chapter 4, addendum 8 (hospital classification) for explanation of classification codes. In essence a 02 patient is the poorest and earns less than R10 000 per year. Thereafter annual income increases through 03 to 04. Other patients have a medical aid.

TABLE 11: PERFORMANCE STATUS, DISEASE STAGE AND EDUCATIONAL LEVEL AT THE TIME OF INITIAL QUESTIONNAIRE COMPLETION (N=100)

DISEASE STAGE:	**III**		**IV**
Whites	11		39
Blacks	14		36
EDUCATIONAL LEVEL:	**Less than grade 12**		**Grade 12 or higher**
Whites	18		32
Blacks	37		13
PERFORMANCE STATUS:	**PS=0**	**PS=1**	**PS=2**
Whites	16	30	4
Blacks	5	40	5

TABLE 12: CHEMOTHERAPY REGIMEN RECEIVED BY PATIENTS

CHEMOTHERAPY	**WHITE PATIENTS**	**BLACK PATIENTS**
Adriamycin	6	6
Adriamycin + Taxane	13	15
Adriamycin-combination (AC or FAC)	6	9
Taxane	12	6
CMF	3	6
MMM	1	0

TABLE 13: EDUCATIONAL LEVEL OF PATIENTS

	No education	**< Grade 8**	**Grade 6 - 9**	**Grade 12**	**> Grade 12**
Whites (41)	0	0	16	16	10
Zulu (15)	6	4	4	0	1
Pedi (16)	1	7	6	1	1
Tswana (11)	1	1	4	4	1

TABLE 14: USAGE OF MEDICATION FOR DEPRESSION AND/OR ANXIETY

DRUG	WHITE PATIENTS (N=41)	BLACK PATIENTS (N=42)
None	14	31
Paroxetine	1	0
Lorazepam +perphenazine +amitriptyline	1	0
Fluvoxamine +bromazepam	1	0
Temazepam	4	4
Haloperidol	1	0
Oxazepam	10	6
Oxazepam +amitriptyline	2	1
Amitriptyline	4	0
Diazepam	1	0
Usage unknown	2	0

5.3.2 DISCUSSION OF DEMOGRAPHY AND CLINICAL CHARACTERISTICS

A number of very interesting and pertinent findings came to light during examination of the baseline demographic information of this patient group. Participation in this quality of life study was offered to all patients with locally advanced and metastatic breast cancer for the study period and the patient sample is thus considered as representative of the breast cancer patients in the Pretoria area of Gauteng, for the period ranging from 1993 to 1999. The ethnic groups were well balanced in numbers for the black patients but there was a bias for the number of Afrikaans patients (see table 7 and figure 1). The question arose whether there are in fact more Afrikaans females with breast cancer, or whether this was a geographical phenomenon. Data supplied by Statistics South Africa, for the 1996 census, supported the fact that the larger number of Afrikaans patients is due to a higher number of Afrikaans-speaking people living in the Pretoria area, than English-speaking people (75.8% Afrikaans versus 24.2% English).

Seven percent more black patients defaulted from treatment than white patients, which can probably be ascribed to less resources to be able to come for treatment (transport and money), ignorance and the influence of a different philosophical culture to healing. In the black cultures the sangoma (traditional healer) is consulted and the prescribed treatment takes place in the patient's home and family environment, whereas the patient is "isolated" from her family in a hospital environment in white cultures.

Seven percent more black patients than white patients were employed, while 9.6% more white patients were staying at home. This reflects the economical realities of the traditionally disadvantaged black population. The pattern for marriage showed that while 73% of the white patients were married, only 31% of the black patients were married.

In general breast cancer is a disease of older women and this general trend is also found for patients in the Johannesburg area as well as for the total female breast cancer population in South Africa. There are thus more post-menopausal females diagnosed with breast cancer in South Africa. At Pretoria Academic Hospital however, the amount of black pre- and post-menopausal breast cancer patients is identical for our sample (see table 8). This same finding was also made by professor L van Rensburg at the Genetics Department of Pretoria Academic Hospital.

This finding needs to be seen in proportion to the population distribution of South African females. My data was collected between 1993 and 1999 and the population figures, and incidence of breast cancer figures for South African females between 1993 and 1995 were used as comparison (Sitas 1998). When the amount of patients in each age group is expressed as a ratio of the total population a bimodal distribution is found for the black patients with a peak at age group 40 – 44 and again at age group 55 – 59 (see table 27). For the white patients a unimodal peak is found in the 55 – 59 age group. For black patients the ratio of patients in the 40 – 44 group is smaller than the ratio of patients in the 55 –-59 age group. This serves to illustrate that there are in fact not more pre-menopausal black females than post-menopausal females in our group, when corrected for population numbers.

There is however an undeniable peak in the incidence of breast cancer in our black patients in the 40 – 44 age group. Whether this is in fact significant is hard to say and needs further investigation.

It is interesting to note that relative to population numbers, the incidence of breast cancer in our white patients is much higher than in the black patients and this is in accordance with the general findings for South African females (Sitas 1998).

A certain bias has however been introduced in that we lose a lot of black patients in the higher age groups because they tend to wait until they have such dire disease and are in such a poor condition, that they have become untreatable are not seen by us at all.

Eighty percent of the black patients had three or more metastases at first diagnosis, versus 51% of white patients, demonstrating that black patients wait longer to seek medical help than the white patients. White patients with an excellent performance status (PS=0) numbered 39% versus 12% of the blacks. Receptor status, was however almost identical for the black and the white patients. At mastectomy 27% of the white patients and 10% of the black patients were node negative. The node negative patients are much less likely to recur than node positive patients.

Thirty four percent of the white patients were inoperable at first diagnosis versus eighty six percent of the black patients. Patients who had had a mastectomy were 29% black versus 68% white. None of the black patients in this sample had adjuvant chemotherapy. This is particularly worrying in the light of the latest findings about the benefits of adjuvant chemotherapy for breast cancer patients.

Substantially more white, than black patients, 66% versus 26% received medication for depression and/or anxiety. Black patients are culturally inclined to be stoical and do not complain readily. There may also be communication barriers between the predominantly white physicians and black patients.

Hospital classification, which is an indicator of financial status, reflects the current disadvantaged status of black patients. Eighty one percent of blacks versus 22% of whites are in the lowest income group. The educational level of the whites shows that 78% have a grade 12 or higher qualification. Only 31% of black patients fall into this educational category.

It is therefore clear that the black patients are very disadvantaged and a huge educational effort is needed to inform the black women of South Africa about the dangers, signs and symptoms of breast cancer. All females should be educated through the media and at the local health care levels about the advantages of seeking medical attention timeously. A guide to the monthly breast examination is also included in chapter 1 addendum 7. Hopefully the Reconstruction and Development Program will contribute towards ameliorating some of these disadvantages in the black population.

5.4 SUMMARY STATISTICS FOR THE FINAL ANALYSIS

Summary statistics for the total sample (N= 100), the white patients (N=50) and the black patients (N=50) separately are shown in tables 15, 16 and 17.

TABLE 15: SUMMARY STATISTICS OF THE INDIVIDUAL QUALITY OF LIFE DOMAINS AND TOTAL SCORES, BEFORE AND DURING TREATMENT FOR THE TOTAL SAMPLE (N= 100)

VARIABLE		MEAN	STD. DEV.	MINIMUM	MAXIMUM
BEFORE TREATMENT	Age	49.31	10.20	26	69
	Physical wellbeing	20.46	5.39	7	28
	Social/family wellbeing	21.37	4.51	11	28
	Relationship with doctor	7.59	1.04	3	8
	Emotional wellbeing	14.07	4.50	1	20
	Functional wellbeing	21.04	5.57	4	28
	Additional concerns	23.52	5.93	8	36
	Total FACT-B score	108.05	18.03	58	144
DURING TREATMENT	Physical wellbeing	18.74	5.71	6	28
	Social/family wellbeing	21.77	4.72	6	28
	Relationship with doctor	7.55	1.14	0	8
	Emotional wellbeing	15.78	4.34	4	20
	Functional wellbeing	20.08	5.98	0	28
	Additional concerns	22.90	6.02	7	36
	Total FACT-B score	106.82	18.42	58	145

TABLE 16: SUMMARY STATISTICS OF THE INDIVIDUAL QUALITY OF LIFE DOMAINS AND TOTAL SCORES, BEFORE AND DURING TREATMENT FOR THE WHITE PATIENTS (N= 50)

VARIABLE		MEAN	STD. DEV.	MINIMUM	MAXI-MUM
BEFORE TREATMENT	Age	50.74	10.19	27	69
	Physical wellbeing	21.72	5.14	7	28
	Social/family wellbeing	23.54	3.47	13	28
	Relationship with doctor	7.62	1.09	3	8
	Emotional wellbeing	14.78	4.15	1	20
	Functional wellbeing	21.62	5.44	9	28
	Additional concerns	25.02	5.22	12	34
	Total FACT-B score	114.3	16.24	73	138
DURING TREATMENT	Physical wellbeing	19.52	5.94	6	28
	Social/family wellbeing	23.18	4.11	10	28
	Relationship with doctor	7.64	0.92	4	8
	Emotional wellbeing	16.22	4.51	4	20
	Functional wellbeing	20.1	6.16	6	28
	Additional concerns	23.54	5.15	12	36
	Total FACT-B score	110.2	19.62	70	145

TABLE 17: SUMMARY STATISTICS OF THE INDIVIDUAL QUALITY OF LIFE DOMAINS AND TOTAL SCORES, BEFORE AND DURING TREATMENT FOR THE BLACK PATIENTS (N=50)

VARIABLE		MEAN	STD. DEV.	MINIMUM	MAXI-MUM
BEFORE TREATMENT	Age	47.88	10.11	26	67
	Physical wellbeing	19.2	5.40	7	28
	Social/family wellbeing	19.2	4.41	11	28
	Relationship with doctor	7.56	0.99	4	8
	Emotional wellbeing	13.36	4.75	3	20
	Functional wellbeing	20.46	5.69	4	28
	Additional concerns	22.02	6.26	8	36
	Total FACT-B score	101.8	17.71	58	144
DURING TREATMENT	Physical wellbeing	17.96	5.41	7	28
	Social/family wellbeing	20.36	4.91	6	28
	Relationship with doctor	7.46	1.33	0	8
	Emotional wellbeing	15.34	4.15	5	20
	Functional wellbeing	20.06	5.86	0	28
	Additional concerns	22.26	6.76	7	34
	Total FACT-B score	103.44	16.66	58	135

5.5 VALIDATION OF THE FACT-B FOR SOUTH-AFRICAN PATIENTS (TOTAL SAMPLE)

Table 18 lists the means, standard deviations (SD) and Chronbach's alpha coefficients generated for the total group, for each of the FACT-B subscales as well as for the FACT-B total score. High mean scores reflect a better quality of life. An alpha of 0.7 or above is indicative of internal consistency of the items. In table 19 the mean scores and Chronbach's reliability coefficients for our sample is compared to the values found by Brady (1997) for American patients.

TABLE 18: FACT-B DESCRIPTIVE STATISTICS: RELIABILITY/ CONCURRENT VALIDITY FOR THE TOTAL SAMPLE (N=100)

Scale	Mean	SD	Alpha
PWB (7-item) before Rx	20.46	5.4	0.7496
SWB (7-item) before Rx	21.37	4.5	0.4698
RWD (2-item) before Rx	7.59	1.0	0.8596
EWB (5-item) before Rx	14.07	4.49	0.6997
FWB (7-item) before Rx	21.04	5.6	0.7530
AWB (9-item) before Rx	23.52	5.9	0.5020
TOTAL (37-item) before Rx	108.05	18.0	0.6950
PWB (7 item) during Rx	18.74	5.7	0.7813
SWB (7 item) during Rx	21.77	4.7	0.5698
RWD (2 item) during Rx	7.55	1.1	0.6232
EWB (5 item) during Rx	15.78	4.3	0.7650
FWB (7 item) during Rx	20.08	5.9	0.8126
AWB (8 item) during Rx	22.90	6.0	0.4927
TOTAL (37 item) during Rx	106.82	18.4	

KEY:

PWB	physical well being
RWD	relationship with doctor
SWB	social well being
EWB	emotional well being
FWB	functional well being
AWB	additional concerns

TABEL 19: COMPARISON OF THE SOUTH-AFRICAN VALIDATED FACT (DURING TREATMENT) WITH THE AMERICAN VALIDATION (BRADY 1997)

Scale	For USA patients		For RSA patients	
	Mean (SD)	**Alpha**	**Mean (SD)**	**Alpha**
Physical Well Being	22.1 (5.3)	0.81	18.7 (5.7)	0.78
Social Well Being	22.7 (5.2)	0.69	21.8 (4.7)	0.57
Relationship With Doctor	7.0 (1.6)	0.78	7.6 (1.1)	0.62
Emotional Well Being	16.3 (3.5)	0.69	12.3 (3.9)	0.77
Functional Well Being	20.6 (6.4)	0.86	16.6 (5.6)	0.81
Additional Well Being	24.1 (6.5)	0.63	21.1 (6.0)	0.49
TOTAL FACT-B	112.8 (20.9)	0.90	98.1 (18.1)	0.70

5.6 COMPARISON OF RACE GROUPS WITH RESPECT TO THE SIX DOMAINS OF THE FACT-B

Hotelling's T-square was employed to assess whether race groups differed with respect to the observation vector (total baseline scores for: physical-, social-, relationship with doctor, emotional-, functional well being and additional concerns) and in the absence of covariates, races were found not to differ.

The difference between the quality of life for each domain during treatment and at baseline is given in table 20 for white patients and table 21 for black patients.

TABLE 20: THE DIFFERENCE BETWEEN QOL SCORES FOR EACH DOMAIN DURING TREATMENT AND AT BASELINE FOR WHITE PATIENTS

VARIABLE	MEAN	STD. DEV.	MINIMUM	MAXIMUM
Physical wellbeing	- 2.20	6.27	-20	10
Social/family wellbeing	- 0.36	3.87	-8	8
Relationship with dr.	0.02	1.10	-4	3
Emotional wellbeing	1.44	5.44	-12	16
Functional wellbeing	-1.52	5.74	-19	8
Additional concerns	-1.48	4.99	-14	10

TABLE 21: THE DIFFERENCE BETWEEN QOL SCORES FOR EACH DOMAIN DURING TREATMENT AND AT BASELINE FOR BLACK PATIENTS

VARIABLE	MEAN	STD. DEV.	MINIMUM	MAXIMUM
Physical wellbeing	-1.24	6.62	-19	13
Social/family wellbeing	1.16	5.91	-19	14
Relationship with dr.	-0.1	1.68	-8	4
Emotional wellbeing	1.98	5.33	-9	16
Functional wellbeing	-0.4	7.01	-21	15
Additional concerns	0.24	5.90	-12	15

2-group Hotelling's T-squared = 5.8979035

F test statistic: ((100-6-1) / (100-2) (6)) x 5.8979035 = 0.93283167

HO: Vectors of means are equal for the two groups

F (6,93) = 0.9328

Pr > F (6,93) = 0.4754

5.7 REGRESSION ANALYSIS TO COMPARE RACES

Comparison of races with respect to:

1. Total baseline scores for: physical-, social-, relationship with doctor, emotional-, and functional well being, additional concerns and total score, initially without a covariate (model has a poor R-square).

2. Then with baseline total scores as cofactor (R-square improved markedly).

3. And then finally by adjusting for age and time between the "before" and "during" FACT-B (covariates). Performance status, stage, education, marital status and concomitant disease were included in the multivariate analysis as risk factors (R-square improved slightly). It was suspected that race and education would be confounded, but by omitting education, the results were not improved and it was therefore retained.

In this section "higher" and "lower" will refer to the sign of the effect and the correct interpretation will again depend on the formulation in the constructs. For all data a 95% confidence interval applies.

The complete regression analysis for physical well being is set out in table 22. Table 23 is a summary of all the statistically significant findings for the regression analyses for each quality of life domain and also for the total FACT-B score.

TABLE 22: THE REGRESSION ANALYSIS FOR PHYSICAL WELL BEING

Physical Well-being	**Coefficient**	**Standard Error**	**P >| t |**
1. Races compared by the change in Physical Well Being (PWB) score during treatment and at baseline:			
Black vs. white	0.96	1.29	0.458
2. Races compared by the change in PWB score during treatment and at baseline, with baseline PWB score added in as cofactor:			
Physical Well-being	-0.67	0.104	0.000
Black vs. white	-0.72	1.118	0.521
3. Races compared by the change in PWB score during treatment and at baseline & with cofactors age and treatment time. Values adjusted for performance status, stage, education, marital status and concomitant disease.			
Physical Well-being	-0.7	0.106	0.000
Age	-0.02	0.056	0.748
Treatment time*	-0.04	0.09	0.65
Black vs. white	-1.43	1.26	0.261
PS=1 vs. PS=0	2.90	1.42	0.048
PS=2 vs. PS=0	-0.83	2.24	0.416
Stage 4 vs. stage 3	0.02	1.29	0.990
Well educated vs. poor education	0.73	1.22	0.552
Divorced/widowed vs. married/single	-0.81	1.48	0.589
Concomitant disease vs. none	-1.62	1.26	0.201

Positive findings are highlighted (where P≤ 0.07).

* Treatment time = the time difference in weeks between the baseline QOL evaluation and the "during" treatment QOL evaluation.

TABLE 23: REGRESSION ANALYSIS SHOWING POSITIVE FINDINGS FOR RISK FACTORS WITH REGARD TO THE CHANGE WITHIN DOMAINS FROM BASELINE TO DURING TREATMENT, WHEN COFACTORS ARE INCLUDED.

Domain Cofactor	**Coefficient**	**Standard Error**	**P >| t |**
Physical well being PS=1 vs. PS=0	2.87	1.43	0.048
Social well being Black vs. white	-1.84	1.08	0.094 tendency
Social well being PS=2 vs. PS=0	4.16	1.77	0.021
Relationship with dr. Stage 4 vs. stage 3	0.59	0.27	0.034
Emotional well being Treatment time	-0.15	0.07	0.036
Emotional well being PS=2 vs. PS=0	3.53	1.71	0.042
Emotional well being Marital status	-1.89	1.13	0.099 tendency
Functional well being Better educated vs. not	2.39	1.27	0.062 tendency
Total FACT-B score PS=1 vs. PS=0	8.2	4.28	0.058

1. There is a significant (p = 0.048) increase of 2.87 in the change of physical well being from performance status PS = 0 to PS = 1.
2. There is a significant (p = 0.015) decrease of 4.7 in the change of physical well being from performance status PS = 1 to PS = 2.
3. There is a tendency toward a significant (0.094) decrease of 1.84 in the change of social well being from white to black.
4. There is a significant (p = 0.021) increase of 4.16 in the change of social well being from performance status PS = 0 to PS = 2.
5. There is a significant (p = 0.034) increase of 0.59 in the change of relationship with doctor from stage 3 to stage 4 disease.
6. There is a significant (p = 0.042) increase of 3.53 in the change of emotional well being from performance status PS = 0 to PS = 2.
7. There is a tendency towards a significant (p = 0.099) decrease of 1.89 in the change of emotional well being from being married or single to being divorced or widowed.
8. There is a tendency toward a significant (p = 0.062) increase of 2.39 in the change of functional well being from being less educated to being better educated.
9. There is a significant (p = 0.058) increase of 8.2 in the change of the total FACT-B score from performance status (PS) = 0 to PS = 1.

5.8 ANALYSIS OF SURVIVAL

The log-rank test for the difference in the survival of the white versus the black patients is shown in tables 24 and 25. The median survival for the total group was 67 weeks, with a range of 9 to 325 weeks (see table 26). A Kaplan-Meier curve by race is shown in figure 5.

TABLE 24: COMPARISON OF SURVIVAL FOR WHITE AND BLACK PATIENTS

Race	**Time at risk**	**Incidence rate**	**N**	**Survival time (weeks)**		
				25%	50%	75%
White	6204	0.0058027	50	51	141	235
Black	4543	0.0070438	50	48	86	180
TOTAL	10747	0.0063273	100	50	96	333

TABLE 25: LOG-RANK TEST FOR EQUALITY OF SURVIVOR FUNCTIONS

Race	**Events observed**	**Expected**
White	36	39.90
Black	32	28.10
TOTAL	68	68.00

$\text{Chi}^2(1) = 0.98$
$\text{Pr} > \text{Chi}^2 = 0.3216$

TABLE 26: MEDIAN SURVIVAL OF THE PATIENT GROUP BY RACE

GROUP	**MEDIAN SURVIVAL (WEEKS)**
White patients (N=36)	87 (09 – 325)
Black patients (N=32)	57 (18 – 180)
TOTAL (N=68)	67 (09 – 325)

TABLE 27: THE INCIDENCE OF BREAST CANCER IN OUR PATIENTS EXPRESSED AS A RATIO OF THE TOTAL POPULATION

AGE GROUP	BLACK PATIENTS	WHITE PATIENTS
30 – 34	0.0043	0.0098
35 – 39	0.0043	0.0156
40 – 44	0.0190	0.0380
45 – 49	0.0050	0.0360
50 – 54	0.0130	0.0570
55 – 59	0.0244	0.1140
60 – 64	0.0125	0.0670
65 – 69	0.0090	0.0220

Peak incidences are highlighted.

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FIGURE 1: PERCENTAGE OF PATIENTS IN EACH ETHNIC GROUP

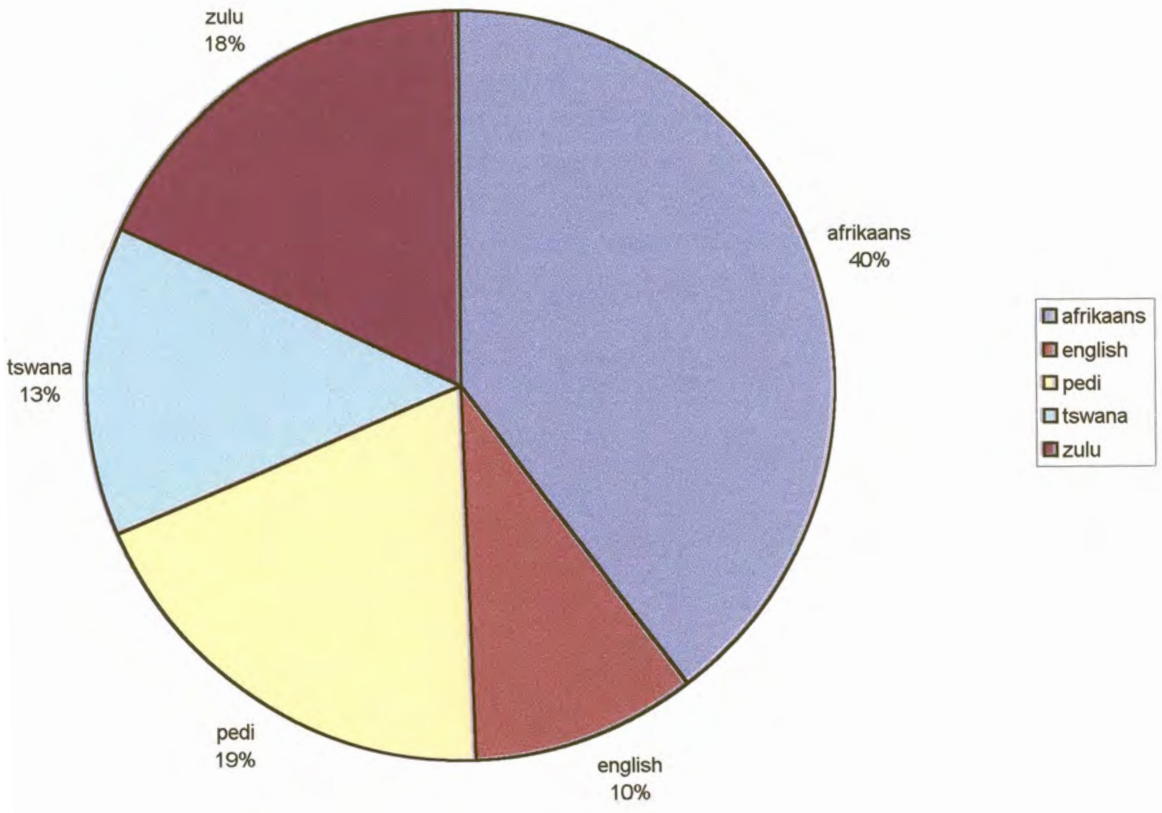


FIGURE 2: MENOPAUSAL STATUS BY RACE

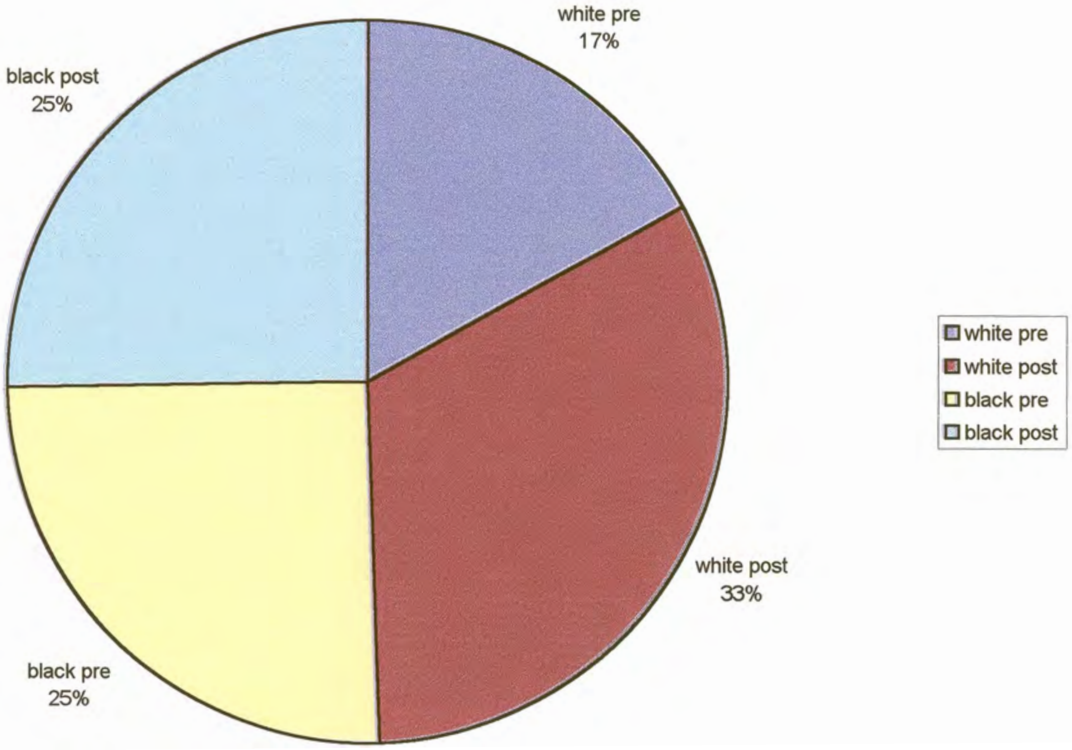


FIGURE 3: AGE DISTRIBUTION OF BLACK AND WHITE PATIENTS

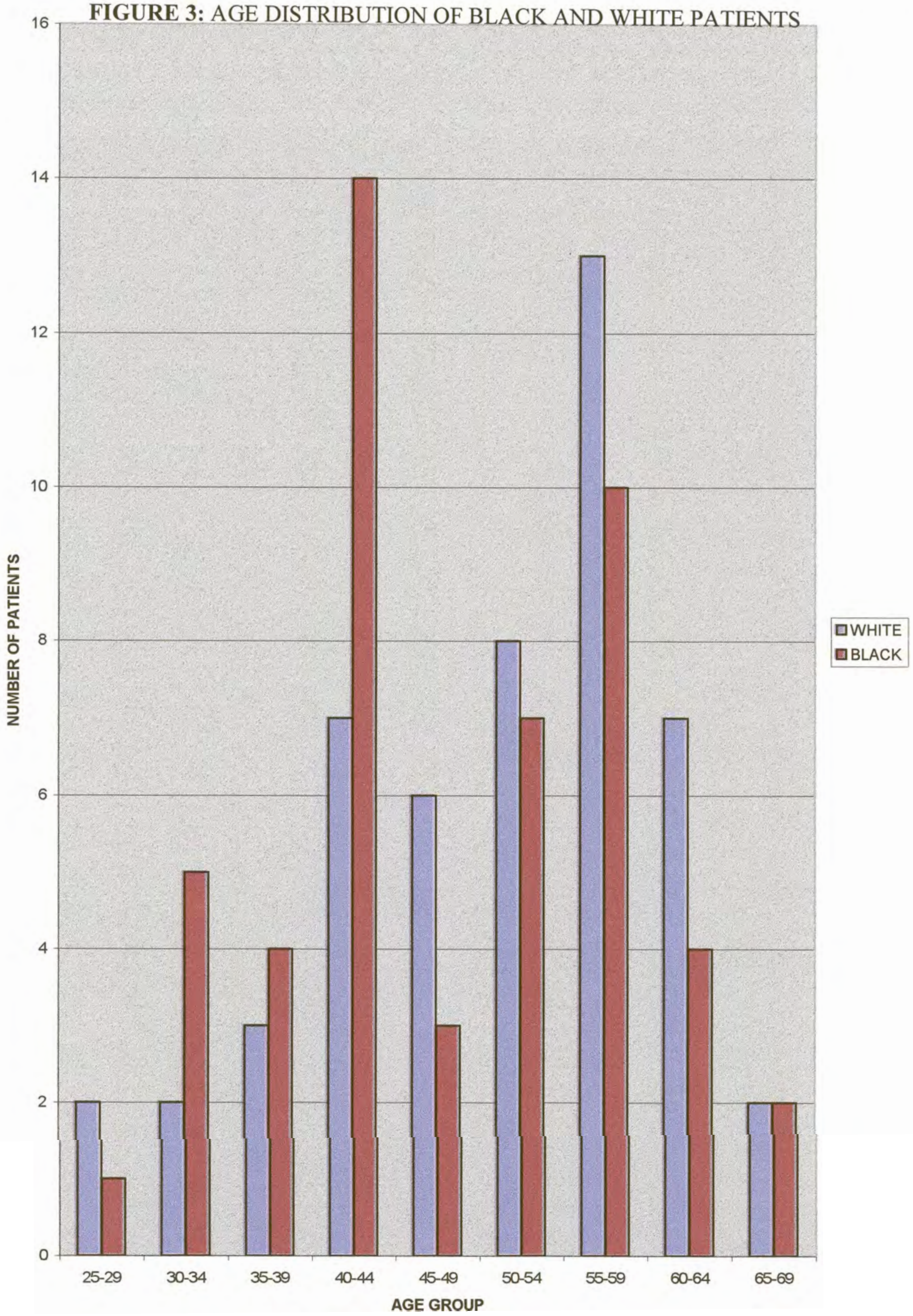


FIGURE 4: CHEMOTHERAPY REGIMEN ADMINISTERED

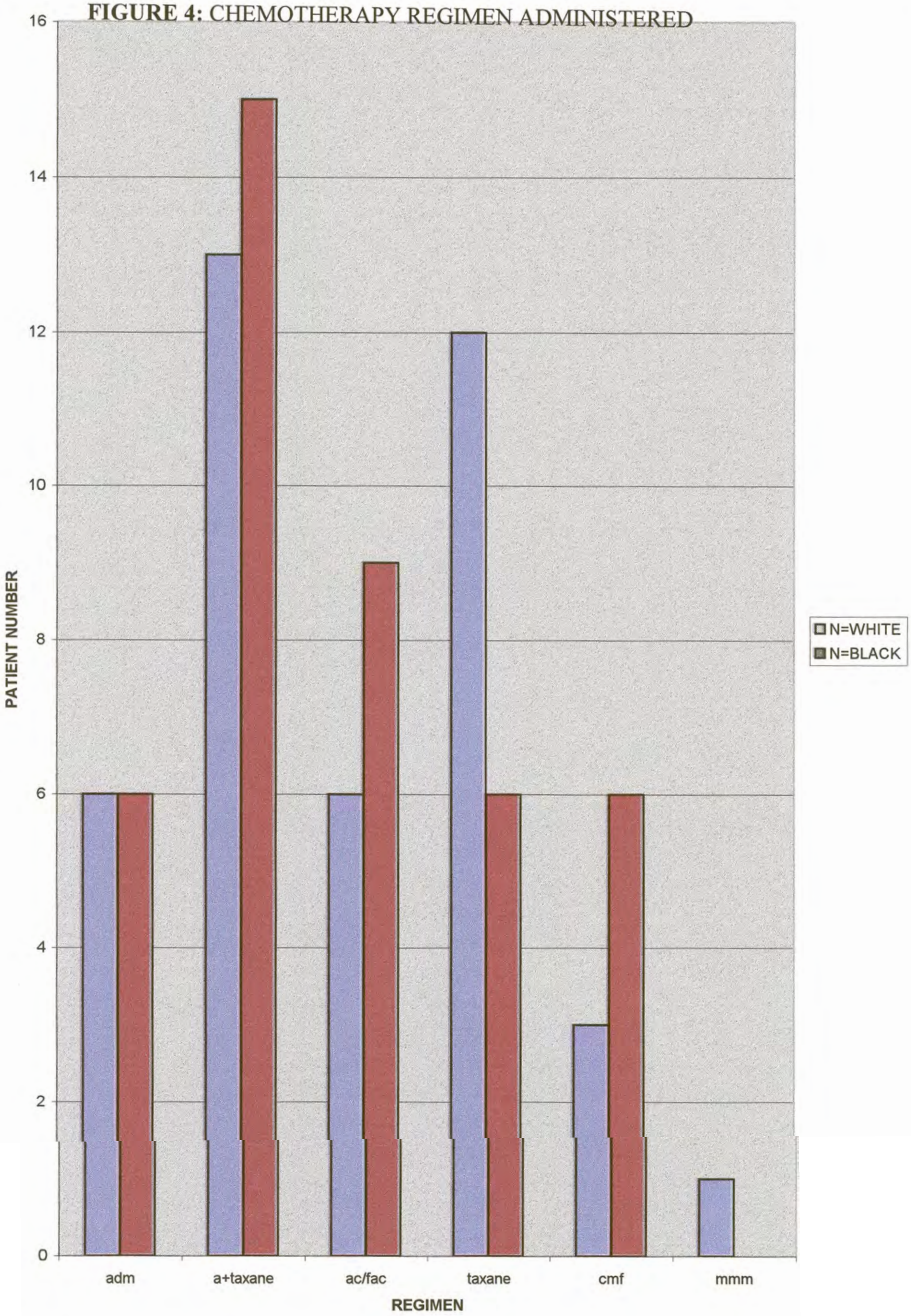
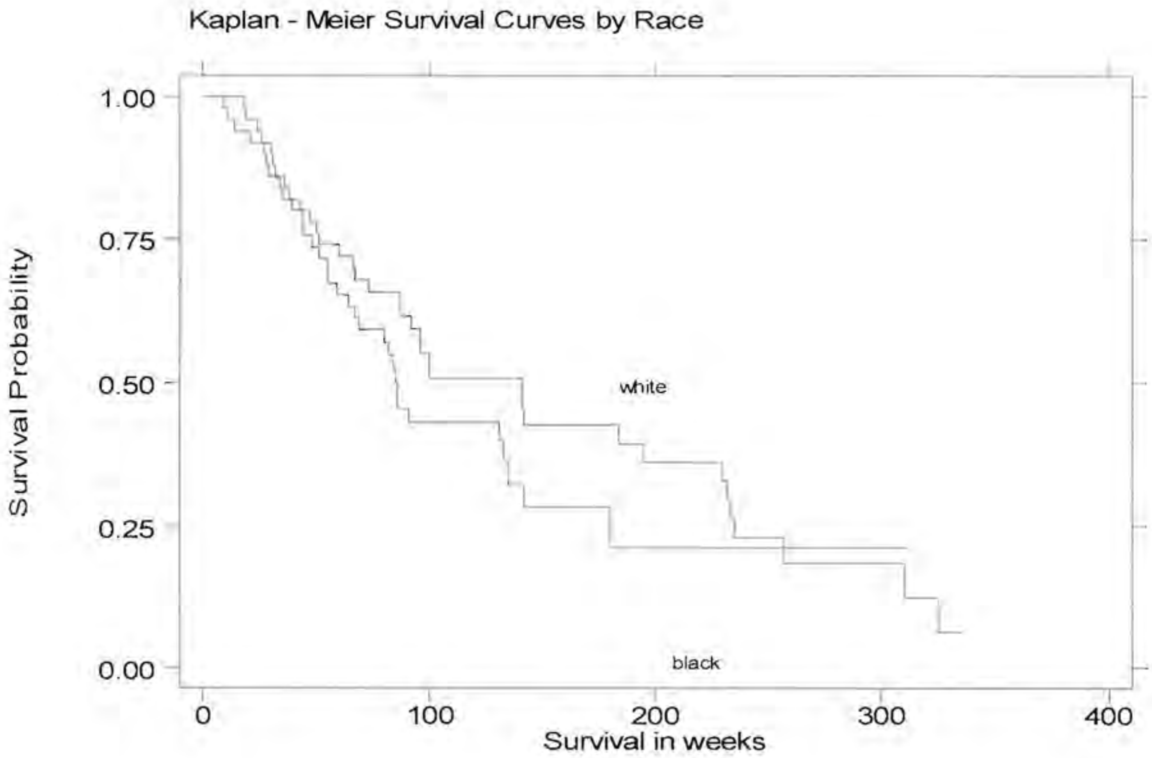


FIGURE 5: KAPLAN-MEIER SURVIVAL CURVES BY RACE



CHAPTER 6: CONCLUSION

The aim of the study was to investigate the quality of life of South African breast cancer patients and to determine the factors that influence quality of life, to determine the impact of treatment on quality of life and to ascertain whether ethnicity has any influence in this context. The findings of this investigation should ultimately be used to establish the utility of quality of life studies and be implemented to improve patient care. All tables referred to in this chapter are to be found in chapter 5.

6.1 VALIDATION OF QUESTIONNAIRES

6.1.1 PEDI TRANSLATIONS

As can be seen from table 1, the reliability of the scale as demonstrated by the Chronbach alpha coefficients is acceptable, ranging from 0.71 to 0.86. The social/family well being scale has a poor alpha of 0.54. None of the items of this scale had negative correlations, but the following items had a very low correlation:

10. I get emotional support from my family.
12. My family has accepted my illness.
13. Family communication about my illness is poor.

For item 13, the word "kgokagano" is used as the translation for "communication". It has been suggested by Pedi-speaking staff memebers that "poledisano" might be a better word to use, because it is closer to the term "communication".

The social/family well being scale was the scale where the most "missing" values had been found after patients had completed the FACT-B. However, a sufficient number of questions had been answered for this subscale and for the total questionnaire to still be acceptable for analysis according to Cella (1994). In view of the poor reliability coefficient for this scale any results involving the social/family well being scale must be ignored or interpreted with great caution.

6.1.2 TSWANA TRANSLATIONS

Reliability coefficients for the individual domains, as seen in table 1, are all 0.84 or above, except the social/family well being alpha, which is again problematic. Any results concerning this domain should be ignored or cautiously interpreted. The additional concerns alpha is borderline 0.69, but still acceptable. Four of the questions of the social/family well being construct were found to have a negative correlation, namely question number:

10. I get emotional support from my family.
11. I get support from my friends and neighbors.
12. My family has accepted my illness and
13. Family communication about my illness is poor.

6.1.3 ZULU

For the Zulu translations, three of the domains have low reliability coefficients (see table 1). The domains are social/family well being, relationship with doctor and additional concerns. Any results for the social/family well being scale should be interpreted with caution or discarded altogether. Items with negative or low reliability coefficients were:

9. I feel distant from my friends.
13. Family communication about my illness is poor.
35. I have been short of breath.
36. My arms are swollen or tender.
37. I feel sexually attractive.
43. I am able to feel like a woman.

For item 13, Zulu-speaking staff suggested that the word “awuxoxi” is a better translation for the term “communication”, than “awu**sa**xoxi”. The staff also says that the Zulu translation for item 38 (“I feel sexually attractive”) is extremely non-specific.

6.1.4 AFRIKAANS

The Afrikaans validations seen in table 2, are all 0.7 or above, when rounded off to one decimal point, except for the relationship with the doctor. Relationship with the doctor shows an alpha of 0.58, which when rounded off to one decimal point, is still acceptable according to Nunally 1978 page 245. The Afrikaans translation is thus completely acceptable.

6.1.5 DISCUSSION

The social/family well being scale is the only quality of life construct, which was unacceptable for all the black language translations. It had the lowest reliability of any subscale for all the languages excepting Afrikaans. It was also the subscale where the most missing items were found after patients had completed their questionnaires, indicating that some of the questions were being misinterpreted or patients felt uncomfortable about answering them. It is important to note that attitudes towards sex and sexuality are much more conservative in South Africa than in the USA and Europe. A lot of patients had difficulty in answering these items. In the black patient group, the questions about sexuality became even more problematic. When a black patient was given the FACT-B as an interview, the patient first had to be asked: "I am about to ask you a question of a very personal nature, may I proceed?" This is mandatory in the South African black cultures.

Another reason for the poor reliability of the social/family well being scale is item 13 ("family communication about my illness is poor"). It has a low correlation in Pedi and Zulu and a negative correlation in Tswana. One explanation for the inconsistency with scoring is that in these cultures, some families do not talk about the illness with the patient once the diagnosis is made. Mtalane (1993) found that although the patients that he had studied informed their families of their diagnosis and prognosis, there was no further discussion of the issue between patient and family. The dying patient was given false reassurance, because family members saw any open discussion or acceptance on their part as hastening death.

Some black patients do not want to discuss their condition with family members at all. Some black men will only discuss their condition with other men. Whereas other black men may discuss an illness with their wives but not with their children.

In the black culture groups saying "my family talks very little about my illness" is possibly not an indication of a poor quality of life, but rather the opposite. Family support to the patient is extremely important, but is limited in some cases, due to the distance and traveling expense for the patient to reach the treatment site. Some black patients even go and stay with distant family members or friends, just to be near to the treatment center.

The social/family well being domain is demonstrative of cultural differences found in the black patient population. Several of the questions in this section are subject to interpretation from the viewpoint of the traditional cultures of the patients. "Family" may not mean the same in a small rural Zulu village as to Western society. Black people sometimes define "family" in a much broader sense to include close friends or neighbors.

Another explanation for the poor reliability of the social/family well being scale is educational status. When the educational level is broken down further than what was done for the multiple regression analysis, it becomes clear that the educational level of the black patients is considerably lower than that of the white patients (see table 13). Forty eight percent of the black patients had an education and reading ability of lower than grade eight, while this did not apply to white patients at all. It is therefore perhaps no coincidence that the entire Afrikaans scale is acceptable and that all of these patients had enough scholastic ability to grasp the concepts that were being tested.

Personality may also play a role in that patients consent to the FACT-B study because they are afraid that their care may be compromised if they don't partake. This is in spite of the fact that it is clearly stated in the informed consent that refusal to take part will not compromise patient care in any way. These patients actually don't want to talk about anything and give unreliable answers. Some patients may have tried so many different remedies that they consider any intervention as useless. They feel that nothing helps them and that their prognosis is so poor and therefore give unreliable answers to the FACT-B interview.

The relationship with the doctor has low reliability coefficients for the Zulu translation. A possible explanation is that doctors tend to have a direct approach. Zulu people don't like to make eye contact they consider it as rude, especially when they are older than the doctor and this may compromise the reliability of this scale.

Overall, the results are encouraging. Although the FACT-B was initially developed in the United States with first world patients in mind, the quality of life dimensions were found to be reliable overall. The discrepancies that occur serve to elucidate the cultural and educational differences of the black patients.

6.1.6 VALIDATIONS FOR THE TOTAL GROUP

The total group validations (see table 18) will not be discussed in detail, because the separate validations for the Pedi, Tswana, Zulu and Afrikaans translations are discussed thoroughly at the beginning of the chapter. Chronbach's alphas for the total group again showed the low reliability of the social/family well being domain. A low reliability for the additional concerns scale was also found. This again confirms that any findings with these two scales should be discarded and that these scales need refinement for South African patient population use. All the other constructs demonstrated sufficient reliability.

6.2 THE INFLUENCE OF TREATMENT ON THE QUALITY OF LIFE OF BREAST CANCER PATIENTS

When comparing the mean scores for each domain and the mean FACT-B score during treatment for our total patient group with mean scores of American patients (see table 19 chapter 5), all the values are similar. The quality of life during chemotherapy, of our group of South African breast cancer patients therefore does not differ significantly from that of American breast cancer patients.

The mean age for the black (47.88 years) and white (50.74 years) South African patients was similar (see tables 16 and 17). The ages of the youngest black (26) and white (27) and oldest black (67) and white (69) patients were well balanced.

Although the pilot project demonstrated an impact of chemotherapy and hormonal therapy on quality of life, these findings can safely be ignored, because it had been found that the statistical analysis for the pilot project had been inadequate.

Despite the clinical benefit that may be associated with reduction of tumor volume, chemotherapy may produce physical or psychological distress that could compromise a patient's quality of life. Conversely, chemotherapy may palliate symptoms produced directly by the tumor, such as pain, dyspnea, or cough, or lessen psychological distress by reducing hopelessness. These effects may improve quality of life, providing benefits that are not reflected by the traditional outcomes assessed in cancer clinical trials, including tumor response, toxic effects and performance status (Seidman 1995).

The mean scores found for each of the quality of life domains "before" and "during" treatment, as well as the total FACT-B score, do not differ for the "before" and "during" treatment time periods (see table 15). Therefore the first major finding of this study is that the quality of life of this patient group was not adversely affected by the administration of chemotherapy. At the same time the quality of life of the patients was also not significantly improved by the administration of chemotherapy.

6.3 THE EFFECT OF RACE DIFFERENCES ON THE QUALITY OF LIFE OF THE PATIENTS

Already before treatment the quality of life of the black patients is worse than that of the white patients, for the following domains: Physical-, social /and family- and emotional well being, as well as for the total FACT-B score. The statistical analysis of the pilot project however, did not control for the factors that might influence quality of life and it was decided to investigate the influence of these factors, i.e. baseline quality of life, effect of treatment, ethnicity, age, educational level, living arrangement, marital status, the presence of co-morbid disease, performance status and disease stage.

A large group of patients (100) receiving chemotherapy had completed both baseline and during chemotherapy questionnaires. This group was selected for the final analysis. Patients receiving front-line, second-line and third-line chemotherapy were included in the analysis, recognizing that patients on second- or third-line chemotherapy have more advanced disease.

The second major finding is that race differences had no significant effect of the quality of life of this group of patients.

6.3.1 HOTELLING'S T-SQUARE

Hotelling's T-square (see tables 20 and 21) was employed to assess whether race groups differed with respect to the observation vector (the changes in: physical well being, social well being, relationship with doctor, emotional well being, functional well being and additional concerns). Vectors of means were not significantly different (p= 0.4754). Note that the sign of the mean values for the construct needs to be interpreted according to the formulation of the questions of the individual constructs. For example all the questions for the construct physical well being are negative (as in: I have pain). Physical well being for white patients therefore had improved during treatment, because the negative sign correlates with how bad it was going with the patient. The mean of –2.2 therefore showed an improvement in physical well being during treatment.

In the absence of covariates, races were found not to differ.

6.3.2 MULTIPLE REGRESSIONS TO COMPARE RACES

We analyzed how the dependent variables were affected by multiple independent variable by the "least squares" method to fit a line through a set of observations. The dependent variables were the individual domains and total score of the FACT-B. The baseline scores of the domains, age of the patients and treatment time were used as cofactors to adjust the relationship between the dependent and independent variables. Risk factors included in the adjustment were: race, performance status, disease stage, educational status, marital status and the presence or absence of concomitant disease (see tables 22 and 23).

All baseline FACT-scores were found to be significant co-factors. Performance status was found to be a significant risk factor. Performance status influenced the following dependent variables: physical well being, social well being, emotional well being and the overall quality of life of patients (total FACT-B score).

There was a tendency toward significance for the influence of race on the social well being of the patients. In view of the poor reliability coefficients for Chronbach's alphas that were found for the Zulu, Pedi and Tswana translations, this finding cannot be stated as an absolute.

6.3.3 SURVIVAL

The log-rank test for survival showed that there was no statistically significant difference in the survival of the white versus the black patients (see tables 24 and 25). The median survival for the total group was 67 weeks, with a range of 9 to 325 weeks (see table 26). A Kaplan-Meier curve by race confirmed that there was no significant difference in the survival curves by race (see figure 5).

6.4 FACTORS THAT INFLUENCE QUALITY OF LIFE

The third major finding was that there were certain factors that influenced the quality of life of the patients.

The factors that were found to be significant predictors of change in quality of life scores were performance status, disease stage and baseline quality of life. Factors that approached significance were race, marital status and educational status. In the analysis of the pilot project race had been found to be statistically significant, but after correcting for the factors that influence quality of life in the regression analysis, it only approaches significance. The distinction in educational status was drawn at grade 12 and higher versus less than grade 12. A finer distinction could probably have been made (see table 13). Table 13 demonstrates that 48 % of the black patients have attained less than a grade 8 education, whereas none of the white patients fall into this category.

Patients with stage four disease had a stronger relationship with the doctor than patients with stage three disease. Stage was thus found to have a significant influence on the quality of life of the patients and specifically in their relationship with the doctor.

There was a tendency towards a significant influence of marital status on the emotional well being of patients. Married or single patients, who are considered to be unstressed in comparison to the divorced and widowed group, had a better emotional well being than the latter group.

There was a tendency towards significance of educational status in that the better-educated group experienced a better functional well being than the less educated group.

The factors that influenced quality of life in this study, were all baseline characteristics of the patients and were not ameliorable to intervention.

6.5 CLOSING REMARKS

The three major findings of the study are:

1. The administration of chemotherapy did not cause an improvement or deterioration in the quality of life of this group of patients.
2. There were no significant differences between the black and the white patients with respect to their quality of life or survival data.
3. Factors that had a significant influence on the quality of life of the patients were performance status, disease stage and the baseline quality of life score.

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