



2809077392

REFERENCE ONLY**UNIVERSITY OF LONDON THESIS**

Degree PhD Year 2006 Name of Author LEARY
Alison

COPYRIGHT

This is a thesis accepted for a Higher Degree of the University of London. It is an unpublished typescript and the copyright is held by the author. All persons consulting the thesis must read and abide by the Copyright Declaration below.

COPYRIGHT DECLARATION

I recognise that the copyright of the above-described thesis rests with the author and that no quotation from it or information derived from it may be published without the prior written consent of the author.

LOAN

Theses may not be lent to individuals, but the University Library may lend a copy to approved libraries within the United Kingdom, for consultation solely on the premises of those libraries. Application should be made to: The Theses Section, University of London Library, Senate House, Malet Street, London WC1E 7HU.

REPRODUCTION

University of London theses may not be reproduced without explicit written permission from the University of London Library. Enquiries should be addressed to the Theses Section of the Library. Regulations concerning reproduction vary according to the date of acceptance of the thesis and are listed below as guidelines.

- A. Before 1962. Permission granted only upon the prior written consent of the author. (The University Library will provide addresses where possible).
- B. 1962 - 1974. In many cases the author has agreed to permit copying upon completion of a Copyright Declaration.
- C. 1975 - 1988. Most theses may be copied upon completion of a Copyright Declaration.
- D. 1989 onwards. Most theses may be copied.

This thesis comes within category D.

This copy has been deposited in the Library of

U n i v College

This copy has been deposited in the University of London Library, Senate House, Malet Street, London WC1E 7HU.

**Quality of life in patients receiving
platinum based chemotherapy for
advanced Non-Small Cell Lung Cancer**

Alison Leary

University College London
Department of Oncology

PhD Medicine (Clinical Studies)

UMI Number: U592236

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



UMI U592236

Published by ProQuest LLC 2013. Copyright in the Dissertation held by the Author.
Microform Edition © ProQuest LLC.

All rights reserved. This work is protected against
unauthorized copying under Title 17, United States Code.



ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

Table of Contents	Page
List of Tables and Figures	iv
Acknowledgements	vi
Abstract	1
Chapter 1 Introduction-an overview	3
1. Introduction	4
1.1 The pathology of non small cell lung cancer	7
1.2 Clinical presentation and diagnosis	9
1.3 Staging and treatment of non small cell lung cancer	11
1.4 The epidemiology of non small cell lung cancer	15
1.5 The lung cancer patient journey	20
1.6 The psychological and social implications of NSCLC	22
Chapter 2 Review of the literature	24
2 A review of the literature-the dimensions of lung cancer and method of review	25
2.1 <i>The cancer journey, the individual and society</i>	30
2.1.1 <i>Issues around suspected cancer and investigation</i>	32
2.1.2 <i>Issues around diagnosis</i>	34
2.1.3 <i>“Having cancer” the person with cancer and the concept of suffering</i>	38
2.1.4 <i>Issues around treatment-doing work</i>	43
2.1.5 <i>Issues around completion of treatment</i>	46
2.2 Toward a generic definition of Quality of Life (QoL)	48
2.2.1 Quality of life and the good life-A historical perspective	50
2.2.2 Quality of life in the literature	54
2.2.3 Measuring quality of life-QoL as an outcome measure	61
2.3 Quality of life in cancer	65
2.3.1 <i>Quality of life and psycho-oncology in the literature</i>	71
2.3.2 <i>Influences on measuring quality of life in cancer</i>	74
2.3.3 <i>Measuring Health Related QoL in patients with cancer</i>	79
2.4 Quality of life related to non small cell lung cancer	86
2.4.1 <i>Non small cell lung cancer and quality of life-concept Clarification</i>	87
2.5 Quality of life in non small cell lung cancer -instruments in the literature	92
2.6 Quality of life in the context of treatment (chemotherapy) For advanced non small cell lung cancer	99

Chapter 3 Methods	116
3 Aims and methods of study	117
3.1 The comparative nature of grounded theory and relationships with scientific positivist tradition	121
3.2 Selection and treatment	124
3.3 Content analysis of the interview data	131
3.4 Method of analysis-HRQoL data	133
3.5 Summary	137
Chapter 4 Results	139
4. Results	140
4.1 Patient demographics for both data sources	141
4.2 The domains of the QLQ 30+LC17	144
4.3 Toxicities	148
4.4 The interview study	151
Chapter 5 Quality of life: The work of cancer and the lens of diagnosis	157
5 Introduction	158
5.1 The lung cancer journey: Doing work	159
5.3 The lens of diagnosis	182
Chapter 6 Suffering in the context of advanced non small cell lung cancer and the worth of treatment	195
6. Suffering	196
6.1 Illness and suffering-having cancer	202
6.2 The lived experience of advanced lung cancer in the context of suffering	208
6.2.1 Psychological well being	209
6.2.2 Physical well being: The worth of treatment	223
6.2.3 Relationships with significant others	240
6.2.4 Health behaviours	245
6.2.5 Spirituality	246
6.2.6 Changes in social role	247
6.3 Summary	252

Chapter 7 Conclusion	253
7.1 Quality of life in NSCLC	254
7.2 Quality of life-The Scandinavian School Vs the Classicists	257
7.3 Implication for practice	274
7.4 Limitations of the study	276
7.5 Areas for further study	282
7.6 Summary	284
Appendices	
Appendix A The EORTC QLQ 30 Version 3 with Lung cancer module	289
Appendix B Patient information sheet	293
Appendix C Common Toxicity Criteria	295
Appendix D Protocol for Study 11	299
Appendix E Scales of performance status referred to in the text	331
References	335

Figures and Tables

Chapter 1

Figure 1.1	The presentation of lung cancer	9
Table 1.1	Prevalence of smoking by socio-economic group	15
Figure 1.2	Continued tobacco use and risk	18
Figure 1.3	CRUK recorded incidence rates in lung cancer	19
Figure 1.4	The lung cancer care pathway-The ten milestones	20

Chapter 2

Figure 2.1	Literature review of quality of life in NSCLC	29
Figure 2.2	Reasons given for non participation in Macmillan National Needs Assessment Study	31
Figure 2.3	Pathway linking social ties to cancer	40
Figure 2.4	A model of research in psycho-oncology	73
Figure 2.5	Quality of life as a causal sequence	78
Table 2.1	Quality of life outcome measures in cancer populations	81
Figure 2.6	Relationships –quality of life as an antecedent	90
Table 2.2	Quality of life in NSCLC-common outcome measures	94
Table 2.3	Issues and practical considerations on collecting quality of life data in lung cancer trials	95
Table 2.4	Specific randomised controlled trials using Gemcitabine	111

Chapter 3

Figure 3.0	The steps included in an interview study	128
Figure 3.1	Questions used to facilitate face to face interviews	128
Figure 3.2	The EORTC QLQ 30 Range and item domain	135
Figure 3.3	The EORTC QLQ Lung cancer module range and item domain	136

Chapter 4

Table 4.1	Patient demographics of the LLCG study	142
Figure 4.1	Compliance (questionnaire returns)	142
Figure 4.2	QoL scores at pre treatment	146
Figure 4.3	Comparison at 12 weeks (QoL scores)	147
Figure 4.4	Haematological toxicity	148
Figure 4.5	Non haematological toxicity	149
Figure 4.6	Examples of clustering codes	155

Chapter 5

Figure 5.1	Patient experience (distribution)	161
Figure 5.2a	Respondent diary	163
Figure 5.2b	The lung cancer patient pathway	164
Figure 5.2c	Communication routes	165
Figure 5.2d	The diagnostic process	166
Figure 5.2e	Work of the first chemotherapy treatment	167
Figure 5.3	Emergent codes from interviews	177
Figure 5.4	The hierarchy of physical position in the MDT	180

Figure 5.5	Observed discrepancy between target groups	183
Figure 5.6	Diagnosis (Distribution)	184
Figure 5.7	The language of communication	190
Figure 5.8	The lens of diagnosis in the respondent group	194
 Chapter 6		
Figure 6.1	Psychological well being (Distribution)	209
Figure 6.2	The relationship between the subjective and objective	219
Figure 6.3	Physical well being (Distribution)	224
Figure 6.4	Relationships with significant others (Distribution)	240
Figure 6.5	The dynamic of the relationship in alleviation of denial	243
Figure 6.6	Health behaviours (Distribution)	245
Figure 6.7	Spirituality (Distribution)	246
Figure 6.8	Changes in social role	247
Figure 6.9	The suffering struggle	252
 Chapter 7		
Figure 7.0	The lung cancer pathway-influencing quality of life through practice	264
Figure 7.1	The comparative properties of quality of life in respondent group	272
Figure 7.2	Implication for practice-factors for consideration	275
Figure 7.3	Sources of data and influences on the researcher	280
Figure 7.4	Quality of life as an area of practice	287

Acknowledgements

Acknowledgements

The author would like to thank for their help and support:

Supervisors Professor Jonathan Ledermann and Professor Ann Bowling, in addition Ms Sandy Beare, Ms Wendy Burford, Ms Anne McTiernan, Ms Philomena Corrigan, Mr Neale Hanvey, Ms Kay Eaton and my colleagues in the Department of Oncology at University College Hospitals NHS Foundation Trust for their on-going support. Professor Louise Boden OBE, Professor John Hartley, and Dr Daniel Kelly My examiners Professor SG Spiro and Professor K Seers.

Ms Lindsey James, Ms Nicky Gower and the London Lung Cancer Group. The Roy Castle Foundation for the grey literature.
My family, my friends and my wonderful colleagues at Millwall FC.

To Jeff Punshon my thanks and *amor vincit omnia*

In memory of
John, Emily and Terry Leary
Florence Chandler
Mattie Haynes
Lucie Griffiths
and GC who kept me company during writing up.

All of the participants in this study were dying from non-small cell lung cancer. They are remembered with grateful thanks as they and their families gave generously of their remaining time and allowed this study to take place.

Abstract

**Quality of life in patients receiving
platinum based chemotherapy for
advanced Non-small Cell Lung Cancer**

Quality of life in patients receiving platinum based chemotherapy for advanced non-small cell lung cancer.

Lung cancer is the cause of 34,000 deaths in the UK each year, with a five year survival rate of only 7.5%. The current treatment for advanced Non Small Cell Lung Cancer is combination chemotherapy but this confers only a small survival advantage. Quality of Life is often proposed as a secondary outcome to most chemotherapy studies as chemotherapy remains palliative. Quality of life is measured using a series of tools, such as the EORTC QLQ 30 that although established and tested for validity are functionally based or focus on physical symptoms. The aim of this study is to explore the meaning of quality of life in this group of patients.

The study utilises use comparative methods (interview n=50, QLQ EORTC 30 data, clinical observation/field notes, medical notes, nursing notes and mapping) to examine the meaning of quality of life in this patient group. This is essentially a collaboration of medical and nursing practice with the aim of understanding what quality of life means to these patients, improving the experience of patients undergoing treatment and offering appropriate psycho-social support.

Content analysis has generated a core theme of patient experience as having an impact on quality of life (negotiation of the treatment calendar, value of treatment broker and interactions with professionals) the overlapping themes are Lens of diagnosis (viewed as atrocity stories), The worth of treatment (despite physical side effects and poor life expectancy, chemotherapy is a focus of hope and allows for adjustment to poor prognosis) and Suffering (psychological and social, for example exclusion from social activities and loss of independence). This study has impacted on the service to cancer patients at a central London NHS Foundation Trust.

Chapter 1

Introduction

1 Introduction

“Malignant disease of the lung is a rare condition. The Middlesex Hospital Reports show only 890 cases of cancer of the Lung, 317 found at post mortem examination since records began.....As for prognosis a fatal termination is inevitable with average duration of the disease [life expectancy] to be 13.2 months.

From Fowler & Godlee 1898
Diseases of the Lung.

“Lung cancer is currently the most common form of cancer worldwide...life expectancy is usually between three to seven months from diagnosis.”

From Boyle et al 2000
Textbook of Lung Cancer

From being a virtually unknown disease at the end of the 19th century, lung cancer has become the most common worldwide cancer. In just over one hundred years lung cancer has become a modern epidemic (Boyle et al 2000) thought to account for over 3 million deaths each year worldwide and 33,400 in the UK (Cancer Research UK 2004), and with a five year survival rate of only 7-12% overall (Cancer Research UK 2005).

Survival from advanced lung cancer has barely improved in the last thirty years (Spiro and Silvestri 2005). However there has been a decline in deaths in the male population and an increase in female deaths. This trend can be seen from the standardised cancer data registry data for the UK (Office of National Statistics accessed 2006).

In contrast one-year survival has improved to some degree. In England and Wales, one year survival in men with advanced Non Small Cell Lung Cancer (NSCLC) has risen from 15% in the 1970's to 25% in 2000/1 (Coleman et al 2004).

In this section, the biology, epidemiology, treatment and cancer as a psychosocial and socio-political phenomenon are examined with respect to laying the groundwork for the main body of this study.

The initial aim of this work was to compare two chemotherapy regimes, for use in the most common type of lung cancer. Non-small cell lung cancer (NSCLC) accounts for about 90% of all lung cancers (King 2000). It is rarely amenable to surgical techniques, because when patients become symptomatic and a diagnosis is made, the disease has usually reached an advanced stage. Despite having few symptoms, about 70% of patients who are diagnosed with Non Small Cell Lung Cancer already have locally advanced or metastatic disease (Souhami and Tobias 2005). Systemic chemotherapy is then usually the treatment of choice.

However as this treatment is rarely curative and increases survival by only a few months, issues such as quality of life and the toxicity of the chemotherapy become paramount. This study examines the meaning of quality of life in patients receiving platinum based chemotherapy agents using a mixed method approach, quantitative health related quality of life data and the analysis of content of one to one interviews with patients who have undergone treatment in this context.

For the quantitative arm this study uses as a vehicle the London Lung Cancer Group Study 11 which is a randomised controlled trial of Mitomycin, Ifosfomide, Cisplatin (standard treatment) Vs Gemcitabine/carboplatin (trial) chemotherapy. The endpoints for Study 11 study were survival, tumour response, toxicity and quality of life (LLCG 1999).

The aim of this work is to focus on the quality of life and related issues in a group of patients receiving platinum based chemotherapies for advanced NSCLC.

1.1 The Pathology of Non-Small Cell Lung Cancer

Here the meaning of the word pathology is used in the context of the study of disease and the purpose of this section is to look at how the disease affects humans. This is from a medical/scientific perspective, but is necessary, as pathology is the main influencing factor on the chosen intervention in clinical practice. The chosen intervention then may have an implicit and explicit effect on the quality of life of a patient and significant group. This perspective is multidimensional in its own right however and not simply a reductionist view. It is therefore one that should be considered as an understanding of the disease and its effects will enhance understanding on a more holistic level.

There are various histological types of Non Small Cell Lung Cancer (NSCLC) the most common type being squamous cell which is classified on the basis of differentiation (approx. 40%), followed by adenocarcinoma and Large cell types (Souhami & Tobias 2005). In oncology practice patients with large cell, squamous and adenocarcinomas of the lung are usually grouped together because these cell types have similar treatment regimens and prognosis. They are termed Non Small Cell Lung Cancers (NSCLC).

In 1998 the World Health Organisation together with the International Association for the Study of Lung Cancer re-classified lung cancer types to ease diagnosis and understanding amongst clinicians (Shimosato 2000). The area of interest here is the invasive malignant epithelial tumours. Only the broad headings have been taken for the purpose of this study, as cell variants are often not reported by the clinical pathology services.

The first of these is *squamous cell carcinoma of the lung*. It is thought to be the most common type diagnosed in the UK at present (Boyle et al 2000) tends to arise centrally in the chest and is very uncommon amongst non-smokers (Macbeth et al 1996).

Adenocarcinomas have the typical neoplastic features when examined histologically and five variant types. They are often peripheral in site of origin (often invading the pleura). On occasion they can arise in fibrotic or scarred lung (Souhami and Tobias 2005). *Large Cell carcinomas* are poorly differentiated cancers, which do not show either histological or cytological features of other cell types (Shimosato 2000).

Although the cells are large and featureless for the most part, the tumour usually has well defined borders and usually arises from the distal or subsegmental bronchus. (Souhami and Tobias 2005).

Most of the patients who present with NSCLC do so as a result of progression of the tumour. Such progression can precipitate the symptoms of dyspnoea, cough, chronic bronchitic illness, haemoptysis and pain. Direct tumour invasion to the left laryngeal nerve may cause hoarseness of voice as a presenting symptom. Other presenting symptoms may be due to the spread of distant metastasis. For example, pain at the site of bone metastasis or Addisonian like symptoms from adrenal metastasis.

Diagnosis is usually made by imaging and then confirmed by histology/cytology often obtained by flexible bronchoscopy. In this way a diagnosis and staging of the cancer can be done with reasonable speed.

1.2 Clinical presentation and diagnosis

Few lung cancers are actually cancers of the lung parenchyma. Most of the tumours seen in clinical practice are found in the large or medium segments of the bronchial tree. Such cancers often present with chest symptoms such as haemoptysis, whereas peripheral cancers grow asymptotically and quite often are found by chance, for example on a chest X-ray. Many clinicians feel the importance of a history cannot be emphasised enough (Bourke and Brewis 2000). Occupational exposure to carcinogens, family history, smoking history and previous chest disease are factors that need careful consideration. The presenting signs and symptoms of lung cancers are shown in Figure 1.1.

Fig 1.1. The presentation of Lung Cancer (after Bourke and Brewis 2000)

Chest Symptoms Haemoptysis Cough Wheeze Stridor Pain	Mediastinal Superior vena cava obstruction Hoarse Voice Pericardial effusion Diaphragmatic palsy Arrhythmia	Chest X-ray Lobar collapse Peripheral nodule Cavitating mass Enlarged hilar nodes Pleural effusion
Neuroendocrine syndromes Hypocalcaemia Inappropriate secretion of ADH.	PRESENTATION OF LUNG CANCER.	Physical Examination Clubbing Lymph node enlargement Localised chest signs
General Symptoms Weight Loss Anaemia Anorexia Lethargy	Paraneoplastic syndromes Peripheral neuropathy Cerebellar degeneration Nephrotic syndrome Lambert-Eaton Syndrome	Metastases Bone: Pain Brain: Fits, hemiparesis Liver: Jaundice Skin: Nodules

Once imaging such as a chest X-ray or CT scan has taken place, a provisional diagnosis is made, as tumours are usually visible on imaging. Further investigation is usually needed to confirm the histology but it is usually at this point that a probable diagnosis is communicated to the patient.

1.3 Staging and Treatment for Non Small Cell Lung Cancer

Staging is the process of medical investigations conducted to discover the extent of the disease. From a clinical perspective, the type of treatment offered, if any, is usually based on the outcome of these investigations. Commonly used investigations are the extended use of imaging, for example bone scanning for bone metastasis, and computerised tomography (CT scanning), bronchoscopy to visualise a tumour and obtain a biological sample for histology or cytology, glomerular filtration rate estimation and estimation of bone marrow and renal or liver function by haematological and biochemical testing. These tests and investigations are also part of the patient journey and should be viewed as such (Cancer Services Collaborative 2001, NICE 2005). The findings of these assessments can have as much impact on the patient journey as diagnosis (Parker et al 2001). This is particularly so if a patient is found to have, for example, poor renal function that would exclude the use of chemotherapy.

After such investigations the disease is then “staged”. The internationally recognised system of staging is known as the TNM system evolved in the middle of the last century and was developed by the Union Internationale Contre le Cancer in 1988 (Goldstraw 2000, 2006). It stages the extent of disease by:

Tumour (primary site) size and invasion of nearby structure (**T**)
Lymph Node involvement (**N**)
Presence of Metastasis (**M**)

Depending on the **TNM** classification, the disease overall is often still given a stage between 0 and 4 by many clinicians. For example a tumour that invades the mediastinum would be T4, no lymph node involvement would be N0 and a bone

metastasis would be M1. This patient would have disease classified as T4 N0 M1.

This patient has stage 4 disease.

The optimum treatment for Non Small Cell Lung Cancer is removal of the tumour (resection) this usually involves removal of a lobe of the lung (lobectomy) or the whole lung (pneumonectomy). Unfortunately as the majority of patients (approximately 80%) present with extensive disease surgery is rarely an option (Souhami & Tobias 2005) This is because the tumour has either spread extensively locally (Stage 3b) or has distant metastasis (Stage 4). If a tumour is technically resectable, pre-existing co-morbidity such as chronic obstructive pulmonary disease may preclude safe and appropriate surgery (Karamanoukian et al 2001). Common sites of metastatic spread are the skeleton, adrenal glands and the brain. The symptoms from these distant sites of spread can cause the presenting symptoms, some of which are very distressing such as brain metastasis causing diplopia.

Treatment options in extensive or advanced Non Small Cell Lung Cancer include radiotherapy and chemotherapy or a combination of the two. Radiotherapy is the use of a precise beam of ionising radiation to induce cell death. This beam also passes through healthy tissue before reaching the tumour and so can also damage the non-cancerous tissue. This is where the unwanted side effects of radiotherapy can be apparent such as fatigue and difficulty swallowing. Much also depends on the intention of the radiotherapy, whether it is palliative or radical (Souhami and Tobias 2005).

Chemotherapy is the term commonly in use to describe a range of cytotoxic drugs. The first chemotherapeutic agents were introduced after the Second World War and have been used for around fifty years (Neal and Hoskins 1994). Chemotherapy, unlike radiotherapy, is a systemic treatment. This means its cytotoxic effects are usually exerted on all fast growing cells in the body. This has implications in terms of side effects. Chemotherapy drugs work in various ways, but are largely cytotoxic because they interrupt the cell cycle causing the cell to arrest and become unable to divide and reproduce (Neal and Hoskin 1994). This happens as cancer cells divide faster than many other cell types in the body. However fast growing cells in the body can be affected such as hair follicles and the lining of the gut (Neal & Hoskins 1994).

In non-resectable, advanced NSCLC treatment options are limited. Any treatment is, at present (2005), unlikely to be curative. Present treatment options are systemic chemotherapy, local radical radiotherapy, surgery and active symptom control. Increasingly biological agents are being considered which target cancer at a molecular level but are in limited use at time of writing.

Due to the nature and stage on presentation, the options of chemotherapy and active symptom control (palliative care) are the most realistic options for patients with stage 3b or 4 disease (Fitzpatrick et al 1998) and recent evidence supports this (Clegg et al 2001, NICE 2005).

Systemic chemotherapy is of most interest here. As the aim of chemotherapy in NSCLC is to palliate symptoms rather than cure the disease, it is worth considering a few important points.

Traditionally, the “success” of chemotherapy treatment has been measured in terms of response of the tumour and survival. Objective response in this context would show only a 30% response (based on World Health Organisation criteria) and modest survival benefits (Middleton et al 2000). However by looking at response in terms of palliation of symptoms the response is 70% (Cullen 1993, Ellis et al 1995)

1.4 The epidemiology of Lung Cancer

Many authors now comment that lung cancer is endemic in society (Boyle et al 2000).

The increased incidence of lung cancer in the last one hundred years has certainly been recognised. One of the causes of this rise is the now axiomatic link with smoking, primarily tobacco. This has implications in terms of lay belief (Chapple et al 2004), and is discussed in Chapter 2. Some authors cite factors in conjunction with direct tobacco use such as low socio-economic status (Ekberg-Aronsson et al 2006). However there has been a small decrease in smoking habits in the UK. Smoking is still prevalent in lower socio economic groups but has fallen by 5% in male unskilled manual groups. The General Household Survey generated by the census (ONS accessed 2006) shows the prevalence of tobacco use in different socio economic classes. This is shown in Table 1.1

Table 1.1 Prevalence of smoking by socio economic group

Great Britain	Percentages			
	Males		Females	
	1998	2000	1998	2000
Professional	16	17	14	14
Employers and managers	22	23	21	20
Intermediate/junior non-manual	25	27	24	26
Skilled manual	34	33	30	26
Semi-skilled manual	39	36	33	32
Unskilled manual	44	39	31	35
All non-manual	22	23	22	22
All manual	36	34	31	29
All aged 16 and over	30	29	26	25

Socio-economic group of the household reference person (excluding those in the Armed Forces and full-time students).

Source: General Household Survey, Office for National Statistics

Since the mid-1970s there has been a decline in the UK death rate for lung cancer among males. This can be closely linked to the proportion of the population who smoke. In 1974 the death rate among all males in the United Kingdom from lung cancer was 110 per 100,000. By 2002 it had declined to 58 per 100,000. In contrast, the lung cancer death rate among females reached its peak of 31 per 100,000 in 1988. Since then the rate has declined very little, and in 2002 it was half that of men. (Office of National Statistics accessed 2006)

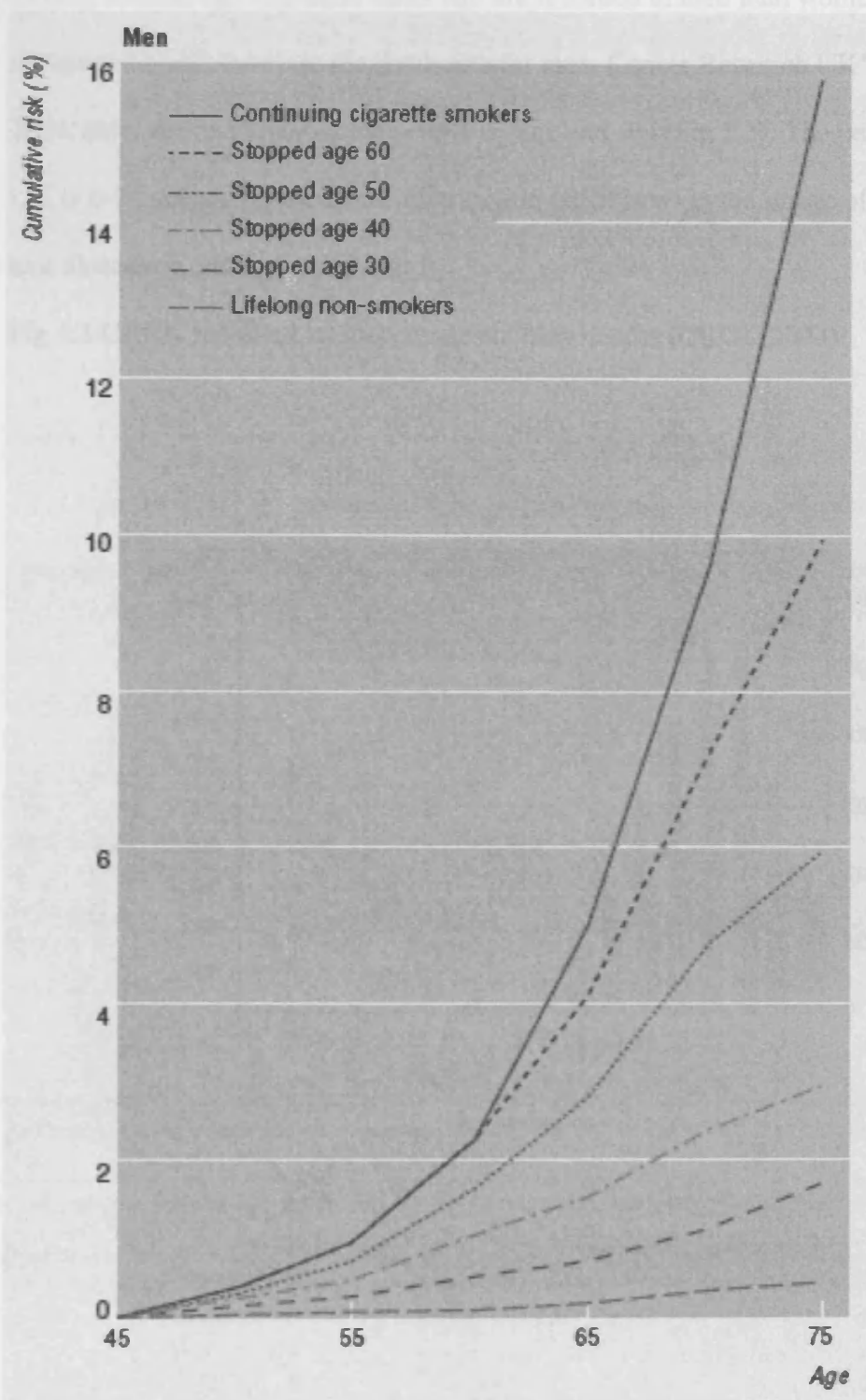
As has been stated, the last one hundred years have seen little in improvement of survival but huge increases in lung cancer death rates worldwide. As one of the few authors taking an epidemiological and historical perspective, Boyle et al (2000) divides the century and epidemiology of lung cancer into four phases.

The first of these phases was the establishment of a causal link between smoking and lung cancer risk in the 1930-1950's. The second phase (from the mid 50's) was the increase in understanding of the aetiology of lung cancer and also the growing awareness that lung cancer was becoming more prevalent and reaffirming the causal link to smoking tobacco. This was, in part, due to the benchmark studies of Doll and Hill (Doll and Hill 1950, 1952, 1954). The body of evidence was so strong that in the USA the Surgeon General was moved to produce an official statement on "Smoking and Health" which caused a worldwide reaction. Phase 3 saw a descriptive epidemiology of lung cancer and the publishing of larger cohort studies (for example the work of the National Cancer Institute in the USA). The fourth phase (from 1960's onwards) charts the rise in smoking related disease (of which NSCLC is just one) and

the present situation. It also charts the way in which smoking habits have changed. For example in the 1970's consumers were made aware of "Tar Levels" and encouraged to smoke low tar products. This seems merely to have changed the histological subtype from squamous cell to adenocarcinoma. (Boyle et al 2000). The reason for the inclusion of Boyle's work here however is to not only summarise the impact of the rise in incidence of NSCLC but also to establish the now almost axiomatic link with tobacco both from a epidemiological/academic perspective and as a perception of the public (UK Lung Cancer Coalition 2005)

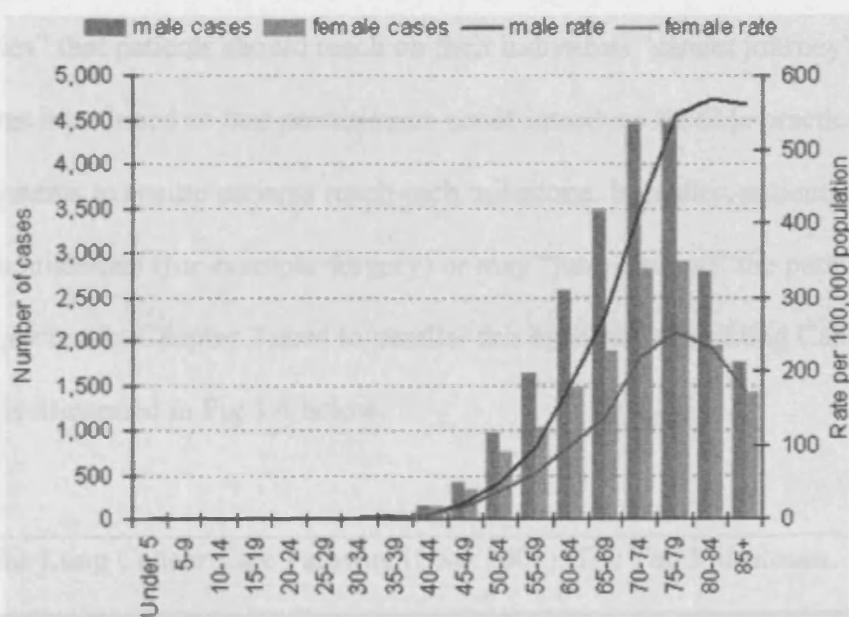
The establishment of a link with tobacco is one that continues to be examined. Richard Peto and colleagues (Peto et al 2000) examine the link between lung cancer and smoking cessation. There is a clear increase in risk associated with continued tobacco use (Fig 1.2).

Figure 1.2 Continued tobacco use and risk (Peto et al 2000)



In addition to socio economic group and tobacco use, NSCLC tends to affect adults in middle to older age and more cases still are recorded in men than women despite the downward trend shown in the death rate for men. Cancer Research UK's figures for 2004 show the incidence of lung cancer by age and sex (Fig 1.3). The peak age in the UK is 6-7th decade, however the distribution range is wide-the image of lung cancer as a disease of old age is shifting.

Fig 1.3 CRUK recorded incidence rates in lung cancer (CRUK 2004)



Age at diagnosis

1.5 The lung cancer patient journey

The format adopted for this section follows that of the lung cancer patient care pathway suggested by the NHS Cancer Plan (Department of Health 2000a) and the Cancer Services Collaborative (CSC) (2001). The rationale for this approach is to illustrate the biomedical, psychological and sociological dimensions of the patient journey and interaction and conflicts of service delivery and social policy. The approach taken here is therefore temporal as opposed to completely reductionist.

The Department of Health Lung Cancer Care Pathway (CSC 2001) consists of ten “milestones” that patients should reach on their individual “cancer journey”. This system was introduced so that practitioners could introduce flexible practice and initiate systems to ensure patients reach each milestone. In reality, patients do not need each milestone (for example surgery) or may “jump around” the pathway. The literature review in Chapter 2 aims to parallel this approach. The Lung Cancer Care Pathway is illustrated in Fig 1.4 below.

Pre-diagnosis	Diagnosis	Chemotherapy	Pre-surgery	Post-surgery
Discharge	Radiotherapy	Follow up	Terminal Care	Bereavement

The impact of the NHS Modernisation agenda is also apparent throughout this study, which has a definite temporal dimension in terms of social policy. This work was initiated in 2000, the same year in which the NHS Cancer Plan (DoH 2000a) was introduced. Little direction in terms of treatment paradigms and management of patient pathways apart from academic collaborative research was available at the time. In contrast 2005 saw the publication of the National Institute for Clinical Excellence (NICE) 170 page guidance on Lung cancer care accompanied by 350 pages of supporting evidence. This reflects the change in social policy intended to deal with the perceived inequalities in accessing specialist cancer care which was the aim of the NHS Cancer Plan.

1.6 The psychological, social and political implications of NSCLC

Cancer has meaning in society, both as a word and disease. It is often thought to be uncontrollable and unpredictable resulting in a short life and painful death with pain being the primary concern of 70% of patients with cancer (Neal & Hoskin 1994). The perception of “cancer” as something to be feared is often based on anecdote or experience of many years ago in the experience of the author. Media such as television also use cancer (inextricably linked with death) for dramatic licence, often with little bearing in reality (Holland 1998). It could be said that cancer is as much socially constructed as it is pathological.

The link between lung cancer and smoking tobacco established by Doll and Hill in the 1950's (Doll and Hill 1954) and subsequent health promotion campaigns have influenced the public perception of lung cancer as a disease of smokers. In a recent survey the UK Lung Cancer Coalition found that 40% of the population considered lung cancer to be self inflicted, despite the fact that one in eight lung cancer patients are never smokers (UK Lung Cancer Coalition 2005). Because of the established epidemiological link with tobacco use, lung cancer patients often feel feelings of stigmatisation and guilt (Chapple et al 2004) which gives an added dimension to their suffering.

Poor five year survival in advanced lung cancer reflects the technical difficulty in developing agents to treat this disease but there is also evidence of influence by other socio-political factors. The Public Accounts Committee has recently issued a report confirming that there is still an identified link between variations in the incidence of lung cancer and levels of socio-economic deprivation (Public Accounts Committee

2006). Poor five-year survival may also be a consequence of lack of investment in lung cancer research. Only 4% of UK cancer research funding goes towards lung cancer research (Roy Castle Foundation 2005).

Lung cancer has become the most common cancer in men in the world. Compared to other cancer types however, less seems to have been written about it. A search of the common databases covering the last thirty years such as CINHALL and OVID reveals a dearth of published work. This is discussed in Chapter 2.

There has been little published work in this area that is specific to the quality of life of patients with Non-Small Cell Lung Cancer outside of the clinical trials literature. This work hopes to contribute to the field by exploring the influences on quality of life in NSCLC in a more global sense, rather than concentrating exclusively on the impact of symptoms.

Chapter 2

Quality of Life-A review of the literature

2 A review of the literature- The dimensions of lung cancer and method of review.

This review begins by examining the literature around cancer and specifically lung cancer as a psychosocial and socio-political entity to provide background and context for the study. Over the lifetime of this study there have been radical changes in the way that cancer is managed in the NHS.

The review then examines the literature in quality of life in four topic areas. These are:

- The understanding of quality of life as a concept-What is quality of life?
- Issues in the context of health and the meaning of the term quality of life
- Quality of life issues in cancer
- Quality of life issues in the context of chemotherapy for advanced Non Small Cell Lung Cancer (NSCLC).

Whilst clinical trial data features heavily in the last topic in lieu of other work, this is not a systematic review of the trials literature as this has been done elsewhere (NICE 2005).

One of the methods used in this study is also reviewed throughout this Chapter. The European Organisation for the Treatment of Cancer Quality of Life Questionnaire version 3 with Lung cancer module (EORTC QLQ-30+LC17) is reviewed along with comparable tools in the section dealing with Quality of Life Issues in Cancer. The second and principal method of this study uses content analysis of interviews with respondents who have recently undergone chemotherapy for advanced NSCLC. This is described more fully in Chapter 3(Methods). As there is very little literature and no

comparable studies that use content analysis in chemotherapy for advanced non-small cell lung cancer and quality of life, a brief overview of content analysis is given here.

Content Analysis is approximately 60 years old but has intellectual roots that can be traced back into human history to the first conscious use of symbol and voice (Krippendorf 2004) Virtually all disciplines within the humanities are concerned with the meaning of symbols, meanings and messages. The use of content analysis in the UK can be traced back to the inquisitorial pursuits of the Church in the 17th century but the term “content analysis” was first used during the second world war by Berelson in 1941 (Berelson and Lazarsfield 1948)

Content analysis entails the systematic reading of a body of text, image or symbolic matter, tabulation and interpretation of that matter. It is an empirically grounded method that is exploratory in process and predictive or inferential in intent (Krippendorf 2004).

Content analysis is a research technique for making replicable and valid inferences from text or other materials. In the context of this study, the interviews with patients undergoing chemotherapy for advanced NSCLC were transcribed and underwent content analysis. According to Krippendorf, data are commonly thought of as representing observations or readings but they are always the products of chosen procedures (Krippendorf 2004). As a technique content analysis relies on several specialized procedures for handling text and these are described in the context of this study in the Methods chapter (Chapter 3). In content analysis data result from the

procedures the researcher has chosen, for example to answer specific questions concerning phenomena.

A search of the databases of the last thirty five years (1970 to present) limiting to English language yield much in terms of literature with respect to lung cancer and quality of life, but little combining the two areas, particularly outside the context of a randomised clinical trials examining quality of life as an end point of a drug trial.

The search used various engines: CINHALL, Medline, Ingenta/EMBASE, SOSIG PsychInfo, The Cochrane Library, OVID and the National Cancer Institute via the HILO portal and search engine for the initial search. As new engines became available in the course of the study, new literature was reviewed via portals such as Google Scholar and British Library ONLINE.

Using keywords and phrases such as “lung cancer” “lung carcinoma” “non small cell lung cancer” “ quality of life” “health related quality of life” “life satisfaction” “global quality of life” “NSCLC” and “chemotherapy related quality of life” and utilising Boolean search techniques and exploding specific phrases, papers were obtained from the databases and via Index Medicus using the search algorithm given in Fig 2.1.

Additionally other material including unpublished studies were sought, this also includes “grey” literature as yet unpublished or personal correspondence.

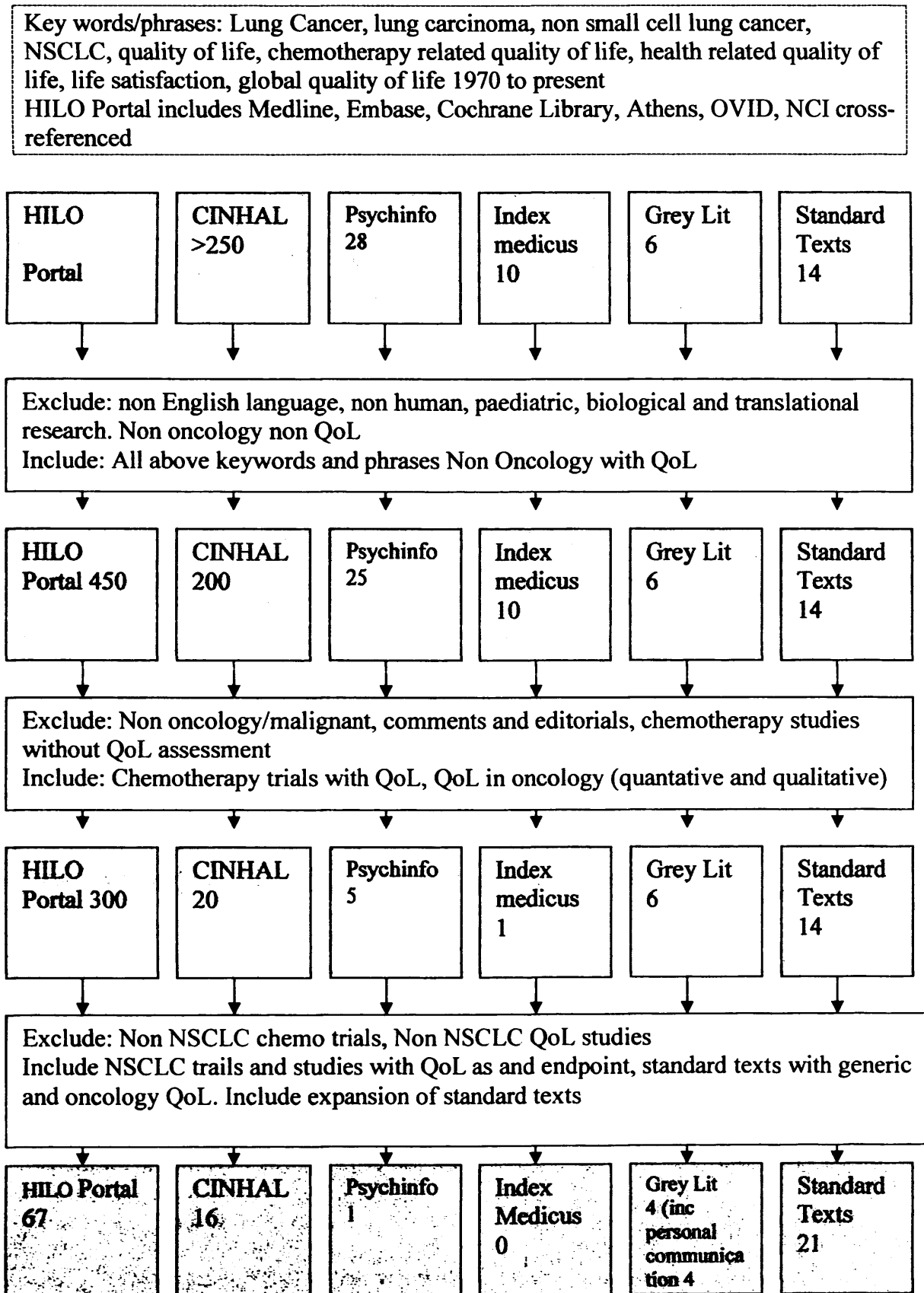
Bibliographies were searched as a source of references and also contact made with experts in the health service, charitable organisations and in industry. Studies reported as posters/conference abstracts were excluded as these are only available in published

form not via electronic portals or printed indices. However some of these led to sources of grey literature.

In addition to published peer reviewed work, a number of standard texts have been consulted to contribute to the medical and scientific strand of this work. Gathered largely from work based in the United Kingdom, Europe, USA and Canada, the following examines the knowledge as it stands in the context of NSCLC.

As the study progressed, both the author and library professionals made repeated searches as themes arose from the interview study which was analysed using content analysis. This is described in Chapters 6 and 7. The rationale for doing so is to elicit more data in which to examine emergent themes of quality of life in Non small cell lung cancer. The results of this process are integrated into the discussion chapters as themes from the qualitative strand emerged and this review is also used as a source of data.

Fig 2.1 Literature review QoL in chemotherapy for NSCLC



2.1 The cancer journey, the individual and society

There is an abundance of trial literature examining quality of life in lung cancer trials much of which is reviewed herein. Nevertheless the experience of the lung cancer journey, including treatment, is something rarely examined. Cancer care and treatment cannot take place in a vacuum as individuals that experience disease are still individuals. This is expressed eloquently by Harvey Cushing :

“A physician is obligated to consider more than the diseased organ, more even than the whole man-he must view the man within his world” Harvey Cushing 1869-1939
(Faull and Woof 2002).

There is much published work on cancer and its meaning. The literature reviewed here, whilst not exclusively examining the advanced NSCLC patient population, aims to place the rest of the review in context. As the aim is to place the quality of life literature in context, the enormous amount of cancer literature has not been fully reviewed here. Instead using the milestones from Fig 1.1 this section aims to illustrate the cancer journey by examining specific contemporary issues.

A study by Krishnasamy and Wilkie in 1999 (pre launch of the NHS Cancer Plan) examined the needs of lung cancer patients, their carers and professionals' perceptions of such needs. This study remains one of very few which looks at these issues in any depth. There are many possible reasons for this, the possibility of nihilism in the treatment of lung cancer or the comparative funding issues (Roy Castle Foundation 2005). It is interesting to note that when Krishnasamy and Wilkie (1999) performed their study, only 35 out of 107 hospital consultants agreed to take part (32.7%). Some

consultants (n=25) did agree to disclose reasons for non participation and this is shown in Figure 2.2

Fig 2.2 Reasons for non-participation in Macmillan National Needs Assessment Study (Lung cancer)

Reason for declining	Numbers reporting reason
Small numbers of lung cancer patients in practice	8
Pressure of work	15
Inadequate records to trace patients	4
Consultants felt study un-necessary/patients needs already known	19
Taking part would be too distressing for patients	13
Study would raise more problems than solutions	17
Needs of lung cancer patients no different to other cancer patients	9

As the consultants approached were those with specific clinical responsibility for lung cancer patients they might be considered the most powerful advocate group, and so the low response rate is surprising. This study is post Calman/Hine Report (CMO 1995) but pre dates the majority of the cancer modernisation agenda. The cancer modernisation agenda in the UK at the turn of the century became a powerful influence for change.

2.1.1 Issues around suspected cancer and investigations-the modernisation agenda.

“Cancer is on of the biggest killers in this country, and we have made it one of the central priorities for the NHS”

Alan Milburn MP 2000

The NHS Cancer Plan (DoH 2000a).

The rationale for inclusion of this section in a work essentially aimed at examining quality of life is illustrated by this quote from Alan Milburn, then Secretary of State for Health (Department of Health 2000a). Cancer is as much a social and political issue as it is a pathology. The NHS Cancer Plan (DoH 2000a) was the basis of the cancer modernisation agenda in England and Wales at the turn of the 20th century.

The four aims of the Cancer Plan were cited as:

- To save more lives
- To ensure people with cancer get the right professional support and care as well as the best treatments
- To tackle the inequalities in health that mean unskilled workers are twice as likely to die from cancer as professionals
- To build for the future through investment in the cancer workforce, through strong research and through the preparation for the genetics revolution, so that the NHS never falls behind in cancer care again. (DoH 2000a)

The ethos of the plan was to be a practical and empowering way of delivering a ten-year strategy and built on previous initiatives such as the Calman-Hine report (CMO Expert Advisory Group 1995).

The NHS Cancer Plan saw the initiation of many service improvement targets in NHS cancer care and delivery. This investment and reform was part of the greater modernisation agenda within the health service (DoH 2000a).

For users of the service this means a more streamlined and confluent approach to care, particularly around the area of first presentation from primary care and into secondary or tertiary referral where many bottlenecks to patient movement had been identified.

One such target demonstrates this. A person going to see a general practitioner in primary care with signs/symptoms of cancer can now expect to see a specialist in secondary care who will initiate investigation within two weeks of presentation to the GP. This allows patients to have equitable access to specialist multiprofessional care, no matter where they live. The Trust in which this study takes place illustrates this.

A patient coming from a primary or secondary centre for a diagnostic/curative thoracic procedure would have waited an average of 38 days in the last quarter of 2001. The implementation of the modernisation agenda cut this time to a mean of 8 days (last quarter 2003) by allowing local initiatives to unblock the pathway, and addressing unnecessary delays (Leary & Corrigan 2005).

The implementation of the modernisation agenda means that the cancer journey is now much faster with an initial target of diagnosis to definitive treatment of 31 days in 2001 (DoH 2000a) and currently a target of GP presentation to definitive treatment of 62 days (DoH 2003).

In a time of uncertainty this allows little time for the adaptation process which can cause increased psychological pain (Houldin 2000) and the “patient journey” along

with the organisation of care for people with cancer can therefore become a much more negative experience than it already is (DoH 2000a).

Another significant area of change in the management of the cancer pathway is the much earlier (often pre-diagnosis) involvement of other healthcare professionals such as clinical nurse specialists and oncologists. Cancer care is now managed by teams rather than, for example, an individual surgeon or physician as was often the norm (CSC 2001). Patients' value having a contactable key professional at all stages of the journey (Schou and Hewison 1999, Krishnasamy and Wilkie 1999, DoH 2000b) and the multiprofessional team has made this a realistic possibility in practice.

2.1.2 Issues around diagnosis-communication

The aim of good communication at the diagnosis of cancer is to reduce uncertainty, enhance a therapeutic relationship and give the patient and their significant others a direction in which to move (Twycross 1997, Ellis and Tattersall 2001). Whilst little is apparent in the literature with regard to communicating a diagnosis of NSCLC, there is much on the communication of a cancer diagnosis and this is worth considering as many patients reflect on this time later in their journey and find that this communication of diagnosis has bearing on how they cope with "having cancer" and its treatment.

Problems around communication and diagnosis often arise from the fear of either party. Professionals do not wish to inflict suffering (Cassell 2004) and in the UK it is usually a non-cancer specialist who communicates a cancer diagnosis. This can be a problem as the communication of a cancer diagnosis has issues of prognosis and

treatment embedded in it, which require specialist knowledge (Schou and Hewison 1999).

There is a significant amount of literature in this area. For example a study from the USA used a 41 item questionnaire to ascertain patient preference for the communication of diagnosis in head and neck cancer. Although those patients questioned had been treated and free of disease for two years, and this is unlikely given the poor prognosis of patients with NSCLC, the paper still has relevance. Head and neck cancers are potentially life threatening and affect breathing and speaking. The study found that patients preferred physicians to communicate the diagnosis of cancer in simple and direct terms, without medical terminology and wanted physicians to be “truthful, caring and compassionate” (Kim and Alvi 1999).

Many doctors find the disclosure of a cancer diagnosis difficult or very difficult (Ellis and Tattersall 1999) coupled with the fact that often the most stressful time for the patient and significant group is the time immediately (first month) after diagnosis (Kruijver et al 2000) it can therefore be seen how this is a potentially very painful start to the journey. The paper by Ellis and Tattersall (1999) also reiterates the need for presenting bad news in an unhurried, honest and balanced way.

This theme continues throughout the literature. Parker et al (2001) found little in the literature about the actual communication of “bad cancer news”. This group from the USA conducted a literature search and found that from 300 papers from 1973-1993 only 23.2% had any descriptive data at all and that 66% of the published work was in the form of letters, opinions, case reports and non-data based descriptive studies. The

authors of this paper note few studies have assessed patient's reactions as to how bad news was conveyed. A study was then conducted by this group examining this issue. It is reviewed here as it is not only of a high methodological standard but the focus is on a patient's rather than clinicians perspective and is one of the few papers available. It should be considered that such news might not only be a diagnosis of cancer but also news of treatment failure or recurrence of disease.

Working with a group of 351 patients with a cancer diagnosis, the authors asked patients to complete a questionnaire that was specifically designed for the project. The authors found that factor analysis indicated that patient preference for the breaking of bad news in oncology could be grouped into three categories. These are content (what and how much information is told) facilitation (setting and context) and support (emotional support during the interaction). The authors also found that women and patients with a higher level of education had higher scores on the content scale (Parker et al 2001).

Further work in this area was conducted on behalf of the Comptroller and Auditor General by the National Audit Office (NAO 2005a) which examined the progress of the Cancer Plan (DoH 2000a) after five years and the changing patient journey (NAO 2005a). The NAO reports improvements overall in the level of services and experiences of patients with cancer. However in terms of communication the NAO reports that there has been only a 6% improvement in communication by medical staff of condition, treatments or tests which patients found easy to understand (62% in 2000 to 68% in 2004) (NAO 2005b).

In literature originating from Europe or the USA in recent years the nature of disclosure of diagnosis of cancer is examined but not whether it is “right” to disclose. This is an ethical question and beyond the remit of this work as clinicians in the UK are socialised to embrace truth telling, however in other cultures this is not always so. This perspective should be recognized, as the UK is a multicultural society. In the context of diagnosis there is a small but significant amount of work on disclosure of cancer in other countries. A paper from Taiwan in the Peoples Republic of China states that older people and those “with lower education” (this term is not defined) are less likely to be told the diagnosis, although this paper also states that disclosure leads to lower intensity of pain (Lin 1999). Two papers from Japan suggest that patients should be told of the diagnosis and then the family should be told with the patient’s permission. This would seem to contrast with current practice whereby the family are told the diagnosis and then decide if the patient should know (Seo et al 2000).

A return to this practice in the UK seems unlikely as there are many issues around consent and such action would to contravene patient autonomy. A study from Portugal based on a questionnaire given to physicians in one city hospital showed that only 71% of respondents would tell a patient a cancer diagnosis and yet 98% would tell the patient’s relatives (Forjaz and Guarnaccia 2001). This paper helps to illustrate the different cultural attitudes to a cancer diagnosis disclosure. This is important in British multi-cultural practice.

Despite honesty being recognised as central to practice, it is essentially a two way process. The psychological adaptation to a cancer diagnosis can lead to illusion and misperception (Beadle et al 2004) and collusion with medical staff (The et al 2000).

2.1.3 “Having cancer”-the person with cancer and the concept of suffering.

Technological developments such as general anaesthesia and microscopy have allowed science and medicine to define cancer. By the early twentieth century, cancer became a disease state in its own right. Due to the limited availability of analgesia and the fact that surgery was not as technically advanced, the person with a tumour would typically have more visible symptoms. Non-healing, fungating wounds, poorly controlled pain and debilitation would have been visible to those around the person. The fact that some of these visible signs may have been similar to those of Syphilis may have contributed to the common belief that cancer was contagious (Holland 1998)

This may account for the stigma that is attached to cancer today and the stigmatising effect which Scambler has defined as “a condition which sets apart the possessor from ‘normal’ people” (Scambler 1991). It is something of an axiom now that cancer is a stigmatising illness. Scambler’s classic work goes on to describe the perceived exclusion of those with rectal cancer as a result of labelling (Scambler 1991). The person becomes the person with cancer despite the previous role they held in society and may still hold. Repeated studies have shown this (Mathieson and Stam 1995).

Lung cancer seems to carry an extra stigma. That is one of blame of self or by society. A recent MORI poll for the Cancer Research Campaign found that 70% of people in the UK thought people who develop lung cancer had “brought it upon themselves” but 77% thought they had as much right to treatment (CRC 2001) Reasons given for this reply by respondents cited tobacco use. The UK Lung Cancer Coalition

commissioned a survey of 956 adults between the 30th September and the 2nd of October 2005 to canvas attitudes toward and understanding of lung cancer. Of those interviewed 40% believed lung cancer to be self-inflicted. There was variation across socio economic groups however. 50% of the AB group said that lung cancer was self-inflicted compared to only 35% in the lower socio economic groups (DE) (UKLCC 2005).

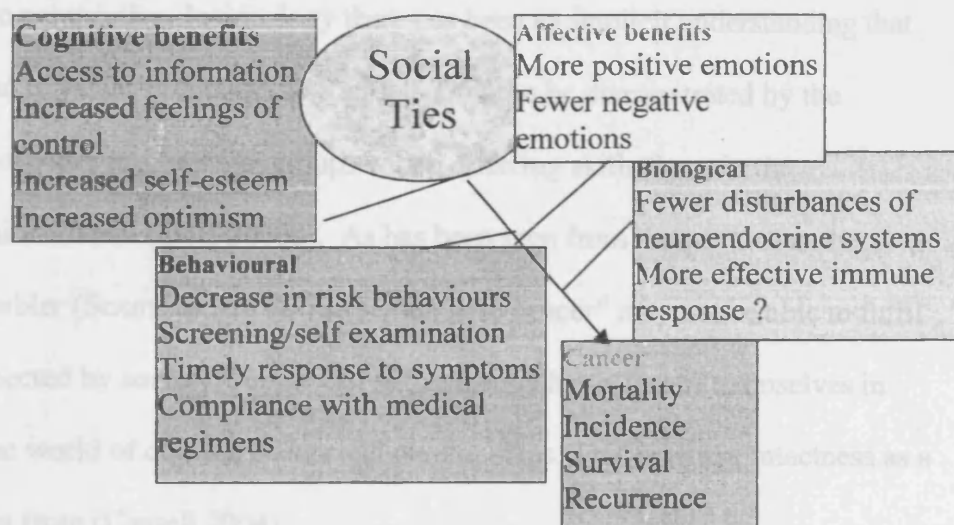
The epidemiology of lung cancer and the link with smoking has already been discussed, but this link is almost ingrained into society and lay belief as a result of many health education initiatives. Tobacco use is recognised as a risk factor in lung cancer but there is limited information about how a smoking history impacts on the emotional distress of those diagnosed with lung cancer. There have been some studies, which examine causal attribution of lung cancer in populations who smoke or have used tobacco in the past. These have shown that past tobacco use correlates with greater emotional distress (Berckman and Austin 1993). It is also thought that anger and resentment may be exhibited by those who have no smoking history themselves but who may have been exposed to second hand smoke at home or work (Sarna 1998). A recent study by Chapple et al reports that participants (adults with lung cancer) felt stigmatised to the point in which they felt the interactions with family, friends and doctors was often affected, with some participants concealing their disease. This occurred in smokers and non smokers (Chapple et al 2004).

In addition, in terms of Parson's classic work (Parsons 1951) of "the sick role" a person with advanced NSCLC cannot be realistically expected to fulfil the obligations of recovery and for the person with advanced NSCLC it is unlikely to be temporary

state. The person with advanced NSCLC may also wish to fulfil the obligation of co-operation with medical practice. This is likely to be chemotherapy that offers little survival benefit. Should persons with advanced NSCLC be exempted from these obligations? Would this obligation extend to prioritising quality of life above other medical treatment?

The person who has cancer as a pathological disease state will also experience the psychosocial dimension of “having cancer”. The benefits of having social ties (and as a corollary, lack of social ties) are illustrated by the model of pathways linking the social environment to Cancer (Helgeson, Cohen and Fritz 1998). The benefits of such social ties are shown in Fig 2.3

Fig 2.3 Pathway Linking Social Ties to Cancer after Helgeson et al 1998)



The nature of suffering is a concept that is gaining credence in oncology. The work of authors such as Eric Cassell (Cassell 2004) who explore suffering as a concept support this. Suffering is of interest as in the media the term is often imbued along with “quality of life” with multidimensional qualities. Like “quality of life” it resists a reductionist approach (see section 2.2).

The concept of suffering has roots as least as far back as the classical scholars, perhaps further, with explicit reference in the *Hippocratic Corpus* and the works of Cicero (Hippocrates trans Chadwick and Mann 1983, Cicero trans Grant 1971).

Suffering can represent physical injury to the person through accident or disease, often this is reacted to by health professionals with solutions borne from a deterministic perspective. In oncology there has been an implicit understanding that those without physical symptoms also suffer. This can be demonstrated by the recognition of other professional groups with a differing skills focus in the multiprofessional team (DoH 2000b). As has been seen from the work of authors such as Scambler (Scambler 1991) “the person with cancer” may not be able to fulfil the roles expected by society. People can suffer from what is lost of themselves in relation to the world of objects, events and relationships. This is where intactness as a person comes from (Cassell 2004).

It is important for clinicians to recognise that the intensity of suffering amongst cancer patients varies widely (Houldin 2000). Recent work has described cancer patients’ needs whilst suffering. Patients wish for nurses to have the ability to see beyond the symptoms-to be affirmed as a person and understood, and to have their needs met

beyond the level of physical problems (Fagerstrom et al 1998) and on a person-to-person level (Gregory 1994). This means offering patients understanding, empathy and compassion through meaningful communication (Gregory 1994, Byock 1994, Houldin 2000).

2.1.4 Issues around treatment-doing work

The majority of patients with advanced Non Small Cell Lung Cancer will die of their disease. In the USA around 178,000 people are diagnosed with lung cancer annually, of these 160,000 will die of their disease (Middleton et al 2000). If resected, there is a 5 year survival rate of 60% (Warren & Faber 2000). Patients with locally advanced or extensive disease have a five-year survival rate (with treatment) of 10-13% (Souhami and Tobias 2005). The median survival for NSCLC that is advanced is four to six months with only 10-20% of patients alive at one year after diagnosis (Dark and O'Brien 2001).

Although palliative chemotherapy is used for many cancers, there is still a reluctance to prescribe this type of treatment for patients with NSCLC, perhaps because the earlier chemotherapies saw no survival benefit and many clinicians saw chemotherapy as unjustified for patients not in a clinical trial. There is also a lay belief that chemotherapy is very difficult to tolerate (Lindley et al 1999). In other types of cancer the ultimate goal of palliative chemotherapy is the palliation of symptoms, not necessarily an increase in survival and so why does this rationale not seem as acceptable in the management of NSCLC?

In the UK only a small number of patients (5%) diagnosed with NSCLC have been receiving chemotherapy (Clegg et al 2001). The principal reason for this seems to have been the still widespread belief that chemotherapy is unacceptable to patients because of toxicity, and clinicians view chemotherapy for advanced NSCLC as

ineffective. A survey of clinicians pre cancer plan found little support for treating NSCLC with chemotherapy (Crook et al 1997).

It has been recognised for some time that NSCLC has been an under invested cancer, the Roy Castle Foundation reports that only 4% of UK cancer research funding is spent on lung cancer research (Roy Castle Foundation 2006). An editorial from the mid nineties referred to NSCLC as the “Cinderella of cancer medicine” (Smith 1994). However even studies from around this time show small gains in survival and quality of life, such as the meta-analysis by Souquet et al (Souquet et al 1993). Studies from around this time do not demonstrate a clear advantage in survival but do begin to show a benefit in terms of symptom control such as pain, cough and breathlessness (Hardy et al 1989). Another review in 1994, concluded that using chemotherapy could give a small benefit in survival, but expressed doubts about the balance between extra time versus toxicity and effect on “quality of life”, this should be a powerful statement but the authors do not actually provide any evidence of quality of life (Marino et al 1994).

In the last ten years, the introduction of platinum based chemotherapy drugs has changed this attitude to some degree because this group of drugs has been found to increase survival overall by small amounts (Spiro et al 2004). In some studies this has included the assessment of health related quality of life, which has also been shown to improve in terms of palliation of symptoms (Dark and O’Brien 2001). The quality of life issue is central to this work, for example is a reported improvement in quality of life a valid one? If the goal of this chemotherapy strategy is palliation of symptoms, it should be a central issue. For some patients the beginning of the “work” of cancer

starts here-with the therapeutic nihilistic approach that is still prevalent toward NSCLC, some patients are required to seek out centres which offer treatment by themselves (Roy Castle Foundation 2003).

Apart from the physical effects of disease and side effects from treatment, the majority of work that has to be done by patients with cancer is around managing the treatment calendar (appointments with key professionals, investigations, infringement into everyday life) (Schou and Hewison 1999). Easier negotiation of the calendar or “cancer trajectory” by standardisation is one of the motivations of initiatives such as the modernisation agenda and the Cancer Plan (DoH 2000a). Many clinicians in practice will appreciate that the cancer trajectory is not always a straight line and this causes more work for patients, physically, organisationally or in terms of emotional labour. Many patients negotiate the calendar by accessing the key professional who has power or influence over the calendar (Schou and Hewison 1999, Leary and Corrigan 2005). This role has now been recognised and supported, usually by means of clinical nurse specialists (DOH 200b) and the recognition of the Key worker role (NICE 2005). It is now recognised that although medical care can reduce the impact of illness, inattentive care can increase the impact of disruption and therefore become a source of suffering (Cassell 2004).

2.1.5 Issues around completion of treatment-abandonment and uncertainty.

“When chronic illness intrudes, it separates the person of the present from the person of the past and affects or even shatters any images of the self held in the future. Cancer with its often insidious, ambiguous presentation and unpredictable course, takes the experience of uncertainty to a higher level”.

Houldin 2000

Following on from the concept of suffering-or perhaps as a dimension of it-is the experience of uncertainty. Illness related uncertainty has been defined as the inability to determine the meaning of illness events, when these events are ambiguous, highly complex, lacking information or when outcomes cannot be predicted (Mishel 1990).

Advanced NSCLC as a disease certainly would engender uncertainty from a pathological aspect alone. Events in the disease course are ambiguous (for NSCLC may or may not respond to chemotherapy) and outcomes in terms of survival cannot realistically be predicted for the individual, it can only be loosely predicted for groups. Add to this is the increased need for and complexity of information required by those who have to negotiate the treatment calendar (Schou and Hewison 1999, NICE 2005) and it is therefore not surprising that patients express fear and have difficulty in adaptation from a psychological perspective.

Research examining illness and uncertainty has shown an association between uncertainty and adjustment (Oberst and Scott 1985), distress (Wineman et al 1996, Fife1995, Wong and Bramwell 1992), spiritual well-being (Landis 1996, Cassell 2004), coping (Schou and Hewison 1999, Christman 1988), and quality of life (Hawthorne and Hixon 1994). The literature offers more studies to support these findings, however nothing in the context of advanced NSCLC.

Uncertainty is sometimes heightened by the end of treatment, when lessening regular contact with health professionals is normal in the UK after the more intense experience of chemotherapy attendances. The literature showed that uncertainty is a continuing stressor (Mast 1998) and may strongly influence adaptive behaviour (Houldin 2000). The feelings of uncertainty and fear produced by feelings of abandonment after treatment can produce the strong need for vigilant behaviour (Houldin 2000, Janis 1967). This is particularly so when patients perceive protective action is primarily dependent on their individual actions (Reutter and Northcott 1994). This is why it is important for patients to feel that they are not alone in the management of their illness. As access to key professionals in the treatment calendar (Schou and Hewison 1999) can be made easier by the key worker (DoH 200b), this may dissipate some of the uncertainty.

In conclusion, words such as “belief,” “suffering” and “meaning,” have often been used to describe the cancer journey and the patient experience. This could be because fear of treatment, recurrence or death causes suffering (Cassell 2004) and is central to that experience. Working with the beliefs and meanings of people with cancer is an essential part of helping people on their own journey (Richer and Ezer 2000).

2.2 Toward A generic definition of quality of life

“Scientists may use rating scales and visual analogue scales to measure pain, and they may even invent scoring systems quantifying types of handicap, but when they talk about measuring quality of life they have gone too far.” (Wulf 1999).

The statement given by Wulff (1999) above, was cited in a review and deconstruction of the concept of Quality of Life (quality of life) (Koller and Lorenz 2002) which demonstrates not only the difficulty of developing such a definition but also the apparent scepticism in the value of doing so.

Quality of life in the literature was apparent in two contexts, authors either seek to define quality of life or measure quality of life. This may seem a logical path to take but it means that the literature lacks integration. For example, this fragmentation makes it difficult for a clinician to introduce quality of life assessment into practice without in-depth exploration of the two areas, unless a formulaic approach is used. This is exactly the situation at present and explains the dominance of questionnaires and quality of life tools in practice, particularly in the context of health economics. Some authors (Hayry 1999) argue for integration of three key questions:

- I. What is quality of life?
- II. How can quality of life be measured?
- III. Why do we need quality of life measurements? (Hayry 1999).

The definition from the Oxford English Dictionary (1995) of quality of life as “...a vague and ethereal entity” serves to illustrate the difficulty in attempting to define quality of life and illustrates the difficulty also faced by the researcher in this area in

trying to find that definition. When quality of life has been discussed in the literature, it has usually been in terms that vary widely from the “need” based theories of authors such as Maslow (Maslow 1954) to expressions of the value or excellence of life and the word quality is being used in an evaluative sense (Meeberg 1993). Authors argue that this is such an enormous area of study that it is almost impossible to define quality of life (Stegbauer 1994). This was also true in application of the term quality of life.

Quality of life is a multi-level concept reflecting macro-societal and socio-demographic influences and also the micro-concerns of individuals’ experiences, circumstances, health, social well-being, values, perceptions and psychology (Bowling et al 2003).

In a recent major undertaking, the Royal College of Nursing sought to define nursing. The consensus defined nursing as “The use of clinical judgement in the provision of care to enable people to improve, maintain or recover health problems, to achieve the best possible quality of life, whatever their disease or disability until death” (RCN 2003). Although in this context, the term quality of life has been used to formulate an important concept, (i.e. defining a whole profession and body of knowledge) no attempt has been made to define the term.

Quality of life became a focus for nursing practice in the 1980’s and as more definitions emerged, the concept receded (Mast 1995). It is possible that as nursing has evolved with such rapidity, many terms have become ambiguous. Quality of life is of particular interest to nurses and nurse researchers, as much value is placed on the

evaluation of nursing interventions and quality of life could be perceived as an outcome measure. This is demonstrated by the liberal use of the term “quality of life” in the nursing literature. The Oncology Nursing Society for example, cited “quality of life” as among its top three priorities without definition (Stetz et al 1995).

The question here is “What is quality of life?” and the aim is to attempt to examine what is meant by the term “Quality of life” in the literature. There have been many attempts to define quality of life and these are explored in more detail in the concept clarification offered in the context of advanced NSCLC later in this chapter. However in a broader sense, quality of life is likely to mean a range of things to different individuals, and so the concept and definitions of quality of life presented in the literature are examined in more detail here.

2.2.1 Quality of life and The good life-Historical perspectives

The first examination of the quality of life in a broad sense has often been attributed to the Greek philosophers of antiquity, such as Aristotle, who valued happiness and a “good life” (McKenon 1947). Such a concept as a “good and useful” life (Plato trans Saunders 1970) can be found in many ancient texts.

The writings of antiquity may allude to quality of life but this has caused conceptual confusion in the literature (Bowling and Windsor 2001). These ideas have been expressed in a variety of ways, for example as a “good life” in the very physical context of “having food and shelter or the price of a horse when in battle, to the faithfulness of trusted friends” (Xenophon trans. Cawkwell 1972). Plato considered a good and happy life the product of a just society, “the good man, because he is

temperate and just, enjoys good fortune and is happy, no matter whether he is big and strong, or small and weak, or rich or poor; and that even if he is richer than Midas or Cinyras' and has not justice, he is a wretch and lives a life of misery." (Plato trans Saunders 1970). Plato and his contemporaries have been cited in work that aims to define quality of life or happiness.

It is apparent from the classical texts that much of Plato's work is heavily influenced by his relationship with Socrates. In the Socratic dialogues it can be seen that the idea of happiness and a good life, which Plato attributes to a just society, is influenced by the Socratic idea of knowledge having an impact on society and the individual.

Socrates argued that knowledge possessed by the individual attracts trust in that individual "knowledge makes one useful and good" (Saunders 1970, Saunders 1987).

Socrates appears to make happiness and "the good life" entirely dependent on moral goodness (Cicero trans Grant 1971) but Cicero argued that it is not simply "moral goodness" that makes life good, but that a "good life" is not quantifiable. Cicero states, "Take for example strength, health, wealth, honour or glory. These are all spoken of by people in general, indefinite terms without reckoning up the exact quantity of each that may be present in any specific case. Now, the same applies to the happy life. Even if it may fall short of perfect happiness, nevertheless it is entitled to be called happy when happiness is the constituent which greatly exceeds all others" (Cicero trans Grant 1971). These themes are carried from antiquity to the present day.

Although it is rare to find the term quality of life in anything prior to the 19th century, there are certainly examples (Meeks and Meeks 1999) of what different individuals

and societal groups have considered as happiness or more profoundly, giving value to life. One of the most obvious examples of this concept in history is the link of everyday life and religion or spirituality. This can be found as far back as pre-dynastic Egypt, and throughout the development of the ancient dynastic Egyptian societies, the reality of daily existence in such times and the happiness and “goodness of living” (Meeks and Meeks 1999) of the people revolved around daily religious ritual, directly to gods or via a mediator (Meeks and Meeks 1999). More recent examples in history are abundant such as the 12th century knights whose sole purpose in life was to protect pilgrims on the pilgrimage to Jerusalem (Burman 1986). The idea of belief giving meaning and value to life is an ideal that still exists today. Although they did not define what quality of life is, these ideas demonstrated the value of the concept and how the concept has engaged minds throughout time.

The use of the phrase in the modern world appears to have been in post war America, and it was used by sociologists and policy makers in reference to the perceived increase in material wealth and consequent improvement in “quality of life” (Carr et al. 1996). Lyndon Johnson, then President of the USA, used the term “quality of life” in his speech to the American public in 1964 to refer to the bounty the post war years brought in terms of material and financial security (Meeberg 1993). The 1960’s also saw the start of the scholarly pursuit of a definition through studies in happiness. The majority conducted by sociologists and psychologists in the USA, studies included examination of concepts such as life satisfaction and well-being with the aim of quantification (Bradburn 1969), and in concord with the ideas of antiquity, what was meant by “the good life” (Gurin et al 1960).

The first proposed theoretical model of quality of life was presented by Lawton in 1983 (Lawton 1983, Bowling 1995) but an early, if implicit, definition of quality of life was introduced after the Second World War by the World Health Organization (WHO).

The WHO defined *health* in 1948 to be “a state of physical, mental and social well-being and not merely the absence of disease” (WHO 1948). This definition has evolved over time, in 1978 WHO stated that individuals have a right to an “adequate quality of life” in the definition (WHO 1978). More recently The WHO Quality of Life Group defined quality of life thus;

“Quality of life is defined as an individual’s perception of their position in life in the context of their culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships and their relationships to salient features of their environment.” (WHO 1993).

This definition has had a profound impact on the design of quality of life assessment and this impact is seen clearly in oncology, most of the reviewed studies herein refer to the WHO definition and it is clear to see how this definition informed quality of life assessment development, particularly throughout the 1990’s (Aaronson 1993, Schou and Hewison 1999). The concept and measurement of quality of life are dependent on the expert rather than lay views of the important constituents (Bowling 2001).

The term “health related quality of life” (HRQoL) as first used in the context of cancer by Aaronson (1990), who argued that factors such as happiness and life satisfaction are “distal to the the goals and objectives of healthcare” and therefore do not adequately capture the effectiveness of interventions (Aaronson 1990). It could be interpreted from Aaronson’s argument that quality of life assessment is only a means to an end. This statement also seems to contradict much of Aaronson’s later work, which is reviewed here. It can be seen from the literature that health related quality of life is increasingly used as an outcome measure of healthcare in evaluative research and clinical trials (Montezari et al 1998).

2.2.2 Quality of Life in the literature

Quality of life is amorphous and subjective (Bowling 1997). Areas that are self-nominated as important to individual quality of life have not always correlated with what is considered important by researchers investigating quality of life (Bowling and Windsor 2001). This amorphous quality was recognised by the early scholars who sought to define quality of life, for example the comment by Campbell et al (1976) that “Quality of life is a vague and ethereal entity, something that many people talk about but which nobody very clearly knows what to do about”. It has been seen from the WHO definition alone that quality of life encompasses a vast range of areas and disciplines such as sociology, health, geography, philosophy and economics reflecting the multidimensional nature of quality of life (Bowling 1997).

In the same way that the WHO definition of quality of life has evolved from one of health, the quality of life literature has been seen to reflect the way that much of the work undertaken in the pursuit of a definition of quality of life is in the health arena. This is perhaps because policy makers and others in the health professions increasingly sought ways in which to evaluate interventions. It has been argued by some authors (Fitzpatrick et al 1999) that the need for the assessment of interventions is one of the motivating forces for the development of the concept of health related quality of life (Cooley 1998).

The aforementioned assessment of quality of life has been traditionally based on a medical or pathological model, with a focus on disability, symptom or decline and focus on role function, such as work and family care (Bowling 2003). Functionalism is a theory, which is based on the interrelationships within the social system, and the consequences of change in such situations (Bowling 1997). Such changes in normal roles are explored by many quality of life outcome measures.

In contrast a search of the available databases cited above using the keywords “Quality of life” now elicit over ten thousand items, particularly from the 1990’s. Through the filtering process described in Fig 2.1 these items become more manageable. Most published work on quality of life seems to have originated in the 1980’s. This work was conducted by sociologists and psychologists examining issues such as housing (Meeberg 1993) and from then onwards the term “quality of life” was found in many different studies from the working environment to health care. Opong et al (1987) stated that quality of life can be conceptualised either as conditions of life or as experiences of life (Opong et al. 1987).

Other recent attempts to define quality of life focus on self-perception and self report in three domains: somatic, psychological and social (Koller and Lorentz 2002).

Zebrack (2000) examined quality of life and cancer survivorship (commonly taken to mean progression/disease free survival of five years or more) and noted a focus on adaptation to change as a principal construct of quality of life. Zebrack then went on to state that by the mid 1990's the term "Quality of Life" appeared to supplant terms like "adaptation" and "psychosocial adjustment" in studies examining outcomes in cancer survivors (Zebrack 2000). This illustrates the fluid nature and the almost erratic use of the term in the literature.

As stated earlier, quality of life has now come to be a prominent part of health care with the growing realisation that the well-being of patients is as important as treating disease or sustaining life which became much more emphatically stated in the 1980's, perhaps because of the increased availability of life-sustaining technology (de Haes and van Knippenberg 1985). Johanna De Haes and Ferdinand Von Knippenberg sought to define Quality of life to some degree.

In their 1985 review of quality of life in cancer patients (a general patient population) they offered six definitions (de Haes and Von Knippenberg 1985):

- The ability of patients to manage their lives as they evaluate it.
- The degree of need satisfaction within the physical, psychological, social, activity, material and structural areas.
- A function of the patient's own endowment, and the efforts made on the patient's behalf by others.
- The global evaluation of the good or satisfactory character of people's life.
- The totality of those goods, services and situations which are articulated as being needed and wanted.
- The output of two aggregate factors: physical and spiritual.

These characterisations of quality of life are not clear or concise (Hayry 1991), however they represent two diverse perspectives. These were those of self-fulfilment and met needs. Hayry also pointed out that philosophical discussions predate medicine (Hayry 1991) and discussions such as those presented by de Haes and Von Knippenberg (1985) presented two facets of what quality of life is: Is quality of life achieving what an individual *wants* or what an individual *needs*?

Other investigators during the 1980's sought to define quality of life in terms of well being (Packa 1989, Meeberg 1993). This was a continuation of the work by investigators during the 1960's and 70's. In contrast Tartar et al(1988) gave a very comprehensive definition of quality of life as “ a multi-faceted construct that

encompasses the individuals behavioural and cognitive capacities, emotional well being, and abilities requiring the performance of domestic, vocational and social roles.” (Tartar et al.1988). This contrasts with an earlier, reductionist, attempt to quantify quality of life with the formula:

$$QL=NE \times (H+S)$$

where QL represents quality of life, H represents the contribution of the individual to family/home, NE represents the patients “natural endowment” and S represents the individual’s contribution to society (Shaw 1977 in Meeberg 1993) It is difficult to accept this as a valid model, mathematically it does not offer mere manipulation of constants. It is difficult to see any relationship between the factors which are all heavily derivative. It should however, be taken in its historical context.

In the late 1970’s quality of life and HRQoL had made only limited appearance in the literature. This formula does not seem to have been developed further in the context of quantification or as an empirical definition of quality of life. Meeberg used this formula to illustrate one end of a spectrum of definitions, and she went on to perform a concept analysis of quality of life that derived four defining attributes, which seem to be in concord with the rest of the literature reviewed here (Meeberg 1993) despite being from the early 1990’s.

They are:

- A feeling of satisfaction with one's life in general.
- The mental capacity to evaluate one's own life as satisfactory or otherwise.
- An acceptable state of physical social and emotional health as determined by the individual referred to.
- An objective assessment by another that the person's living conditions are adequate and not life threatening.

The definition of Shin and Johnson (1978) who suggested that quality of life consisted of "the possession of resources necessary to the satisfaction of individual needs, wants, desires. Participation in activities enabling personal development and self actualisation and the satisfactory comparison between oneself and others" contrasted with the earlier definitions, particularly from antiquity (Plato Trans Saunders 1970). The latter definition appears to imply that personal and financial resources are key to good quality of life.

Other attempts to define quality of life have included the subjective, such as Andrews & Withey's concept that quality of life is an affective response to one's role, situation and values (Andrews and Withey 1976). It would seem that the concept of quality of life in the literature that pre dates the 1980's was still strongly connected with the "goodness of life" (Zautra and Goodhart 1979) concepts from antiquity (Plato Trans Saunders 1970).

Definitions of quality of life range vastly from the holistic WHO definition (WHO 1993) through social and physical well-being of patients to the ability to lead a fulfilling life (Bullinger et al.1993). Nursing and other health related literature yields the majority of quality of life references (Koller and Lorentz 2002) but there is little given in the way of definition of the term. quality of life has been viewed until recently, as a constant (Carr et al. 2001). There is recognition now in the literature that this is not so (Carr et al 2001).

Recent work does not try to define quality of life with one phrase and a trend can be seen from the late 1990's of encompassing previous definitions whilst exploring the meaning of the concept of quality of life in greater depth (Bowling 2003, Carr 2001, Addington-Hall and Kalra 2003). An example of this is the idea of quality of life as an individual and subjective concept and therefore countering the concept of quality of life as a constant or the gap between expectations and experience causing differing perceptions of quality of life (Carr 2001). Recent investigators have made explicit assertions that quality of life is not related to health, contrary to the current literature, but is related specifically to disease (Koller and Lorentz 2002).

There was no consensus in the literature as to what quality of life is, in particular with reference to health (Carr et al. 2001) or health related quality of life (HRQoL). Instead a variety of concepts and definitions have been presented. Despite many references to quality of life in the literature, the term was often used but few real attempts have been made to define it. It seems that quality of life resists definition, reflecting the amorphous nature of the concept. (Fitzpatrick et al 1998).

2.2.3 Measuring quality of life-quality of life as an outcome measure

“Like Humpty Dumpty, researchers and clinicians alike seem to think that quality of life can mean anything they want it to mean, regardless of the concerns of the patients themselves”.

Sonja M Hunt
Individual Quality of Life 1999

There was much debate in the literature with regard to the measurement of quality of life (Zebrack 2000, Aaronson 1991, Fitzpatrick et al 1998). As quality of life has defied definition, is it possible to measure? Measuring the immeasurable is counter to positivist tradition. In addition who should measure quality of life? (Fitzpatrick et al 1998, Slevin et al 1988). The theme of doubt that quality of life could be measured was woven into the literature, for example:

“For a scale of any kind to be meaningful there must be an agreed unit of measurement. In other words scientific measurement is inherently reductionist-concerned with one type of entity only-whereas quality of life is multifactorial, and the factors are inherently incommensurable, no matter how complex the mathematics. Hence the attempt to produce “quality of life scales” is bound to fail.”

Downie 1999

Most of the literature pertaining to health interventions discussed functional status or health-related quality of life (HRQoL). Effectively these were patient outcome measures, used to assess interventions in patient populations (Byrne 1992, de Haes and von Knippenberg 1985). These outcome measures and instruments used in cancer populations are discussed in Section 2.2

Investigators agree that quality of life is multidimensional (Bowling 2003, Zebrack 2000, Fitzpatrick et al 1998). As Testa and Simonson (1996) pointed out, different studies have focussed on different domains, for example physical, psychological and performance (Testa and Simonson 1996). The findings of Beretero and Ek (1993)

demonstrated the need for multidimensional tools. In their study, Bereto and Ek (1993) found that patients verbalised their perceptions of quality of life and how it varied over time with regard to illness state, perspectives on survivorship and relationships. They found that the diagnosis of a serious or life threatening illness resulted in a higher priority being given to existential and psychological factors over other domains (for example physical) (Beretero and Ek 1993). These findings suggest that investigators need to assess the values that patients place on different dimensions of quality of life and evaluate those dimensions.

The literature offered a diverse range of outcome measures, and as a result of the process illustrated in Fig 2.1, patient based outcome measures were the only ones examined.

Seven major types of patient based outcome measure are available in the literature (Fitzpatrick et al 1998). These were:

Disease specific: Developed to provide patients' perception of a disease or health problem. These instruments have a specific range and could detect changes in condition or disease state over time (Patrick and Deyo 1989). These instruments are limited in that they can only be used in the population with the disease (and not healthy control groups).

Site specific Assess quality of life or outcomes with respect to specific part of the body, for example the Oxford Hip score (Dawson et al 1996)

Dimension specific: These instruments assessed one aspect of health status, for example depression (Beck et al 1961)

Generic: These instruments are designed to capture a variety of aspects of health and illness states. They can therefore be used in a wide range of studies.

Summary item: These instruments are single items that invite respondents to verbalise health status by a small number of questions. The main disadvantage is brevity, however this also means less time demands on respondents.

Individualised: Individualised measures allow respondents to select issues which are of concern to them and not pre-selected by the investigators.

Utility: These instruments have been derived from economics and decision theory with the aim of estimating patient preference.

Fitzpatrick and colleagues (1998) also recommend eight criteria which investigators should apply to the selection of an instrument. These were appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability and feasibility (Fitzpatrick et al 1998)

Validity in quality of life research has more facets than the reproducibility of a purely reductionist method. Bowling describes validity as: (Bowling 1997)

Content Validity: The components of the measure should cover the attributes that need to be measured.

Face Validity: A form of content validity, Is the measure the right one from an obvious standpoint?

Construct Validity: The validity of underlying factors (constructs). A more abstract approach for testing the development of hypothesis.

Criterion Validity: The closest comparison to validity in reductionist approaches.

Criterion validity tests validity against a “gold standard” which is difficult to do in HRquality of life as this does not exist. Criterion validity is further divided:

Concurrent Validity: Defines how substantial the scale is, usually in comparison to a sucessessor.

Predictive Validity: Does the measure predict future differences?

These criteria should be considered in the selection of an instrument.

2.3 Quality of Life in Cancer

“Survival rates and side effects have become the dominant constructs of cancer treatment and cancer care, to the detriment of more supportive and patient focussed approaches. The concept of quality of life introduced to address this has failed to temper the language of oncology.”

Jessica Corner
The Robert Tiffany Lecture 1996
9th International Conference on
Cancer Nursing

Incidence, survival and mortality have historically been used to map cancer pathology and treatment (Fraumeni et al 1993) and this is reflected in Corner's assertion (Corner 1997) and confirmed by Alan Millburn's statement at the launch of the NHS Cancer Plan (DoH 2000a). The oncology literature is dominated by studies in which five-year survival, prognosis and tumour response are the main themes. This is not surprising but as the primary language of cancer they reflect the fear of the disease and support the association of cancer with death. The introduction of quality of life and HRQoL has not tempered this language; however it is the criticism of the over-emphasis on survival as the sole legitimate aim of treatment, which led to far greater consideration of factors such as quality of life (Corner 1997).

Oncology was one of the first areas of medicine to include the assessment of the impact of treatment on functioning as part of the treatment agenda. The work of Karnofsky and colleagues being an example of this (Karnofsky et al 1948, Schou & Hewison 1999). In general terms, cancer is difficult to cure and most types of treatment induce some kind of toxicity. In the late 1970's and early 1980's consideration of quality of life began to emerge in the oncology literature. Some authors have attributed this to technological progress and the increasingly complex

treatment options that became available (de Haes and van Knippenberg 1985).

Technology has increased lifespan in the western world and also meant that it is possible to keep humans alive for longer with chronic illness (Gerhardt 1990).

Chronic illness shifted the biomedical agenda in the latter part of the last century, through the changing population of acute care institutions, where some of the first qualitative studies of chronic illness took place (Gerhardt 1990). The first of these examined quality of life in patients with chronic illness (Strauss and Glaser 1975) and concluded that much of the work of acute care institutions is the management of the acute phases of chronic illness. Ten years later, Strauss and co-workers described how advances in medicine had now produced a group of chronically ill people who had to function in society (Strauss et al 1985).

This work set the foundations for quality of life to become a biomedical issue (Schou and Hewison 1999), and the biomedical model of acute illness is often criticised for its inability to deal with chronicity and the illness experience (Illich 1976, Levanthal et al 1982). A new model was called for, it needed to be multidimensional and holistic (Engel 1977, Cunningham 1986). One of the largest advocates of the importance of quality of life in the context of living with chronic illness, was the emergence of the hospice movement in the 1960's and 1970's.

As has been shown, definitions of quality of life vary widely (Bowling 1997, Fitzpatrick et al 1998). The WHO (WHO 1993) definition is the one that seems to have informed the oncology literature to the greatest degree (Zebrack 2000), as this definition emphasised the multi-dimensional nature of health and well-being. Two

themes emerged from the oncology literature in the context of quality of life. The first was that quality of life is a broad term, and this leads to difficulties when comparing studies. The second was that quality of life is multidimensional and included physical, psychological and social components (Aaronson et al 1991, Hopwood 1992, Testa and Simonson 1996, Fitzpatrick et al 1998).

It is the biomedical model that continues to dominate clinical practice. Physicians and other professionals set goals for cancer patients and then assess progress. Quality of life assessment is an extension of this process in the context of cancer treatment. Investigators (Schou and Hewison 1999) found that some clinicians considered including a patient's own assessment of treatment in this form is in conflict with the need to have clear and concise measures so as not to interrupt the flow of a time pressed clinic or clinician and an increased patient burden (Schou and Hewison 1999). This view re-enforced the biomedical model and was in direct opposition to that of multidimensional and holistic care (Barkauskas 2002).

Generally quality of life in oncology is operationalized as functional status (Aaronson et al 1988, Holland 1992). The adoption of quality of life assessment in oncology has been influenced by the inclusion of quality of life assessment in clinical trials in the context of outcome measures (Byrne 1992) and so there has been a strong argument that quality of life in oncology essentially still has a biomedical focus through a dependence on a "functional living" perspective (Schipper 1984, Schou and Hewison 1999, NICE 2005).

This perspective has evolved from the early performance indicators, which were based on functional ability (Karnofsky et al 1948) and activities of daily living scales (MacDowell and Newell 1987). In many instances HRQoL is often extended to include other domains such as financial or global quality of life (Aaronson 1991) but essentially, non-function specific issues receive little consideration in the literature. In focusing on functioning, quality of life assessment developers have continued to focus on pathology and some authors argue, severely restricted the study of psychosocial aspects of cancer and it's treatment to detecting psychopathology and the measurement of distress in patients (Schou and Hewison 1999, Holland 1992).

Catruvedi (1991) stated that the quality of *life* is not the same as the quality of *function*. What seems to be missing from quality of life assessment in cancer is a sense of *meaning* of the experience of cancer and treatment for an individual. The term *meaning* gives some depth to functionality, but is not merely an extension of functionality. Meaning can include issues of understanding and acknowledgement from professionals and ideas about support (or non-support) from professionals or others, the nature of choice in treatment and the different experiences of the treatment trajectory or even treatment cessation. There have been authors who supported a shift from the "distress" model of psycho-oncology toward a positive exploration of the meaning in the experience of cancer and treatment (Fife 1995).

The psychological aspects of quality of life have been heavily linked to function and coping strategies. Using this method has resulted in assessing stress or distress felt by the patient in respect to diagnosis, treatment or prognosis and not assessing quality of life (Schou and Hewison 1999). Again the influence of the biomedical model arising

from pathology is clear and so is its origin in the Cartesian philosophy of the body as a machine (Bowling 1997). Studies available in the literature (Spiegel 1997, Schou and Hewison 1999) have examined various aspects of psychological response and “functionality” in this way.

In the cancer literature examined other than that for NSCLC (for example breast and gynaecological cancers) there was a wealth of literature examining reaction to treatment, to prognosis or diagnosis, self-esteem and sexuality but little literature on the healthcare context such as professional-patient relationships that have positively affected information giving in terms of optimism or pessimism (Spiegel 1997).

McCorkle et al (1989) defined quality of life as “functional capacity, symptoms and perceptions of health”.

It can be said then that quality of life in the cancer literature is still based in terms of a functional approach that gives conventional biomedical perspectives priority. Such an approach would seem to fail to take account of the personal experience of people with cancer. Patients’ experience of treatment, of the health care system and of living with cancer are all aspects of the social experience of illness (Holland 1992, Somerfield and Curbow 1992, Testa and Simonson 1996, Schou and Hewison 1999) and require more attention than they have received in the oncology literature. There is a lack of empirical research in this area (Zebrack 2000).

It has become apparent that the effect of non-small cell lung cancer (NSCLC), and cancer in more general terms, cannot be considered only in terms of pathology.

Holistic practice is based on a broad knowledge of many issues that affect people with

cancer. In the last half of the twentieth century more has been understood of the psychological effects of health and illness and the context of health and disease in relationship to the rest of life. The teaching of these ideas certainly makes up a significant part of the clinical pre-qualification curricula of various disciplines in the UK. This work was clinically based and so it is appropriate to examine the issues around this area particularly in the oncology setting.

The exploration of issues such as the effect of cancer on the individual and the group is now often termed psycho-oncology or psycho-social oncology, a discipline which has developed as a sub speciality of oncology over the last thirty years as psychological factors were seen to influence the experience of people with cancer (Holland 1992).

There was a detectable pressure from within the psycho-oncology literature for the “scientific” measurement of quality of life using tools such as questionnaires (Schou and Hewison 1999, Holland 1992, Holland 1998, Bowling 2003). The tools thus developed and considered supported the idea of measuring pathology, not only physical but also psychological. This framework was assumptive and it has also been suggested that psychological morbidity in cancer patients has been overestimated (Meyerowitz 1993, Bowling 1997).

Two types of conceptual definition of quality of life have been used in psychosocial oncology, global quality of life and health related quality of life. The main differences noted were that global quality of life sought to learn more about the character of life whereas health related quality of life sought to examine disease symptoms, side

effects of treatment, psychological distress and functioning (Kaasa and Mastakaasa 1988).

2.3.1 Quality of life and Psycho-oncology in the literature

Over the last thirty years investigators have written about the social construction of health and illness. This has formed the basis for much of the groundwork of psychosocial oncology. It is worth reviewing some of the work that made significant changes in the way that health and illness are viewed in a psychological and sociological context. This is because it is important to understand the psychological and sociological importance of illness so as to better understand the impact of cancer.

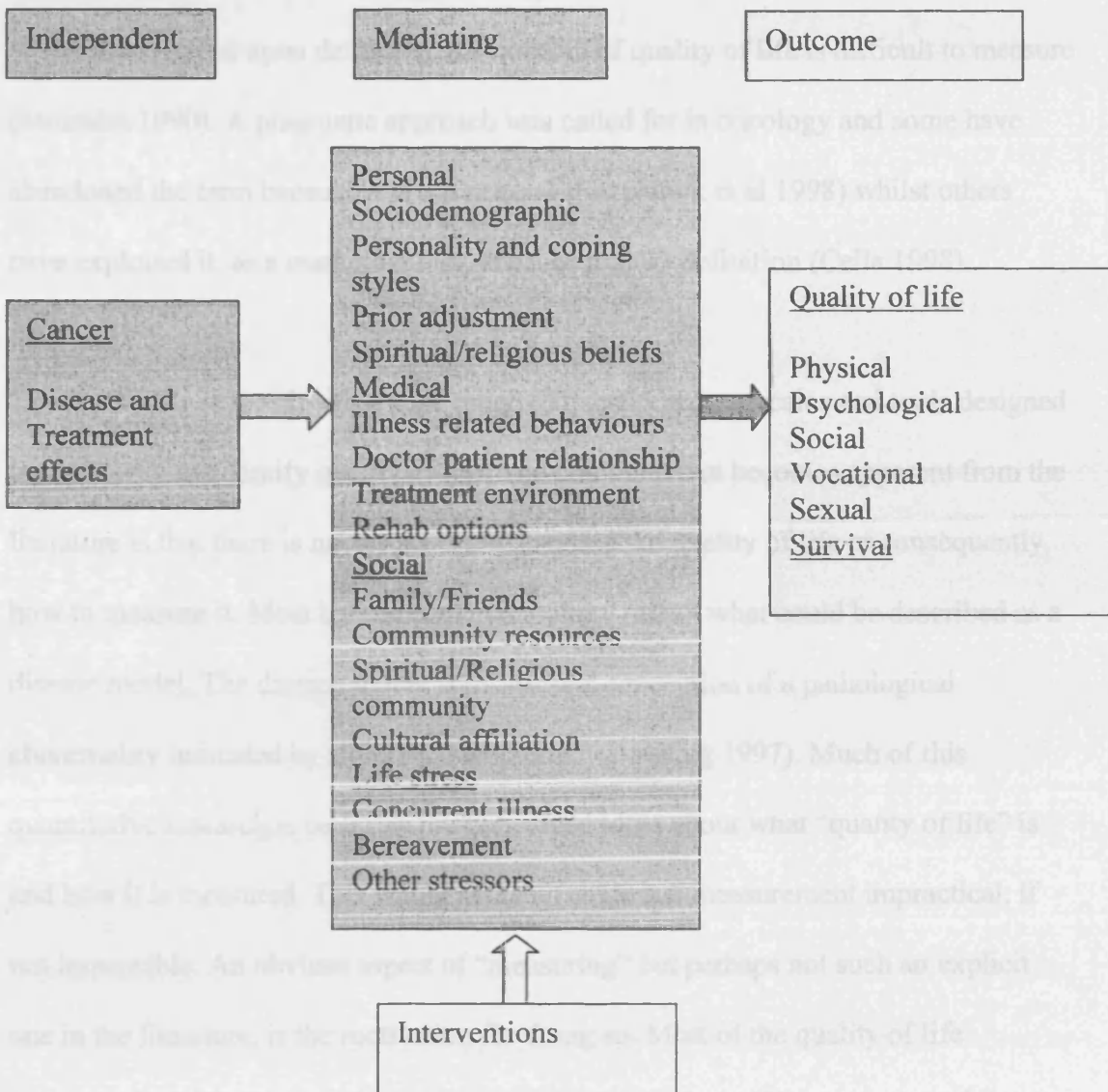
A study on the lay belief of illness was conducted by Herzlich in the late twentieth century (Herzlich 1973). Herzlich found that the people she interviewed perceived illness as external, the result of a way of life. Health in contrast was perceived as internal to the individual. Three dimensions of health were identified. The absence of illness or “health in a vacuum”; an innate ability determined by constitution or temperament “a reserve of health” and a sense of equilibrium. The population that Herzlich interviewed consisted of eighty middle class French people but the results of her study have been confirmed.

A seminal study in the UK also illustrated these different dimensions of lay beliefs of what health is (Pill and Scott 1982). In the study by Blaxter and Paterson (Blaxter and Paterson 1982) some references were made to the absence of disease but for the majority of the mothers they interviewed from low social class backgrounds, defined health as functional, with many distinguishing between “normal” illness which could

be accommodated and “serious” illness such as heart disease or cancer, which required a major shift in coping strategy. Central to psycho-oncology research are quality of life issues and the integration of this research into patient care (Holland 1998), but the issue arises once again of the domination of psychosocial oncology by psychopathology (Mathiesen and Stam 1995, Schou and Hewison 1999). Lay belief in lung cancer causes is reflected in the UKLCC study (UKLCC 2005) that has been discussed but reflects the findings of earlier authors such as Blaxter and Patterson (1982)

One of the most prominent influences of psychosocial oncology on quality of life in the literature was the concept of coping, and there were many studies in the literature devoted to the idea of cancer patients coping (Sommerfield and Curbow 1992). Many of the self report quality of life tools that featured “coping” assumed that there is coping to be done. This is because quality of life assessment research in oncology has been orientated to assessing coping with interventions. The model shown in Fig 2.4 illustrates this (Holland 1998).

Fig 2.4 A model of research in psycho-oncology (Holland 1998)



Current quality of life assessment in cancer is still rooted in the need to assess interventions. This is reflected in the cancer literature on quality of life, the majority of which is based on chemotherapy/radiotherapy trials (Anderson et al 2001, Crino et al 1999, Geddes et al 1990). This is also a typically nomothetic style of the functionalist perspective. Bowling (1997) argued that quality of life is assessed from a nomothetic perspective and this approach was very apparent from the literature.

2.3.2 Influences on measuring quality of life in people with cancer

Can quality of life be measured? How can one measure that which cannot be defined?

Without an agreed upon definition, the concept of quality of life is difficult to measure (Molzahn 1990). A pragmatic approach was called for in oncology and some have abandoned the term because it is too general (Fitzpatrick et al 1998) whilst others have exploited it, as a marketing tool, because it lacks definition (Cella 1998).

The researcher is faced with a huge range of questionnaires, scales and tools designed in some way to quantify quality of life. The one thing that becomes apparent from the literature is that there is no agreed “gold standard” of quality of life or consequently, how to measure it. Most instruments in oncology reflect what could be described as a *disease model*. The disease model is a “medical conception of a pathological abnormality indicated by signs and symptoms” (Bowling 1997). Much of this quantitative research is based on pre-conceived ideas about what “quality of life” is and how it is measured. This would make an empirical measurement impractical, if not impossible. An obvious aspect of “measuring” but perhaps not such an explicit one in the literature, is the motivation for doing so. Most of the quality of life literature found in non-small cell lung cancer is in the form of assessments originating from clinical trials (Stephens and Hopwood 2000).

Some leading cancer nurses argue that quality of life measures “miss the point” (Corner 1997) as this type of assessment is too reductionist and has little to contribute to cancer nursing as therapy.

There seems to exist a dualism in the quality of life literature between a philosophical-theoretical approach, and the literature, which could provide guidelines for methods for “real life clinical situations” (Hayry 1991). Hayry suggests three different motives for choosing methods (Hayry 1991):

- Respect for the sanctity of life
- Respect for scientific efficiency
- Respect for human autonomy

This is rather confusing, particularly the first point, and would be difficult for clinicians to accept. This is because the inference given by the term sanctity of life is one of *prolonging* life. Taking advanced non small cell lung cancer as an example, which is a severely life limiting disease (Neal and Hoskin 1994, Souhami and Tobias 2005) it is possible to prolong life in terms of quantity but at the cost of quality, this could also apply to many palliative situations.

There was implicit and explicit opinion in the literature over the validity of attempting to measure quality of life (Carr 1991, Fitzpatrick et al 1998). This is not an allusion to Wulff (Wulff 1999), some of the doubt has arisen due to methodological issues of measuring the unmeasurable. This applies in oncology quality of life. An example of which is the view that instruments based on the WHO definition (WHO 1993) are fundamentally flawed. Authors such as Koller and Lorentz (2002) have cast doubt on the WHO definition of quality of life and put forward a three-component outcome model. Using the usual outcome measures to assess HRQoL in terms of disease and symptomatology, only half of the picture is presented. The other half is composed of hermeneutic constructs and it is only when the two are combined that agreement on a

successful outcome or endpoint can be reached (Koller and Lorentz 2002). This does concur with the growing opinion in the literature that quality of life, or satisfaction, can only be accurately assessed by the individual (Carr 2001, Cohen 1996).

Cella (1998) examined cancer specific quality of life/HRQoL instruments concluding that collectively thirty different domains or dimensions could be identified. Cella then went on to rationalise these and suggests seven distinct dimensions of quality of life in the instruments he reviewed. These were: (Cella 1998)

- Physical concerns (symptoms and pain)
- Functional ability (activity)
- Family well-being
- Emotional well-being
- Treatment satisfaction (including financial concerns)
- Sexuality/intimacy (including body image)
- Social functioning

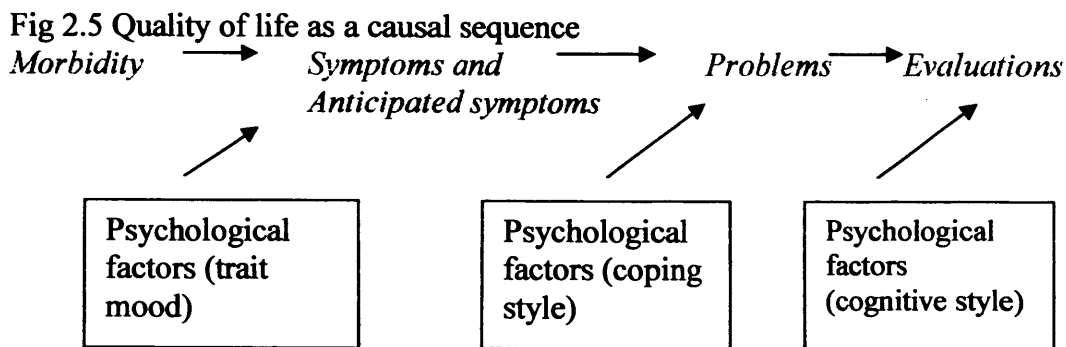
Cella's review is thorough and useful in examining and rationalising the body of work that exists, however it does cover an enormous range and amount of quality of life work and to some degree over rationalises this work. Like many other similar works, it also fails to encompass one of the fundamental difficulties of quality of life research, that the reductionist and deterministic approach of medicine is most clearly expressed in symptom management (Benner and Wrubel 1989). It is still a useful piece when considering the selection of a tool however.

In people with cancer the value of the medical interventions offered has often been gauged in terms of quantity of life (Clegg et al 2001, Corner 1997). More recently, as can be seen from the following section, there has been a move towards evaluating interventions in terms of quality also. There have been a number of studies that have assessed quality of life in people with cancer. Much of the published work was however in the form of a secondary endpoint to a randomised clinical trial, usually using chemotherapy treatments (Clegg et al 2001, NICE 2005).

In a number of cancers, particularly breast cancer, there have been more studies with quality of life as a primary endpoint. The application of these data to NSCLC has been limited due to the much wider variation in prognosis and symptoms as well as the social context of the tumour site. As has been seen, people with breast cancer have been viewed by society as “victims” whereas people with NSCLC have been perceived as being in some way to blame for their disease (Cancer Research Campaign 2001, UKLCC 2005).

Much of the quality of life data that exists in the cancer literature originates from clinical trials, this has been particularly apparent in non-small cell lung cancer studies but the fact applies to cancer studies generally. Quality of life is usually a secondary outcome measure (Clegg et al 2001). It is common for quality of life data in studies to be presented separately from mortality and morbidity data. Although many quality of life tools examine symptoms by self-scoring, the data is rarely correlated with, for example, toxicity scores or other objective data (Clegg et al 2001). Quality of life scoring has reported the subjective experience of those symptoms. It has been seen that factors such as mood and anxiety influence scoring in quality of life in cancer

patients (Jones et al 1989) and so it would seem a logical step to try to correlate subjective and objective data in some way. An interpretation of this linking is given by Michael Hyland in that quality of life is a causal sequence (Hyland 1999). This is shown graphically in Fig 2.5



The first stage of this causal sequence morbidity causes symptoms and what is reported is the subjective experience of these symptoms. People with anxious or depressed mood may report more or intense symptoms (Hyland 1999). The second stage is for symptoms (or anticipated symptoms) to cause problems, however the symptoms may not cause problems or they may be minor ones. This is again dependent on psychological factors and coping strategies. The final stage is for patients to evaluate. This is an important stage and one that is not commonly considered in quality of life as Hyland states (Hyland 1999) and anecdotally many people with cancer re-evaluate what quality of life means to them and this is a complex relationship, those with problems are not necessarily unhappy or experiencing what they would consider lower quality of life.

In conclusion, it has been shown that although a substantial amount of work exists, it does so with the aim of measuring HRQoL in clinical trials (Clegg 2001). However

assessment of quality of life can lead to a substantial level of intervention in the context of cancer care, particularly from a nursing perspective (Ryan 1996) and become an outcome measure, subsequently improving care (Lindley and Hirsch 1994).

2.3.3 Measuring Health related Quality of Life in patients with cancer

A number of tools have been introduced over the last fifty years with the aim of quantifying or assessing HRQoL. To have reviewed all of these tools would have been an enormous task, and beyond the remit of this work.

The instruments reviewed here were those used primarily for assessing HRQoL in patients with cancer and were disease based. HRQoL became a factor in cancer management with the growing realisation that cancer therapies aimed at cure are often accompanied by side effects (McMillan 2000). It can be seen from the brief introduction above, that to even attempt to measure quality of life or HRQoL, any tool must have certain attributes. It has been shown that instruments need to be *multidimensional*, (Bowling 1997) and need to measure all aspects of life that may be affected by a life limiting illness. Such instruments must also be *sensitive* to the area in which they are used and the client group (Patrick and Deyo 1989). They must also provide allowance for the collection of *subjective data* from the patient (McMillan 2000). It was stated earlier that instruments need to be *valid and reliable* (Schipper et al. 1984) although this seems axiomatic, it does infer that quality of life is a constant.

The measures presented in this section are not exhaustive but represented the majority of studies from HRQoL literature for cancer. These measures were also represented in

the HRQoL literature for the NSCLC studies, particularly clinical trials. This also included work, which used the palliative based scales (McMillan 1994). These papers have a focus on a hospice setting and patients receiving palliative care. The most commonly used measurement tools in cancer in the literature of the last thirty years are represented in Table 2.1. The palliative care setting was one of the first arenas in which quality of life was investigated in cancer care. A study of sixty people by Hinton (Hinton 1975) in the end stages of cancer examined issues such as “a sense of satisfaction with life” and concluded that greater satisfaction with life indicated that “dying was less troublesome”. The issue of the quality of time left to live having more importance than the quantity, is in direct opposition to Hayry’s “sanctity of life” motivation of quality of life (Hayry 1991).

Quality of time verses quantity of time is a concept entrenched in palliative care literature and education (Tywcross 1997, Faull and Woof 2002) but the idea of maximising “quality of life” in education and clinical practice is virtually never defined or measured and yet many editorials and papers argue the importance of doing so (Tywcross 1987, Cella 1992, Ahmedzai 1993).

Table 2.1 Quality of Life Outcome Measures for Cancer Populations

(After McMillan 2000, Bowling 1997)

Tool	Year of Publication	Dimensions assessed	Self reported?	Style/length	Validity/reliability data? (tested)	Limitations
Karnofsky Performance Index Quality of life index	Karnosky et al 1948	Physical/subjective functioning	No	Linear score	Yes	Not self reported, not specific QoL
	Spitzer et al 1981	Outlook, support networks, Activity, health	No	Interview Structured questionnaire	Yes but questioned in later years (Slevin 1988)	Some confusion over dimensions
Hospice QoL Index Functional Living Index (Cancer) Quality Of Life Index (cancer) Functional Assessment of Cancer Therapy-General (FACT-G) Quality of Life Questionnaire-cancer EORTC QLQ 30.	McMillan 1996	Physical/Functional social/spiritual, Financial	Yes	25 rated items	Yes	Content validity limited to hospice setting
	Schipper et al 1984	Physical, psychological, family/social, somatic sensation	Yes	22 Likert items	Yes	Difficult to complete, subts over construct validity
	Padilla et al 1983 Ferrans et al 1990	Symptom control, physical/psychological wellbeing	Yes	14 VAS items	Yes Has not undergone extensive testing	Little used.
	Cella et al 1993	Physical/functional social/emotional relationship with doctor	Yes	23 Likert Items	Yes	Functionally based
	Aaronson et al 1993	Symptoms, Function (physical/emotional/social) Financial	Yes	30 items additional modules available	Yes	Function and HRQoL biased

An argument often given for not assessing quality of life in people who are receiving palliative care is that they are too vulnerable (Waldron and O'Boyle 1999) but this is an assumption that has not been tested, it also makes huge assumptions about a specific population. It is possible that because of this perceived vulnerability that measurement scales were developed.

The first of these measurement scales for use in the cancer population was the Karnofsky Performance Index. It is still in use today although the use of this measure has varied somewhat to become a measure of performance and as a proxy for functioning (Montezari et al 1998). One of the first health professionals to assess health related functioning in medicine, and the effect of one of the first palliative chemotherapeutic agents for lung cancer, was Karnofsky in the late 1940's (Karnofsky et al. 1948). Karnofsky's aims were to palliate symptoms from tumours and in particular "bronchogenic carcinomas". With no means to measure symptom relief, Karnofsky and colleagues developed a system of objective and subjective improvement in the patient group. The subjective part of the assessment was a "subjective improvement" of "good, fair or none".

It is difficult to ascertain from the original paper who measured or assessed the subjective aspect (doctor or patient) but over time the assessment has evolved into the Karnofsky Performance Index (KPI) which is usually an assessment by a practitioner. This is the most often criticised aspect of the KPI alongside its crudeness and focus on physical functioning (Bowling 1997). However it should be taken in historical context. Karnofsky's group did not define or even use the term quality of life in the 1948 paper, however it is used as a proxy for quality of life in the present day

(Montezari et al 1998). This has been seen in the literature where the KPI has been used alongside other, more recently developed, tools such as the EORTC QLQ-30 (Anderson et al. 2001, Burris et al. 1997). The limitations of the KPI centre on the fact that this is a practitioner, rather than self reported, measure.

The *Functional Living Index-Cancer (FLIC)* was developed in the 1980's predominantly for use in clinical trials (Schipper et al 1984). It was a 22 item Likert style format on a scale of 1 to 7. It is a self-report measure and, from the literature, it was used predominantly in the 1980's and early 1990's. Validity was confirmed by comparative studies with other instruments (Schipper et al 1984, Finkelstein et al 1988) however reliability was not assessed by the authors (Schipper et al 1984) and some authors state that the literature does not provide evidence of reliability studies of FLIC (McMillan 2001), and has been criticised for the method of scoring which may make the scale too crude to use clinically (Aaronson et al 1988) however there was limited evidence of reliability (Morrow 1992)

The *Quality of Life Index (QLI)* was developed by Padilla and co-workers (Padilla et al 1983) as a self-report instrument designed to measure quality of life in cancer populations. It consisted of a 14 items that are rated using a visual analogue scale. The domains examined were symptom control, physical well-being and psychological well-being. The advantage of the Quality of Life index was ease of completion and simplicity (McMillan 2001). The validity of the QLI was examined in four groups of subjects (healthy volunteers n=43, outpatients receiving chemotherapy n=43, outpatients receiving radiotherapy n=39 and inpatients receiving chemotherapy n=48) and significant differences found between the groups, with the non-patient group

scoring highest which the investigators claim supports construct validity (Padilla et al 1983) but the details of the group (eg age, demographics and physical function) are not given. Subsequent studies confirmed reliability (Ryan 1985).

Quality of life index (Cancer Version) QLI-CV This instrument was developed from the QLI by Ferrans and Powers (1985) who suggested that individuals values may have a variable impact on quality of life. This approach led to individuals weighting satisfaction items with importance. The QLI-CV is a thirty-five item instrument which aims to assess global quality of life (Ferrans et al 1990). The QLI-CV used domains such as health and functioning, socio-economic, psychological/spiritual and family. This instrument has been validated against the QLI and in general oncology use (Ferrans 1990).

Functional Assessment of Cancer Therapy-General (FACT-G) is a self-report instrument that was designed to measure HRquality of life in cancer patients receiving therapy (Cella et al 1993). This 28 item instrument can also be augmented with site, disease or treatment specific adjuncts. The FACT series of instruments have been subject to validation and reliability studies (Cella et al 1993, McMillan 2001) and are in current usage.

European Organisation for the Treatment of Cancer Quality of life Questionnaire (EORTC QLQ Version 3) This instrument has become one of the most apparent in the cancer literature. It was developed by the EORTC primarily for use in clinical trials (Aaronson et al 1993, EORTC 2005). The EORTC QLQ addressed the domains of function, symptom control, financial, global health and global quality of life. It has

been validated in 13 countries and translated into different languages (McMillan 2001). The QLQ also has disease specific modules such as the QLQ 30+L17 (Lung cancer module) and this is explored in more depth in Chapter 3.

2.4 Quality of life related to Non Small Cell Lung Cancer

Lung cancer is an area where quality of life assessment has had an impact. As was seen earlier, many patients with lung cancer present in the advanced stages of the disease and there is little benefit from most treatments in terms of quantity of life and so advanced lung cancer is seen as disease that is treated in a palliative setting.

Despite the work of Karnofsky in the 1940's (Karnofsky 1948), until recently very little was written about the Quality of Life of people with lung cancer of any type. In Splinter's 1990 review of 142 clinical trials in NSCLC, only 10 had any form of quality of life measurement apart from a physician assessed recording of performance status (Splinter 1990). Splinter's work has dated, generally the proliferation of quality of life assessment has been as a secondary endpoint to survival in chemotherapy drug trials.

From the mid 1990's papers began to appear which reviewed and supported the idea that quality of life should be an endpoint in such studies (Kosmidis 1996, Hopwood and Thatcher 1990, Gralla 1994). These studies often employed a medical and pathological perspective. It has been noted by authors (Stegbauer 1994, Cooley 1998) that there is a notable lack of theoretical quality of life work in the lung cancer patient population. The recent work in quality of life is driven by the cancer modernisation agenda, but still centres on clinical trials and HRQoL (NICE 2005).

2.4.1 Non small cell lung cancer-Health related quality of life (HRQoL) concept clarification.

This section serves as an exploration of the definition of terms for the rest of the work. The aim is to gain insight into areas such as the philosophical construction of the concept of quality of life in advanced NSCLC, particularly in the clinical context.

Many disciplines, such as philosophy, have placed value in concept development but as Rodgers and Knafl (1993) pointed out that as clinicians we “tend to know much more about how to tackle empirical concerns than we do about means to solve conceptual barriers to progress” (Rodgers and Knafl 1993). Certainly it would seem that to investigate not only the empirical but also to go some way to resolving conceptual problems would add something to the understanding of the individual practitioner and the profession as a whole. This section introduces conceptual clarity by the use of concept development and analysis.

Concept analysis and development is a challenge to define. In the context of nursing, concept analysis entails synthesizing existing views of a concept and distinguishing such views from other concepts (Knafl and Deatrck in Rodgers and Knafl 1993).

Concept clarification was the main focus of the various methods of achieving this.

Concept analysis has gained popularity as a basis for much of the underpinning knowledge of clinical practice. This is perhaps much more so in nursing practice as much of the published work on the use and value of concept analysis has been from a nursing perspective. This could be due to the paradigm shift that has occurred in

nursing in the last twenty years or so that has moved the fulcrum of nursing as an activity from ritual to evidence based practice for example the work of Binnie and Titchen (1999).

There was very little literature available on the conceptual analysis of quality of life in NSCLC. A search of the literature revealed only one explicit concept analysis of quality of life in NSCLC (Cooley 1998) and once a concept has been defined in such a way perhaps the question is “Is another concept analysis necessary?” It may not be necessary to re-define the concept but it could be argued that such a concept is not static. Most things change over time. This analysis was well researched and insightful and it is unlikely that a new concept analysis would have contributed much to the body of knowledge. However there was a strong argument for a critique and expansion of Cooley’s work, which is focused very much on the population of North America and appeared culture specific (for example, references to a system of healthcare that has significant differences from those in the UK). Cooley had to limit the amount of literature reviewed and analysed, reviewing fifty papers, published in English that used patient self-reports of quality of life. Phase one and two trials were excluded as they were deemed to have “limited applicability to persons with NSCLC” but no rationale for doing this is given. The strength of Cooley’s work was the focus on individuals with NSCLC.

Since the late 1980’s and the work of those such as McCorkle et al (1989) the evolution of definition’s of quality of life in NSCLC became much more apparent. Upon reviewing the literature, a definite shift can be found to a more global approach and a broadening of health related quality of life. From the mid 1980’s (for example

Bakker et al 1986) the focus of investigation shifted from functioning and physical symptoms to a more global approach. This is also reflected in the tools reviewed previously.

From the literature there has been an emerging consensus that there are at least four major dimensions of quality of life in NSCLC that relate to health including functional status, physical symptoms, emotional function and social function.

Functional status was defined by normal day to day living activities, and then further subdivisions of this with respect to performing the everyday activities of daily living such as bathing and dressing, and role responsibilities such shopping and working.

Physical symptoms are the physical symptoms of the disease or treatment that is referred to. *Emotional function* refers to the affect, which included positive and negative, for example depression and anxiety (Cella 1989). *Social function* Schipper et al (1990) referred to the maintenance of relationships with family and friends. Some authors maintain that this dimension has been under-used (Schipper et al 1990).

As a result of this work a definition of quality of life in non-small cell lung cancer has been proposed:

“Quality of life in the context of NSCLC is the impact of the disease and/or treatment on the functional status, physical symptoms, affective state and interpersonal relationships as evaluated by the person with cancer.”

(Cooley 1998)

Cooley argued that an obvious antecedent for self perceived quality of life is that an individual must have the ability “to make a cognitive appraisal of his or her life”

although she offered no evidence, this seems somewhat axiomatic and was rare to see such an explicit expression in the literature.

From the literature other antecedents became apparent:

- Antecedents for *functional status*: Chemotherapy, co morbidity, income, kilocalorie status, prior weight loss, time since surgery. (Bakker et al 1986, Sarna et al 1993)
- Antecedents for *physical symptoms*: Chemotherapy, co morbidity, gender, income, no surgical treatment, age, stage of disease, smoking. (Bakker et al 1986, Sarna 1993a)
- Antecedents for *emotional function*: age, spousal support, and time since diagnosis. (Sarna 1993b, Quinn et al 1986)
- Antecedents for *social function*: age, marital status. (Sarna 1993b)

This was clarified somewhat by the explanation that Cooley viewed health related quality of life as an antecedent to global quality of life (Fig 2.6) and also introduced the importance of physical health as perceived by many to be on of the most important self-disclosed factors in a cognitive appraisal of quality of life or predictor of life satisfaction (Girzadis et al 1993).

Fig 2.6 Relationships between physical health, health related quality of life and global quality of life. (Cooley 1998)

Physical Health* ⇒ *Cognitive Appraisal* ⇒ *Health Related Quality of Life* ⇒ *Global Quality of Life

This paper is difficult to critique. It is well researched examining sixty-five papers, and is the first of its kind. There is no real comparison to be made with other works as

there is little written on the subject from this perspective. Cooley recognises this, particularly the lack of work on the emotional and social function.

The clear message from all the definitions reviewed in the literature demonstrated that there is still much ambiguity. However a useable definition of quality of life in NSCLC is at hand in the work of Cooley (1998). There was a virtual non-existence of any spiritual or existential dimension to the concept by the papers reviewed. Zebrack (2000) noted that this dimension was important to patients and certainly anecdotal experience would tell us this also. Spiritual care is also a mark of holistic practice (Barkauskas et al 2002). It is hard to see how spirituality could not influence the perception of global quality of life as “spiritual well-being can have a positive impact on the individual’s ability to cope with the physical manifestations of the disease process” (Walsh, Crombie and Reveley 1999).

2.5 Quality of life in Non Small Cell Lung Cancer: Instruments in the literature

Since the 1970's it has been common practice to use performance status as a prognostic indicator in lung cancer practice (Montezari et al. 1998). This arose from Carlens' Vitagram (Carlens et al. 1970) used to plot survival against performance status. Studies over the next twenty years appeared to confirm this proxy relationship (Montezari et al 1998), demonstrating that performance status is a good predictor of quality of life, or rather an indicator of psychological, physical or symptom distress (Montezari et al. 1998). Although using performance status as a proxy for quality of life has been controversial, studies have shown correlation between performance status and global quality of life in some populations of lung cancer patients (Osoba et al. 1994). In practice performance status continues to be used as a proxy for more thorough quality of life assessment (Montezari et al. 1998, Tishelman et al 2000) and some authors caution against its continued use as a proxy for quality of life, having made direct comparisons in patient groups (Koller et al. 2000).

In the literature many instruments are used to assess quality of life outcomes in cancer patients (Table 2.1) and this statement applies equally to lung cancer. From 1990 onwards however the assessment of quality of life has utilised a core of instruments that are examined in more detail here and illustrated in Table 2.2. The development of the majority of the instruments that are cancer and cancer site specific have been developed as a result of increased activity in clinical trials. Hopwood (1998) offers practical points to consider in this context that would serve as a guide to any

researcher choosing an instrument specifically for quality of life assessment in NSCLC and this has been shown in Table 2.3 (Hopwood 1998).

Table 2.2 Quality of life in NSCLC: Common outcome measures shown in context as used in the reviewed literature.

Tool	Purpose	Year of publication	Dimensions assessed	Self reported?	Style/length	Validity/reliability data/tested	Limitations
KPS	Performance status	Karnofsky 1948	Physical functioning	No	Rating	Yes	Not multidimensional
ECOG	Performance status	Zubrod 1960	Physical functioning	No	Rating	Yes	Not multidimensional
Sickness impact profile	Generic	Bergner et al 1981				Yes	Length
DDC	Continuous Drug Trials	Geddes et al.1990	Overall function and symptoms	Yes	Daily completion of self rated items	Yes	Limited domain measurement
RSCL	Generic/symptoms		Symptoms	Yes	Questionnaire	Yes	
LCSS	Lung cancer specific			Yes + observer	Questionnaire	Yes	
FACT-L	Lung cancer specific		Multidimensional physical wellbeing, relationship with carers	Yes	44 item questionnaire	Yes	Aimed at assessing lung cancer symptoms, not treatment effects
EORTC QLQ 30+LC17	QLQ-30 plus lung cancer specific module	Bergman et al. 1994	Global/physical/social and symptoms domains	Yes	Questionnaire 30 + 17	Yes	Functional HRQoL

Table 2.3 Issues and practical consideration on collecting QoL data in NSCLC trials.

	Theoretical Perspective	Practical consideration
Patient sample size	Large numbers of patients with NSCLC	Minority of patients with NSCLC treated in trials
QL Outcomes	Well defined domains, well constructed instruments available	Clinicians reluctant to change traditional endpoint from survival
QL study design	Straightforward in theory, guidelines exist	Instrument selection, timing, sample size more difficult in clinical practice
Measuring palliation	Symptoms can be quantified by QoL measures and analysed	Definition of palliation not agreed
QL data collection	Assumes patients attend per protocol	Compliance problematic in palliative centres
Clinical value of QL end points	QL can be summarised numerically to show differences in treatment options	Treatment options not always clear cut. Scores have limited value when discussing treatment options with patients

In the literature many different tools were utilised to assess quality of life in lung cancer. These ranged from generic performance status instruments (e.g. WHO Performance status) to cancer site-specific tools. There were three instruments in common usage in the context of thoracic oncology and they are examined here and examples of instruments of performance status are given in Appendix E.

Lung Cancer Symptom Scale (LCSS). This instrument was developed in the 1980's at the Memorial Sloan-Kettering Cancer Center in the USA. It was based on an empirical conceptual model insofar as the LCSS attempts to depict to the quality of life dimensions or domains associated with the symptoms and, subsequently, the treatment and palliation of lung cancer (Hollen et al. 1994). Essentially the LCSS examined the physical and functional aspects of quality of life, focussing on the major lung cancer symptoms and the effect of the symptoms on function and performance

status. It is somewhat unusual as it was made up of two reporting components, one for patients to self-report and one for professionals as assessors of the patient. The administration of this tool made it easy to use. The development team found that the patient scale took eight minutes to complete and the professional assessment two minutes on average (Hollen et al. 1993). The LCSS has been used in a number of chemotherapy trials, and in common with many other quality of life instruments, this was the motivation for its development. This tool has been used and validated in a trial setting (Hollen et al 1993, Hollen et al. 1997, Lutz et al. 1997) and across age, gender and culture (Hollen et al 1999) but it is the least used of the three selected tools based on this review. There were no negative critiques of this tool, it seems merely to have been superseded by other instruments. Although there are no negative critiques of the LCSS found in the literature, the LCSS does focus very much on the physical and functional domains. It is not multidimensional. The development team cited its use as an assessment tool in therapeutic studies as the reason for its limited domains, such as the exclusion of spiritual/social/psychological aspects (Hollen et al. 1994) but perhaps this is the reason for the LCSS decreasing popularity with researchers.

The Functional Assessment of Cancer Therapy-Lung version 3 (FACT-L v3) is a self-reported 44 item questionnaire which is divided into two parts. The first part is a 34 item general/oncology based HRQoL and the second part, consisting of 10 items, is lung cancer specific. The focus of the items in part two is a measure of lung cancer related symptoms rather than HRQoL or QoL. The principal use of the FACT-L, in common with many other instruments, was in clinical trials. Both the LCSS and FACT-L have been validated and are considered reliable tools (Hollen et al.1993, Cella et al. 1995, Hollen and Gralla 1996), however fast becoming the most popular

instrument in the literature is the European Organisation for the Treatment of Cancer (EORTC) Quality of life questionnaire (QLQ).

The EORTC QLQ instrument evolved as a result of a desire by the EORTC to evaluate interventions in cancer therapies. A study group on Quality of Life was initiated by the EORTC in 1980 to develop a brief and practical quality of life measure (Aaronson 1991). The group developed the original 42-item questionnaire that used self-report. This was reduced to 36 items in the early 1990's (Aaronson 1991). The current thirty item (EORTC QLQ Version 3) is a multidimensional questionnaire encompassing five functional domains: physical, role, cognitive, emotional and social. Three symptom domains: nausea & vomiting, pain and fatigue, and single items such as a self rating VAS of own quality of life. Patients rate each item using the terms "not at all" "a little" "quite a bit" and "very much". It also includes a self rated global VAS (Aaronson et al. 1993). In recent years a 13 item lung cancer site specific module has been added (Aaronson et al. 1993, Bergman et al. 1994).

The EORTC QLQ-30+LC 17 was developed during the 1990's primarily as a tool for assessing quality of life in lung cancer patients entered into clinical trials. Aside from the recommendations of the FDA, a growing realisation by researchers of the palliative nature of lung cancer treatment has contributed to the increased use of quality of life instruments in trials and particularly the QLQ 30+LC 17 (Krzaowski et al. 2002). The reason for the increased use of the QLQ 30+LC17 could be the multidimensional nature of the instrument. The tumour specific module includes not only lung cancer symptom items (haemoptysis, dyspnoea, cough) but also items based

on effect of treatment for lung cancer (trouble swallowing, hair loss, pain, parasthesia) which researchers have found useful in the evaluation of interventions (Montezari 1998).

Some authors questioned the validity of the QLQ 30+LC17, and the other site specific modules as being hybrid instruments (Cella et al. 2002) and yet these instruments continue to be adopted by large research groups, increasingly as the only quality of life outcome measure in clinical trials. This instrument has undergone extensive testing including in its original form and has been adapted into many different languages (Aaronson 1991, EORTC 2005) which makes it attractive to researchers. The EORTC QLQ 30+LC17 is included in Appendix A. The EORTC QLQ in various forms has also been tested across age, gender and disease (Cella et al 2002). The EORTC QLQ was also designed with clinical trials in mind. As trials are becoming more collaborative and taking on an international approach, the tested cross-cultural validity of EORTC QLQ means it is very appealing to research groups.

2.6 Quality of life in the context of treatment (chemotherapy) for advanced Non Small Cell Lung Cancer.

The following section is a review of the literature found which focused on the use of gemcitabine in trials in which quality of life is an endpoint, usually a secondary endpoint, to survival. Many of the following studies reviewed take the same approach, the comparison of two treatment modalities within a randomised controlled trial.

Although the quality of life is a secondary endpoint in these trials and so is investigated to varying degrees, the absence of more descriptive data means that these studies are the major source of work available. The aim here was to review and critique the work that has been done.

The WHO definition of health (WHO 1947, WHO 1993) has been used to develop quality of life studies in cancer. In 1985 the Food and Drug Administration (USA) encouraged Quality of life to be an outcome measure in oncology clinical trials. This is a very salient point in that this work uses a clinical trial as a vehicle, and reflects the way that attitudes have changed in the UK with collaborative and commercial studies now also encouraging the use of quality of life as an outcome measure (for example the Medical Research Council 2000). This is supported by the fact that there was little dedicated literature prior to the mid 1980's.

The impact of the FDA recommendations of the late 1980's was apparent in the literature. Some form of quality of life measurement was included in most of the chemotherapy based clinical trials. It should also be considered that many of the

published trials receive sponsorship or financial support from pharmaceutical companies although this is usually declared.

The meta-analysis performed on behalf of the Non Small Cell Lung Cancer Collaborative Group (NSCLCCG) concluded that pessimism in the treatment of NSCLC has turned to cautious optimism. This 1995 paper in the BMJ (NSCLCCG 1995) was then updated as a Cochrane review in 2000. This review demonstrated the problem well as it showed that chemotherapeutic agents used in NSCLC have changed considerably since the 1980's, from alkylating agents to platinum based therapies such as carboplatin.

The most difficult problem with chemotherapeutic agents is non-specificity. Most chemotherapeutic agents affect healthy tissue causing toxicity. Over the last eight years the introduction of the four "new generation" drugs may shift this outlook further. The new generation drugs, of which gemcitabine is one, use a novel approach. Gemcitabine is a pyrimidine antimetabolite rather than a true alkylating agent, and has a broad spectrum of anti tumour activity (Drabitsaris et al 2002). Theoretically this means that such compounds should be more tumour specific, have less side effects and more reversible toxicity. This has been further demonstrated by the UK Gemcitabine study that showed that although only 20% of patients had a response in tumour volume, it also showed 50% had improvement in symptoms (Anderson et al 2000).

Based on the available evidence of the late 1980's and 1990's (up until 1998), the Clinical Oncology Information Network (COIN) published guidelines. These

guidelines concluded that it was appropriate to offer chemotherapy to selected patients, usually in the context of clinical trials. The general consensus of most clinicians of the time can be summed up by the quote from the guidelines “strong evidence of only a modest effect on survival, with no clear evidence of benefit in terms of quality of life” (Macbeth 2000).

Subsequent authors commented on the “nihilism surrounding lung cancer in the United Kingdom” that such reports engender (O’Brien & Cullen 2000). In 1998 the so-called new generation drugs had not yet entered common usage in the UK, they were starting to be used in clinical trials and so it could be argued that previous work supporting the nihilistic approach is even less valid.

In terms of patient preference, the Health Technology Assessment (Clegg et al 2001) of new generation drugs acknowledged that there was very little in the literature on which to anchor patient perception and attitudes to chemotherapy (Clegg et al 2001). This has resulted in seeking patient’s views from a patient support group, The Roy Castle Foundation. The Roy Castle Foundation operates a telephone support and information service, which receives approximately 100 calls per month. About 25-30% of these are from patients or carers seeking alternatives to best supportive care (Roy Castle Foundation personal communication with author 2003, 2006).

The opinions of those who contacted the helpline include the following:

- If there is a possibility that chemotherapy could be beneficial, either by extending life or by maintaining quality of life, patients feel they should have the option of receiving this therapy
- Patients are aware (from doctors, media, internet and others) that new drugs are available and may have activity against NSCLC and therefore offer hope in a condition in which outcomes are poor.
- Faced with an incurable disease, worsening symptoms and a short life expectancy, sufferers do not feel that cost should be a factor in deciding treatment options.
- Inequality in access to therapies, which are available in the private sector and in other countries, is seen as unjust.
- Patients often have the impression that their doctors believe that lung cancer has such a poor outlook that referral to a specialist oncology service is not worthwhile.

(Clegg et al 2001, Roy Castle Foundation personal communication with author 2003, 2006).

One of the new generation drugs, Gemcitabine, is examined as part of this study. It is usually used in combination with another drug either Carboplatin or Cisplatin. These drugs are usually given as an intravenous infusion every three weeks (one cycle) four to six times on an out-patient basis. This is described in more detail in Chapter 3. This review identified several randomised controlled trials (RCT's) which use gemcitabine in advanced non-small cell lung cancer but usually have survival and tumour response

as a primary endpoint and quality of life assessment as a secondary endpoint. As seen previously, at present people with advanced (non operable) NSCLC have an extremely poor prognosis. Why then is quality of life only a secondary endpoint to these studies? Most trials offer poor survival benefits if any.

A number of these RCT's are examined here but this is not a systematic review of the trials literature, excellent reviews have been performed both as Health Technology Assessments (Clegg et al 2001) and by the National Institute of Clinical Excellence (2005) from which guidance on the treatment of advanced NSCLC has been published. The trials included herein reflect the literature at the start of the study, prior to the qualitative arm taking place.

In 1992 a study was published that set the tone for the use of chemotherapy in NSCLC. The use of cytotoxic chemotherapy in NSCLC has always been controversial, but the review identified a number of agents, such as Cisplatin, in use that were having a small impact of survival. Response rates to single agents were found to be approximately 20% and the authors felt unable to recommend single agent chemotherapy for NSCLC (Ihde 1992). As the 1990's progressed more novel agents became available, such as Gemcitabine. In addition some clinicians were asking patients to become involved in combination chemotherapy (two or more cytotoxic agents). This change in culture has been slow, with many clinicians still reluctant to offer chemotherapy, often citing cost or side effects as the rationale.

A study by the Joint Lung Cancer Study Group (Sweden) used the QLQ-30+LC17 module as part of a RCT in advanced NSCLC examining best supportive care (BSC) Vs chemo (Carboplatin+Etoposide). Patients in the chemotherapy group reported better overall physical functioning and symptom control compared to the BSC group. Scoring in the psychosocial domains showed little difference. The chemotherapy group had a median survival of 29 weeks compared to the BSC group, which had a median survival of 11 weeks (one year survival 28% Vs 8%) (Helsing et al 1998).

The Joint Lung Cancer Study Group study was fairly typical in terms of methodology and findings. Such studies enrolled patients with advanced disease (Stage 3b or 4) who generally have a poor prognosis from a medical perspective. In a similar phase II study examining safety and efficacy of a cisplatin-gemcitabine combination chemotherapy, the authors found little survival benefit but high efficacy in the palliation of symptoms reflected by the scoring of HRQL via the QLQ 30+LC17 (Krzakowski et al 2002).

Despite the FDA recommendations and the inclusion of some form of quality of life assessment in most trials, quality of life continues to have less relevance than the focus on survival or time to progression. A large review which pulled together much of the chemotherapy trials in NSCLC gives only brief reference to quality of life (Haura 2001), despite the fact that by definition all chemotherapy for advanced NSCLC is palliative (Spiro et al 2004).

Some studies in the literature focused on quality of life and treatment decision-making. A recent study by Detmar et al (2002) examined the reasons for modifying or

stopping chemotherapy in patients with advanced cancers. This study examined physicians self reported reasons for changes or cessation of chemotherapy using changes in health-related quality of life (HRQoL). Physicians reported that HRQoL was a major factor in decision making, The authors used audiotape to record the physician/patient interaction and found that although the physicians perceived that they used HRQoL as a guide to treatment decision making, in practice this was not so. In this study 70% of patients with no tumour progression or serious toxicity but with seriously impaired HRQoL continued on the original treatment plan (Detmar et al 2002). This disparity between perception/quality of life assessment by medical staff and lived experience of patients undergoing palliative chemotherapy is not newly discovered (Hopwood and Thatcher 1990) however little has changed in practice despite this knowledge.

This study used as a vehicle a chemotherapy trial and seeks to examine in greater depth the quality of life aspect of the study. The vehicle for this study was a randomised controlled trial and compares two combination chemotherapy regimens. The two regimens are the standard Mitomycin, Ifosfomide and Cisplatin and the experimental arm of Gemcitabine and Carboplatin and a full explanation can be found in the Methods chapter. The primary endpoint was survival and secondary endpoints were tumour response and quality of life. This study was co-ordinated by the London Lung Cancer Group and funded by the Cancer Research Campaign (now Cancer Research UK). It has no commercial funding. In design it was comparable to many other studies which also use quality of life as a secondary endpoint however quality of life data was captured at more frequent intervals (daily) rather than periodically.

With such a small survival benefit for such chemotherapy regimens this study was expanded to gain more insight by focusing on quality of life from a more qualitative perspective. It should also be considered when examining the trials based quality of life data and results, that methods of collecting quality of life data in this way has already been called into question, particularly the variability of data quality (Stephenson and Hopwood 2000). The FDA recommendations and available evidence (Clegg et al 2001) now require investigators to collect some form of quality of life data and, as some authors view it, at the cost of rigour (Stephenson and Hopwood 2000) and some groups still choose not to collect HRQoL data (Georgoulas et al 2001). In addition, the use of the most appropriate quality of life tool is paramount (Gunnars et al 1997).

In contrast to this perspective, some authors argued that assessing quality of life in the context of a study is an intervention in its own right with a therapeutic benefit as it offers an interaction to the patient that would not otherwise occur (Bernhard et al 1995). This issue was reflected in a study that compared self reported quality of life, using the EORTC QLQ 30, to compare quality of life to disease course and medical records (Velikova et al 2001). This study demonstrated that physical domain health related quality of life issues are noted in medical records but functional domain issues were recorded in between 1% and 25% of the notes and more often (20% and 76%) on use of the QLQ-30 (Velikova et al 2001).

Many of the past RCTs comparing combination chemotherapy in advanced NSCLC, including some assessment of quality of life have been subjected to review and meta-analysis. A review that focused on the quality of life demonstrated the benefits of

chemotherapy in terms of quality of life and asserts that there is no longer a convincing argument for not offering chemotherapy to patients with advanced NSCLC (Klatersky & Paesmans 2001). It should be noted that these studies once again focused on health-related quality of life using instruments such as the EORTC QLQ30+LC17 rather than global quality of life and this restricted the value of the perspective offered.

Among the numerous chemotherapy RCT's where quality of life is a secondary endpoint were studies which examined the use of chemotherapy and the patients lived experience. These studies were few but as the emphasis towards global quality of life shifts, they may become more commonplace. Such studies were often based on a patients own or projected experience of chemotherapy. This took the form of offering patients a number of scenarios, for example, x weeks survival against y degrees of toxicity. Asking patients to project what they would find acceptable or unacceptable seems counter intuitive in terms of methodology but in fact is the reality of clinical practice.

The choice between accepting and rejecting chemotherapy for patients with advanced NSCLC is an exceptionally difficult one. In the study by Tamburini (Tamburini et al 2000) four groups were given three scenarios projecting survival and toxicity of receiving chemotherapy. The groups were made of patients with NSCLC (n=104), patients with benign respiratory disease (n=129), healthcare workers (n=140) and students (n=120).

The scenarios presented were optimistic neutral or pessimistic. Relative to the other groups the NSCLC patients showed a consistently higher degree of uncertainty about whether to accept or reject chemotherapy. The NSCLC group also had the lowest rate of acceptance of the optimistic and neutral scenarios and in contrast the highest rate of acceptance of the pessimistic scenario. The NSCLC group also had the highest percentage of constant answers, independent of the scenario presented, particularly the answer "I don't know" (Tamburini et al 2000). An earlier study (Silvestri 1998) stands out in the literature as it uses scripted interviews to determine to what extent patient's would "trade off" between survival and toxicity (n=81). In this study the authors found that patients varied in what they would be willing to accept in terms of toxicity (the usual outcome measure in HRQoL). Several patients would accept chemotherapy for a survival benefit of one week while others chose not to accept chemotherapy for a survival benefit of 24 months. The median survival threshold for accepting chemotherapy was 4.5 months for mild toxicity and 9 months for severe toxicity. Most patients would not choose chemotherapy for the survival benefit of three months but would if it improved quality of life, however the authors did not say how or if they determined what an acceptable quality of life would be (e.g. possible gains of survival were measured in units of time, but potential quality of life not assessed, benefits in treatment were measured as benefits in survival) (Silvestri et al 1998).

Although the work of Silvestri et al (1998) does have limitations, assessment of quality of life in this setting would allow clinicians and patients to effectively discuss the trade offs when considering various treatment options, particularly those which

are perceived to have little benefit in terms of survival such as chemotherapy (Hopwood 1996, Grilli et al. 1993, Silvestri et al. 1998).

As gemcitabine is a third generation drug, comparisons (usually as RCT's) with older regimens or best supportive care contributed heavily to the literature. As third generation drugs have only been in use for about seven years in the UK, including on a trial basis, this has limited the amount of literature, examples of which are given in Table 2.4.

Table 2.4 Specific RCTs using Gemcitabine in advanced (Stage IIIa inoperable, Stage IIIb and IV)

Author (Year) and study details	Outcome measures	Adverse events
Perng et al 1997 GEM Vs CIS+VP open RCT n=53 No support declared	Tumour response and survival Survival GEM 37 weeks CIS+VP 48 weeks No QoL data collected	CIS+VP arm, higher toxicity for Haematology, nausea and vomiting
Bokkel-Huninik et al 1999 GEM vs CIS+VP open RCT n=147 Supported by Eli Lilly & Co	Tumour response and survival Survival (median) GEM 6.6 months, CIS+VP 7.6 months QoL (QLQ-30+LC13) no significant change from baseline in either arm	Grade 3-4 toxicity recorded in both arms
Cardenal et al 1999 GEM+CIS Vs VP+CIS n=135 Supported by Eli Lilly & Co	Tumour response and survival Survival (median) GEM 8.7 months, VP 7.2 months QoL (QLQ 30+LC 13) both groups saw improvement in pain, cough, haemoptysis No improvement in dyspnoea in either arm	Grade 3-4 haematological toxicity, grade 4 neutropenia twice as high in VP arm
Crino et al 1999 GEM+CIS Vs MIC n=307 No support declared	Tumour response and survival Survival GEM+CIS 8.6 months MIC 9.6 months QoL (QLQ-30+LC13) worse alopecia in MIC arm less pain in GEM+CIS. Both arms record improvement in insomnia and cough. Not significant difference in arms	Haematological toxicity in both arms. Grade 3-4 nausea and vomiting in MIC Arm
Anderson et al 2000 GEM + BSC Vs BSC Open RCT n=300 Supported by Eli Lilly & Co	Tumour response and survival Survival (median) GEM + BSC = 5.7 months BSC alone 5.9 months QoL (QLQ-30+LC17) at 4mths >10% improvement in many domains for GEM group	Low 3-4 toxicity Nausea & vomiting Lethargy, myelosuppression Flu like symptoms in GEM arm

Continues overleaf

Author (Year) and study details	Outcome measures	Adverse events
Sandler et al 2000 GEM+CIS Vs CIS open RCT n=522 Supported by Eli Lilly & Co	Tumour response and survival Survival (median) GEM+CIS 9.1 months CIS 7.6 months QoL (FACT-L) Both arms noted decrease in HRQoL	Higher rate of haematological toxicity in GEM+CIS arm
Georgoulas 2001 Docetaxel+Gemcitabine Vs Docetaxel+Cisplatin n=406 Supported by Aventis	Tumour response and survival Survival (median) Docetaxel+CIS 10 months Docetaxel+GEM 9.5 months <i>No QoL assessment</i>	Increased toxicity associated with Docetaxel arm
Jassem et al 2002 Gem+Cis phase II n=80	Tumour response and survival (Complete response in 7%) Survival median 11 months QoL QLQ-30+LC17 improvements in many physical domains	Grade 3-4 haematological malignancy
Danson et al 2003 MIC Vs GEM CARBO N=372 supported Eli Lilly & Co	Tumour response and survival Survival (median) MIC/MVP 248 days GEM+CARBO 236 days QoL QLQ 30+LC 17/13 High attrition rate	Grade 3-4 Haematological toxicity Greater alopecia in MIC arm
Rudd et al (2005) MIC Vs GC N=422	Tumour response and survival Median survival MIC 7.6 months GEM+CARBO 10 months QoL QLQ 30+LC 17 as discussed herein	Grade 3-4 Haematological toxicity Greater alopecia in MIC arm

Table 2.4 Specific RCTs using Gemcitabine in advanced (Stage IIIa inoperable, Stage IIIb and IV) (continued)

The quality of life assessment is a secondary or tertiary endpoint and even omitted in some studies.

In recent randomised controlled trials from the last fifteen years quality of life has been recognised as being a factor, and in at least one trial, the primary endpoint. The study by Anderson (Anderson et al 2000) compared gemcitabine to best supportive care (BSC). This RCT used the EORTC QLQ-30+LC17 and also the SS14 symptom scale. The QLQ 30 was used at two and four months to test 25 variables (QLQ used at every cycle, e.g. every four weeks). Of these 25 variables, six showed improved scores of > 10% at two months. Five of these were in the gemcitabine arm and one in the BSC arm. Five of the twenty-five variables showed a 10% or greater decrease in quality of life, three of these were from the BSC arm and two in the gemcitabine arm. After four months six variables showed a 10% or greater increase in quality of life scores, all in the gemcitabine arm. Four variables showed a decrease in quality of life of 10% or more and three of these were in the BSC group (with alopecia being the gemcitabine variable). An improvement was seen by 38% of the gemcitabine group and 24% BSC patients at two months, followed by 44% of gemcitabine group and 25% BSC group at four months. At six months overall improvement was seen by 31% gemcitabine patients and 22% of the BSC group. (Anderson et al 2000).

This study By Anderson et al (2000) is encouraging in that quality of life is an endpoint and the breadth of the assessment undertaken, but the study lacks detail as to what exactly BSC consists of. Best supportive care by its nature is palliation of symptoms and some of these techniques such as analgesia using opiates and palliative radiotherapy are very effective in terms of symptom control (IASLC 2000). The use of BSC usually applies to the experimental group as well as the control (to do otherwise would be unethical), however the use and type of BSC used is not included in the paper. Another RCT compared gemcitabine vs cisplatin+etoposide reporting

quality of life with the EORTC QLQ-30+LC17, and demonstrated no significant difference in the two groups after six cycles (approx five months) of treatment, only in one domain (alopecia) in the cisplatin group showed a reduction (Bokkel-Huninik et al 1999). A similar study using gemcitabine+cisplatin Vs cisplatin+etoposide also using the QLQ-30+LC17, found no change from baseline in functional or global domains, but improved symptom scores such as cough, pain, insomnia and haemoptysis. There was no change in dyspnoea and there was an expected decrease in the symptom domain for alopecia in the etoposide group (an expected side effect of the drug) (Cardenal et al 1999).

In a study similar to the one that is the vehicle for this study, Crino et al compared gemcitabine+cisplatin vs. MITC (mitomycin, irinotecan and cisplatin). quality of life was reported using the QLQ-30+LC17, and once again, no significant difference was found between the two groups, apart from alopecia in the MITC group (Crino et al 1999). However, there was some decrease in physical functioning and worsening of nausea but improvement in pain, insomnia and cough. Sandler's group compared gemcitabine+cisplatin vs. cisplatin using FACT-L to measure quality of life. They found no significant changes at all from baseline (Sandler et al 2000) but this could be because the FACT-L tends to focus on symptoms rather than global or HRQoL.

In a later phase II study, Jassem and co-workers (Jassem et al 2002) used quality of life as an endpoint using the QLQ-30+LC17 in combination therapy, gemcitabine+cisplatin, in a group of 80 patients with NSCLC. In common with most of the chemotherapy regimens Jassem's group found common toxicity of grade 3-4 in myelosuppression, but improved domains in global (22%), functional (19-37%),

dyspnoea (36%), fatigue (45%), chest pain (38%) haemoptysis (77%) and cough (44%). It is unclear if there is any decrease from baseline in this study however as this data is not included and also as it is a phase II open trial, there is no control group for comparison (e.g. BSC).

An important point to consider when evaluating these studies in the context of quality of life is the amount of detailed information on the elements of BSC given. It is standard practice (IASLC 2000) to palliate symptoms with drug therapy and radiotherapy (e.g. pain, breathlessness etc) in lung cancer but little information, if any, is given on the method and frequency of use, or non use, in any of the studies mentioned above. This must be considered when assessing the perceived benefit of palliation by chemotherapy. The aim of the studies examined was to bring better therapeutics into practice. As a range of quality of life assessments are used this makes direct comparisons between studies difficult

The main criticism of oncology quality of life assessment in the context of trials in particular, is the firm grasp of the functional that dominates these studies. QOL in cancer is still rooted in functionalism and biomedicine prevails. The vast majority of studies use nomothetic measurements of quality of life (Bowling 1997). This approach may be dismissive of what is important to patients and its continuance to the expense of other methods will be at great cost to clinicians, researchers and patients.

Chapter 3

Methods

3 Aims and methods of the study

The aim of this study was to examine quality of life, and the meaning of “quality of life” in patients receiving platinum (Cisplatin/Carboplatin) combination chemotherapy for advanced Non small cell lung cancer (NSCLC).

The original aim of the study was to collect quantitative and qualitative data and to perform a comparison. As this study has evolved a revised methodology was required to analyse the data generated. The review in Chapter 2 demonstrates the difficulty in defining quality of life and a direct comparison in the light of this would be unrealistic. The futility of direct comparisons of the data in a purely empirical context is also demonstrated in the results chapters 4, 5 and 6.

In order to examine the meaning and interpretation of the term “quality of life” in patients receiving platinum based chemotherapies for advanced NSCLC two principle methods of data collection were employed. Data collection consisted of HRQoL data in the form of the EORTC QLQ 30+LC 17 and in addition interview data with 40 patients undergoing palliative chemotherapy for advanced NSCLC. Data from the EORTC QLQ 30+LC 17 was analysed using the EORTC CD ROM package. In addition a manual mathematical operation was performed on the HRQoL data. Data from the interviews was analysed using content analysis. Both of these methods are described herein.

Content analysis is a quantification of qualitative data (Silverman 2001) and so the data generated from both components of the study is ultimately quantitative. After communication with experts in the field, a revised methodology of grounded theory was considered but as most of the work, such as the literature review, had already been done this was considered inappropriate. However elements of grounded theory and positivism are comparable in terms of theory generation. This is considered in the concluding chapters and the philosophy of grounded theory and empirical positivism are considered here.

Fieldwork began approximately 18 months before the start of the interviews, and three months prior to registration for a higher degree. Participant observation and reflection in practice of the decision making process in the Lung Cancer Multidisciplinary Team (MDT) Meetings across several North London Hospitals occurred. Such meetings are the cornerstone of care delivery in the cancer modernisation agenda but many teams already used the format prior to 2000.

The clinic fieldwork coincided with this. It was an observation by the researcher prior to the commencement of the study that patients in clinical trials were required to fill in EORTC QLQ 30 questionnaires, but that in different tumour/prognosis groups different concerns were vocalised.

The researcher worked in practice with three patient groups at the time of this observation-approximately 120 patients per year. The three patient groups were those with ovarian, colorectal or lung cancer. Patients with ovarian or colorectal cancers were receiving adjuvant chemotherapy regimens and had a good prognosis. These patients expressed concerns or wished to discuss topics in practice that were reflected in the functional nature of EORTC QLQ 30, such as working, symptoms, side effects of treatment and meeting the deficit of activities of daily living.

Lung cancer patients who were receiving chemotherapy with a stated palliative intent appeared to express a much wider variety of concerns in practice that were not reflected in the quality of life instrument such as issues around death and dying, serious and sudden impairment of social function, psychological distress including suicidal ideation, trust issues with staff or issues around collusion.

These observations lead to an initial review of the literature, which yielded little in NSCLC populations apart from the drug-based studies reviewed herein. Continued observation of the MDT meetings as a participant in practice and as part of on-going audit process along with further review of the literature revealed a lack of study into this aspect of quality of life. The omnipresence of HRQoL in lung cancer in the literature was not supported with any qualitative data, and the sensitivity/validity data offered for the HRQoL measures were normothetic as has been seen (Bowling 1996).

What is apparent from the cancer literature, including the lung cancer literature reviewed in Chapter 2, is the exclusivity of qualitative or quantitative data presented in studies. This can be for many reasons but the growing recognition of cancer care as a multiprofessional activity (DoH 2000a) requires a multifaceted approach to enquiry in an area as subjective as quality of life.

The research problem is lack of knowledge reflected in the literature and therefore in clinical practice and this can be addressed as two specific research questions; in this case “What do patients receiving chemotherapy for NSCLC consider to be factors affecting quality of life?” and “What is the meaning of quality of life to these individuals?”

Outcomes based research as opposed to purely experimental design is now becoming more prominent in the study of palliative oncology in order to learn about the social construction and subjective experience of cancer-for the seriously ill person there is unlikely to be one objective “truth”. This kind of work can facilitate the understanding of a social phenomenon (such as the lived experience of having chemotherapy for advanced NSCLC) in natural rather than experimental settings (Strang 2000).

3.1 The comparative nature of grounded theory and relationships with scientific positivist tradition.

The construction of a theory, which is grounded in data from various sources, has been an established method in social science research since the 1960's. In addition to the interview studies, observational field notes and reflections in practice were also influences in the data collection and synthesis process.

The literature offers two approaches to what is termed "grounded theory" as the two founders (Barney Glaser and Anselm Strauss) diversified the application and use of the theory (McCann and Clarke 2003). The approach adopted here is sympathetic to the one developed by Strauss and Corbin (1998) which favours an active approach by the researcher. It was not possible to adopt Glaser's independent approach in this study due to the researchers own experience with the patient group and professional relationships have already been established, hence the influence of being a participant and actively involved in audit of the service.

Comparison is at the heart of the process of grounded theory. The interview data is compared as per the methods, and this in turn is compared to the literature and the field notes. In addition the coding of the interviews produces many margin notes and all of these are used, in comparison, to locate an emergent theory. In positivist traditions, theories unify, they go "beyond, beneath and behind" phenomena that empirical study reports (Rosenberg 2000). Both grounded theory and positivist tradition rely on emergent theory generated by synthesis and examination of

phenomena, despite the utilisation of different methods. From the literature there is an almost tangible sense of incompatibility between science and the humanities.

However the examination of phenomena tolerates the philosophy of either perspective. Many of the social science texts seem to equate scientific rigour with the reproducibility of controlled experimentation. Science is much broader concept than this- science is the acquisition of knowledge about the world (Diamond 2005). The nature of grounded theory and positivist traditional and determinism are actually closely linked in this way-the generation of theory (by different rigorous techniques) that examines phenomena.

Unlike the reductionist principles employed by science and medicine, which are prescriptive about the presentation of data, the presentation of data which is gained from a mixed method study with a large qualitative input which is then subject to quantitative analysis can tolerate a more flexible approach. It is for this reason that the rest of this work is formatted thus. This is not at the cost of rigour but simply because the huge amounts of data generated support a theory and the difference in collection methods mean that each study will have unique aspects of presentation, particularly in terms of narratives which are used to illustrate experience (Silverman 2003).

By using a mixed method approach the aim was capture data that was not available to QOL researchers previously in this area. As Strauss and Corbin note (Strauss and Corbin 1998) much of what is termed “qualitative research” is qualitative techniques such as observation and interview, which is then quantified. This study is no exception to that. Content analysis of the interview data is the primary form of data

analysis in this study; this is a reflection of the inexperience of sociological research methodology and training in scientific method of the researcher.

The author's initial observations of different patient groups using the available tools to "measure" quality of life generated an inconsistency within clinical practice-empiricism apparently had failed in this situation but this does not mean the failure of positivistic approach. In grounded theory, the researcher begins with an area of study and allows the theory to emerge from the data. As grounded theory has developed it has attained an increasingly rigorous approach and this can be seen from the literature. It would have been a useful method to use in the context of this study-the exploration of the comparative data collection techniques and the resulting data would add dimension. The approach taken in this study has elements of the philosophy of grounded theory and positivism embedded in it.

Objectivity from the materials is required for fair representation of the data. The intention of the study was to interview participants using the topic guide (Fig 3.1) until saturation.

Unlike reductionist methods, objectivity does not mean controlling variables, but being open, a willingness to listen and the ability to "give voice" to the respondents (Strauss and Corbin 1998). In addition the use of both the technical and non-technical literature is required to give an overall perspective. Narratives from respondents were subjected to content analysis. This was done manually due to budgetary constraints and a coding strategy was developed and applied to the verbatim transcriptions. The

addition of the qualitative data allows some shift of focus (Bowling 1997). The quantified, qualitative data will add another dimension in this way.

3.2 Selection and treatment

This study primarily uses as a vehicle, a multicentre randomised controlled trial (Study 11 London Lung Cancer Group, since published as Rudd et al 2005) that compared two chemotherapy regimens in NSCLC. The sample size of patients chosen by the investigators (the London Lung Cancer Group) was 387. This was judged to be the minimum size for measuring toxicity and quality of life and for detecting any significant shortfall in terms of survival for the trial group.

The regimens were Mitomycin/ Ifosphomide/ Cisplatin (MIC) as a standard treatment arm versus Gemcitabine (difluorodeoxycytidine)/Carboplatin (GC) as trial therapy. At the time of the study, Carboplatin was not licensed for use in NSCLC and therefore a DDX licence was applied for and granted. The treatment was as follows: (London Lung Cancer Group 1999)

GC 21 day cycle:

Gemcitabine $1200\text{mg}/\text{m}^2$ IV day 1 and day 8
Carboplatin (AUC 5) in mg IV day 1

MIC 21 day cycle:

Mitomycin $6\text{mg}/\text{m}^2$ IV day 1
Ifosfomide $3\text{g}/\text{m}^2$ IV day 1
Cisplatin $50\text{mg}/\text{m}^2$ IV day 1

In addition: Pre-medication with 3mg IV Granisetron and 8mg IV Dexamethasone day 1 with Metaclopramide 20mg 8 hourly prn (as required) post chemotherapy anti-emetic regimen was administered. This was altered depending on clinical indication/patient preference. Prophylactic antibiotics (oral) were also give day 8 to day 21 of each cycle to minimise risk of neutropenic sepsis and respiratory infection. The choice of antibiotic was left to the discretion of the clinician. Four treatment cycles are given in total.

Eligibility Criteria

Patients were eligible to enter the study if they were over eighteen years of age, able to give informed consent for both the chemotherapy study and the extended quality of life study, had adequate bone marrow function as assessed by full blood count including white cell differential, adequate renal function allowing the administration of platinum based chemotherapy by biochemical investigation and creatinine clearance or glomerular filtration rate. Patients were excluded if life expectancy was less than eight weeks, not fit for chemotherapy because of concurrent medical conditions or had symptomatic brain metastasis which required immediate radiotherapy or raised issues around consent. All patients had a confirmed histological or cytological diagnosis of NSCLC.

Both male and female patients were eligible. Each patient received a written information sheet prior to consenting (Appendix B). The local regional ethics committee for University College Hospitals London (NHS Trust) approved each part of the study. As the group was extended past the original Study 11 group, the sampling emphasis became more qualitative (Chapters 5 and 6).

In order to assess quality of life in patients with NSCLC, two methods of data collection were utilised: Self completed questionnaires and open-ended interviews. Each patient was asked to self-complete the EORTC QLQ-30 Version 3 with the attached LC 17 lung module (EORTC 1995)(Appendix A) before randomisation and at the first follow-up visit. The first follow up visit is at the end of cycle four. The timing of this visit is dependent on chemotherapy toxicity but was scheduled to be 4-5 months from randomisation. This tool was chosen as it has been validated (Bergman et al 1994, *ibid*).

Patients were monitored by pre-chemotherapy assessment of toxicity (of the previous cycle) using the Common Toxicity Criteria (CTC Appendix C) (LLCG 1999), including haematological and biochemical, and haematological toxicity at nadir (day 10 of each cycle). Supportive care was given if required, to treat toxicity or for the palliation of symptoms, for example blood transfusion for the treatment of chemotherapy induced anaemia. Disease assessment in the form of chest x-ray was also performed prior to each cycle and CT scanning and/or assessment of metastatic sites as clinically indicated. Patients were also given palliative radiotherapy if clinically indicated at any point in time, for example the treatment of haemoptysis or pain control. Serious adverse events such as febrile neutropaenia, which requires intravenous antibiotics, were reported to the investigators.

Basic demographic data was collected such as sex, age and occupation or previous occupation if retired, educational level, changes in occupational pattern since

diagnosis and self selected ethnic-grouping data. The length and location of the interviews was also recorded.

In addition to the QLQ 30+LC17, semi-structured face-to-face interviews were used. Interviews were the chosen methodology as they allow flexibility in response and allow for probing and follow up questioning (Bell 1999). The aim of the interview was to elicit information and to examine issues that arose which were not evident from quality of life outcome measures.

Sampling for the interview study was performed via a cross sectional approach (Baruch 1981). However after interviewing 10 participants saturation was becoming apparent. The themes from the patient narratives indicated that some contamination may have occurred as the researcher had clinical responsibility for these patients. To increase objectivity patients were interviewed (n=40) for whom the researcher had no clinical responsibility. As the study of the phenomena is the aim, sampling is conducted to a different methodology. In outcomes based research the aim is often not to draw a representative sample at random from a population, but to identify certain groups or individuals who experience circumstances relevant to the phenomenon being studied (Mays and Pope 1996).

Approaching the area of qualitative research entails defining some parameters to ensure rigour. It has been seen in Chapter 2 that quality of life is a subjective, complex

and an empirically difficult phenomenon. This means that unlike the reductionist methodology of measuring the objective, concepts must also be considered in consideration of the subjective.

Interviews are a the most common way of collecting talk (Payne 1997) and qualitative research method is concisely, if simply, summarised by Peter Strang in Fig 3.0 (Strang 2000)

Fig 3.0 The steps included in an interview study (Strang 2000)

1. Thematizing
2. Designing
3. Tape recorded interviewing
4. Transcription (plus field notes)
5. Naïve reading to gain an overall picture
6. Preliminary themes and coding (decontextualisation)
7. Comparison of codes and categorisation of data
8. Detailed analysis of data
9. Condensation of data
10. Recontextualisation

The interview is a recognised methodology in eliciting information (Moser and Kalton 1971). The framework of questions used to guide the interview was based on preliminary data gathered in clinical practice, where the disparity between the topics of patient led therapeutic conversation and the items used by outcome measures first became apparent. This constituted pre-test.

The interviews for this study used five questions as a guide. These are shown in Fig 3.1

Fig 3.1 Five questions used to facilitate the face-to-face interview.

What do you consider to be a good quality of life? (expand/paraphrase to “What makes life good?”)
What do think affects your quality of life most? (expand/paraphrase to “What things affect your life?”)
How has having lung cancer affected you?
How has chemotherapy affected your quality of life? (expand/paraphrase to “How has chemotherapy affected how you feel/what you do?”)
Do you think having chemotherapy was worthwhile?

This was to allow for greater flexibility in response, and also to allow for variations in literacy ability and allowed for the inclusion of patients who would be excluded from the questionnaire study due to inability to read English.

Open questions were used and those given in Fig 3.1 served to facilitate the interview.

However deviation from the format was permitted to capture a wide range of responses and allow for focus in the interviews at the indication of the respondent.

The interviewer aimed for a neutral approach however interaction by the interviewer was also permitted if appropriate, for example areas of sensitivity such as expressed anger or anticipatory grief.

The aim of the interview was to elicit subjective responses such as perception of quality of life and narratives of the experience of undergoing chemotherapy for advanced lung cancer-essentially how do people undergoing treatment for advanced lung cancer construct quality of life? (Silverman 2003).

The interviews were tape-recorded with the permission of the respondents and took place in the patient’s own home or that of the patient’s relative/carer. This allowed for a question and answer format to transform in to a more conversational style.

Patients taking part were assured of their anonymity that and no data gathered via the interview would be passed on to the clinical team except with the explicit wish of the respondent.

The interviews were transcribed verbatim and underwent content analysis (Silverman 2003, Krippendorf 2004)). These data were then analysed using manually using Excel and coded by the author alone due to limited resources. These themes were elicited using key words and phrases (for example worry/worried/worrying) and for narratives (Strang 2000)

3.3 Content Analysis of the interview data

Content analysis, sometimes referred to as textual analysis, is a standard methodology in the social sciences on the subject of communication content. Lasswell (1965) formulated the core questions of content analysis: "Who says what, to whom, why, to what extent and with what effect?". Holsti (1969) offers a broad definition of content analysis as "any technique for making inferences by objectively and systematically identifying specified characteristics of messages".

Content analysis enables the researcher to include large amounts of textual information and identify systematically its properties such as the frequencies of most used keywords and phrases by detecting important structures (Silverman 2001). Such amounts of textual information must be categorised according to a certain theoretical framework, providing at the end a meaningful reading of content.. The creation of coding frames is inseparable to a creative approach to variables that exert an influence over the content of the text.

Lasswell proposes that every content analysis should depart from a hypothesis (Lasswell 1965). As an evaluation approach, content analysis is considered to be quasi-evaluation because content analysis judgments need not be based on value statements. Instead, they can be based on knowledge. Such content analyses are not evaluations. On the other hand, when content analysis judgments are based on values,

such studies are evaluations (Frisbie, 1986). There is certainly an element of evaluation in this study as the narratives are also examined in the context of the textual content.

The responses from the semi-structured interviews were open coded. Collecting data in this way can give a great deal of insight (Bowling 1997) Coding was done by using key words in context (KWIC) and key phrases (Krippendorf 2004) and subjected to tabulation.

Root codes elicited from analysis and tabulation of interview data are given below:

Preliminary root codes:

- *Communication*
- *Psychological wellbeing*
- *Physical wellbeing*
- *Family and significant others*
- *Health behaviours*
- *Spirituality*
- *Patient experience*
- *Lifestyle changes*

Repeated tabulation is a method of achieving validity in content analysis and was used in this study. Data was repeatedly tabulated by the researcher to elicit and then validate root and eventually, branch codes.

3.4 Method of analysis-HRQoL EORTC QLQ 30+LC 17 data

The EORTC QLQ 30 is composed of both multi item scales and single item measures.

These are grouped as domains and include three symptom scales, a global health status question, five functional scales, and six single items. High scores represent high levels of response and so a high score for function indicates a high level/healthy function, however a high symptom score represents a high level of that symptom.

The principle for scoring is the same in all-estimate the average of items that contribute to the scale (this is the raw score) as: (if for example items 1,2,3)

$$\text{RawScore RS} = (I_1+I_2+I_3\dots I_n)/n$$

and then use a linear transformation to standardise the raw score (0-100).

Functional scales:

$$S = \frac{[1-(RS-1)]}{[\text{range}]} 100$$

Symptom scales and Global status:

$$S = [(RS-1)/\text{range}] 100$$

Range is the difference between the maximum and minimum possible value of RS

The scoring table for the EORTC QLQ 30 Version 3 is shown in Fig 3.2 as shown in the EORTC Scoring Manual (Fayers et al 2001).

The linear transformation performed on the raw score as described above was performed within a scalar range (this data represents scalar permutations). A linear transformation is a function between two-vector spaces-it preserves linear combinations (Boas 1983). In the language of abstract algebra a linear transformation is a homomorphism of vector spaces.

Taking as definition and first consequences (in this proof only the homogeneous linear transformation is shown-other transformations are possible but not of relevance in this study):

$$f(x+y) = f(x) + f(y) \text{ (additivity)}$$

$$f(ax) = af(x) \text{ (homogeneity)}$$

$\equiv f$ preserves a linear transformation, that is for any vectors $x_1 \dots x_m$ and any scalars $a_1 \dots a_m$ the equality:

$$f(a_1 x_1 + \dots + a_m x_m) = a_1 f(x_1) + \dots + a_m f(x_m)$$

holds. Thus a scalar linear transformation *within* a scalar range-it indicates one point. (Boas 1981). This means that multiple data can be expressed as one integer.

Figure 3.3 The Lung Cancer Module is scored in conjunction with the QLQ 30 for the Scoring Manual (note the LC 13 and 17 are identical modules)

Figure 3.2 The EORTC QLQ 30 Version 3 range and corresponding item domains.

	Scale	Number of items	Item range*	Version 3.0 Item numbers	Function scales
Global health status / QoL					
Global health status/QoL (revised)†	QL2	2	6	29, 30	
Functional scales					
Physical functioning (revised)†	PF2	5	3	1 to 5	F
Role functioning (revised)†	RF2	2	3	6, 7	F
Emotional functioning	EF	4	3	21 to 24	F
Cognitive functioning	CF	2	3	20, 25	F
Social functioning	SF	2	3	26, 27	F
Symptom scales / items					
Fatigue	FA	3	3	10, 12, 18	
Nausea and vomiting	NV	2	3	14, 15	
Pain	PA	2	3	9, 19	
Dyspnoea	DY	1	3	8	
Insomnia	SL	1	3	11	
Appetite loss	AP	1	3	13	
Constipation	CO	1	3	16	
Diarrhoea	DI	1	3	17	
Financial difficulties	FI	1	3	28	

*Item range is the difference between possible maximum and minimum values or response to items (most take values from 1-4 hence range is 3)
Revised from Version 1.

The Lung Cancer Module consists of 13 items specific to that disease. Scoring the Lung Cancer Module (LC13 or 17) is done using the same mathematical operation and the module is shown in Fig 3.3.

Figure 3.3 The Lung Cancer module used in conjunction with the QLQ 30 for the Scoring Manual (note the LC 13 and 17 are identical modules)

Scale name	Scale	Number of items	Item range*	QLQ-LC13 Item numbers	†
Symptom scales / items					
Dyspnoea [†]	LCDY	3 [†]	3	3,4,5	X
Coughing	LCCO	1	3	1	
Haemoptysis	LCHA	1	3	2	
Sore mouth	LCSM	1	3	6	
Dysphagia	LCDS	1	3	7	
Peripheral neuropathy	LCPN	1	3	8	
Alopecia	LCHR	1	3	9	
Pain in chest	LCPC	1	3	10	
Pain in arm or shoulder	LCPA	1	3	11	
Pain in other parts	LCPO	1	3	12	

* "Item range" is the difference between the possible maximum and the minimum response to individual items.

† The dyspnoea scale should only be used if all three items have been answered. Some respondents ignore question 5 because they never climb stairs; in this case, the score for the dyspnoea scale would be biased if it were based upon the other two items. Hence if item 5 is missing then items 3 and 4 should be used as single-item measures.

This data can be handled using various statistical packages that are commercially available. This study utilised the data handling package designed by the EORTC to manipulate and analyse these data. Much of this analysis was verified manually to ensure no systematic errors were in place and to explore the possibility of comparison with the interview data..

In addition, to elicit any possible comparisons the linear transformations were repeated on the raw scores at the most basic level. Initially the researcher intended to obtain a raw score from each respondent by administering the EORTC QLQ-30 at time of interview due the change in study group (i.e. interviewing outside of the Study 11 group) but 40 exclusive questionnaires did confer enough power for the

required mathematical operation. This meant a return to the original Study 11 data raw scores, which were then re-examined and were robust enough for the required serial linear transformation as described.

3.5 Summary

As a mixed method is used in this study it is important not to lose sight of the aims. This study is a clinical study and primarily based on the experiences, feelings and social context of the patients who undergo treatment for advanced NSCLC. The aim of the study is not to generalise to an entire population with these data, but to understand the experience of this group. As has been seen in Chapter 2, patients experience cancer as a journey-this cannot be measured purely in terms of tumour response or survival but it is hoped that the findings of this study in context will influence the researcher in practice:

“Although we do not create data, we create theory out of data. If we do it correctly then we are not speaking for our participants but rather we are enabling them to speak in voices that are clearly understood and representative. Our theories, no matter how incomplete, provide a common language, a set of concepts, through which research participants, professionals and others can come together to discuss ideas and find solutions to problems. Yes we are naïve if we think we can “know it all”. But even a small amount of understanding can make a difference” Strauss and Corbin 1998

The methods described herein have generated enormous amounts of data, which are discussed in the following chapters.

Chapter 4

Results

4 Results

The results presented in this chapter consist of the two streams of data central to this study. The interview study data and the QLQ 30+LC 17 data were subjected to the mathematical operations described in Chapter 3 to elicit comparative factors. As the content analysis of the interviews also includes the use of narratives, much of the data generated by the interview study is examined in Chapters 5 and 6.

Data collected from the EORTC QoL Questionnaire with LC-17 module for lung cancer is presented below. The EORTC QLQ 30+LC 17 is included in Appendix A. EORTC QLQ-C30 + LC17 Raw data collected by the London Lung Cancer Group is shown here as it was subsequently subjected to the mathematical operations described in Chapter 3 to elicit any comparable factors between the QLQ 30+LC 17 and content analysis of the interviews.

The demographics from both the LLCG Study 11 group (source of HRQoL data) and the interview study (source of content analysis data) are given here.

4.1 Patient demographics for both data sources

Patient demographics of the interview study

The nature of this study and the theoretical approach taken means that full results are given in context within the Discussion (Chapters 5 and 6)

Respondent demographics of the interview study are as follows:

28 males and 12 females interviewed 5 EFL (Greek, Turkish, Spanish and

Portuguese) 8 considered themselves as from a BME origin

Mean age was 54 years (range 35-81)

Working Pattern

25 already retired

8 changed working pattern because of cancer/treatment

7 continued in full or part time employment as previously i.e. no change in work pattern.

Smoking History

2 Lifetime non-smokers, 15 current smokers, 23 ex smokers

Educational background

28 had no post-compulsory education, 8 had A level/NVQ/Apprenticeships, 4 had higher education qualifications (professional/technical/graduates)

Performance status

ECOG performance status:

0 for 12, 1 for 15, 2 for 11 and 3 for 2 in the period three to six weeks after completion of last cycle of chemotherapy.

Chemotherapy received

8 MIC 32 Gem/Carbo. Only 12 of those in this group took part in the LLCG Study 11.

Table 4.1 Patient demographics of the LLCG study (Rudd et al 2005) *and the interview study for comparison.(CA)

	<i>GemCarbo</i>	<i>MIC</i>	<i>CA*</i>
	N=212	N=210	N=40
Age (Years)			
Median	62	63	54
Range	40-81	34-81	35-81
Sex			
Male	147 (69%)	149 (71%)	28 (70%)
Female	65 (31%)	61 (29%)	12 (30%)
ECOG Status+			
0	64 (30%)	44 (21%)	12 (30%)
1	124 (58%)	133 (63%)	15 (37.5)
2	9 (19%)	29 (14%)	11(27.5%)
3	5 (2%)	4 (2%)	2 (8%)
Stage			
IIIB	95 (45%)	105 (50%)	NA
IV	117 (55%)	105 (50%)	NA
Pathology			
Squamous	85 (40%)	89 (42%)	NA
Adenocarcinoma	79 (37%)	70 (33%)	NA
Other NSCLC	48 (23%)	51 (24%)	NA

+ECOG performance status: A description of performance status and the use of such scales is given in Chapter 2.

The number of forms received by the LLCG for analysis compared to the number expected is shown in Figure 4.1

Figure 4.1 Compliance (number. received / number. expected) of QoL form received centrally by London Lung Cancer Group

	GC	MIC
	Within 7 days	
Pre-treatment / cycle1	193/212 (91%)	192/210 (91%)
Cycle2	154/184 (84%)	157/189 (84%)
Cycle3	142/165 (86%)	134/152 (88%)
Cycle4	118/143 (83%)	108/134 (81%)
	Within 14 days	
6 weeks from randomisation	158/199 (79%)	159/192 (83%)
12 weeks from randomisation	96/180 (53%)	99/175 (57%)
6 months from randomisation	10/153 (7%)	11/119 (9%)

Note from Figure 4.1 at how 12 weeks from randomisation the attrition rate for QLQ 30+LC module has risen. Only 53% and 57% respectively in each chemotherapy group completed questionnaires. 12 weeks from randomisation is the approximate time at which respondents are interviewed.

Possible reasons for this attrition rate include death of respondent and increasingly poor performance status. As these questionnaires are commonly given out at clinic visits and patients with poor performance status are more likely to be cared for by community teams with few or no visits to the clinic. Interviews took place in respondent's home allowing capture of low performance/high ECOG score patients. In comparison a higher percentage of respondents had poorer performance status in the interview study than in Study 11. This is shown in Table 4.1.

4.2 The Domains of the QLQ 30+LC 17 by question.

The domains measured by the QLQ-30 are presented below-data from each domain represents a group of questions from the questionnaire.

Outcome measures-the domains of QLQ-30 have been coded for ease of presentation:

EORTC QLQ-C30	Domain	Question Number
Functional scales	PF: physical functioning	Q1-Q5
	RF: role functioning	Q6-Q7
	EF: emotional functioning	Q21-Q24
	CF: cognitive functioning	Q20, Q25
	SF: social functioning	Q26, Q27
Global health status	QL	Q29, Q30
Symptom scales/items	FA: fatigue	Q10, Q12, Q18
	NV: nausea and vomiting	Q14-Q15
	PA: pain	Q9, Q19
	DY: dyspnoea	Q8
	SL: insomnia	Q11
	AP: appetite loss	Q13
	CO: constipation	Q16
	DI: diarrhoea	Q17
	FI: financial difficulties	Q28

QLQ-LC17 (Lung Cancer Specific Module)

Symptom scales/items	LCCO: coughing	Q31, Q32
	LCHA: haemoptysis	Q33
	LCDY: dyspnoea	Q34-Q37
	LCSM: sore mouth	Q40
	LCDS: dysphagia	Q41
	LCHO: hoarseness	Q39
	LCPN: peripheral neuropathy	Q42-Q44
	LCPC: pain in chest	Q38
	LCHL: hair loss	Q45
	LCHU: upset by hair loss	Q46
	LCFE: fever	Q47

Range of scales/items

All scales/items except QL are from 1 to 4 with the smaller the value the better. QL ranges from 1 to 7 with the larger the value the better. The rationale for this method and background of content is given in Chapters 2 and 3.

Analysis dataset parameters set by the LLCG but as standard practice.

Forms with less than 80% items completed were excluded

Scales with less than 50% items completed were excluded.

Data from QLQ analysed using the EORTC CD Package ratified by the London Lung Cancer Group findings. Figure 4.2 below illustrates the pre-treatment (baseline) HRQoL scores for the Study 11 (Rudd et al 2005) group. As described below the real numbers shown in this and the accompanying figures/tables are *ranges*.

Ranges are the comparable factors in many HRQoL tools including the QLQ 30.

Subjecting the data to the mathematical operations described in Chapter 3 gives a series of values as real numbers which can then be compared to corresponding values as those in Figure 4.3 (values at 12 weeks-approximate time of interview).

Figure 4.3 also shows comparison of the two scores (baseline Figure 4.2 and 12 weeks). Figure 4.4 also includes the cumulative SD and p values. These should be noted-in the comparison data the p values for some domains (such as social function 0.85) are very high. This is probably due to the attrition rate within the groups however should be considered in the interpretation of these data. This is because these data seek to represent a facet of quality of life in the global sense. Given the low confidence of these data can it do this?

Figure 4.2 QoL at pre-treatment (before chemotherapy for NSCLC)

Scale	GC				MIC				Total		
	n	mean	median	sd	n	mean	median	sd	n	mean	median
EORTC QLQ-C30											
Functional scales											
PF	189	1.87	1.80	0.65	189	1.84	1.60	0.66	378	1.85	1.80
RF	188	2.18	2.00	1.03	189	2.28	2.00	1.03	377	2.23	2.00
EF	190	1.91	1.75	0.76	190	1.93	1.75	0.73	380	1.92	1.75
CF	190	1.52	1.50	0.68	190	1.51	1.50	0.64	380	1.51	1.50
SF	189	1.89	2.00	0.90	190	1.96	2.00	0.92	379	1.92	2.00
Global health status											
QL	190	4.41	4.50	1.45	190	4.58	4.75	1.32	380	4.49	4.50
Symptom scales/items											
FA	190	2.14	2.00	0.75	190	2.18	2.00	0.77	380	2.16	2.00
NV	190	1.31	1.00	0.59	190	1.31	1.00	0.58	380	1.31	1.00
PA	190	1.83	1.50	0.89	190	1.78	1.50	0.85	380	1.80	1.50
	189	2.30	2.00	0.89	190	2.33	2.00	0.97	379	2.31	2.00
DY	189	1.98	2.00	0.99	190	2.11	2.00	0.97	379	2.04	2.00
SL	189	1.89	1.00	1.06	189	1.96	2.00	1.04	378	1.93	2.00
AP	189	1.66	1.00	0.94	190	1.53	1.00	0.81	379	1.59	1.00
CO	189	1.20	1.00	0.55	188	1.09	1.00	0.31	377	1.14	1.00
DI	187	1.63	1.00	0.95	189	1.65	1.00	0.91	376	1.64	1.00
FI											
QLQ-LC17 Symptom scales/items											
	192	2.28	2.00	0.78	192	2.30	2.00	0.84	384	2.29	2.00
LCCO	192	1.23	1.00	0.53	192	1.27	1.00	0.63	384	1.25	1.00
LCHA	192	1.95	1.75	0.71	192	1.95	1.75	0.77	384	1.95	1.75
LCDY	192	1.23	1.00	0.58	192	1.19	1.00	0.57	384	1.21	1.00
LCSM	191	1.28	1.00	0.69	192	1.31	1.00	0.72	383	1.30	1.00
LCDS	191	1.64	1.00	0.95	191	1.60	1.00	0.91	382	1.62	1.00
LCHO	192	1.36	1.00	0.52	192	1.39	1.33	0.55	384	1.37	1.33
LCPN	191	1.64	1.00	0.84	192	1.66	1.00	0.84	383	1.65	1.00
LCPC	191	1.03	1.00	0.16	188	1.04	1.00	0.27	379	1.03	1.00
LCHL	131	1.11	1.00	0.47	127	1.16	1.00	0.56	258	1.14	1.00
LCHU	192	1.15	1.00	0.47	186	1.13	1.00	0.47	378	1.14	1.00
LCFE											

* % of patients with score >2 (quite a bit / very much) for all scales except for QL which was % of patients with score <4 (below average health status).

All scales/items measured by EORTC QLQ-C30 and QLQ-LC17 questionnaires were balanced across the two treatment groups at the pre-treatment. The majority of patients did not experience or experienced a little difficulty in QoL.

Figure 4.3 Comparison at 12 weeks (± 2 weeks) from randomisation

Scale	GC					MIC					Total	
	n	mean	median	sd	%*	n	mean	median	sd	%*	Diff / sd **	P
EORTC QLQ-C30												
Functional scales												
PF	95	1.82	1.80	0.61	32	97	1.88	1.80	0.67	33	0.06/0.64	0.63
RF	95	2.13	2.00	0.93	37	98	2.26	2.00	0.96	44	0.13/0.95	0.35
EF	95	1.72	1.75	0.61	22	98	1.65	1.63	0.66	12	-0.07/0.64	0.20
CF	95	1.49	1.00	0.61	12	98	1.51	1.50	0.65	9	0.01/0.63	0.87
SF	95	1.86	2.00	0.82	27	98	1.93	2.00	0.93	26	0.07/0.88	0.85
Global health status												
QL	94	4.82	5.00	1.31	21	98	4.66	5.00	1.22	16	0.18/1.26	0.25
Symptom scales/items												
FA	95	2.10	2.00	0.74	38	98	2.25	2.00	0.79	40	0.15/0.77	0.22
NV	95	1.23	1.00	0.43	4	98	1.39	1.00	0.58	9	0.16/0.52	0.04
PA	95	1.51	1.50	0.59	12	98	1.49	1.25	0.66	9	-0.02/0.62	0.64
DY	95	2.11	2.00	0.86	29	96	2.11	2.00	0.93	30	0/0.89	0.94
SL	95	1.74	2.00	0.88	16	98	1.65	1.00	0.79	15	-0.09/0.83	0.61
AP	95	1.54	1.00	0.81	14	97	1.70	1.00	0.89	16	0.16/0.85	0.16
CO	95	1.34	1.00	0.66	6	98	1.50	1.00	0.84	14	0.16/0.76	0.23
DI	95	1.17	1.00	0.48	2	98	1.16	1.00	0.53	3	-0.01/0.50	0.64
FI	95	1.47	1.00	0.77	11	98	1.71	1.00	0.97	18	0.24/0.89	0.10
QLQ-LC17												
Symptom scales/items												
LCCO	95	1.86	2.00	0.64	19	93	1.89	2.00	0.71	24	0.03/0.67	0.87
LCHA	95	1.05	1.00	0.22	0	93	1.05	1.00	0.34	1	0/0.29	0.51
LCDY	95	1.80	1.75	0.61	27	93	1.72	1.50	0.67	25	-0.08/0.64	0.19
LCSM	95	1.24	1.00	0.54	5	93	1.26	1.00	0.57	6	0.02/0.55	0.92
LCDS	95	1.07	1.00	0.26	0	92	1.17	1.00	0.51	3	0.1/0.40	0.18
LCHO	95	1.44	1.00	0.68	6	93	1.42	1.00	0.73	8	-0.02/0.70	0.59
LCPN	95	1.39	1.33	0.40	5	93	1.44	1.33	0.58	10	0.06/0.49	0.73
LCPC	95	1.46	1.00	0.67	9	93	1.34	1.00	0.60	2	-0.12/0.63	0.22
LCHL	95	1.56	1.00	0.66	7	92	2.65	3.00	1.08	53	1/1.05	0.000
LCHU	70	1.39	1.00	0.75	10	88	1.63	1.00	0.97	17	0.24/0.89	0.12
LCFE	94	1.07	1.00	0.30	1	93	1.03	1.00	0.18	0	-0.04/0.25	0.31

* % of patients with score >2 (quite a bit / very much) for all scales except for QL which was % of patients with score <4 (below average health status).

**diff = mean of MIC – mean of GC

P values calculated using χ^2 apart from age, in which t-test was used. All statistics performed on the advice of trials centre statistician.

4.3 Toxicities

All Toxicities were recorded using the Common Toxicity Criteria described in

Chapter 3. Toxicity has been included here as along with performance status it is used as both a foundation for health related QoL scales. Occasionally it is also a proxy for, quality of life. The rationale and literature for this has been described in Chapter 2.

It is both toxicity and overall QoL domain scoring that will be compared with the interview study.

Figure 4.4. Haematological Toxicity for patients who received at least one cycle of chemotherapy

<i>Reported worst toxicity by grade</i>	<i>GemCarbo N=200/202* %</i>	<i>MIC N=201/202*%</i>
Anaemia		
0	2	4
1	26	32
2	61	24
3	7	8
4	2	1
Leucopenia		
0	27	24
1	23	26
2	28	22
3	19	22
4	3	6
Neutropenia		
0	28	34
1	13	12
2	24	21
3	21	18
4	13	15
Thrombocytopenia		
0	45	48
1	28	38
2	3	6
3	11	4
4	13	3

*206 patients received at least one course. Data Unavailable for 6 patients on GemCarbo

Figure 4.5 Non Haematological Toxicity for patients who have received at least one cycle of chemotherapy.

<i>Reported worst toxicity grade</i>	<i>GemCarbo N=197 (%)</i>	<i>MIC N=202 (%)</i>
Allergy		
0	93	97
1	5	2
2	1	1
3	1	0
4	0	0
Nausea		
0	36	23
1	37	35
2	22	29
3	5	12
4	0	1
Vomiting		
0	64	45
1	20	26
2	12	19
3	3	8
4	1	2
Alopecia		
0	58	17
1	36	26
2	6	48
3	1	9
4	0	0
Rash		
0	79	94
1	14	3
2	7	2
3	1	0
4	0	0
Constipation		
0	52	39
1	30	36
2	16	17
3	2	7
4	0	0
Infection		
0	70	72
1	6	8
2	16	12
3	7	6
4	1	1
Stomatitis		
0	71	66

1	18	27
2	10	5
3	1	2
4	0	0
Diarrhoea		
0	82	83
1	12	12
2	4	3
3	2	2
4	1	1
Anorexia		
0	51	51
1	32	23
2	12	19
3	5	6
4	1	1

Toxicity data is included here as part of the original comparative study was to determine if the reason cited by some clinicians as a limiting factor in quality of life is a valid one.

4.4 The Interview Study

Interviews were transcribed verbatim and subsequently subjected to content analysis. Content analysis of the transcribed scripts was performed manually and managed on an Excel spreadsheet. As Krippendorff suggests (Krippendorff 2004) such texts generate huge amounts of data and this study is no exception to that. A total of 3,802 responses were coded by content. Initial analysis was performed for structure and elicited narratives (e.g. atrocity stories) and a second was then undertaken to elicit themes (Mishler 1996, Benit et al 2005).

These transcribed responses were tabulated. Repeated tabulation lends reliability to the method and data. In addition such tabulation enables the creation of representation of frequency, illustrated by histograms. The histograms generated from these data can be found in Chapters 5 and 6, which deal with the interpretation of the content analysis data.

On examination of these data there was apparent clustering of coded responses.

These are presented below and using a dendrogram to summarise in Figure 4.6. These data are further examined in context in the following chapters.

1 Root code Communication HP and Patient

- 1.1 How diagnosis was communicated (positive or negative)
- 1.2 Attitude of those communicating diagnosis (positive or negative)
- 1.3 Willingness/reluctance of health professionals to discuss life expectancy
- 1.4 Willingness/reluctance of health professionals to discuss information needs
- 1.5 Willingness/reluctance of health professionals to discuss fear/emotional distress
- 1.6 Atrocity stories of pre diagnosis (communication)
- 1.7 Atrocity stories of diagnosis (communication)
- 1.8 Not being able to discuss with HP
- 1.9 Feelings of shock, numbness or distance

2 Root code Psychological well-being

- 2.1 Ability to adjust to diagnosis/prognosis
- 2.2 Ability of significant others to adjust to diagnosis/prognosis
- 2.3 Suffering-Inability to adjust to diagnosis/prognosis
- 2.4 Suffering-Inability of significant others to adjust to diagnosis/prognosis
- 2.5 Feeling independent
- 2.6 Feeling Isolated (psychological)
- 2.7 Suicidal ideation
- 2.8 Emotional distress*
- 2.9 Labile mood*
- 2.10 Depression*
- 2.11 Feeling fear of unknown (eg suffering "what happens when you die?")
- 2.12 Feeling well (psychological)
- 2.13 Feeling relief
- 2.14 Experiencing other mental health problems
- 2.15 Change in body image
- 2.16 Suffering caused by uncertainty
- 2.17 Feeling guilty (smoking)
- 2.18 Feeling guilty (other)
- 2.19 Feeling determined/not giving up
- 2.20 Feeling disbelief
- 2.21 Feelings of failure
- 2.22 Feelings of Anger

*As defined by patient affecting QoL-not always confirmed as a pathology

3 Root code Physical well-being

- 3.1 Experiencing symptoms (e.g. dyspnoea, haemoptysis, orthopnea) associated with lung cancer
- 3.2 Experiencing symptoms not associated with lung cancer (eg other chronic conditions)
- 3.3 Experiencing side effects of treatment considered to have detriment to quality of life^
- 3.4 Experiencing side effects of treatment considered not to have detriment to quality of life^

- 3.5 Feeling well
- 3.6 Experiencing improvements in symptoms
- 3.7 Physical effort of treatment (eg hospital visits) fatigue

^Side effects of treatment on QoL as defined by patient-not by CTC

4 Root code Relationships with significant others

- 4.1 Willingness of family/others to discuss diagnosis/prognosis
- 4.2 Reluctance of family/others to discuss diagnosis/prognosis
- 4.3 Concerns about future of family (children, partner)
- 4.4 Experiencing difficult reactions of family and others (eg anger, denial, exclusion from social activities)
- 4.5 Refusal to discuss with others
- 4.6 Support from family/others
- 4.7 Planning for the future

5 Root code Health behaviours

- 5.1 Giving up smoking
- 5.2 Not giving up smoking/smoking more
- 5.3 Eating healthier
- 5.4 New belief in alternative (complimentary) therapy

6 Root code Spirituality

- 6.1 Affirmation of religious belief
- 6.2 Interest in spirituality
- 6.3 Interest in "afterlife"
- 6.4 Rejection of previous religious beliefs

7. Root code Patient experience

- 7.1 Level of service (eg waiting time) prior to oncology positive
- 7.2 Level of service (eg waiting time) prior to oncology negative
- 7.3 Level of service (eg waiting time) within oncology positive
- 7.4 Level of service (eg waiting time) within oncology negative
- 7.5 Scheduling of investigations prior to chemotherapy positive
- 7.6 Scheduling of investigations prior to chemotherapy negative
- 7.7 Options and alternatives presented prior to oncology positive
- 7.8 Options and alternatives presented prior to oncology negative
- 7.9 Options and alternatives presented within oncology positive
- 7.10 Options and alternatives presented within oncology negative
- 7.11 Feeling of trust in medicine/medical team prior to treatment
- 7.12 Feeling of mistrust in medicine/medical team prior to treatment
- 7.13 Feeling of trust in medicine/medical team on treatment (oncology)
- 7.14 Feeling of mistrust in medicine/medical team on treatment (oncology)
- 7.15 Control of treatment decisions/choices
- 7.16 Perception of control issues around circumstances of own death
- 7.17 Experience of therapies as positive (eg context of hope, access to experts)

- 7.18 Experience of therapies as negative (side effect or useless)
- 7.19 Access to specialist nurse (eg lung CNS, chemo nurses) positive/negative
- 7.20 Access to doctors positive/negative
- 7.21 Access to others positive/negative
- 7.22 Community support positive/negative
- 7.23 Flexibility/negotiation of treatment calendar and support services (eg OPA booking/transport) positive
- 7.24 Flexibility/negotiation of treatment calendar and support services (eg OPA booking/transport) negative
- 7.25 Abandonment
- 7.26 Persistence (in accessing services)
- 7.27 Information needs prior to treatment positive/negative
- 7.28 Fear of treatment/what to expect

(positive and negative as defined by patient perceived effect on QoL)

8 Root code Atrocity stories non communication

- 8.1 Pre diagnosis (eg >2 visits to GP with herald symptoms before action)
- 8.2 Diagnosis
- 8.3 Post diagnosis/pre treatment
- 8.4 On treatment

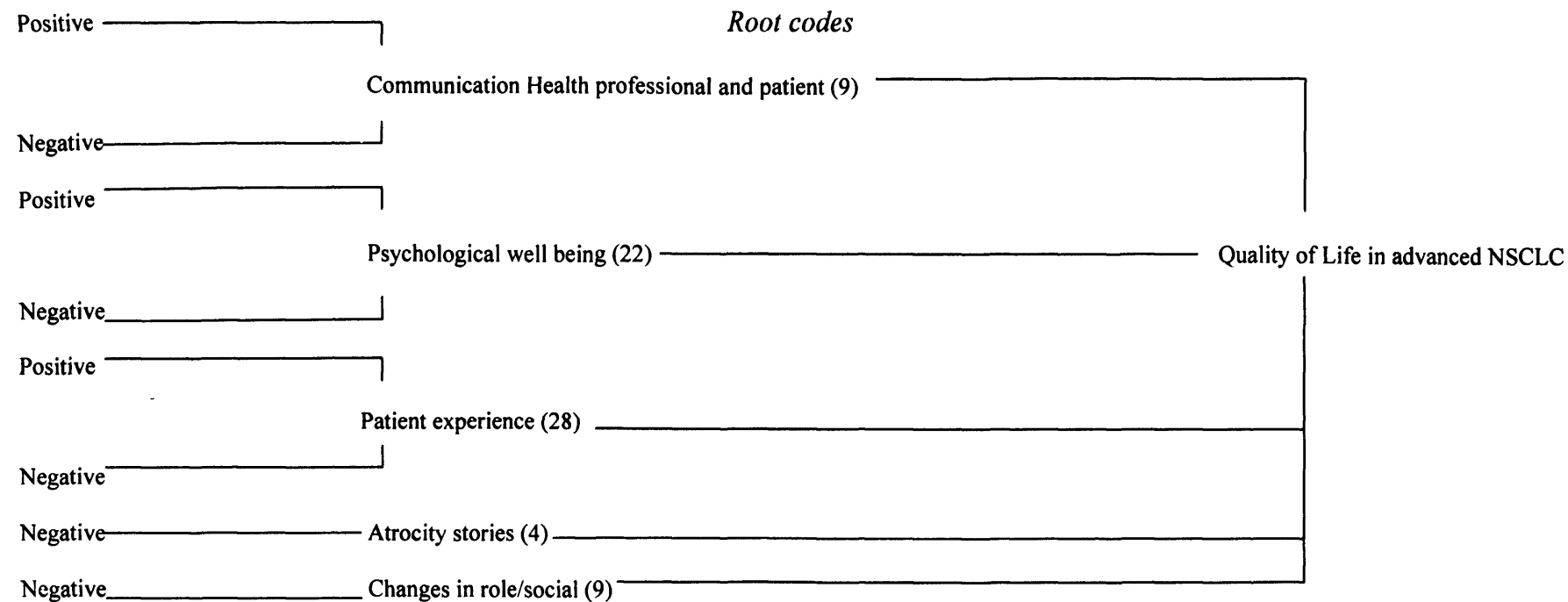
9. Root code changes in role/social

- 9.1 Changes in working patterns/giving up work
- 9.2 Change in financial circumstances positive
- 9.3 Changes in financial circumstances negative
- 9.4 Change in social activities and interaction positive
- 9.5 Change in social activities interaction negative
- 9.6 Changes in independence/mobility negative
- 9.7 Feeling isolated (mobility/socially)
- 9.8 Leading a "normal" life
- 9.9 Suffering-not leading a "normal" life

10 Root Code Miscellaneous

Figure 4.6 Examples of clustering of codes using a dendrogram of the tabulated interview results to the first level. Root codes are shown with numbers of branch codes in parenthesis show responses.

Branch codes



The two streams of data gathered by HRQoL and content analysis will be compared and contrasted to examine the meaning of quality of life in this patient group.

The findings of these data are used to elicit meaning of what quality of life means to patients who have advanced NSCLC in the following chapters.

Chapter 5

Quality of life

The work of cancer

and

The lens of diagnosis

5.Introduction

The result of coding produced root codes and a wide distribution of branch codes.

At a high level, from the content analysis of the interview data four themes were identified. These were compared across the scripts and with the published literature.

In addition comparisons were sought with the EORTC QLQ-30 data. There is much overlap but two of them have such synergistic properties they are presented in one chapter

The four themes are:

- Doing work
- Suffering
- The lens of diagnosis
- The worth of treatment

The themes of Doing work and The lens of diagnosis appeared to have overlap and so are considered in this Chapter. The worth of treatment an Suffering are considered in the next.

5.1 The Lung Cancer Journey-doing work

Using line-by-line analysis of content, this was the dominant theme. The dominance of this theme was the reason for sampling outside of the study group. In the initial sample of ten for which the researcher could not attain clinical isolation, saturation in this category was reached very quickly. Comparison of scripts of this initial group showed saturation and possible influence (originally thought to be contamination) of the respondent group by the therapeutic relationship shared between the researcher and the respondent. Subsequent interviews for which the researcher had no clinical responsibility yielded a similar result-fast saturation of this topic and possible data redundancy.

From the coded, tabulated responses, 29% (1,101) described aspects of the patient journey. The importance of this journey was explained in Chapter 2 and is also recognised in the UK by the various guidance published by the Department of Health, such as the NHS Cancer Plan (2000) and the subsequent initiatives.

Comparisons of the EORTC QLQ data, the literature and the current Department of Health initiatives are part of the comparison process with the interviews and patients own realities to explore the meaning of quality of life in the context of the patient journey.

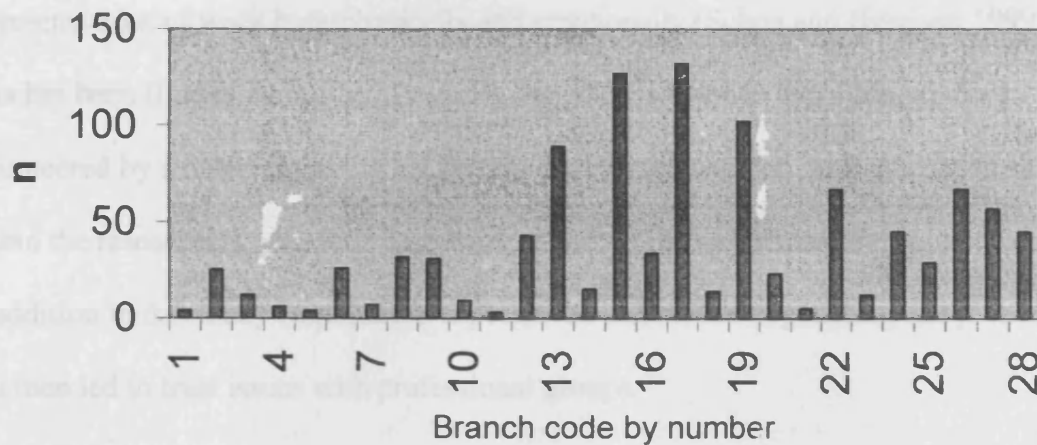
This is an area that is not covered by the functional status questionnaires such as the QLQ 30 + LC 17, although such tools do contain items such as assessment of physical function, emotion and social/role which may affect ability to negotiate the journey; it is not possible to extract information about specific influences on these domains. The responses from the lung cancer patients covered a wide variety of topics that have been coded into 28 branch codes:

Twenty-eight branch codes by open coding and content analysis for the root code patient experience.

- 1 Level of service (eg waiting time) prior to oncology positive
- 2 Level of service (eg waiting time) prior to oncology negative
- 3 Level of service (eg waiting time) within oncology positive
- 4 Level of service (eg waiting time) within oncology negative
- 5 Scheduling of investigations prior to chemotherapy positive
- 6 Scheduling of investigations prior to chemotherapy negative
- 7 Options and alternatives presented prior to oncology positive
- 8 Options and alternatives presented prior to oncology negative
- 9 Options and alternatives presented within oncology positive
- 10 Options and alternatives presented within oncology negative
- 11 Feeling of trust in medicine/medical team prior to treatment
- 12 Feeling of mistrust in medicine/medical team prior to treatment
- 13 Feeling of trust in medicine/medical team on treatment (oncology)
- 14 Feeling of mistrust in medicine/medical team on treatment (oncology)
- 15 Control of treatment decisions/choices
- 16 Perception of control issues around circumstances of own death
- 17 Experience of therapies as positive (eg context of hope, access to experts)
- 18 Experience of therapies (negative)
- 19 Access to specialist nurse
- 20 Access to doctors
- 21 Access to others
- 22 Community support
- 23 Flexibility/negotiation of treatment calendar and support services (eg OPA booking, transport) positive
- 24 Flexibility/negotiation of treatment calendar and support services (eg OPA booking, transport) negative
- 25 Abandonment by service
- 26 Persistence
- 27 Information needs prior to treatment
- 28 Fear of treatment

The distribution of these responses is shown below in Fig 5.1, however this is not usual practice in medical sociological research. The decision to include distribution is that it is valid data, which can be used for comparison and quantification of such data is common practice in content analysis (Krippendorff 2004).

Fig 5.1 Root code Patient Experience



Patient experience was given as a basis for many quality of life issues in advanced NSCLC. This root code reached saturation quickly in the first ten respondents. As the researcher was initially part of the Study 11 research team and had a clinical responsibility for these respondents as patients, the researcher then interviewed patients outside of Study 11. This decision was made for two reasons. In addition to the reason just given-a possible bias toward the interviewer, another reason was the adoption by the National Institute of Clinical Excellence of the Gemcitabine/Carboplatin chemotherapy combination as best practice in advanced NSCLC. This meant that patients no longer received one of the chemotherapy regimens (MIC). It would have been unethical to continue the study in such a way.

The cancer patient experience or journey is a complex one to which the considerable investment by the current government attests (DoH 2003). Many of the sources of frustration or stress for cancer patients arise from access problems or bottlenecks (Leary and Corrigan 2005) even when a clear path based on clinical evidence is apparent. Mapping of the lung cancer pathway at one central London NHS Trust revealed 72 actions between GP referral and definitive treatment, which in real terms, represents a lot of work both physically and emotionally (Schou and Hewison 1999). This has been illustrated in Fig 5.2a and b. Fig 5.2.a is from an appointment diary volunteered by a respondent. Fig 5.2.b demonstrates the mapped lung cancer journey within the researchers own cancer network as part of the modernisation agenda work. In addition to this many respondents experienced difficulties negotiating this journey that then led to trust issues with professional groups.

The remaining figures of this section demonstrate lower level mapping of aspects of the patient journey, particularly the aspect of communication between professionals, patients and organisations. The various complexities of communication are shown in Fig 5.2.c. Two points of the journey have been selected to illustrate the complexity of the process and the negotiation the patient has to deal with. These are shown at outpatient diagnosis (Fig 5.2d) and the process of receiving a dose of chemotherapy (Fig 5.2e)

Fig 5.2a Offered by a respondent 54, female during interview. An appointment diary. This diary was primarily for recording appointments but demonstrates the work of a lung cancer patient.

It starts with visit to chest clinic in a large district general hospital that is also a cancer unit after abnormal x-ray findings by GP.

21/10 AM chest clinic (this identified the need for investigation)

28/10 AM Bronchoscopy

5/11 AM Chest clinic (no results from bronchoscopy available-return next week-should have had CT already but appointment not until 11/11)

11/11 AM CT Scan

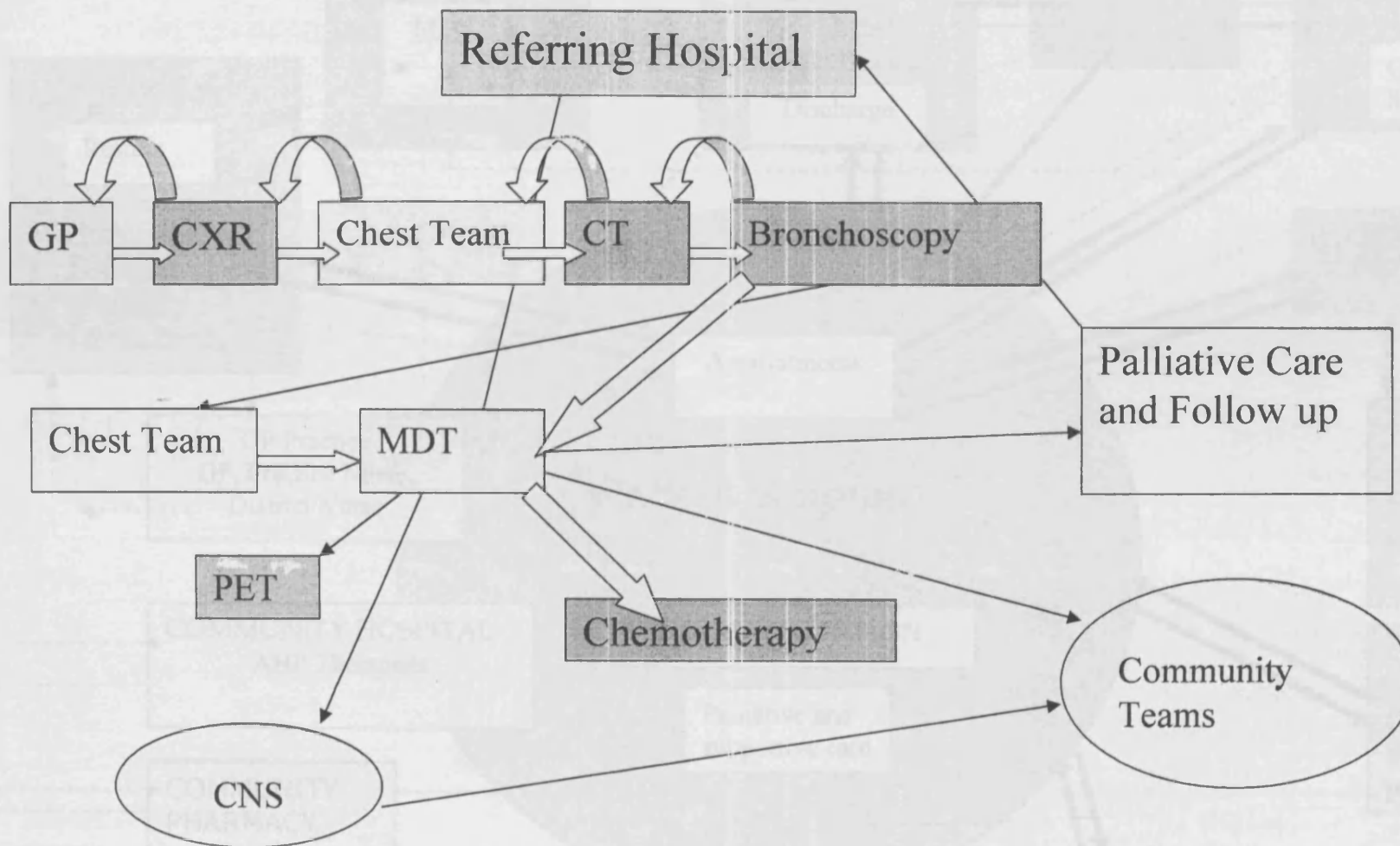
12/11 AM Chest clinic results show lung cancer-might be operable refer to surgeon.

The respondent then waited a month for an appointment to see the surgeon in outpatients at a surgical clinic. The surgeon told her she was not operable and would refer back to the chest clinic. After waiting two weeks for an appointment she rang the chest clinic to find no re-referral had been received. The chest team had to liaise with the surgical team to confirm the findings and the respondent was seen in the chest clinic two weeks later.

5/1 AM Chest clinic referral made to oncology team and Macmillan nurse

The respondent finally received her first course of chemotherapy almost three months after her first visit to the chest clinic. Given the prognosis of NSCLC and the Department of Health guidelines for the treatment of cancer wait times, waiting three months exceeds all targets and represents work for the respondent.

5.2b Lung cancer pathway-the work of having cancer (abridged-assumes GP initial visit) the actual pathway as mapped in one central London trust consists of 72 steps.



5.2c The different communication routes required for the journey (mapped by SE and North Central CN)

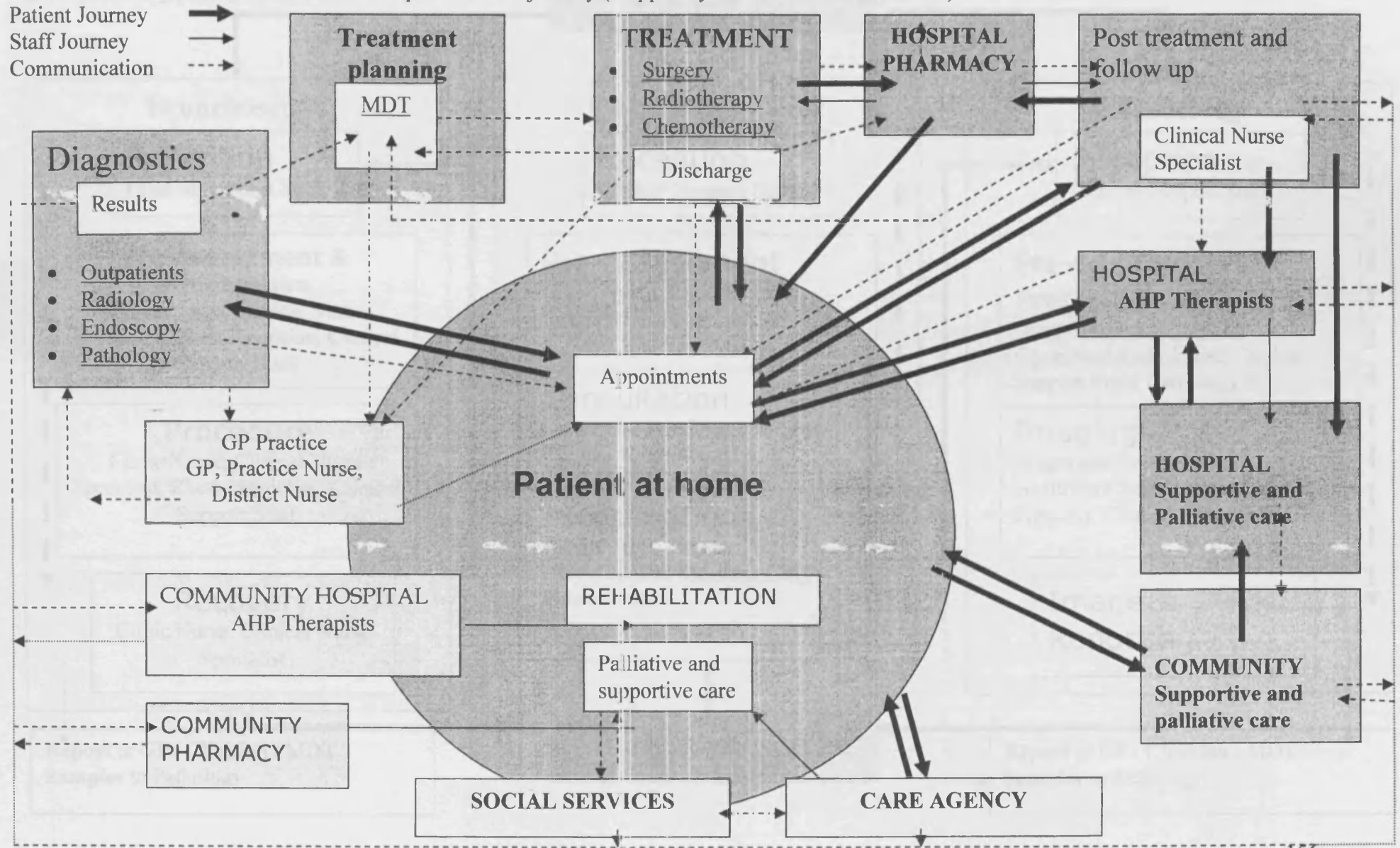
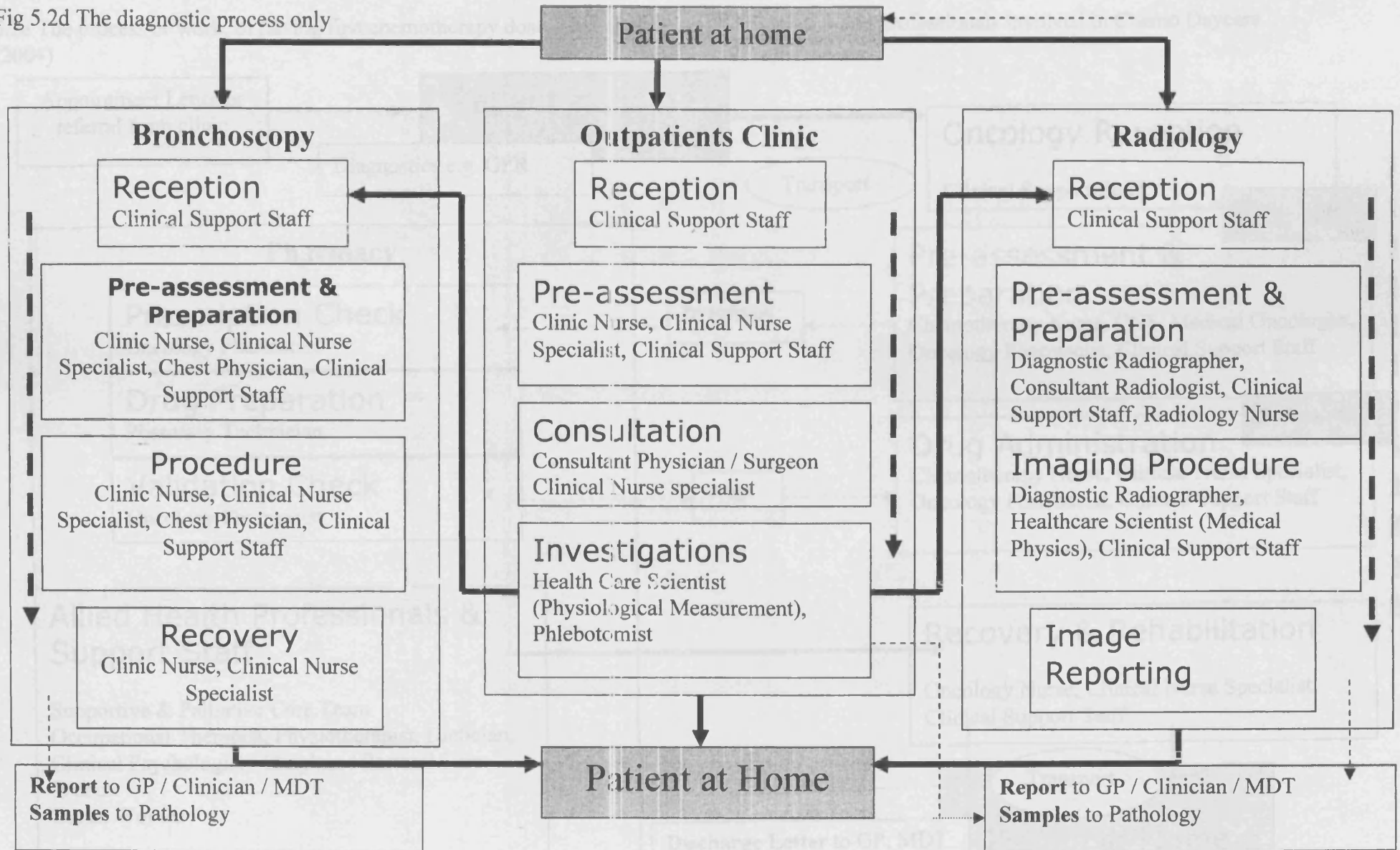
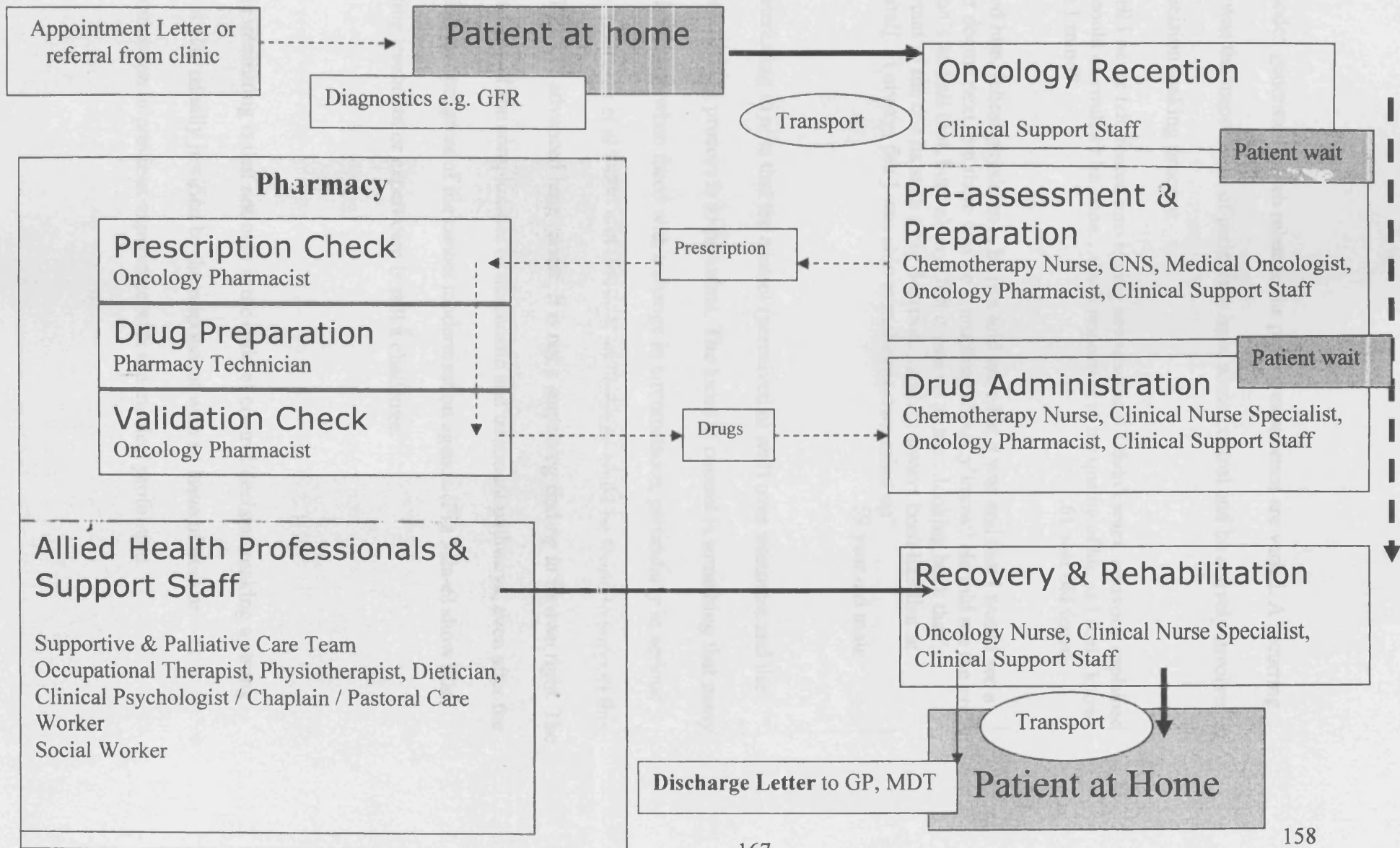


Fig 5.2d The diagnostic process only



5.2e The process or work, of having first chemotherapy dose (Gemcitabine and Carboplatin) and professionals involved in Chemo Daycare (2004)



The codes generated which relate to the patient experience are varied. A recurring issue was the importance of patients to have some control and be actively involved in the decision making process:

“...well I never felt, forced into having any treatment I didn't want. everyone explained what could or couldn't be done...that's important in my quality of life as I feel I know where I stand”
61 year old female

“I liked him, [chest physician] , he just told me what it was and that I would see a cancer doctor next..but there was no...mucking about..y'know? He told me the pro's and con's and all that, but I always felt it was up to me...looking back that's important to me cos its such a big decision...and its always been like that at [hospital]...I always felt I was able to make my own mind up”
59 year old male

It is interesting to note that the control (perceived or real) over treatment and the decision making process is so prevalent. The locus of control is something that many try to hold onto when faced with a change in circumstance, particularly in serious illness, (Burgess et al 1988) and although no literature could be found to support this specifically in advanced lung cancer, it is not a surprising finding in its own right. The examination of the complexities of diagnostic and treatment pathways, even after the inception and progress of the cancer modernisation agenda (Fig 5.2a-e) show that accessing treatment or expert care is still a challenge.

What is interesting is that not only is the code of control/decision making a strong one, it is also usually justified by the respondent with an issue of trust or communication in previous experience with the medical profession.

This can be seen by the amount of atrocity stories that were presented.

The narratives elicited included a number of “atrocity stories” which are situational accounts of encounters with medical professionals and were first identified in the 1970’s (Webb and Stimson 1976, Dingwall 1977).

Atrocity stories usually appear at the inventory stage of interviews with patients (Baruch 1981) and portray a situational encounter in which the parties’ involved display different perceived characteristics. The patient is portrayed as an emotional, feeling person whereas the medical professional is depicted as cold and emotionless. In total 47 atrocity stories were elicited from the narratives of forty patients. In this study the atrocity stories did appear at the inventory stage and were often referred to throughout the course of the interview. Similar to the findings of Baruch (1981), patients paid close attention to the realities in which they locate themselves and members of the health professions as two separate realities.

Thirty-eight were narratives around diagnosis and communication with the respondent’s general practitioner. The most common topic that was subsequently coded was repeated visits to the GP before investigation or referral (35) where the GP acts as gatekeeper to acute services. This example demonstrates not only the interruption and work of the journey but also the breakdown in trust:

“I went to my doctor [GP] and he said I had an infection....um... a chest infection, the antibiotics were not much help, I kept going back and after about three months...I think I saw him about five times.... I went to the (ref hosp) for the X ray, that’s when they found it...I try to see the lady doctor since then or the young one...he [GP] doesn’t know what he is doing”
58 year old man.

There were three narratives in which the probable diagnosis was delivered by the GP told as an atrocity story as the respondents expressed that they were not able to meet the complex information needs expressed by the respondent which is a recognised facet of cancer care (NICE 2005) although the respondents referred to the GP as “caring”, “kind” and “wonderful”. An example from a 46 year old man:

“Well I asked....you know how long...he said probably....about six months...he [GP] didn't know about any treatment...Mentally and emotionally I was down, I was just waiting for the six months to come around....even when Dr X [oncologist] said you can't tell...I had it in my head...six months”

Another example was given by a 68 year old woman, who had a likely diagnosis communicated by her GP, after which she did not appear to have been referred to a local chest physician for some weeks as per the Department of Health Target Waits causing anxiety

“...but any time I had spare time I was in the depth of despair....I was very conscious of walking around with this cancer inside me...it felt like a time-bomb waiting to go off, I've become very intolerant and impatient”

Six stories were around the diagnosis milestone within the acute sector and encounters with chest physicians. These stories were all centred on communication. The respondents had been diagnosed in different acute hospitals and all had told atrocity stories as gate keeping encounters.

A 78 year old woman told of her experience of communication of diagnosis by a chest physician:

“.....I knew something was wrong before...I knew it was serious so I was expecting it to be cancer...well, he told me what it was and I wanted to know the ins and outs and what comes next...but that was it, next patient! He was already at the door! And he wouldn't look me in the eye, as if he were embarrassed or something.”

Two stories were around an unexpected treatment plan change and change in prognosis, these stories depicted the circumstance and perceived realities of the patient and the healthcare professionals involved. An example of this is shown below. This story was told by a 54 year old woman who was thought to have operable lung cancer. On admission for surgery she complained of diplopia and consequently underwent a CT scan of the head. The CT revealed brain metastasis, making the patient inoperable, and this news was communicated to her at 9pm the evening prior to surgery by the anaesthetist, an encounter which she recalls:

“he said...sorry to tell you, you won't be having an operation tomorrow, you've got cancer on your brain...here I am left on my own...and not only that, I sat there, obviously in tears and this nurse came up to me and said....I wasn't noisy cos I don't cry noisy...'well I think you should go to bed now and rest for the night' and I was, like, hang on, have I just been told I'm dying or have I dreamt it?”

One story was told by a 62 year old male respondent who was originally diagnosed and treated for Non Small Cell Lung Cancer and histology re-review revealed a Lymphoma. This narrative was around the communication of the change of diagnosis and consequent expressions of lack of trust with the medical team.

“..well at (ref hosp) they got the type of cancer wrong didn't they...first I had this then I had that-they don't have a clue, I was angry”

Many of the stories told were of GP encounters, which still featured despite patients being some six months from initial visit. The story of repeated visit to the GP before diagnosis/investigation was the most common. Non Small Cell Lung Cancer is difficult to diagnose and it is not surprising that repeated visits may have been necessary. Respondents often made personal, professional or moral judgements about the GP.

Change of emphasis/professionalisation of patient

Studies such as clinical trials and quality of life studies in which treatment is depicted as anonymous and asocial process-taking place independently of individual agents (Schou and Hewison 1999) demonstrates well the point Cassell (Cassell 2004) makes about the ontology of medicine. The human body as an organism with a disease to be cured or measured-but no concept of that state occurring within a dynamic system-this is where cancer treatment in the reductionist sense begins to fail for people with cancer.

Respondents recounted a narrative in which they became professionalised and learned to “work the system”. This was important for maintaining control and independence which was often referred to in terms of quality of life:

“...after what happened at [hospital] we really learnt...you have to work the system, otherwise you loose out”
62 year old male

“...I usually organised my chemo for when I had no work or work when I knew I would be OK to work...that made a big difference...I’m self employed so it was good for me and the family...that I could organise the times I had the chemo and at the start, some of the tests as well”
42 year old male

“...you can’t just accept the first thing you are told, press for more information, more things that may be available to help you”
70 year old female

Hospital and community staff were cited as an important factor in managing or mis-managing the treatment calendar and there is evidence of the value of what The et al (2000) refer to as the treatment broker.

The negotiation of the treatment calendar and the work of having cancer is the basis for much of the cancer patient experience and consists of attitudes of staff, willingness and helpfulness, interactions at crisis points, flexibility, trust, professional credibility and a sense of fairness. It is important to note that the majority of respondents came from units and centres around southeast England. Twelve had specifically sought a second opinion of the team at the centre in which this study is based after receiving a first opinion at the referring unit which was not to their, or their family's, own personal satisfaction.

"...the thing about going to (cancer centre) I just feel they know what they are doing, not like at {ref hosp} I think they will do their best for me, our quality of life is affected because I know I can trust [consultant] and [CNS], they will look after us and I can just get on with things."
54 year old female

"...basically they told me to go home and die at [ref hospital], I thought [expletive] that, I'm only 59. My son went on the internet and saw [cancer centre] so I went back to [ref hospital] and said I wanted to go there. It was no trouble, they wrote me a letter and did it really quick and Dr [consultant] said I could have chemo."
59 year old male

This needs to be considered as an element of the group are therefore self selected and had already presented strong opinions on what constitutes the "good" patient-professional interaction. This has been explored in the context of atrocity stories but comparisons of these data will be made in the next section which also examines the lens of diagnosis-how respondents repeatedly returned to the initial stages of the journey.

The linear and temporal mode of structure is prominent in western society (Knudston & Suzuki 1992) and so illness is experienced in the context of the individual's

calendar. Calendars have the role of embodying goals, motivations and limitations; these can be social norms for some groups for example having children by a certain age or the expected length of one's own life, what Schutz and Luckman refer to as social structures of relevance (Schutz and Luckman 1974) Humans in western society have personal or private calendars, and these incorporate tasks of daily life, goals and responsibilities. Authors such as Sacks (Sacks 1989) believe these personal calendars operate at much deeper levels. In this deeper way, individuals locate specific close relationships, for example marriage, within them.

A diagnosis of cancer will have an impact on the personal calendar, and the diagnosis of an advanced NSCLC for which treatment, if offered, is likely to be palliative, will have a significant impact-for if no other reason but as an indication that the lifespan of the personal calendar is likely to come to an end much sooner than anticipated.

A cancer diagnosis also introduces a new calendar an illness or treatment calendar (Schou and Hewison 1999).

The dominance of functionalism in quality of life neglects this social dimension. The social dimension of quality of life is shown in the context of illness and of treatment calendars. Professionals have power over the treatment calendar because they manage it within a patient-professional relationship that is unequal. Professionals hold knowledge and choose when patients have access to that knowledge. The professional management of the calendar is bound up in the traditions of biomedicine (Schou and Hewison 1999). This may equally not be the desire of the professional group but is directed by institutional culture or political agenda or limited resources.

The treatment calendar seems largely ignored in the quality of life literature and yet seems to have impact on patients' quality of life as the topics for discussion, which explicitly asked respondents about quality of life, elicited so many experience narratives which allude to the treatment calendar.

The impact of the treatment manager or agent is profound (or treatment broker as referred to by Anna Marie The et al 2000) as when this job is done well, a better quality of life is provided for the respondent.

The issue of calendar negotiation and the treatment broker was a recurring code. The qualities of the staff were reiterated in these narratives. Of particular importance was the consultant medical staff, staff in the chemotherapy unit and the lung cancer nurse specialist who were all referred to in the context of agent or broker. The respondents also emulated the role that these professionals played to some degree as a means of gaining control. The establishment of a therapeutic relationship in hand with patient professionalisation was important to quality of life. Consultant medical staff offered consistency throughout treatment, particularly in terms of prognosis:

“.....well after the GP, that really unsettled me....Dr [consultant] was more, I dunno...*reliable* I suppose...the business with the y'know six months...he never said that...he was honest....*he'd say*...”we don't know-it depends on how you react to treatment” and well...he is a cancer doctor so that made me feel better in a way...not like a death sentence....that made life better”
67 year old male

“...when I go to [cancer centre] I usually see [consultant] and that's great because you don't usually see the consultant with other things, you see a junior doctor and it's a different one every time....you have to go through the whole thing again and again and sometimes you just don't feel like it”

59 year old female

The staff in the chemotherapy unit were valued by respondents particularly in terms of information giving, dealing with the practicalities of chemotherapy such as managing side effects, lifestyle changes and accurate information giving:

“the girls in the chemo suite, they were brilliant. I was so nervous about having the chemo, I was sick before I even went. If it hadn’t been for [CNS] I wouldn’t have even come back to hospital after they told me, I was so scared”

62 year old male

“..its good to have someone you can call, no appointment...just ring....At one point I wanted to stay with my sister for a couple of days, and it was nice to be able to ring and ask..”do you think that would be OK?”..its reassurance...when so much changes in one’s life...even simple decisions become difficult...its very reassuring to know that most of the time a simple phone call will help”.

72 year old female

The introduction of the “key worker” a pivotal role in the multidisciplinary team which acts as a navigator of the journey has recently been introduced as part of the latest stage of modernisation (NICE 2005) but this role has been fulfilled by the clinical nurse specialist in lung cancer. The narratives from the respondents demonstrate how this role is viewed and valued as the principal one for negotiation of the cancer patient journey-the principal treatment broker.

“...we found it all very confusing, particularly at first but [CNS] was very good, I remember she rang us the next day to see how we were”

74 year old male

“...oh and [CNS] she was so good, I know I kept asking the same things over and over again. [CNS] helps me a lot, if I cant get there [clinic] she will help me change the appointment-if you just ring up yourself you can’t get an appointment for weeks-its always full. The time I was too ill, she rang to see why I didn’t come and got me an appointment for the next week. I can just ring her if I am not well-my own doctor [GP] he is not a cancer specialist it takes a lot of worry out of it”

68 year old male

Common codes which emerged from this data do not appear to support the view of the therapeutic nihilists. From an experience perspective few respondents commented on chemotherapy as a negative experience and this can be compared with and confirmed by, the physical experience data which is presented in context in the next section..

The patient experience is characterised as hard work and yet work that will have a positive outcome:

“I think its important to try....Dr [consultant] was pretty straight I knew it was not gonna make the cancer go away but at least I was trying...for me and the kids...at least we gave it a go and I dunno if I would have felt bad if I hadn't tried it”

48 year old male

It is difficult to compare these findings with the large cohort EORTC QLQ 30 data from Study 11. There are not common domains for patient experience and so any comparative data analysis in the statistical sense (for example a rank-spearman) would not yield helpful or reliable data data.

In summary the emergent coded responses of the negotiation of the treatment calendar are given in Fig 5.3

Fig 5.3-Emergent codes

- Negotiating the treatment calendar and its complexities
- Gaining control
- Sharing decision making
- Access to a treatment broker
- Being supported by Health Professional and/or family
- Negotiation of the pathway difficult but seen as a positive action

Who makes the decisions? The dynamic of the Multidisciplinary Team.

The Cancer Plan (DH 2000) is explicit about the nature of clinical decision making in cancer care. Decisions should be patient centred and multidisciplinary in nature. For each type of cancer there should exist a core and extended multidisciplinary team to ensure equitable decision-making. This is explored here, as a number of respondents were self-selected. Twelve actively sought chemotherapy or other treatment at the centre after being either refused chemotherapy or offered best supportive care at the referring hospital. These narratives and the other gatekeeper atrocity stories have become a core theme of this data. The existence of these narratives prompts reflection—these narratives demonstrate an experience that is contrary to the cancer modernisation agenda.

The multidisciplinary team is directed by the work of the modernisation agenda to review and audit their work (Department of Health 2000a). This includes activity such as peer review and publication of tumour board minutes in the public domain. Transparency is encouraged and review is required to ensure equity of care (Department of Health 2000a).

The decisions made for this group of patients do not seem to have followed the standard MDT format as proscribed by the Department of Health Cancer Plan (2000a) and modernisation agenda. The MDT field notes of the researcher were re-examined in the context of this data for comparison. How are these decisions made and who makes these decisions?

The observed work of the MDT meetings from the fieldwork across one cancer network produces an interesting power dynamic. The MDT functions as a group rather than a team, with personality, positional authority and established relationships influencing power. There is an alpha decision maker in each group who is a chest physician. The decision making process is altered when the alpha decision maker is not present and a beta decision maker becomes apparent. The beta decision maker is also influential when the alpha decision maker is present generally by affirming the decisions of the alpha decision maker. If the characteristics of group Vs team behaviour are considered (Belbin 2003):

Team working

Mutual Trust
 Freedom to express views
 Process issues part of the work
 High level of commitment
 People work together
 Work through conflict
 Common objectives
 Open
 Decisions are made by consensus

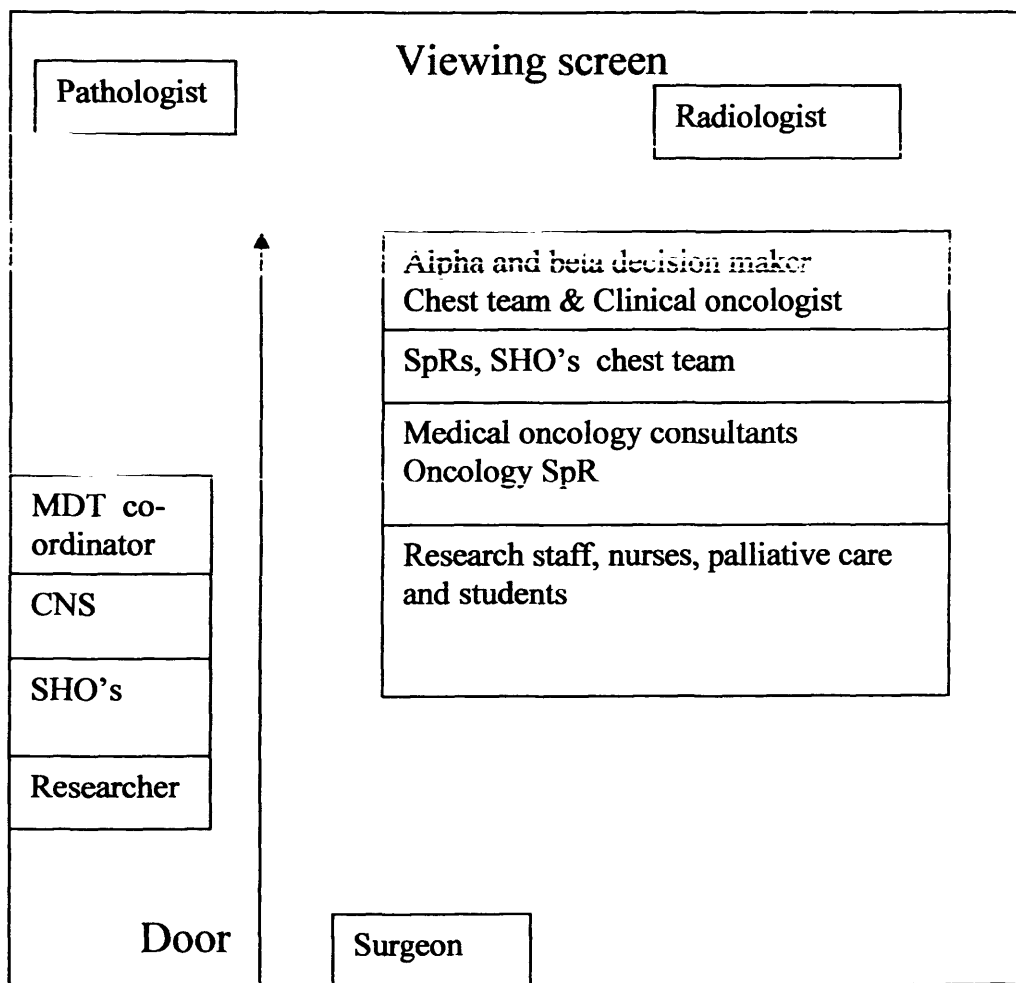
Group working

Trust is measured
 People negotiate
 Process issues worked on covertly
 High level of commitment
 People co-operate to get the job done
 Conflict is accommodated
 Politics are at play
 Feelings not part of work
 Information passes on a need to know basis

The observed behaviour of the core and extended MDT's reflect functioning as groups rather than as teams as there is little consensual decision making, instead opinions are elicited from the group with perceived positional authority being the determinant factor to the hierarchy of the group and subsequent influence on the decision making process. The hierarchy of the group is reflected by attitudes, willingness to contribute to discussions and even seating patterns within the meeting,

these patterns were consistent over months or in some cases the five years of the study. Some positions are fixed by external influence for example the pathologists have an assigned position at the microscope and the radiologists near the projector however in one meeting the radiologist/nuclear medicine physician was the beta decision maker:

Fig 5.4 The hierarchy of position in the MDT meetings



From this dynamic it is possible to consider the decision making process. The evidence presented in Chapter 2 informs that performance status is the best predictor of coping with chemotherapy and yet the majority of the observed decisions in the

MDT meeting utilised chronological age and occasional social factors to make treatment decisions. It is not surprising that this method could result in variations of equity. As the work of cancer and the patient pathway appear to impact directly on quality of life, the function of the MDT as originator of decision-making is of paramount importance. A process of peer review is the method of quality assurance used by cancer services across England and Wales that originated from the Cancer Plan (DH 2000). Teams are encouraged to look at their own practice and regularly audit their own service. In this way a dynamic system of improvements can be facilitated. In addition teams from Networks out with the cancer centre appraise and observe the MDT in a formal system of analysis.

5.3 Lens of diagnosis and quality of life

“Illnesses become narratives very rapidly. Some sense is sought of time and sequence, for one’s self and others. The past confusion is explained, the present situation requires a story, and the future presents the possibility of terrifying resolutions.”

Jackie Stacey (1997)
Teratologies-a cultural study of cancer.

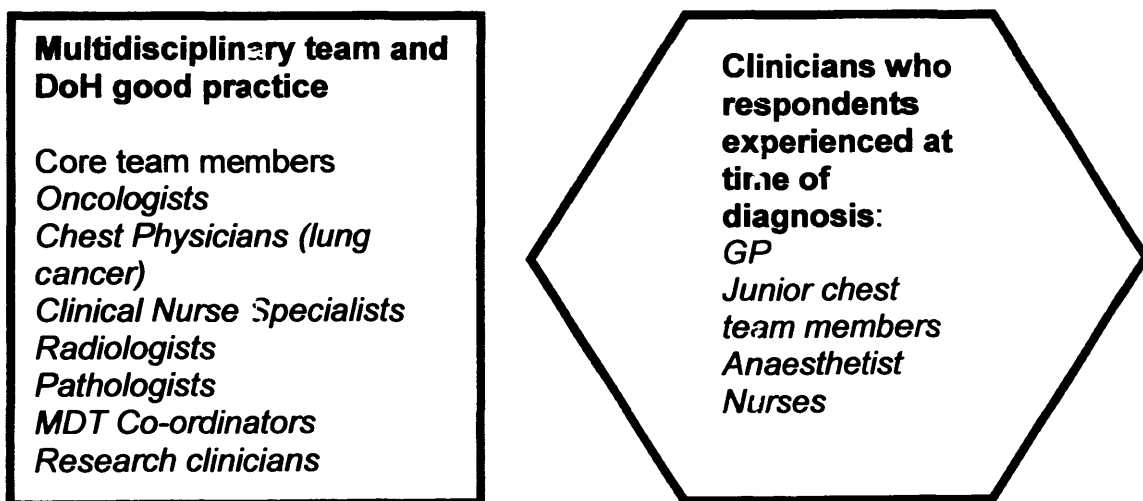
It is interesting to note how often the time of diagnosis is part of the narrative. The author quoted above is a sociologist who has written about her own experience of ovarian cancer. Stacey (1997) asserts that narratives offer a way of ordering events and assigning roles, it gives a temporal continuity and spatial coherence. The diagnosis of cancer is likely to be a negative life experience, and the pathology of non-small lung cancer and probable prognosis and life expectancy is one that is recounted as negative by the respondents, but the manner and communication of diagnosis, particularly the frequency of atrocity stories, is surprising.

Observational fieldwork of the multidisciplinary team meetings across one cancer network was undertaken prior to the study and at various convenience points within the study lifetime. Reflection and audit are encouraged as peer review by the DoH (DoH 2000). The observation of behaviour and attitudes of staff in these meetings does not match the perception of the patients. Yet narratives of the time of diagnosis are seen not only as negative in the patient-clinician relationship, but almost as amoral.

A possible reason for this is the groups observed in fieldwork. No respondent received a diagnosis from an oncologist of any grade or a clinical nurse specialist. Chest physicians were the object of some of the negative diagnosis narratives but these individual physicians were not observed by the researcher in the MDT setting as they were from outside the cancer network in which this study is set.

This is significant in terms of the modernisation agenda as it demonstrates that those who receive training, guidance and are the followers of best practice do not deliver the diagnosis. The implication is that best practice is not being followed because the modernisation agenda is not being correctly targeted (Fig 5.5).

Fig 5.5 The observed discrepancy between target groups when delivering the cancer modernisation agenda. A potential for the source of atrocity stories?



For those with serious illness there is seldom one objective truth and the patient experience may change over time (Strang 2000). Respondents seemed to be consistent historians. Examination of the medical notes shows consistency for example of histories given in clerking.

The coded responses around the communication of diagnosis represent approximately 10% of the responses by content analysis with codes as follows:

- 1 How diagnosis was communicated,
- 2 Attitude of HP,
- 3 willingness/reluctance of HP to discuss life expectancy,
- 4 Information needs not met,
- 5 Reluctance to discuss emotional distress,
- 6 & 7 Atrocity stories,
- 8 NA
- 9 Feelings of shock numbness or distance at diagnosis

Fig 5.6 Distribution within this root code:



Communication of diagnosis and communication of cancer bad news is still rarely examined although a process of change does seem to be underway. Some scholars such as Robert Buckman assert that the less than optimal delivery of bad news is part

of the socialisation of medicine. Buckman (1996) suggests that part of the culture of medicine for many years was to avoid the truth, as the writings of de Sorbriere (1672) who thought that truth telling would jeopardise practice.

In 1961 Oken's seminal study into disclosure of cancer diagnosis by American surgeons showed that 90% of surgeons in the USA would not routinely discuss a diagnosis of cancer with the patient. Novack (Novack et al 1979) repeated the study to find a shift in attitude. Less than twenty years later, Novack et al found that 90% of physicians now would speak to patients about a cancer diagnosis. In the twenty-five years since Novack's work there have been many social, political and legal arguments to support truth telling. The legal argument has prevailed in the USA, however in the UK and Europe, there is still a reluctance to discuss such issues. This is an issue in UK healthcare because of social, economic and educational migration. EU working practice and free trade agreements make working in the UK an attractive educational experience for doctors from countries where a reticence to share information may be socially acceptable.

In 1993 Thomsen et al found that 60% of European gastroenterologists did not tell patients a of a cancer diagnosis unless the patient asked. In Italy Grassi et al (2000) found that of 675 physicians about 45% agreed a patient should always be told of a cancer diagnosis, however only 25% would routinely do this.

Buckman also points out that it is not only the content but the delivery of what is said to patients. He points out that there are many reasons for not wanting to do this part of the job such as the ongoing need to provide support, but also makes clear that it is a

responsibility that is not optional and that “if breaking bad news is done badly, patients and their families (or often their lawyers) may never forgive us”. Perhaps this is why patients with advanced NSCLC used diagnosis as a lens through which to view the rest of their journey.

Respondents narratives often referred back to the time of diagnosis throughout the interviews, not just at the inventory stage.

“I have been going through it from the day I was told....when he first told me my first thought was about death and then in a split second it was for my children.....”
49-year-old male

R: “that day keeps coming back, when I got the x-ray results, mostly a night or when I am on my own, I go over it again and again in my mind. That has affected my quality of life I think”

I “in what way?”

R “it comes back when don’t expect it, it stops you doing normal things.”

54-year-old woman

This lens of diagnosis seems to overlap with the atrocity story. The respondents view the rest of their journey through this lens:

“I keep going back to it...it seems so unfeeling...like he was embarrassed or something”

Cassell (2004) remarks on the wholeness of the past tense, to a time before illness.

This is also offered by others such as Scarry (1985) who remarks: “What is remembered in the body is remembered well”

This was a recurring narrative. Respondents often referred to themselves in such a way. Common phrases such as “before I was ill” or “before the cancer” often prefixed narratives about a good quality of life:

“before I found out about the cancer we had just been to New York, we had a good quality of life then”
68 year old woman

If the concept of the treatment calendar is considered at this point, the early illness and then treatment calendar has influence. At the diagnosis and pre-diagnosis milestones the life calendar undergoes disruption. Newly diagnosed patients are threatened with disruption and probably cessation of their life calendar. In addition the life calendar is subsumed by the illness/treatment calendar-future plans give way to medical commitments and the sick role. This may be why respondents used the past tense to describe the person without cancer as themselves.

Information needs being or not being met were also cited as having an effect on quality of life at diagnosis. This has been shown previously in the context of the GP and atrocity story-particularly in the context of life expectancy. This fulfilment of this need was often met at the cancer centre and in particular by the specialist nurse, chest physician or oncologist:

“I just felt finally someone knew what they were talking about and what to do next, things were a lot better after that”
54-year-old woman

“Don’t tell me to go away and don’t worry about it, I need to know that its, that I can continue on my own...I mean maybe other people don’t want that...they need to be told fibs”
69 year old woman

These issues around information reiterate the issues around trust. If incorrect or inconsistent information is given that is later contradicted, the patient-health professional relationship is damaged. This has been recognised for many years, particularly in nursing and has been verified by a recent National Audit Office report (NAO 2005). Much of the transfer of information is at the pre diagnosis or diagnosis milestone when information needs are high:

R “after the bronchoscope I had at [referring hospital] he [chest physician] said “well I did see something down there but its probably nothing to worry about, it doesn’t look too nasty, but you know, we’ll wait for the thing to come back” and I thought what a thing to say....and then it came back *cancer*”

I “do you think he should have said something different?”

R “C [daughter in law] worked in the department and she said he was optimistic, until he knew I feel actually It’ed be better not to say anything at all, you know take a few samples but not tell you: it looks OK and then a week later you get a smack in the gob like that”

I “do you think it made a difference.....the way you heard the diagnosis?”

R “yeah it was much worse, more of a shock, that’s really affected my life I think, cos you know, we weren’t expecting it really, I don’t smoke or anything, then he just said “you’ve got cancer do you want to talk to [Macmillan nurse] our Macmillan nurse?” and I got out of there and thought, wait a minute he’s just told me I’m dying.”

I “right”

R “ but it hadn’t sort of struck me or I hadn’t digested it.....It was like well here it is and you’ve got that much to live and.....I couldn’t talk to [Macmillan nurse] and I just got out of there.....that time has affected things I think...it being such a shock and no-one knowing if I could get any treatment.....they tell you different things”.

54 year old woman

Many cancer diagnoses offer some hope of recovery and return to the “normal” previously functional self. This is playing the part of the sick role, as expressed in Talcott Parson’s seminal work (Parsons 1951) of the social rights and obligations of the sick. To comply with treatment and become well again-to take up a useful role in society in return for the support of society during illness. Patients with advanced lung cancer are unlikely to fulfil this obligation as it is likely to be an illness without recovery, which respondents expressed as a factor affecting quality of life.

Lung cancer still seems to be surrounded by therapeutic nihilism, expressed at time of diagnosis, which respondents cited as having an impact on quality of life:

R “it just all sounded so final, you know, have some steroids-go off and die – life is over....well that’s a bit unfair really, they were very nice at [ref hospital] and said they would get a Macmillan nurse to see us. My sister in law lives in the states and when [wife] spoke to her, she went to see a friend who is a doctor, I think he looked up something from the Internet because a few days later lots of information arrived about treatment and so forth, chemotherapy and radiotherapy and some experimental treatments, we knew then that we had to find some way of getting these treatments, to try them, that it wasn’t the absolute end for us-that improved the outlook and by default, quality of life.”

I “in what way do think it improved your quality of life?

R “I think....its about having something, anything really, some hope after all the doom and gloom (laughs)!”

62 year old man

The denial or displacement of the word cancer at diagnosis was cited by respondents as a negative part of the process:

“I knew something wasn’t right.....it was a shadow on my x-ray, I’d had a cough for about three months and my GP sent me for an x-ray, he said they found a shadow and I thought cancer straight away cos that’s what they call it.”

70 year old man

“I saw lots of people...I can’t remember who they all were, but I remember this doctor at [referring hospital] he told me about the growth that they saw on the scan. I was really shocked when the other doctor came round, I know now he was the cancer doctor, and said I could go to [cancer centre] if I wanted, for chemotherapy...I thought, hang on that’s for cancer so I asked him, like, have I got cancer and he said it was cancer...no one had said it was cancer before.” 69 year old man

In the national study referred to at the start of Chapter 2 by Krishnasamy and Wilkie (1999) the language used to communicate diagnosis was one of the items examined in needs assessment in lung cancer patients. Although this study is now seven years old and pre-dates the majority of the Department of Health cancer initiatives, it is one of the few pieces of work involving lung cancer patients and there is nothing more recent that is comparable in the literature.

Krishnasamy and Wilkie (1999) found that only 58% of individuals (n=115) had been told they had cancer or lung cancer. The use of language in this study can be seen in Figure 5.7

Fig 5.7 From Krishnasamy & Wilkie 1999-use of language in the communication of NSCLC

Language used to describe illness	Number of patients using language	Number of doctors using language
Cancer	30	30
Lung Cancer	67	64
Specific Diagnosis	19	21
Malignancy	4	7
Shadow	4	2
Growth, lump, tumour mass	70	72

These authors also report that in their study, 10% of respondents felt not at all prepared when asked if they had received information about treatment.

There is a reticence of those working outside of cancer settings to use the word cancer. Jackie Stacey (1997) quoted at the start of this chapter recalls her own story of the mid 90's, of her surgeons telling her she will receive chemotherapy for her cyst. This is also the lived experience of the researcher. Upon approaching patients to take part in clinical chemotherapy trials, occasionally patients would not be aware that the disease they were being treated for was a cancer. However, after two years ethnographic research (unpublished) as a participant observer in thoracic surgical unit, the researcher found this practice of avoidance to be common.

The most common method of delivering bad news such as unsuccessful lung cancer or some diagnostic surgery, was a "hit and run" technique. This involved delivery of diagnosis in the anaesthetic recovery area before patients were fully awake and with poor recall. This avoided interaction with patients and even in this situation euphemisms were often used particularly the word "growth". This was common in observed surgical practice over a two year period.

Ward rounds are part of the medical ceremony (Dingwall 1977) of surgical life, and an average surgical ward round of eight patients took approximately twelve minutes. This demonstrates the lack of social interaction in surgery and possibly other medical specialities in which patients are diagnosed and treated before they have access to an oncology service. Ward rounds from the oncology members of the same multidisciplinary team take over one hour to see six patients.

The modernisation agenda in cancer has attempted to address this issue in terms of communication, but only very recently (NICE 2005) and only in clinical areas such as oncology, haematology and palliative care. This is one of the few measures that examines and intends to address the quality of the service provided, rather than the dominant factor which is to provide an increased quantity of service (Dingwell 2001) to meet set targets such as wait times. Such reforms do not address the underlying issue, one of fear of the professions to talk about cancer. Respondents have used words such as “embarrassment” and described closed body language that demonstrates the reluctance to discuss the subject “he just looked at his feet” or “he just left” Patients on wards sometimes describe blocking behaviour or in outpatients “he was at the door” signifying the end of the consultation at diagnosis. This is closure on the terms of the health professional, and not the patient who may leave or be left without all information needs being met.

An articulate example of this is again given by Jackie Stacey in her experience on a surgical ward as a cancer patient:

“shortly before I left hospital one of the more sociable nurses sits on a patients bed down the row from me and starts to chat about her work. What are her ambitions, one of the patients asks her. She would love to work in oncology, she replies. Suddenly she catches sight of me she, blushes with embarrassment. Unaware of the reason for this mood change the patient asks her what oncology is. The whole ward falls silent. “it’s.....” she glances nervously in my direction, hesitates and never finishes her sentence, she had better get on with her tasks she announces. Have I a disease so unspeakable I wonder to myself?”

Cancer is still an illness that even health care professionals try to avoid. A study by Jessica Corner (Corner & Wilson-Barnett 1993) showed that newly qualified nurses found the meaning of cancer to mean poor prognosis and associated with death. Much

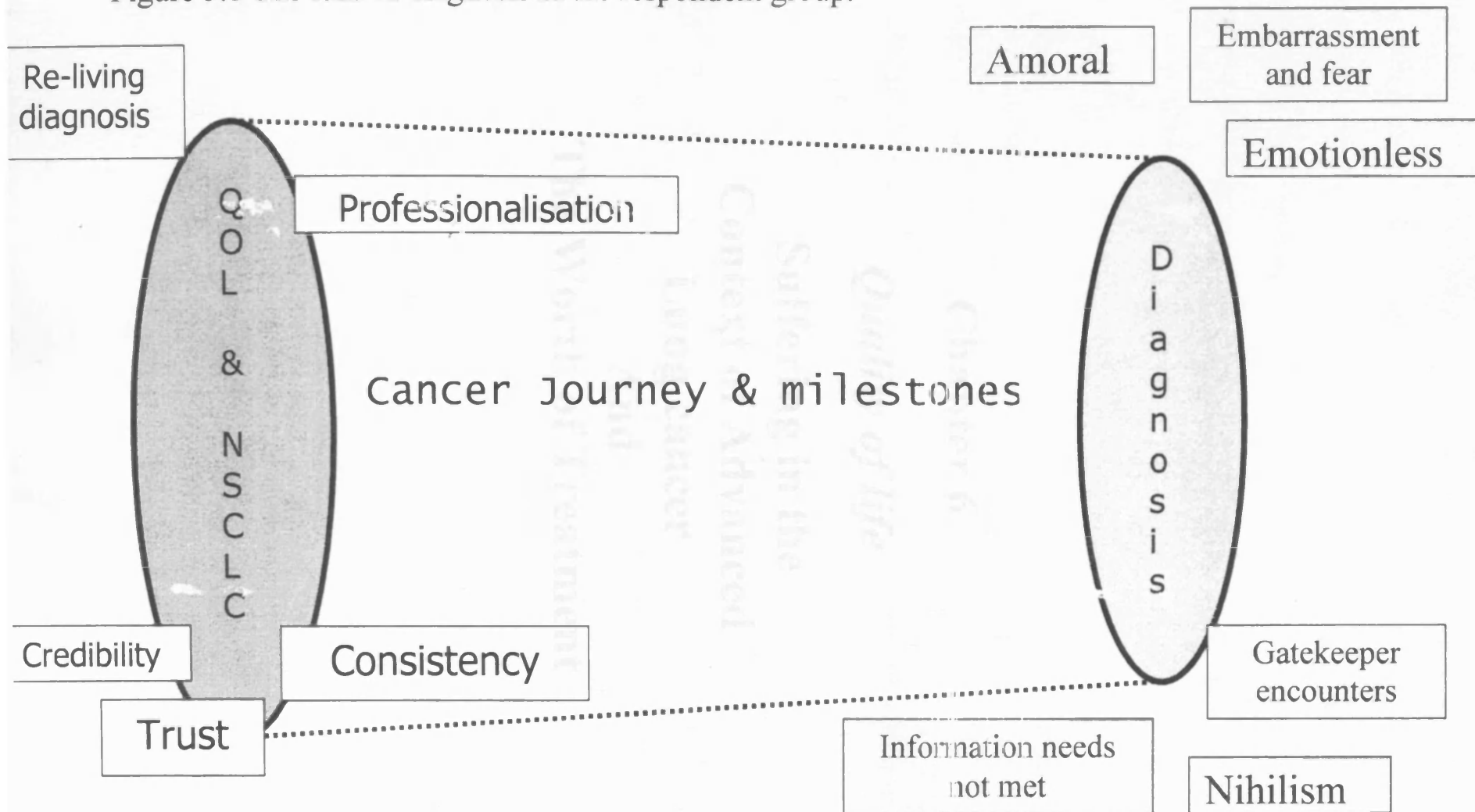
more recently the same issues have been raised in nursing and are being addressed through education (Steginga et al 2005, Leary 2005) and work has been done in areas such as palliative surgery which supports the unprepared nature of the practitioners working in this area in dealing with the emotional burden of this work (Galante et al 2005) but little has changed when considering staff attitudes. Such negative attitudes have a negative effect on the quality of care.

Respondents spoke at length of the experience of diagnosis, pre diagnosis and in one respondent's case, re-diagnosis of lung cancer, some typifications can be made:

- Repetitive theme-not just at inventory stage
- Often viewed as atrocity stories
- Rest of journey is focussed through

The lens of diagnosis constructed from responses is shown in figure 5.8

Figure 5.8 The lens of diagnosis in the respondent group.



Chapter 6

Quality of life

Suffering in the Context of Advanced Lung cancer

And

The Worth of Treatment

6 Suffering

Much theoretical work has been done in the last thirty years, which examines the concept of suffering. While suffering is associated with illness and is a facet of human nature, it has only recently been accorded any legitimacy within the health care literature and the professions (Cassell 2004, Morse and Johnson 1991), it is now recognised as an entity in cancer nursing practice as part of assessment and holistic care delivery (Houldin 2000).

In this chapter the majority of the respondents narratives and the analysis of the accompanying data is presented. Although the patient journey and the work of cancer provoked the most typical and greatest number of responses in one core theme, the majority of the data can be grouped into context of suffering.

This data consists of respondent narratives and coded responses. Data collected at time of interview and the majority of the EORTC QoL 30 data collected as part of the original study. This section therefore examines the physical, psychological, social and functional coded data. From the interviews these are root codes of:

- Psychological well-being
- Physical well-being
- Relationships with significant others
- Health behaviours
- Spirituality
- Changes in role/social function

The EORTC QLQ 30+LC17 domains reflect this data:

The functional domains

Physical functioning

Role function

Emotional function

Cognitive function

Social function

Symptom scales

Nausea and vomiting

Pain

Dyspnoea

Insomnia

Appetite loss

Constipation

Diarrhoea

LC+17 domains (specific lung cancer domains)

Cough

Haemoptysis

Dyspnoea

Sore mouth

Dysphagia

Hoarseness

Peripheral neuropathy

Pain in chest

Hair loss

Upset by hair loss

Fever

Global quality of life

These data from the interview studies are compared to the EORTC QLQ 30 data, which strives to quantify quality of life and as, has been shown in chapter 2, does so largely from a functional perspective. Do these data support a quality of life as interpreted by respondents as one in which there is suffering?

What is suffering? It is as subjective a term as quality of life but unlike QoL there seems to have been little pressure from areas such as the psycho-oncology movement to, in some way, measure suffering in the same way that quality of life is “measured”. Suffering as an entity or the relief of suffering is not seen as an achievable endpoint. This is puzzling as the apposition of the relief of suffering in medicine is entrenched through western history as the study of the classical schools. Much of the literature on suffering originates in disciplines such social science, medical sociology, anthropology and nursing. These disciplines hold an advantage in the examination of the lived experience of lung cancer patients, as they are not confined to the occasional limitations of deterministic or reductionist methods of study that require integer outcomes.

Science is capable of such action as it deals with generalisations, but medicine deals with individuals-this resonates back to the classical period, a conflict between the emphasis on theoretical knowledge and the actual experience of the doctor with *this*

patient (Zaner 1988). Despite its purposeful individualistic approach, medicine is also trapped by technical rationality-practitioners are seen as technical problem solvers (Schon 1991). This means that physicians are caught in a dichotomy between the application of science to a population and the treatment of an individual and suffering is an individual experience.

The benchmark of the modern medical literature on suffering was the work produced by physician Eric J Cassell in 1982, who noted that medicine tends to focus on the body, whereas suffering is an experience of the whole person. After further work, he states in 1992 that is not possible to divide problems into physical, psychological and social aspects because suffering is an experience of the whole person as a state of distress induced by the threat of loss of intactness or disintegration no matter what the cause.

The preface to his work *Eric Cassell, a physician*, (Cassell 2004) explains this line of reasoning in an articulate manner:

“The test of a system of medicine should be its adequacy in the face of suffering: this book starts from the premise that modern medicine fails that test. In fact the central assumptions on which twentieth century medicine is founded provide no base for an understanding of suffering. For pain, difficulty breathing or other afflictions of the body, superbly yes, for suffering, no. Suffering must inevitably involve the person-bodies do not suffer-persons suffer.

Eric J Cassell

The Nature of Suffering and the Goals of Medicine 2004

Suffering was further developed in the context of nursing/caring by Kahn and Steeves (1986) who proposed that a person experiences suffering when some crucial aspect of self, being or existence is threatened. The fact that advanced NSCLC is currently a life limiting disease would constitute a threat to the integrity of the person. In later work Kahn and Steeves (1995) developed the clinical relevance with the help of aphorisms from suffering-summarized with an understanding of suffering experienced by the whole person (Arman and Rehnsfeldt 2003).

Rodgers and Cowles (1997) examined suffering as a concept in the nursing literature and concluded the suffering is “an individualised, subjective and complex experience that involves the assignment of intensely negative meaning to an event or perceived threat”

Although suffering is a concept that is hidden by everyday English in everyday life as concepts such as pain, anxiety and fear, it is unlikely that these words alone will capture the meaning of suffering (Arman and Rehnsfeldt 2003). Suffering occurs in many life situations and has many levels of meaning. To alleviate suffering a person must be triggered by something so that the struggle for development takes place. The struggling act of suffering demands a compassionate other to confirm the suffering (Lindholm and Eriksson 1993) which might lead to meaning as a shared experience or as Rehnsfeldt proposes, in communion (Rehnsfeldt 1999).

Authors such as Frankl (Frankl 1984) take a philosophical tone, which originates from the classical schools and also has spiritual undertones:

“We must never forget that we may also find meaning in life when confronted by a hopeless situation, when facing a fate that cannot be changed. For what then matters is to bear witness to the uniquely human potential at its best, which is to transform a personal tragedy into triumph, to turn one predicament into a human achievement. When we are no longer able to change a situation, we are challenged to change ourselves”

V. Frankl 1984

Frankl asserts, like Cassell, that the person rather than just the body, experiences suffering.

Medicine is where patients with lung cancer (or any other disease for that matter) turn to alleviate suffering. The ontology of medicine reflects physical embodiment with the emphasis on curing disease. Medicine not only pathologises quality of life by using functional scales to measure a subjective experience, it also pathologises suffering as it can only reply to such challenges with pathology which can be treated. If Cassell’s line of thinking is adopted, does medicine fail patients with lung cancer if it does not seek to alleviate their suffering?

6.1 Illness and suffering-having cancer

There is a dearth of qualitative literature examining the lung cancer population and it has not proved possible to find qualitative literature that deals specifically with suffering in lung cancer. This is despite utilising the specialist search mechanisms employed in Chapter 2, specialist historical and archive searches performed by library professionals at University College London, The British Library and a search of the Steinberg Collection- a collection of nursing and related theses which dates back to the 1950's.

There is however a growing body of knowledge around suffering in the cancer population which gives perspective, particularly as some of this work is from palliative care. Medical sociologists and nurse researchers are examining the experience of cancer and the attendant experience of suffering.

Much of the literature on suffering in cancer appears to come from Scandinavia, a study by Hallorsdottir and Hamrin (1996) interviewed nine people in recovery/remission from cancer and found an overriding theme of "experiencing existential changes" which had the sub themes of uncertainty, vulnerability, isolation, discomfort and redefinition, A study by Kuppelomaki and Lauri (1998) examined suffering in patients in the palliative stages of cancer. They found evidence of Physical, psychological and social suffering-the psychological and social suffering was underpinned by the physical- the disease and the treatment of the disease.

Arman and Rehnsfeldt (2003) explored suffering in patients with breast cancer (different stages/prognosis) and found that the early stages of the experience caused a sudden disruption and disintegration of the person with the evident awareness of death being significant to the individual. This experience caused the individual to suffer.

Suffering is a personal matter, unique to the individual experiencing it. Suffering has temporal quality for example Cassell (2004) states that fear always involves the future (for example a fear of what will happen rather than what is happening) or that the lived past is projected into the future and suffering is anticipated which in turn causes suffering in the present “one can suffer again the injuries of yesterday” (Cassell 2004). Persons also suffer when they have lost. When the relationships with others, the physical world, the future is lost, suffering occurs because the intactness of the person is lost.

A cancer diagnosis represents many of these facets. Uncertainty in the future, possible loss of future, loss of relationships with the physical world, social environment and loss of independence because of the work of negotiation of the illness and treatment calendar are just a few example of this. Cassell gives an excellent example in cancer of the facets of suffering in the individual

A thirty five year old sculptor with cancer of the breast that has spread widely was treated by a competent physician...At every stage the disease and the treatment was a source of suffering to her....She was constantly tortured by fears of what tomorrow would bring, each tomorrow worse than today heralding sickness, pain or disability-never as the beginning of better times. She felt isolated because she could not do the things other people could do, she feared her friends would stop visiting her and she feared she would die.”

This is an excellent illustration of the multifaceted nature of suffering of the person.

This woman had severe physical pain and other physical symptoms that caused her to experience suffering. However she also suffered threats that were to her personal and social existence. She suffered the effects of the disease and the effects of the treatment that caused not only physical suffering but feelings of loss in terms of her appearance and her abilities. Her disease caused her to lose her means of living and the pride associated with it, along with her professional identity. Finally she also suffered from her own perception of a future that was anticipated with fear and loss.

Cassell (1998,2004) also points out the relevance of meaning. Chapter 2 referred to the meaning of certain issues in cancer, such as the word “cancer” the meaning of pain etc. An example was given in Chapter 5 to illustrate communication is repeated here to show “meaning”. This demonstrates the meaning ascribed to the word “shadow” by a 70 year old gentleman:

“I knew something wasn’t right.....it was a shadow on my x-ray, I’d had a cough for about three months and my GP sent me for an x-ray, he said they found a shadow and I thought cancer straight away cos that’s what they call it.”

70 year old man

It is important to acknowledge the meaning ascribed to language—indeed it can be argued that this is the function of language. For the same word, event, object or relationship, a person may have simultaneously experience a cognitive meaning, an emotional or affective meaning, a bodily meaning and a transcended or spiritual meaning (Cassell 1985). Meaning in suffering is important because although unique to each individual it is a shared process—almost all humans suffer in their own way. Although a shared human experience the language of suffering is unique and personal to each individual (Rodgers and Cowles 1997).

Human suffering is not viewed as the opposite of health, but is integrated into human life (Fredriksson and Eriksson 2001). Suffering is compatible with health if the suffering is bearable (Arman and Rehnfeldt 2003).

The ontology of health has three dimensions. *Health as having/doing*: The person is focussed on health problems and external matters such as health behaviours, disease and medicine. *Health as being*: The persons deeper needs and longings, these can be beyond articulation and strive for a balance or harmony, *Health as becoming*: is a process of reconciliation, the person reconciles themselves to the present situation as is able to face suffering and death. The person then strives for development, to become more whole (Fagerstrom and Bergbom 1998).

Ontological suffering in cancer (or any life/person threatening illness) is described in a similar way (Fredriksson 1998) *Having* suffering is experienced as sorrow, fear and

alienation. *Being* suffering includes more intense feelings such as distrust, distrust, hopelessness and a lack of freedom. The *becoming* of suffering the existential perspectives are examined such a life and death.

Cassell argues that the grip of this is loosening (Cassell 2004) particularly in medicine. Medical ontology has been to view the patient as the unlucky recipient of a disease to be treated-in the strict ontology of medicine the disease is the focus of the attention-it would not matter which individual had it, the effect would be the same. In the observed practice of some members of the cancer multidisciplinary team the ontology is undermined with a prevailing attitude of a disease that is integrated into the life of the person. Many comments from members of each multiprofessional team across the cancer network demonstrated this via a degree of empathic response to the life situations of the patients, for example if the patients had young children. The observed confirmation of this was through the medical-technical roles of the pathologist, radiologist and surgeon whose speech deferred to the ontology cited by Cassell of the abstraction of a disease process.

Is it possible to control or alleviate suffering? Certainly that is often the professed aims of the healthcare professions. Suffering remains a complex issue and requires work by the person with cancer often faces suffering in terms of loss. This can be a cascade of loss such as threat to the person, failure of treatment and loss of body image (Houldin 2000). The reasons for suffering are variable and the nursing literature supports meeting the person in their suffering and moving with them as the compassionate other as they go through the experience (Byock 1994). Nurses seek to

understand the suffering of the person with cancer by offering authentic presence and empathic caring (Houldin 2000). The impact of bearing witness to suffering often creates suffering in clinicians. This suffering may cause those professionals to maintain emotional distance and not make time available to patients or focus on the treatment or disease (Klagsbrun 1994). This in turn will change the perception of the person with cancer to that professional.

As indicated in the introduction to this Chapter, suffering has recently been accorded legitimacy in the literature. Over the last twenty years the concept of suffering has become more widely accepted and a thus a component of this work.

6.2 The lived experience of advanced lung cancer in the context of suffering

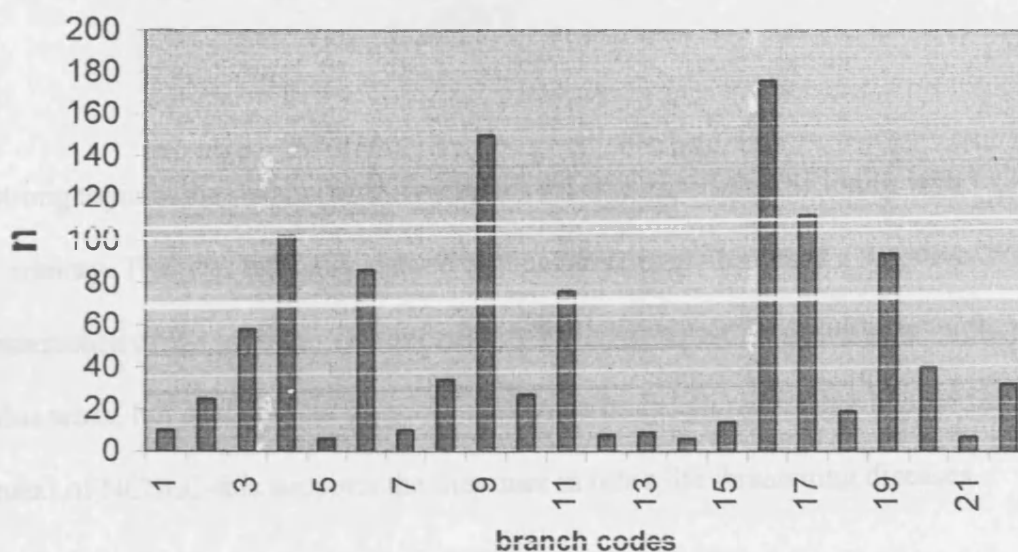
The literature can offer little that is specific to the population of advanced non-small cell lung cancer in terms of suffering. Specific searches for NSCLC and suffering (of anything other than linked purely to physical parameters) yielded one paper (Benedict 1989) which was utilised a basic Likert scale from “very much” to “none at all” arranged over five points. However the findings presented here are compared to the other literature which examines suffering in poor prognosis patients in addition to the other sources of data aforementioned.

The coded responses from respondents were a response to explicit questions asked about quality of life. These narratives have been framed within the context of either the experience or alleviation of suffering. The responses themselves are also framed as narratives, with particular reference the *having*, *being* and *becoming* of suffering. The responses in comparison with the other data begin to give meaning to the experience.

6.2.1 Psychological well-being

Psychological well-being was the most diverse and prominent root code, second only to patient experience from the interview studies. The range of coded responses is presented in Fig 6.1

Fig 6.1 Root code Psychological Well-being



- 1 Ability to adjust to diagnosis/prognosis
- 2 Ability of significant others to adjust to diagnosis/prognosis
- 3 Suffering-Inability to adjust to diagnosis/prognosis
- 4 Suffering-Inability of significant others to adjust to diagnosis/prognosis
- 5 Feeling independent
- 6 Feeling Isolated (psychological)
- 7 Suicidal ideation
- 8 Emotional distress*
- 9 Labile mood/mood swings*
- 10 Depression*
- 11 Feeling fear of unknown (e.g. suffering "what happens when you die?")
- 12 Feeling well (psychological)
- 13 Feeling relief
- 14 Experiencing other mental health problems
- 15 Change in body image
- 16 Suffering caused by uncertainty (e.g. not being able to make plans)
- 17 Feeling guilty (smoking)
- 18 Feeling guilty (other)

19 Feeling determined/not giving up
20 Feeling disbelief
21 Feeling Failure
22 Feeling Anger
*as defined by respondent

All of the respondents talked about the psychological impact of disease, particularly around diagnosis and patient experience. For this reason the responses of patient experience and psychology are not mutually exclusive.

A strong topic in the respondents' narratives was the experience of living with uncertainty. This was typically viewed as a negative experience and a negative consequence of the journey. The uncertainty of living with illness has been explored in this work, but as this is such a prominent topic it is explored further here in the context of NCSLC-this supports the literature in other life threatening diseases.

Illness related uncertainty is highly complex and as a construct uncertainty has both a perceptive and cognitive component (Houldin 2000). Mischel (1990) developed a theoretical model of uncertainty in illness organised around four categories:

- 1, Antecedent factors, which precede and contribute to the perception of uncertainty, such as illness severity, personal beliefs and social support
- 2, Uncertainty and its personal appraisal as a threat or opportunity
- 3, Problem focussed and emotion-focussed coping
- 4, Adaptation

These elements are all apparent in typical responses:

“..quality of my life....its about doing the normal everyday things....since I’ve had this....the treatment’s not been too bad, I go to work and do all the normal things I used to do, but I can’t make plans anymore and that’s really difficult. I can’t say to my girl, “don’t rush your wedding plans, get married in the summer” like she wants to instead of rushing on account of me”
60 year old man

“when I’m doing things its OK, I feel OK, its when I’m on my own, my mind just starts...I suppose you cant help it really....my mind just wanders off and I start thinking about things, you know the kids, E [husband] how are they going to get on after I’m gone.....Its hard when you don’t know when...how long”
54 year old woman

“I kept on at work, they said I could take the sick or retire on medical grounds but I’m only part time and I’d really miss it you know, its company and it stops me thinking about things”

R “how does it help?”

“seeing other people, they are a good bunch there [work] there is no point worrying about things, I cant do anything about it and I don’t know when I will get ill and have to stop”
64 year old woman

In common with the respondent quoted above, living with uncertainty and the suffering associated with this was linked with emotional distress or changes in affect:

“I get so angry at times, for no reason....I just fly off the handle...I never used to get so angry”
62 year old man

“I get so frustrated at times, I think its because you cant do anything about it, you don’t know what’s going to happen, what its going to be like”
54-year-old woman

The experience of uncertainty is personal, and has degree of significance to each person. The personal perception of uncertainty appears to play a major role in

appraisal of and coping with the situation. To understand the situation it is necessary to place the illness in its biographical context-what life was like before the illness intruded, what hopes were lost or changed (Corbin and Strauss 1998). This can also be viewed in the context of the illness calendar as described in Chapter 5, the temporal nature and expectations of the person. It is not the cancer-the disease per se- that is feared, but what a cancer diagnosis represents, the multiple meanings of a future in which cancer diagnosis will dictate.

There does not seem to be a relationship between illness severity/progression and uncertainty (Hilton 1988, Mast 1995) Uncertainty in cancer is also a personal experience. Patients need to construct personal meaning of the illness to understand the event within their own lives, the appraisal of a situation as dangerous and the perception of a high level of uncertainty and thus vulnerability, results in greater disturbance in psychological and emotional well being (Wineman et al 1996, Houldin 2000).

Because of the subjective experience of uncertainty, it is not possible to generalise from the literature which coping strategies effectively reduce the emotional distress caused by uncertainty. For the respondents, distraction was a technique mentioned by many:

“I needed people who needed me, you know, so many people were depending on me to do good jobs for them” 72 year old woman

“I had to go to work, so I didn’t allow my self time, I call it a luxury to be depressive because then you can just pack up and give up” 62 year old woman

Some respondents focused on the experiences of others-helping others cope with treatment acts as a distraction and comparisons of those “worse off”

“For C it all seems so unfair. There is no sense to that of course, anything can happen at any time but.... its almost as if her life has been stolen....” 69 year old woman

Emotional distress is a recurring sub theme, and can be seen as labile mood, depression, fear of unknown and suicidal ideation.

Two respondents talked about dealing with uncertainty and gaining control through suicidal ideation, some fear of the unknown at the end of their lives (in the embodied sense rather than purely the existential) both with sub themes of psychological isolation:

[This selection also demonstrates the ethical difficulties of interviewing those who are dying and have potential vulnerability. R=Researcher]

“well I often wonder what people are thinking, people like me. they probably do find ways of getting out”

R “hmmm”

“pulling the plug, it costs a lot”

R “Really?”

”yeah, you have to go abroad”

R ”you are very frank about it, it obviously concerns you quite a lot and you have given it a lot of thought”

“well yes, if you feel you can control it you know, and a way that is fair to everyone else, you just cant tell anyone else in the family.....”

R “yeah?”

”.....there’s no real dialogue about it. They have their problems facing up to that issue. If I could talk to them maybe I could convince them that [inaudible] with dying in horrible circumstances, what are the alternatives? They could see it makes sense.”

R “Do you see the end of your life as being like that? From listening to you, and I know we are going a little off track here but it concerns me, you seem to have decided that the end of your life is going to be a really terrible experience”

“It could be if I loose all control, and obviously I am bound to loose control. If they said at the beginning that it’s the kind of illness where you are walking down the street and you just drop dead, so, no, if it was that it would be quite a relief actually”

R “right”

“If you could just, have a heart attack or something and then you’re gone and that would be better. Have you got something that induces a heart attack? [both laugh] but really, I am gonna need more drugs and control is gonna be taken away from me because of the drugs. That’s the thing about quality of life, having control is a big part of quality of life”
48 year old man

[Interviewer further explored fears around death and psychological distress-this respondent agreed to referral by the researcher to a local psychologist and handover of some information to his local palliative care team]

or

“I cant see myself going out as a hero, I don’t know, jumping of off the white cliffs of Dover....I did see that as the practical answer to a problem that’s facing me. That doesn’t mean I am suicidal or a danger to myself, it means the answer to a problem that is my head at the moment”
60 year old man

and

“...quality of life is going to deteriorate, and there must be some level at which, and we cant get into times cos doctors wont tell you, I cant ask my doctor to terminate everything today cos I’ve had enough, well I can but they wont take any notice”

R “hmmm.....how do think quality of life will deteriorate?”

“ its going to be harder to make my own decisions....and then...having to rely on other people for everything”

64-year-old man

This shows the *having, being and becoming* of suffering in cancer described by others and explored in the beginning of this chapter (Fredriksson 1998).

The becoming of suffering is seen, the work being done by the respondents narratives show how each respondent is working through their own experience.

Quality of life as a psychological construct

Respondents' narratives use the term "quality of life" explicitly in the psychological themes. In other themes there was occasional usage of the phrase, however in the psychological theme and sub themes the term was used to describe issues around control of life choices, depression, mood changes, uncertainty and fear of the unknown:

"I don't know...the more I try to cope with it all the worse my quality life seems"

48 year old man

Is quality of life a psychological construct? From these data it seems likely. The idea that quality of life is best understood as a psychological state has gained popularity over recent years-Rapley calls this "cultural common sense" (Rapley 2003). Chapter 2 explored definitions-or lack of-when considering quality of life as an entity. As a psychological construct it makes much more sense. Cummins et al offer a theory of a biological, hard wired brain state, and Cummins (2001) provides a homeostatic model to support this. Cummins argues that since the seminal studies of Campbell et al

(1976) the view that personal or subjective well-being is made up of affective or cognitive components has become accepted. This is referred to as subjective well-being.

In the examination of six national samples, Crocker and Near (1998) concluded that the distinction between the affective and the cognitive is illusory but Cummins group have continued using this dichotomy with interesting results.

The presumed cognitive element of subjective well being from Cummings suggests that personal evaluations of this dimension are generated via the internal computations of multiple comparisons. The net satisfaction from this is described as a positive linear function of the perceived differences between what one *has* versus

- What one wants
- What others have
- The best one has had in the past
- What one expected to have in the past
- What one expects to have in the future
- What one deserves
- What one needs

Although this can be interpreted in the context of suffering and is comparable to the narratives elicited from the respondents, it is not clear what kind of mathematical operation would be needed to validate this (i.e. function of x and y) to yield net satisfaction.

Some of Cummins work is confusing; a commentary given by Mark Rapley (2003) about the internal calculation of subjective well-being with its dual component state (cognitive and affective) confirms this. Whilst Cummins insists on an affect and

cognitive component as separate, his biological (or indeed mathematical) theory relies on the combination of these distinct areas to yield *subjective quality of life (SQOL)* (Cummins 1997).

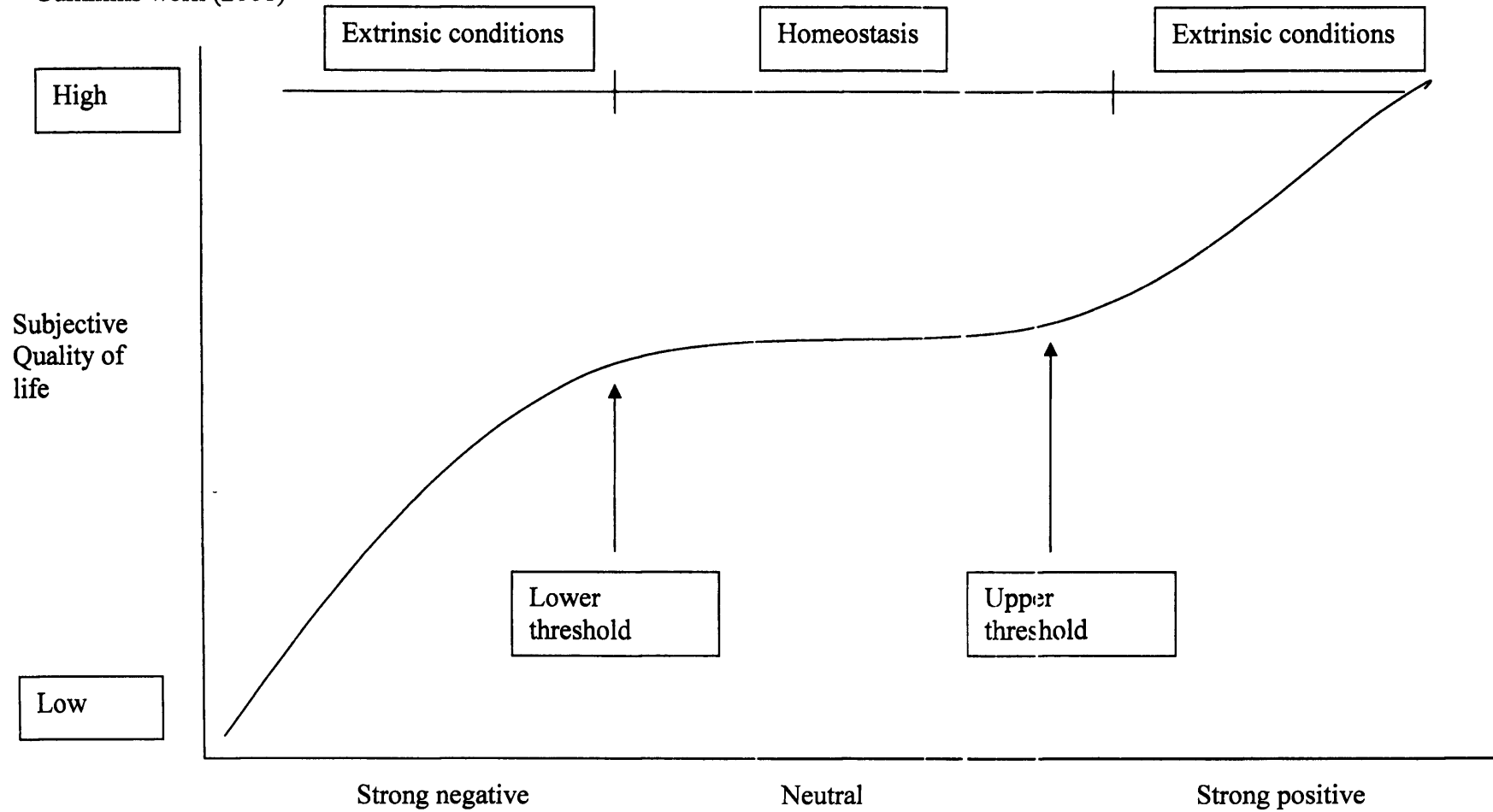
Cummins et al (2005 in press) state that SQOL can be expressed as a normative empirical standard, in the western population mean SQOL lies between 70-80% and claim that measuring such values reflects biologically based human universals (Cummins 2001). This would mean that on average people are around 70-80% satisfied with their quality of life-but 70-80% of what? What does the remainder represent? These questions are not tackled. The reason for the inclusion of this work here is that it offers a psychological origin rather than functional. Although it is difficult to grasp in its entirety, some strong themes emerge, particularly in the internalisation and process of quality of life as a psychological phenomenon. This merely re-enforces the futility of measuring such a subjective experience.

Whilst the work of Cummins, Campbell and commentators propose to describe the biological components of subjective well being-that subjective well being is not principally dependent on circumstance as the American ideologists would purport, the shared variance between satisfaction reports of the highest coefficient cited-a value of 0.65 (Bowling 1996, Cummins 2005 in press, personal communication with author) equates to a mere 42%-this does not support the studies of satisfaction as merely internal but a role for circumstance must exist.

The difference could be explained by life events. Much of Cummins work is done at equilibrium without consideration to extremes of extrinsic factors. In light of this a relationship between these subjective and objective features must be considered.

Figure 6.2. The respondents in the interview study did not “list” explicitly.

Fig 6.2. The relationship between these subjective and objective features and extrinsic factors including the possible plateau explanation for Cummins work (2001)



The data given by the LLCG QoL study via the QLQ 30+LC 17 also re-enforces the subjective nature of quality of life in the psychological context. The content analysis of the narratives of 40 patients who have undergone platinum based treatment for advanced NSCLC has provided a rich insight into the experience, the suffering associated with the experience of the disease and the treatment, the experience of negotiating the illness and treatment calendar, the psychological perspective in this instance and yet from the QLQ 30+LC 17 data very little of this experience, of what the respondents considered quality of life, is reflected.

The scoring in the domains that could be associated with suffering caused by uncertainty or other psychological factors i.e. the emotional or cognitive domains are not specifically given in any of the papers reviewed in the literature review and are certainly not examined in any detail. If these scores are endpoints, albeit secondary endpoints, to palliative chemotherapy trials why effectively are only two very broad aspects measured? Emotional and cognitive items of the QLQ 30 are firmly based in the functional domains and in the study by Rudd (Rudd et al 2005) the confidence in even these scores has dropped by the 12 week measurement (Figures 4.2 and 4.3).

The scoring from the LLCG study (Rudd et al 2005) did not show appreciable worsening in these domains but perhaps this is because the baseline was already at over 30% in both groups for the emotional domain and 14% GC arm and 12% for MIC arm in cognitive domain (baseline % of those scoring “quite a bit” or “very much”). This is surprising as the narratives are rich in such data. The sensitivity of the EORTC QLQ30+LC17 has been tested, but it is nomothetic.

This re-enforces the initial review, authors such as Montezari et al (1996) who ask patients to nominate items for quality of life scales also find that family life, health and social life are cited as important and as yet not considered in any depth by trial groups.

6.2.2 Physical well-being and the worth and work of treatment.

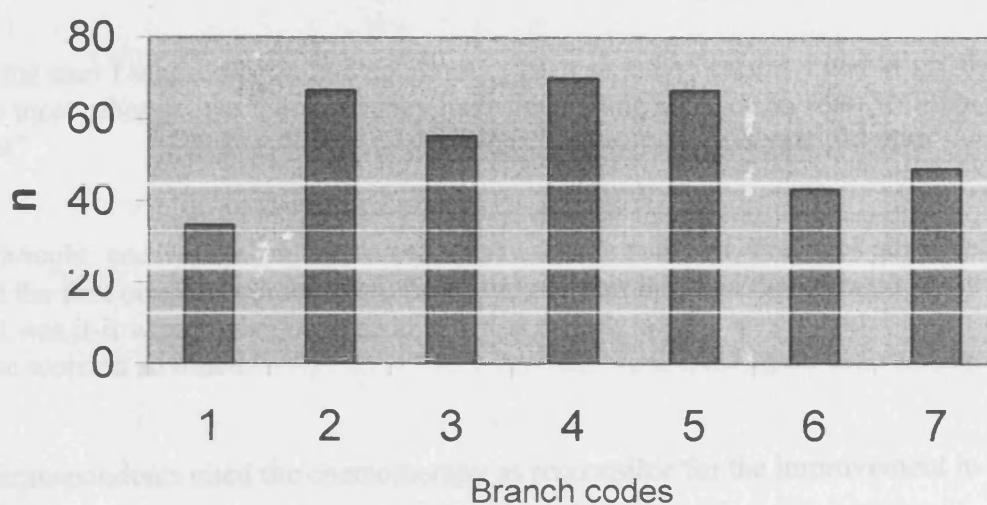
From the field notes made at MDT meetings across the cancer network (the joint cancer centre and three cancer units) the physical side effects of the chemotherapy regimens was cited in the decision making process, along with age but rarely performance status (indeed performance status was rarely recorded in the medical notes prior to chemotherapy). An observation of twenty such decisions yielded data as part of the internal peer review process. Functional/performance status was discussed only in two cases, as it was poor. Decisions were made on the basis of chronological age for example a typical response to the presentation of a 42 year old, a clinician remarked up how young the patient was and therefore it was important to try despite the poor performance status of the patient.

The most dominant factor from the field notes was the prevalence of predicting the impact of side effects of the drugs used and whether patients would tolerate these.

The interviews yield a surprising response. It can be shown from Fig 6.3 that physical well-being is remarkably understated in this group of patients, with physical narratives making up only 10% of the total responses. This could be for many reasons. The patient group was partly self-selected, 12 actively sought out treatment after being offered supportive care or older regimens in other unit/centres. These respondents had taken part in a chemotherapy trial, which has performance status and other inclusion/exclusion criteria (listed in Chapter 3). This study used the same criteria, principally that the respondents had survived the course of treatment.

Despite this if the ECOG score of patients at time of interview is considered (13 had ECOG 0, 15=1, 10=2 and 2 had and ECOG score of 3 and were in the terminal phase of their illness) this should be associated with considerable obvious physical and functional impairment. Why is this not reported by the respondent?

Fig 6.3 Root code Physical well-being



- 1 Experiencing symptoms of NSCLC,
- 2 Experiencing symptoms not associated with NSCLC,
- 3 Experiencing side effects having a detrimental affect on QoL,
- 4 Experiencing side effects not having a detrimental effect on QoL,
- 5 Feeling well,
- 6 Experiencing improvements in symptoms,
- 7 Physical effort of treatment (eg fatigue)

The respondents did report the effects of both the chemotherapy and of the NSCLC, however, they were reported without emphasis. This could be because respondents were interviewed approximately one month after treatment, after the work of the treatment and much of the negotiation of the calendar has been completed.

The typical responses involved minimising the effects of treatment. One respondent who experienced grade 2 CTC nausea and vomiting which required admission describes his experience:

“...I mean...it was no-where near as bad as I thought.....err...I was sick a few times but I’ve had worse hangovers...”
56 year old male

For many respondents the experience of chemotherapy was not as deleterious as the anticipation and fear of chemotherapy:

“at the start I was really wound up about it, I felt sick the first day I had to go, then you meet other people there and they have been going a bit longer than you-that helps a lot”
68 year old man

“I thought. god you know. this is going to make me really ill, but I was surprised, I had the first one, I remember that, they give you this drip and then you go home and that was it-it would have been good to know exactly what it was like and I wouldn’t have worried so much.”
54 year old woman

Four respondents cited the chemotherapy as responsible for the improvement in symptoms for example:

“I only had breath for six words...I would say to my children those six words and they would say ‘What did you say dad?’ and I didn’t have enough breath to say those six words again and I would get irritable and spread out to everyone around me but that’s got a lot better”
48 year old man

Although respondents talked about side effect of treatment in terms of quality of life for example:

“I think the steroids had a much more impact on my quality of life than the chemotherapy, I am sensitive to them, I just COULD NOT sleep. I would get about three hours [sleep] a night, I watched a lot of News 24!”
62 year old man

or

“the chemo did affect me-I just felt, I don’t know how to describe it really, just rough I suppose, tired and washed out. It just made doing things harder, but I was feeling down so that could have been the reason...its hard to say” 64 year old woman

As many referred to existing co-morbidity such as arthritis or migraine:

“I have had migraine for years, I have more now but I do have them when I am under stress-I have been feeling stressed about it all” 62 year old woman

Physical domains are the predominant areas of assessment for the versions of the EORTC QLQ 30, both in terms of the main body of the questionnaire and also the LC 17 lung cancer module (Appendix A).

How then do these functional measures compare with the lived experience of undergoing chemotherapy? From the Study 11 data (Rudd et al 2005), patients undergoing platinum based chemotherapy do report physical effects of treatment and disease. The LLCG Study 11 group are reported in Chapter 4, where the raw data can be found for the EORTC QLQ 30+LC 17 (see Figures 4.2 and 4.3 in Chapter 4).

The LLCG Study 11 data is rich with physical and functional data. The authors’ state that the patients in the gemcitabine/carboplatin arm experienced less nausea, vomiting, constipation, alopecia and this regimen was associated with fewer hospital admissions. These data are derived from scoring systems (the Common Toxicity Criteria (CTC) expanded NCIC 1994 Version Appendix C) or a defined factor-hospital admission. The nomothetic nature of the CTC is absolute. Although self reported, a healthcare professional grades toxicity. Some scores are based on numerical/observed data e.g. episodes of vomiting in 24 hours or renal toxicity as

measured by serum creatinine) others are much more subjective (e.g. lethargy) but all pertain to a physical sign or symptom.

Rudd et al (2005) also state that in addition to the observation that patients experienced less nausea, alopecia and other physical effects associated with toxicity Rudd et al (2005) observed “patients experienced better quality of life”. This statement refers to the overall findings of the QLQ 30 EORTC data but the word “experience” is an interesting choice. These data represent a group-the LLCG went into detail when collecting QLQ data-they used not only the QLQ 30+LC 17 but also daily diary cards (The full protocol for Study 11 is given in Appendix D) but can the homogeneous data produced from this group be termed as “experience”? In Chapter 2 the experience of cancer as subjective was supported by evidence. So what do Rudd et al (2005) and the previous studies of this design refer to when they refer to “better quality of life”?

The data from the LLCG QLQ 30 EORTC LC+17 study is comprehensive. A common feature of the EORTC based work in the literature is the limitations of the data-handling tool for the QLQ 30. Limitations are examined in Chapter 7 however need to be considered here as factor into interpretation. Baseline data with variance is available and is usually based on the two most negative responses (“quite a bit” or “very much”) aside from interpretation of these terms by respondents (how much is “quite a bit”?). the recorded score is percentage from baseline of those answering with these responses essentially determined from the raw score.

Overall there is no appreciable decline between baseline scores and those at end of treatment (12 weeks). In the physical domain there is some improvement with mean raw score of 1.87 (n=189) in the GC arm at baseline and 1.82 (n=95) at 12 weeks. There are similar findings in the symptom specific scores. Pre treatment percentage of those reporting in the physical domains (i.e. the “quite a bit” or “very much” responses) 26% and at 12 weeks 32% which does represent an increase in those reporting worsening physical function. However as can be seen from the baseline mean scores, the attrition rate should be considered (GC group 189-95=94 non reporters an attrition of almost 50%). What happened to this group? Research groups such as the LLCG factor into studies for attrition as part of the sample size/power (see Appendix D) and some of this group may simply have been lost to follow up or decided not to take part in the study, however it is more likely that this attrition rate was due to death or ill health (respondents only filled in the questionnaire when coming to the cancer centre) and so these factors are inadequately captured. This factor has been recognised by the group (Brown et al 2005) and others (Donaldson and Moinpour 2005). The interview study can contribute to this missing data in terms of experience. The method of interview was in respondents own home, this allowed poor performance (ECOG 2 and 3) respondents to take part.

Re-review of the literature in Chapter 2 reveals little mention of attrition rate (although decrease in survival is given and therefore implicit reasoning) and no paper mentioned the impact of attrition on QLQ scoring-despite the efforts to power such studies statistically.

The symptom scales exhibit a drop in percentage of reporting (representing improvement in symptom specific symptom) for example cough GC arm pre treatment of the LLCG Study 11 reports a 46% response, which becomes 22% at six weeks and 19% 12 weeks.

It could be the apparent improvement in physical symptoms coupled with the steady physical domain scores from questions 1-5 account for the low reporting of physical symptoms by the respondents in the interview study.

The toxicity recorded in the subgroup compares with the LLCG study, but yet again there is minimal reporting of these physical symptoms in the respondents' interviews. The greatest range occurred in haematological toxicity, which is defined by haematological parameters (i.e. bone marrow function) and is unlikely to produce physical symptoms unilaterally but can lead to detrimental health states such as infection or bleeding. The exception to this is anaemia and 22 respondents used words which described fatigue such as "washed out" "tired" or "no energy". Data from the medical notes informs that 15 respondents required one or more transfusions during treatment.

During observation in the field, at MDT meetings and other arenas for clinical decision-making the physical consequences of offering the patient chemotherapy were the dominant arguments. In the decision making process observed, the reasons for not offering chemotherapy to patients was noted. The physical argument was the only one offered. On occasion social reasons were given to support this decision (for example

homelessness) or chronological (as opposed to biological) age, but the primary apparent decision was based on physical status or probable decline in physical status.

From the respondents perspective the experience of chemotherapy and the physical effects of the disease and treatment were generally referred to in retrospect:

“the chemo didn’t affect me as much as I thought, I think its important to try....Dr X was pretty straight I knew it was not gonna make the cancer go away but at least I was trying...for me and the kids...at least we gave it a go and I dunno if I would have felt bad if I hadn’t tried it”
62 year old male

“I felt tired a lot of the time, but I think that was partly due to the going backwards and forwards [to cancer centre] I suppose I just knew....well its chemotherapy....you know its going to be hard, that’s what puts people off it”

72-year-old female

“I put it off for a long time, I thought if its not going to get rid of the cancer...you know, what’s the point of going through all that....I put it off for a few weeks...I was talking to B [wife] about it, she said you might as well try it-I think I did for her really, otherwise its just....well....waiting to die I suppose”

60-year-old male

“I wanted the treatment very badly, despite what the doctors at [referring hospital] said about it not being a cure-how can they expect you not to do anything? Just write you off like that? You need some hope to hang onto”

54-year-old female

Chemotherapy was seen as hope in response to questioning about quality of life. It has been shown in earlier sections how authors such as Cassell (2004) and Houldin (2000) have expressed suffering in terms of existential plight and perceptions of a lost future. Intense unhappiness results from the loss of the future and its expected profile. Hope is necessary for successful life; it is in this dimension of existence that hope dwells (Cassell 2004).

Macintyre (1979) is often quoted as a result of his work into hope

“Hope is in place precisely in the face of evil that tempts us to despair, and more especially that evil that belongs specifically to our own age and condition. The presupposition of hope is, therefore, a belief in a reality that transcends what is available as evidence”

Alisdair Macintyre 1979

Chemotherapy as a focus for hope was a recurring narrative as was chemotherapy not as an option or even a choice but a necessity. Hope is one of the most cherished ideas in western culture (Omer and Rosenberg 1997) and hope is seen as adaptive for coping (Lazarus and Folkman 1984). This is a controversial point, others do not agree that hope is always adaptive (and conversely that despair is always maladaptive) (Bennett and Bennett 1984).

The loss of hope is cited as a feature of some psychiatric disorders (Beck et al 1985) and for some is essential to maintaining a “fighting spirit” (Houldin 2000). This can be seen from some of the themes in the psychological responses-not giving up was cited as a factor in good quality of life.

The cancer nursing literature supports the value and necessity of internal sources of hope, for most part irrespective of the course of disease (Ersek 1992 Ballard et al 1997). Post-white et al (1996) describe five central themes influencing hope for cancer patients:

- Finding meaning
- Relying on inner resources
- Affirming relationships
- Living in the present
- Anticipating survival

Post-white et al (1996) also found individual variability to define hope. In addition Ballard et al (1997) found that patients with newly diagnosed and recurrent disease did not differ in levels of hope, but differed in the type of hope expressed. Patients with recurrence and thus poor prognosis tended to express hope in terms of faith whereas the newly diagnosed expressed hope in terms of medical technology. In this study the respondents, although poor prognosis patients in terms of survival, express hope through medical technology in the form of drugs (chemotherapy). If Ballard's interpretation is accurate, this may be because although the respondents were a poor prognosis group, they were also newly diagnosed.

In terms of patient outcomes, there is some evidence that hope can enhance adjustment to illness (Christman 1990, Ersek 1992, Omer and Rosenbaum 1997). Spencer et al (1997) suggest that the acknowledgement of despair over the lost possibilities of a life or future lost can activate the will and trigger hope. This is very

much embedded in specialist cancer nursing practice and was observed in interactions between patients and the Clinical Nurse Specialist in lung cancer at the cancer centre as part of the researcher's own reflection on practice as a Clinical Nurse Specialist.

As has been seen, nursing literature supports meeting the person in their suffering and moving with them as the compassionate other as they go through the experience (Byock 1994). Nurses seek to understand the suffering of the person with cancer by offering authentic presence and empathic caring (Houldin 2000). This accompanying on the journey of adaptation is recognised by the respondents.

“Its good to have someone you can just ring up and you don't have to put on a show”

72-year-old woman

“You've got to keep coming back to [cancer centre] its so nice having someone there”

68-year-old woman

The CNS's and experienced medical staff dealt with and supported hope by employing the strategies observed by Morse and Doberneck (1995). These are reality-based strategies for supporting hope:

- A realistic assessment of threat
- The envisioning of alternatives and the setting of goals
- Preparing for negatives outcomes
- A realistic assessment of personal and external conditions and resources
- The solicitation of supportive relationships
- The continuous evaluation for signs that re-enforce the selected goal
- A determination to endure

“Even though you always have to wait...its worth going to [cancer centre] I feel better going there because they always have something positive to say, I think its important to hope for the best sometimes”
56 year old man

Houldin (2000) also remarks that hope and despair are two sides of the same coin.

The coexistence of hope and despair is observed throughout the narratives and authors such as Kegan (1982) argue that one cannot exist without the other. As Spencer et al state-acknowledge the limits of hope, understand the associated emotions of despair and grief and rejoice in the discovery of new possibilities. This may seem trite; however hope is a process, a dynamic process that will change over time and circumstance. As Houldin states (2000) “For hope to be enduring and adaptive, as much as possible for each individual, it should be rooted in reality. When hope is based on illusions fuelled by false assurances it can cause considerable anguish”

Chemotherapy as work to be done

Chemotherapy was seen as a focus for hope, despite its meaning and fear. How did the respondents view the experience and reconcile medical factors (known poor response rate) to the hope given? In addition-despite recorded toxicity-what other features account the low prevalence in the physical theme?

Typical responses involved hope (as has been seen), fear, a view that there is no other realistic choice and influence of others. The nature of conversations around chemotherapy and quality of life reflect these and also the view that once the decision to have chemotherapy is made it becomes, perhaps simplistically, work to be done.

“I had the chemo because I thought it might be a chance, I didn’t like the thought of it but all happened so quick I didn’t think about it, but what else could I have done?”

64-year-old man

“I knew I just had to get on with it, no choice in the matter...I was not about to just give up and die”

69 year woman

“I suppose.....quality of life, it was a lot of work...very involved...going to see Dr [oncologist], then for the blood tests and then the chemo then start all over again, more blood tests and that.....I did feel tired but who knows why that is...it could have been the travelling...the transport used to go and pick up lots of other people so sometimes it took ages to get to [cancer centre]”

68-year-old woman

The respondents seem to “factor in” that chemotherapy would involve work, both physical work and psychological work. Doing work is part of negotiation of both the illness and treatment calendar (see Chapter 5) and as has also been discussed the social meaning of the word chemotherapy induced fear in respondents.

Respondents did not expect the experience of chemotherapy to be pleasant or even neutral-they described negative attributes to the meaning when told about chemotherapy as a treatment to advanced NSCLC. Some respondents even sought out chemotherapy despite this fear as the fear of losing control or having few options apart from death in narratives.

The narratives inform the researcher of the experience of chemotherapy and the minimisation of the physical effects demonstrates several things:

- Chemotherapy discussions occur, by necessity, at the pre treatment milestone, close to diagnosis and involve the loss of future and a social meaning of the word “chemotherapy” before professionalisation has begun.
- Respondents expected chemotherapy to involve work and be difficult to cope with.
- A temporal quality-the chemotherapy had been completed at interview and was viewed as work completed.

“...erm looking back...yeah the first one seemed to shrink it down and I think that gave me more time...Early on...see...quality of life...its not in your hands...early on the doctors told me I had 30% chance of seeing next Christmas, but I might not reach *this* Christmas and the seed was planted in that split second, and that dragged me down for six months. He was telling me I'd only got six months. Why he said it in that way...I don't know....my quality of life was instantly affected and the chemo made me think I was....I suppose...buying more time...”

48 year old man

Abandonment-treatment as social interaction

As can be seen from Section 6.2.3 below, the support of others during the cancer journey is a recurring topic. The support gained is from a variety of sources such as family and friends. It should also be noted that some respondents verbalised feelings of increased uncertainty or abandonment. This may reflect the temporal qualities of the journey-respondents were interviewed on completion of treatment, were waiting for follow up and some were waiting for disease reassessment (i.e. response). From what has been shown it is not unreasonable to expect increased uncertainty at this point in the journey.

Schou and Hewison's work (1999) examined the journey and these authors have researched the effect of treatment as a social interaction. This is reflected in Chapter 5, the work of cancer. The work of negotiating the treatment calendar and attendance at the cancer centre ensures regular contact with health professionals and other patients. When treatment such as chemotherapy stops some respondents expressed feelings of abandonment:

“while you are going for the treatment, you are going to the hospital a lot...and you see all the people there.....erm...the nurses and that.....but now I've finished, what happens now?”
56-year-old man

or a respondent in the final stages of her disease had care handed over to a local community team:

“I'm not fit enough to go on the transport now, [oncologist] said I can go back if I need to, anytime, erm....it's a bit odd thinking I won't be going there again...its nice to think I can go back if I need it.....the new Macmillan nurse is lovely but its not the same as people you know”.
54-year-old woman

Or

“I’m a bit worried about what happens next, my next appointment is in a month....and that’s....that’s the next big thing to get through”

R “in what way?”

“because it’s the results....the x-ray, it might find something...and that’s it now...like...I’m on my own”

72 year old woman

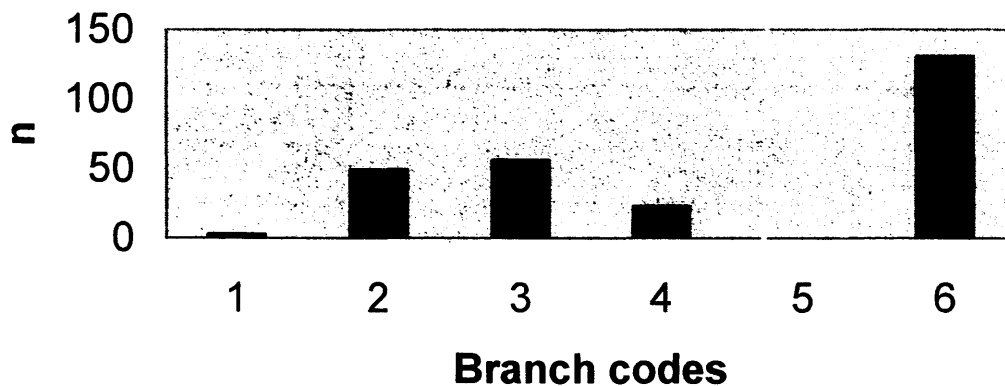
Abandonment is beginning to be recognised along with survivorship issues in the literature. It is rarely acknowledged in practice although observation of practice and reflection of practice by the researcher demonstrates how team members would arrange follow up at units or in the community if not necessary at the cancer centre. There has been observation within this study of the professionalisation of the respondents but this has been within institutional context-respondents become adept at negotiation within a specific institution. Loss of this relationship implies that the process has to start again-not from the beginning as before, but respondents see it as having a negative effect. It involves repeating some of the work completed, increases uncertainty levels and occurs at an unstable point in the journey.

Some authors argue that issues around abandonment are generated from the “either-or” idea of palliative care-that patients are treated actively or are referred to palliative care services (Byock 2000) but not both. This leads to a clear end of treatment-referral to palliative care services boundary. Even if early referral to community palliative care takes place (standard practice in the cancer centre) respondents had little contact with community teams during treatment. Authors such as Daugherty (2004) are more provocative and issue a challenge to oncologists working with patients who have advanced cancers-that the oncologists themselves present obstacles to palliative care

whilst patients are receiving active treatment, even with such a poor response rate as those with lung cancer. Daugherty (2004) views this as an ethical issue for medicine in the creation of obstacles access and adaptation to palliative care is diminished.

6.2.3 Relationships with significant others

Fig 6.4 Rcot codes Relationships with significant others



1 Willingness of family/others to discuss diagnosis/prognosis

2 Reluctance of family/others to discuss diagnosis/prognosis

3 Concerns about future of family/children (also in psychological 16)

4 Experiencing difficult reactions from other (denial, exclusion from activities)

5 Refusal to discuss with others

6 Support from family/others

Supportive relationships helped respondents cope with the disease process, negotiation of the illness and treatment calendars and the distress associated with uncertainty. This has been shown in the literature (Mast 1995, Houldin 2000).

It has been shown how hope (Post-white et al 1996) is central to adaptation to difficult life situations and that hope-affirming relationships are a way of creating this.

The observed practice of the CNS and senior medical staff affirmed the observations of Morse and Doberneck (1995) discussed in the previous section.

Is it finding these relationships with others who are closer than professionals that also facilitates hope?

Supportive relationships were given by all respondents as important coping factors.

The depth and level of these reports varied a great deal but all respondents included at least one narrative, which illustrated support of others outside of an institution.

Twenty respondents also cited experiences of others close to them who did not wish to or could not engage in any acceptance of the respondent's situations. This will be examined in the context of denial. Supportive relationships and societal role are discussed in section 6.2.6 Changes in role/social function.

Denial

Half the respondents cited denial or reluctance/unwillingness by those they considered close to them, to discuss issues around their illness as an experience in their journey.

The intensity and number of narratives varied. One powerful example has been cited in Section 6.2.1 of the 48 year old man who wished to discuss issues around his own death with his close family:

".....there's no real dialogue about it. They have their problems facing up to that issue. If I could talk to them maybe I could convince them that [inaudible] with dying in horrible circumstances, what are the alternatives? They could see it makes sense."

Denial is often cited as a coping mechanism (Ness and Ende 1994) and in a poor prognosis group is more likely to be an adaptive mechanism (Lazarus 1983).

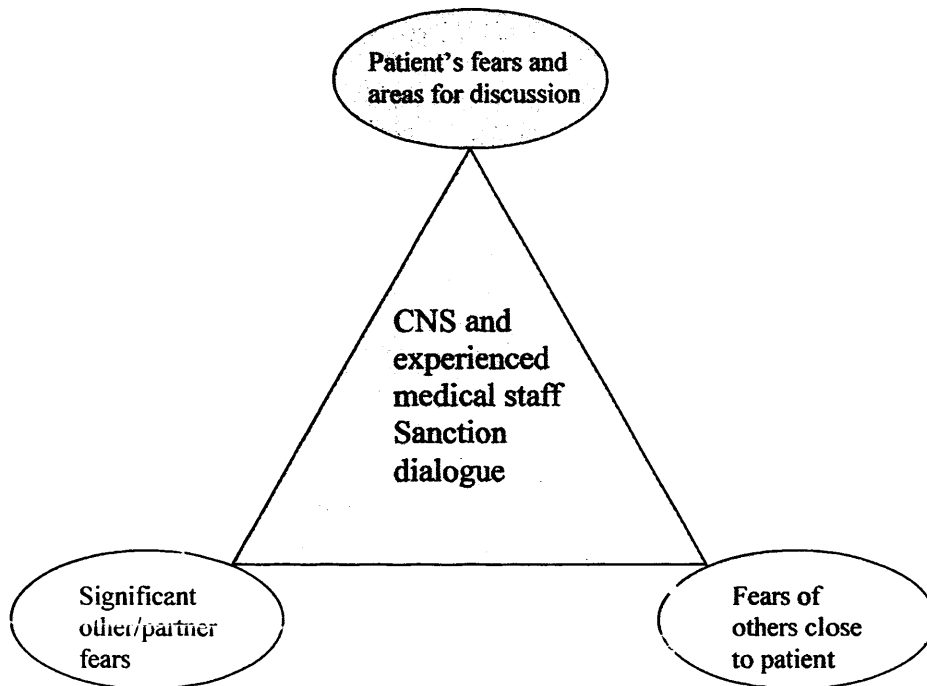
However, perhaps because of the phase of the treatment/illness calendar that the respondents were in at time of interview, they were largely grounded in reality. The

denial narratives dealt almost exclusively with significant others. Denial offers psychological protection when dealing with distressing information (Goldbeck 1997) and in cancer patients is eventually replaced with other coping mechanisms-perhaps this is why the respondents did not deny their situation.

Denial cited here by respondents takes the form of psychological protection but would become an issue if it became collusion. Observed and reflective practice of the lung cancer CNS role demonstrated an interesting set of interactions. During a four year period of this study the researcher was employed as both a lung research CNS and a CNS in thoracic surgery.

Patients did not disclose concerns for fear of upsetting their significant other and the significant other would use denial or reluctance to discuss with the patient and yet be able to articulate fears to the CNS-the CNS being the only one in receipt of both sets of fears (Fig 6.5). The CNS can then facilitate communication by giving permissions and sanctioning communication by using reflective/questioning techniques between all or selected parties.

Fig 6.5 The dynamic of the relationship in alleviation of denial



The CNS role is central to the dissolution of situations that lead to collusion in particular, at a pace sensitive to the patient and others. Techniques such as open questioning and active listening facilitated this. As denial is a technique used to protect not only oneself but also close others, it is important that clinicians not only identify denial but also the motivation for it. The denial or reluctance of others caused suffering in the respondents who experienced it:

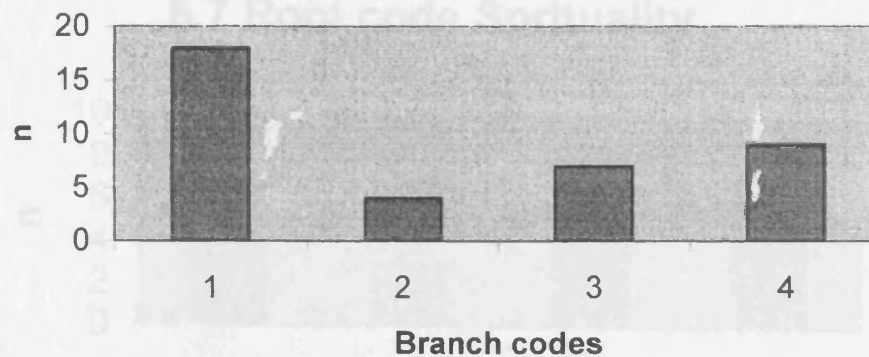
“I suppose its just too much...all at once, my husband drives me to distraction. The way....but I know my illness has had a bad effect on him as he's slowed down so much: of course he's 77.....he needs so much help now and... GOD! Before my illness he didn't need this much attention...he just can't cope and wont talk to me about it...he just goes off!”

76-year-old woman

The relationships that respondents had with others who were close to them were threatened by the experience of advanced NSCLC and this in turn was cited as a factor in quality of life.

6.2.4 Health behaviours

Fig 6.6 Root code Health Behaviours



1 Giving up smoking

2 Smoking more/not giving up

3 Deliberate change in eating habits (healthy eating)

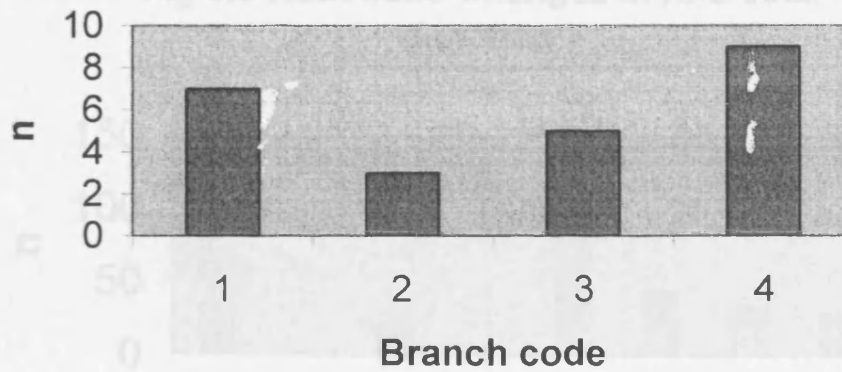
4 New belief in alternative or complementary treatment/practitioners

There were few references from respondents in terms of health beliefs. Considering previous work done by those such as Chapple (2004) and the associated guilt of tobacco use, this is surprising. Only one respondent out of forty had decided to try complementary health practices and lifestyle change in terms of diet.

The issue of tobacco could be due to the demographic of the group (2 lifetime non-smokers, 15 current smokers, 23 ex smokers), a desire not to discuss this subject area or as the trigger questions were quality of life ones, no association with the topic. This topic is further explored in context of social role and function in Section 6.2.6)

6.2.5 Spirituality

6.7 Root code Spirituality



1 Affirmation of religious belief

2 Interest in spirituality/non religious

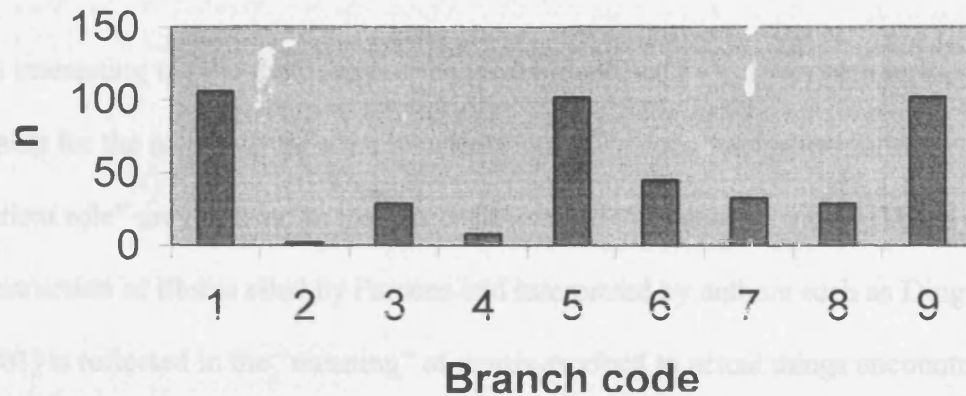
3 Interest in the “afterlife”

4 Rejection of previous religious belief

Few references were made specifically about spiritual life in the context of quality of life. The narratives which included explicit spiritual references (as opposed to existential plight which is grouped with psychological themes) all referred to spirituality in the context of religion. One respondent rejected their previous religious belief system and one had affirmed religious belief.

6.2.6 Changes in role/social function

Fig 6.8 Root code Changes in role/social function



- 1 Changes in work pattern/giving up work
- 2 Changes in financial circumstances (positive)
- 3 Changes in financial circumstances (negative)
- 4 Changes in social activity/interaction (positive)
- 5 Changes in social activity/interaction (negative)
- 6 Changes in independence/mobility (negative)
- 7 Feeling isolated (Socially/ mobility)
- 8 Leading a normal life
- 9 Suffering not leading a normal life (social role)

The literature review for this study examined social role and meaning in a broad sense. The work of Talcott Parsons (1951), Graham Scambler (1991) and Robert Dingwall (2001) have all examined the meaning of illness in society, the social construction of illness and the meaning and impact of ill health.

It is interesting to note that many of the issues identified by authors such as these are present for the respondents in the interview study. Parsons "sick role" followed by "patient role" are reflected in the cancer illness and treatment calendars. The lay construction of illness cited by Parsons and interpreted by authors such as Dingwall (2001) is reflected in the "meaning" of words ascribed to actual things encountered (for example the meaning and lay interpretation of chemotherapy and its attribution to a negative experience and hard work or the meaning of the word shadow on an x ray and its interpretation to by the respondent as cancer).

Social role and the maintenance of social role was cited by respondents when asked about quality of life. Changes in social role and activity was generally a negative experience, for example a 69 year old woman with bone metastasis who could no longer drive:

"I think having a good quality of life is about having...about being able to do things. The biggest change that came to my life with the cancer was the fact that my mobility was very restricted"

69-year-old woman

Role and social activity were used as coping techniques (such as distraction). In order to deal with uncertainty and regain control, respondents used the mundane as a focus for hope. The loss of the mundane and associated independence caused suffering both in terms of loss and in terms of distraction:

“I used to work for the council...maintenance work, you know? There was a big gang of us and we was always out and about. I used to moan to [wife] about getting up early in the morning...I used to get up at five am but I wish I could do that now.”

56-year-old man

or

“... I think its important to have a normal life.

R “In what way?

”Well, when I was diagnosed with this, I was like, well you know shattered, I gave up smoking years and years ago, I couldn’t believe it, but soon after, the next week I think, I went back to the site, and I have been working ever since. I get to sit in an office all day and the blokes are really good blokes you know, but I went straight back to work. I know some people would’ve taken to their bed but to be honest that would ave just killed me stone dead.

R “Do you think work helped you then?

“God yeah! I go to work, see me mates, we have a laugh, I am not thinking cancer, cancer, cancer all day like at hospital and it takes my mind off it all for a bit, its just normal and I am doing all right. We will be OK for money but I really don’t like the idea of giving up work.... Oh yeah, its not just the work, it’s the company I suppose, at work I am just another bloke on the site, not the bloke with cancer d’ya know what I mean?”

Some respondents felt physically well at diagnosis and even through treatment. This led to expression of “being a fraud” (72 year old woman) and guilt at being able to (or encouraged to) assume a sick role without feeling physically ill:

“I didn’t know what to do with myself really you know? Dr [GP] signed me off sick like, from [workplace] for the chemo...but I felt alright, a bit of a fraud really”

59-year-old woman

This was despite recorded CTC grade 1 of lethargy due to treatment and treatment for anaemia by transfusion before the last cycle of chemotherapy (approximately one month prior to interview).

Guilt is now becoming a recognised issue in lung cancer, but as these findings show perhaps from a different viewpoint than the link with tobacco.

“I want to describe, not what it is really like to emigrate to the kingdom of the ill and to live there, but the punitive and sentimental fantasies concocted about the situation: My subject is not physical illness itself, but the uses of illness as a figure or metaphor. My point is illness is not a metaphor Yet is hardly possible to take up residence in the land of the ill unprejudiced by the lurid metaphors with which it has been landscaped”

Susan Sontag 1977

Sontag’s work (Sontag 1977) was a reply to the growing construction of the metaphorical in cancer from the 1960’s. This can be seen today in the self help literature for example the popular books of authors like Louise Hay which continue to grow in popularity. The metaphorical basis of cancer originates (like other metaphorical origins of disease) from the lack of knowledge of cause and therefore cure (Stacey 1997). Authors like Stacey (1997) and Sontag (1991) refer to the often insidious nature of many cancers. Whilst the epidemiological link between lung cancer and tobacco was established in the 1950’s by Doll and Hill (1953) NSCLC is often advanced at presentation and remains insidious. This lends lung cancer to metaphorical meaning:

“ I keep wondering if I could have done anything to stop it, I gave up smoking twenty years ago-being self employed is stressful and wonder if that didn't help”

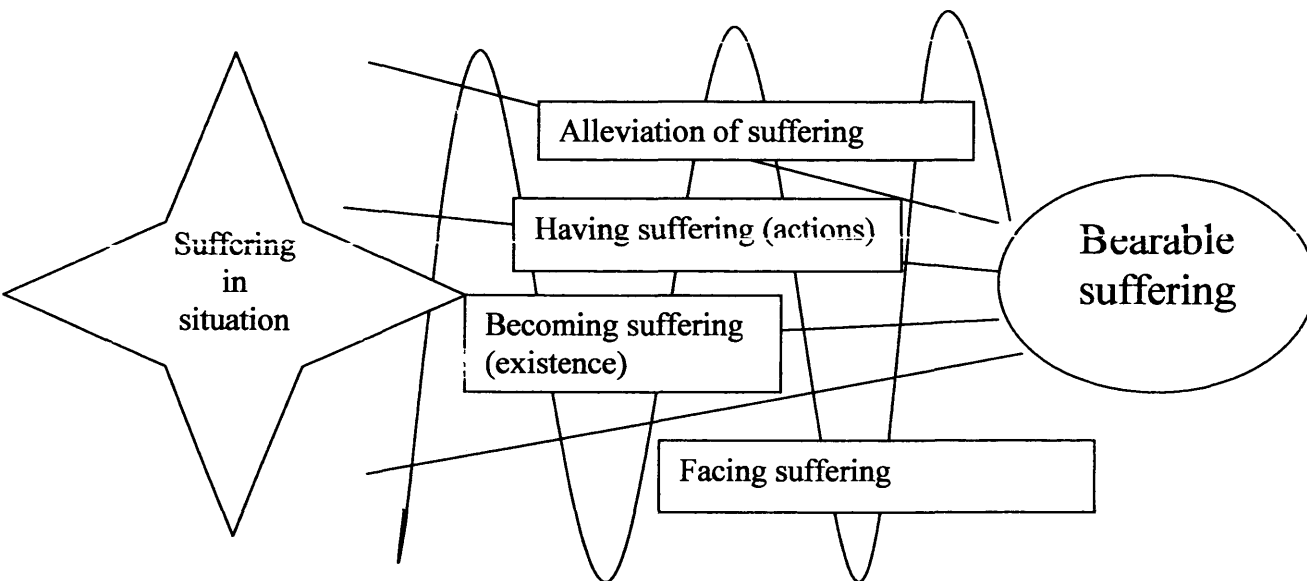
52 year old man (ex smoker)

Guilt featured in few of the narratives and this expression of guilt with the life style choice of smoking has begun to be explored in the literature (Chapple et al 2004) but by comparatively few. Two responders were never-smokers and 23 declared themselves ex-smokers at time of diagnosis and interview. Although some respondents did mention regret of tobacco use, this was not a typical response. Guilt seemed to be associated more with the fraudulent nature of assuming the sick role under false pretence and therefore not fulfilling societal obligations. Perhaps this is the reason for less self-professed guilt. However there is a paucity of literature in this area with which to compare these findings. It may be that the respondents do not view a link between smoking and guilt as a quality of life issue.

6.3 Summary

Suffering is “immobile and quiet” (Eriksson 1997) but with the support of compassionate others the person can turn toward the development of suffering (Arman and Rehnsfeldt 2003). To ease suffering the person with lung cancer needs to be able to do this in a safe environment physically, emotionally, socially and spiritually. This is shown graphically in Fig 6.9

Fig 6.9 The suffering struggle in ontological dimensions (after Arman and Rehnsfeldt 2003)



This gives meaning to quality of life in the experience of these patients.

Chapter 7
Conclusion

7.1 Quality of life in patients receiving platinum based chemotherapy for advanced non-small cell lung cancer-the contribution of this thesis.

Five years has lapsed since the start of this study, the modernisation agenda has become entrenched into NHS cancer practice in the UK, the role of multiprofessional care is recognised by the Department of Health and yet the literature in advanced NSCLC reflects the literature of the late 1990's. A return to the current (2005) literature in NSCLC reveals the continued dominance of trial data using HRQoL assessment tools such as the EORTC QLQ 30 and similar functional tools.

In many ways this is understandable. Despite its ideals of equitable good quality cancer care for all, the modernisation agenda has only increased the need for measurable outcomes-target waits, user involvement and performance are all factors, these outcomes are used as the measures of success, which both further entrench and even encourage the misuse of tools such as quality of life and HRQoL assessment measures.

In a target driven NHS the need for outcomes is influential, however within the academic writing reviewed herein, the conceptual work around quality of life constantly reiterates the controversial nature of these tools. Authors such as Ann Bowling, Mark Rapley and others who have spent a large part of their professional careers examining both global quality of life, life satisfaction and HRQoL have cautioned against the misuse of these tools. quality of life indicator tools are nomothetic and measure what they seek to measure-health related quality of life.

This study sought to examine quality of life from the respondent's perspective, to give meaning to and to articulate the experience of treatment for advanced NSCLC.

Quality of life is subjective and a wholly individual experience-should the sceptics win the day? Is it possible to construct a theory of quality of life in advanced NSCLC from the findings presented herein?

Accepting that each individual has his or her own quality of life experience is central to this. It is not enough to construct a theory, as a general theory would have to be heavily qualified. Instead two main areas have become apparent:

- *In talking to patients who have undergone chemotherapy for advanced NSCLC lung cancer there are common themes, which they associate with quality of life*
- *The HRQoL data of Study 11, whilst valid, reflects only a small component of what the respondents considered to be quality of life.*

By comparing the data generated through the interviews and subsequent content analysis and coding, the observational work and the EORTC QLQ data from Study 11 it has been possible to see concepts that are similar or dissimilar, and in many ways this has been exceeded. The work has also allowed comparison of how researchers in medicine view quality of life and how patients undergoing the experience of chemotherapy for advanced NSCLC view quality of life.

It appears that the researchers who use HRQoL tools do not view an artificial image of quality of life, but they do view an incomplete one, a view that is taken directly from the medical ontological viewpoint. The data generated from respondents reflects the multidimensional nature of quality of life, particularly the concepts of the classicists “good life” of which HRQoL is a very limited part. This can be seen from the technical literature used to support the quality of life work in NSCLC and medicine in general. An apt illustration of this is the technical literature that has roots firmly in the (reductionist) Scandinavian school and social indicator movement and yet often draws on or quotes the classical school at the start of papers.

The quality of life data in the NSCLC literature remains resolutely functional. Each of the tools used, despite individual differences, shares a functional perspective. So how can theories of quality of life for those experiencing platinum based chemotherapy for advanced NSCLC be generated? The same measures are being used without review as those used in the 1980's—they are merely repackaged and revalidated along side existing measures. In addition very few poor performance status patients are given the opportunity to record HRQoL. HRQoL tends to be measured in the clinic and supposes that patients are fit enough to attend. The high attrition rate of HRQoL studies such as those in Study 11 (Rudd et al 2005) reflected this. Note at how 12 weeks from randomisation the attrition rate for QLQ 30+LC module has risen to 53% and 57% in each chemotherapy group. 12 weeks from randomisation is the approximate time at which respondents are interviewed. The interviews took place in the respondent's home allowing capture of the poorer performance status patients. In this way this work has contributed in capturing a varied group of performance status patients' responses.

7.2 Quality of life-The Scandinavian School versus the Classicists

A variety of themes have been generated from the content analysis and much of the findings are psycho social or experiential rather than the functional findings of the EORTC QLQ 30+LC 17 domains. Finding comparative data between the QLQ 30 data and the thematic analysis is a challenge. This is partly due to the perception and meaning of quality of life in an academic and societal context.

“ The idea of quality of life as a measurable indicator of the great society’s achievements has, since it’s inception, been inseparable from the notion of progress”

Mark Rapley 2003

The assertion of Rapley (Rapley 2003) reflects the growing trend of authors in quality of life research to reflect upon the concept of quality of life. This comment is an allusion to the dominance of the social indicator movement from which the functionally focused so-called “Scandinavian School” (Rapley 2003) originated and has been shown in Chapter 2.

The Scandinavian School concept of quality of life is based on the writings of authors such as Drenowski (1974), Erikson (1993) and the application of this work, particularly in cancer, by authors such as Niels Aaronson (Aaronson 1993).

Erikson and Uusitalo (1987) frame quality of life as the resources needed for the individuals welfare, such as money, physical energy, social support. Scandinavian thought focuses exclusively on objective indicators of living. This conceptualisation

of quality of life fits with the desire to establish outcomes in Medicine, Nursing and Psycho-oncology (Holland 1998) and it is therefore unsurprising that this approach has gained authority.

It is apparent from the results presented in Chapter 4 that the dichotomy of quality of life as interpreted by each of the different theoretical schools is illustrated. The Scandinavian School which focuses on functionalism and is the predominant method of assessing quality of life in the context of clinical trials, and indeed, almost all of medicine as it adopts the medical ontology cited by Cassell (Cassell 2004) to a high degree.

A review of the quality of life literature in Non Small Cell lung Cancer demonstrates the dominance of such thinking. This is because the vast majority of literature examining quality of life in patients with advanced (non operable) NSCLC is originated from clinical trials funded by agencies such as the pharmaceutical industry or independent research groups. Scientific work needs measurable outcomes and this has contributed to the rise and dominance of the Scandinavian School and its associated philosophy.

The literature reviewed for this work, although rich in functional quality of life data, makes no reference to the social indicator movement in the clinical papers. Some background information is given in most papers on the post war WHO definition and President Lyndon Johnson's speech in the 1964 (for example Aaranson et al 1988, 1991, 1993) but only as much as is given to Aristotelian (i.e. Classical) ideas in the introductions of the papers reviewed.

This finding echoes the work of Haura (Haura 2001) in which NSCLC trials were reviewed and only brief mention was given to quality of life as defined in any convention, despite the assumption of the authors, that chemotherapy for advanced NSCLC is palliative. In addition when Kong and Gandhi (1997) reviewed 265 papers reporting HRQoL assessment in clinical trials, only 21% reported any HRQoL validity data. This has also been seen in this study; very few studies reviewed provide definitions of QoL, sensitivity or validity data.

The main milestones of development of quality of life assessment tools and their influence or non-inclusion into the assessment of quality of life in people receiving chemotherapy for advanced NSCLC have been demonstrated in Chapter 2. However the acceptance of the dominance of the functionalists and the Scandinavian School as a principal influence is only now being recognised as more medical sociologists examine the literature. The common theme of the Scandinavian School and its founders is that it applies quality of life as individual welfare needs with outcomes, but on a societal level- does this mean it is an appropriate concept to apply to the individual person dying of cancer?

Much of the literature, particularly that which views quality of life “measurement” with scepticism (for example Downie 1999, Hunt 1999) reiterates the subjective nature of quality of life. It is the *individual* nature of quality of life which is the flaw of much the work of the functional, social indicator and societal movement and this individual nature is now becoming recognised in the literature-it is not enough to simply:

“...represent social facts independently of personal evaluations and in contrast to subjective indicators which rely upon the individual perception and evaluation of social conditions” (Noll 2000).

The literature available in NSCLC quality of life is almost exclusively consists of data from clinical trials and therefore the functional Scandinavian School. The QoL literature from a sociological perspective is almost exclusively classical but not in the context of NSCLC. The generation of a theory of quality of life in patients receiving platinum based chemotherapy must therefore be embedded in both schools.

Quality of life as an academic concept is still young. Although the classical theorists and philosophers have discussed the idea of quality of life and the good life for centuries, as an academic area of study in the reductionist sense it is surrounded by “conceptual confusion” (Rapley 2003). This can also be seen in attempts to clarify the conceptual confusion of quality of life. The work of Mary Cooley (Cooley 1998) who has undertaken one of the few qualitative studies in advanced NSCLC goes some way to tackling this issue.

Conceptual clarity is an enduring problem in quality of life studies and is likely to be so until a consensus exists. The futility of reaching a consensus in such a subjective area has been debated and beyond the remit of this work. However this study has given insight into the experience of quality of life in advanced NSCLC, particularly in the context of chemotherapy and adds to current work by taking a mixed method (i.e. not exclusively HRQoL) approach.

From the data generated in this study the respondents generated four core themes when quality of life was discussed. These themes are reflected in an extremely limited way by current HRQoL tools, if at all. This thesis adds to the body of knowledge by eliciting these themes.

The core themes from the respondents were:

- The work of cancer
- The lens of diagnosis
- Suffering
- The worth of treatment

These are summarised as follows and should be included when any debate where quality of life in patients with non small cell lung cancer is aired.

The work of cancer

This elicited most of the responses in the interview study. The amount of responses and the rapidity of saturation was the reason for interviewing outside the study group. The experience of being a patient and the work involved in having cancer was cited as a factor of quality of life. Respondents found that negotiating the illness and treatment calendars required effort, particularly the beginning of the journey, before they had learned the systems of the institution, which, once familiar with, they could have some control over.

Gaining access to health professionals at crisis points was also important to respondents. Gaining reassurance in the early stages, having a treatment broker (usually the Clinical Nurse Specialist) who dealt with the complexities of the treatment calendar and normalised (as opposed to pathologised) the distress of cancer.

Having access to treatment brokers such as CNS's or medical staff was valued in terms of quality of life as the respondents perceived that staff made life easier for them, at a time of distress and alienation these professionals were seen as caring and having the respondents best interests as central to the care they provided. This has to be considered in the light of the atrocity stories revealed however which is discussed in the lens of diagnosis.

Taken in the context of the Milestones identified by the Department of Health (2001) there are clearly areas in which input from professionals and service improvements could be targeted to improve quality of life as described by the respondents. This is

shown in Fig 7.0. HRQoL does not capture this element of what respondents considered a major influence on quality of life. Patient experience is largely measured through patient satisfaction surveys, which are also limited in scope and, for many clinical environments, availability and specificity.

Fig 7.0 The Lung Cancer Care Pathway (DoH 2001). The Ten Milestones. Influencing Quality of life factors at different points through practice-minimising work.

Tackle causes of atrocity stories
 Accurate information given

Suffering: Psychological, Social, Emotional and Physical

Confluent, timely co-ordinated care with access to the appropriate professionals

Specific information and support through suffering

Pre Diagnosis	Diagnosis	Chemotherapy	Pre surgery	Post surgery
Discharge	Radiotherapy	Follow up	Terminal care	Bereavement

Abandonment

Abandonment and change

The lens of diagnosis

Contrary to the findings of qualitative work in other cancers, the respondents did not narrate with a beginning-middle and end. The respondents typically returned to diagnosis throughout the narratives. They viewed the rest of the journey through the lens of diagnosis and compared experiences, particularly subsequent experiences with professionals, back to the time of diagnosis.

The narratives of diagnosis typically took the form of atrocity stories as examined in Chapter 5. Not only were these experiences centred around the pre and peri diagnostic element of the journey, the professionals were imbued with characteristics that were negative (e.g. amoral, cold or incompetent). The respondents recounted these narratives, generally around first contact with healthcare for this episode.

Placing these stories in context is difficult. It could be argued that at such an emotive time, emotions such as anger would influence the respondent. This is hard to dispute and the nature of this study is to allow the respondents to tell their story. If this interaction did provoke anger, that is surely a valid experience.

However the respondents did not emote anger-more a sense of injustice, particularly those who were not offered or refused chemotherapy at the time of diagnosis or those who had to make repeated visits to their GP with explicit symptoms. Other expressions in the context of atrocity stories included the inconstancy or inaccuracy of information that caused anxiety, mismanagement of the treatment calendar (for example repeated visits to clinic for results which were not available) and coldness,

insensitivity, embarrassment or a sense of being rushed when diagnosis was communicated.

The respondents recount how at diagnosis their experience is re-organised by the medical staff and how the medical staff set the agenda to fit in with first the illness and then the treatment calendar. The respondents organise their illness narratives as a coping mechanism, which is then upset. This means that healthcare professionals do not consider large sections of what the respondents considered important to quality of life in the early illness calendar. The early phase or lens of diagnosis becomes the mechanism through which subsequent encounters are viewed and can also be seen at the end of treatment when some respondents expressed abandonment.

HRQoL tools do not reflect this experience or facet of quality of life directly. In current practice this area is not examined and yet is considered a factor influencing quality of life by respondents.

Suffering

Respondents expressed the suffering of cancer as cited previously by other authors in the narratives of quality of life. In particular the respondents expressed ways of dealing with suffering as being influential in the quality of their lives.

Physical, psychological and social factors contributed to suffering, the meaning of cancer, the suffering of loss such as perceived loss of future, loss of social function, loss of societal role and loss or change in close relationships such as the denial of close others all contribute to the suffering experienced.

Physical suffering is reflected in the HRQoL assessment tools. The QLQ 30+LC 17 gathers information about HRQoL in this group but as has been shown; the respondents focus few of the narratives on physical experience of treatment or even of lung cancer, in some cases despite recorded toxicity or symptoms. This implies that the QLQ 30+LC 17 is not reflecting quality of life in this instance but rather a small fraction of what is considered quality of life by the respondents. The QLQ 30+LC 17 has domains which are designed to assess quality of life in terms of role and psychology. The validity of these domains is not questioned here but the scope of these domains is. They are extremely limited. Psychological issues have a strong presence in the narratives and these are not reflected by the QLQ 30+LC 17.

Access to knowledgeable, reliable, credible and approachable healthcare professionals was cited by respondents as a factor in quality of life in the context of the alleviation of suffering. This was from different perspectives. Trust, attitude and credibility of

professionals was important to respondents, particularly to those who had recounted atrocity stories. Accessibility and negotiation of the treatment calendar was also given as an influencing factor as was handling difficult situations such as reluctance by close others to discuss illness, treatment and prognosis.

Normalising and acknowledging the distress of cancer was also cited by respondent in the context of discussions in the psychosocial dimension of the work.

Professionalisation of the respondents (gaining knowledge about NSCLC and treatment, becoming familiar with the mechanisms of the institution) and the process of doing work contributed to quality of life in terms of coping with a difficult situation. The struggling act of suffering demands a compassionate other to confirm the suffering (Lindholm and Eriksson 1993) which might lead to meaning in communion (Rehnsfeldt 1999). The value of CNS as treatment broker and the compassionate other was integrated into the narratives, as was the value of the relationships in terms of honesty and trust with the senior medical staff. This value of honesty and trust as integral to the relationship with staff extended to the acceptance of truth telling when the news was bad.

The reasons for suffering are variable and the nursing literature supports meeting the person in their suffering and moving with them as the compassionate other as they go through the experience (Byock 1994). Nurses seek to understand the suffering of the person with cancer by offering authentic presence and empathic caring (Houldin 2000) as discussed in Chapter 6. The impact of bearing witness to suffering often creates suffering in clinicians. This suffering may cause those professionals to maintain emotional distance and not make time available to patients or focus on the

treatment or disease (Klagsbrun 1994). This in turn will change the perception of the person with cancer to that professional. This can be linked back to the lens of diagnosis in the context of atrocity stories, for example the use of words like embarrassment by respondents when describing the experience of diagnosis.

The worth of treatment

The worth of treatment was the fourth theme derived from the comparative data. Respondents viewed the treatment as a focus for hope and as a social interaction, including professionalisation. The physical work of treatment was minimised by participants in the interview study despite observed and recorded toxicities during treatment.

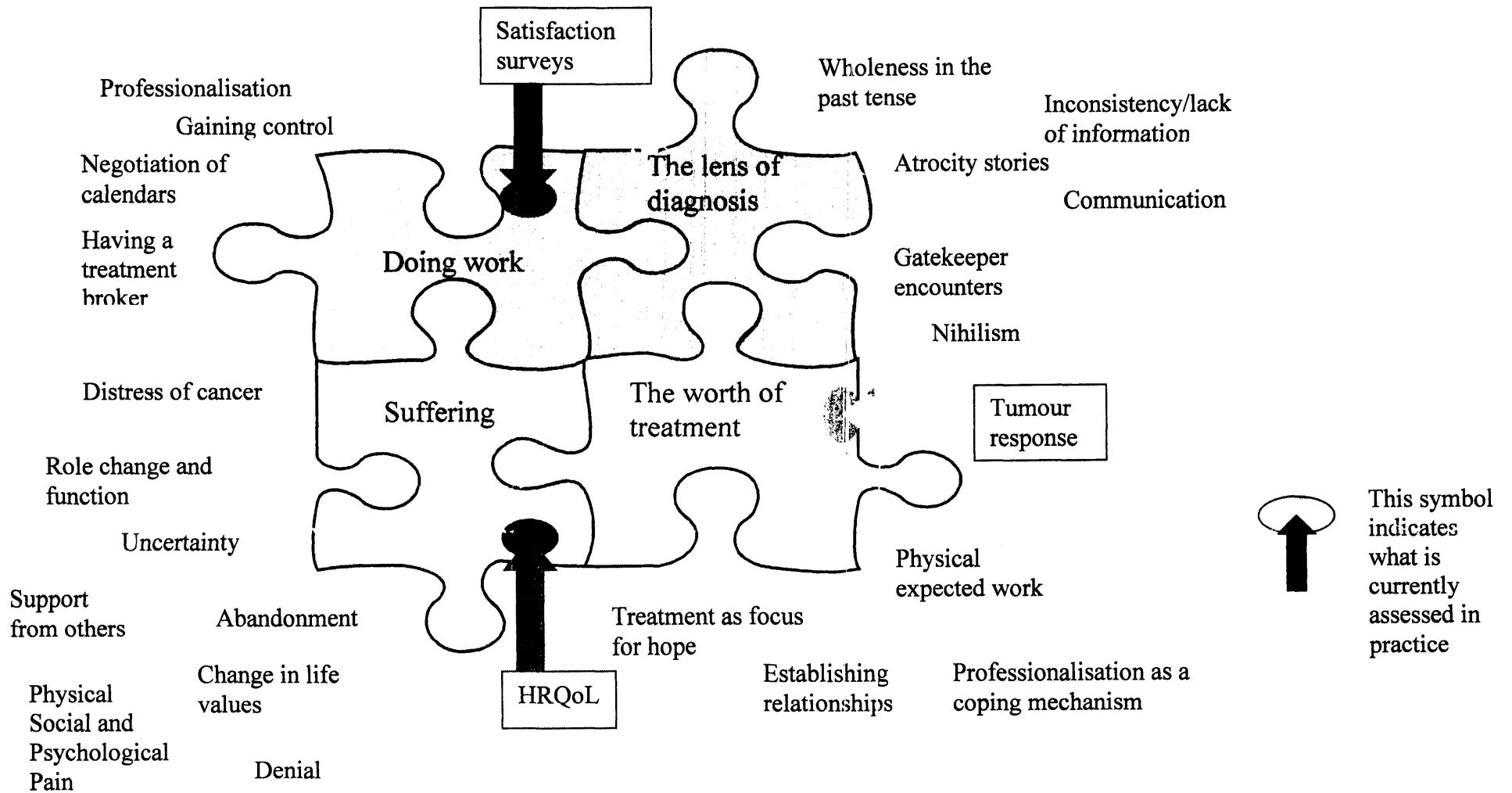
Respondents generally expected chemotherapy to be hard work and had already completed the work at time of interview. The issue of respondents minimising the physical effects of chemotherapy has been raised in the seminar series that has accompanied this work. The question of whether respondents minimised chemotherapy adverse effects for fear of discontinuation of treatment has been considered. Respondents were interviewed outside the original study group so as to gain a clinical independence from the researcher-the researcher had no clinical contact with the group interviewed apart from a researcher-respondent relationship. The researcher identified herself as such, only revealed a professional background if questioned and asserted independence from the MDT, this is also reflected in the participant information sheet (Appendix B). The other factor to consider is that respondents had completed chemotherapy at time of interview and so discontinuance was not a threat. It was not standard practice in the centre to consider refractory treatment at the time of the interviews.

Respondents may have not considered physical side effects, although experienced, to be associated with quality of life in this way. Respondents recounted how they expected chemotherapy to be physically difficult. Some respondents experienced better symptom control as a result of the chemotherapy and this is reflected in the LLCG QLQ 30+LC 17 data quite clearly. As twelve of the respondents were self selected and sought out a centre where treatment would be available, treatment in the context of hope and adaptation to the suffering of cancer seems a plausible explanation.

The worth of treatment in practice is measured only in terms of tumour response, which given the effectiveness of current regimens in terms of response seems simplistic. It is time to look at chemotherapy more widely as not only a possible treatment for NSCLC but also as a source of hope and adaptation at a time of suffering. For the respondents the expected effort and the attempt allowed time for the patient and family to adapt.

The four themes are shown in Fig 7.1 as what respondents considered facets of quality of life when receiving platinum based chemotherapy for advanced non small cell lung cancer.

Fig 7.1 The comparative properties of quality of life in patients receiving platinum based chemotherapy for advanced NSCLC



These findings reflect the subjective nature of quality of life. The core themes have evolved to give insight into the experience of NSCLC from the conceptual arguments of psychological perspectives to applied clinical practice and the social indicator movement.

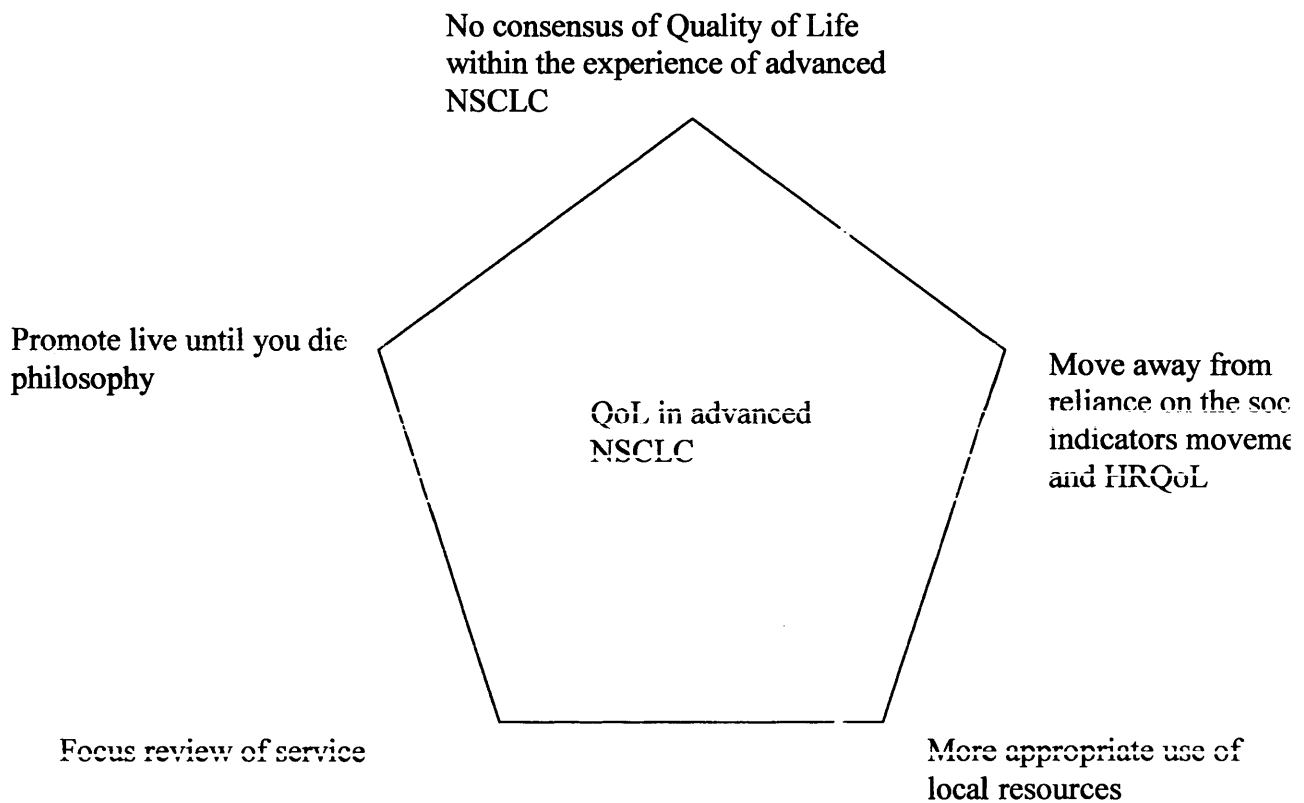
7.3 Implications for practice

From these data, the themes that predominate as factors of quality of life for the respondents were largely psychological factors or experiences of being in the role of a patient.

The respondents identified psychological factors which are often pathologised such as labile mood, but can equally be argued to be part of the distress of cancer given its meaning in society. Living with uncertainty and loss is considered to be important in narratives associated with quality of life rather than physical functioning. The cancer journey and the negotiation of the illness and treatment calendar constituent a core theme of quality of life for these respondents.

This infers that considerable improvement in quality of life as defined by the respondents could be achieved through service improvement and the cancer modernisation agenda. Cancer treatment calendars and cancer care need to be integrated to achieve confluence and improve quality of life. The recognition of the importance of the key worker/treatment broker as a central role needs to be affirmed. The CNS as central to psychological support needs to be recognised. The importance of the source of atrocity stories also needs to be recognised and tackled to improve quality of life in patients receiving chemotherapy for advanced NSCLC. Timely and appropriate information and an opportunity to discuss the experience needs to be available. For these participants, the negative experience of chemotherapy was expected; the factor that impacted on their quality of life was the amount of disruption it caused and the support available. Implications for practice are shown in Fig 7.2

Fig 7.2 The implications for practice-factors for consideration in practice



Although the modernisation agenda has been an active part of cancer services in UK for five years, and covers the common cancers such as lung cancer, there has been little specific work for this group of patients and yet the provision of services is cited by respondents in this study as being important to quality of life.

7.4 Limitations of the study

The literature in the area of NSCLC is limited in terms of quality of life. The trial data is plentiful but functional. This was despite utilising the specialist search mechanisms employed in Chapter 2, specialist historical and archive searches performed by library professionals at University College London and the British Library. This was in addition to the conventional searches performed by the researcher as documented. A search of the Steinberg Collection, a collection of nursing and related theses held by the Royal College of Nursing library that dates back to the 1950's revealed no thesis that had lung cancer in the title or as a keyword. Lung cancer remains a poorly funded area of research and despite awareness campaigns has made little progress in eliciting public support.

The lack of consensus at an academic level was both a limitation and an asset to the study. A limitation as the original aim was to test a hypothesis and essentially the sensitivity and use of the QLQ 30+LC 17 in this group. The lack of consensus means no "gold standard" can be ascertained and there is no benchmark at a level other than HRQoL. A respondent asked the researcher "How do you measure quality of life?" This limitation allowed the study to open up, to explore quality of life and the experience of chemotherapy at a much more global level and to examine its meaning in the context of the patient experience.

The group of respondents were self-selected. Although convenience sampling was used to recruit, twelve of the respondents had sought chemotherapy after a second opinion at the cancer centre. In qualitative research the aim is to gain insight to the experience rather than produce a representative sample and results that can be generalised into the wider population and so this is more of a consideration than a limitation.

The authors' inexperience of qualitative methodology can be considered a limitation to the study. Data was collected pre study however the formation of hypothesis and testing of hypothesis was the original aim of the study. This is why the format of the study and theses (i.e. inclusion of a literature review) has not been changed. However in terms of data collection and handling this lack of experience is likely to be an influencing factor. For example, a reason for performing the study was the observed reaction of respondents in the original trial studies to the QLQ 30+LC 17. The reactions of respondents on completing the questionnaire for the first time included levels of distress at the questions such as "Have you coughed up blood?" This would sometimes provoke a response question to the researcher of "will that happen to me?" This data was never recorded

The data generated from the QLQ 30+LC 17 should also be considered. From this HRQoL data in the original study by the LLCG there is no appreciable deterioration of global or domain HF QoL. In fact within some domains there is an improvement in HRQoL. It is necessary to be cautious of this data in so far as it too is incomplete. The attrition rate for the QLQ study was high, probably due to severe decrease in function

and death of participants. This means that an incomplete picture of HRQoL is presented. This has been recognised by authors as discussed herein.

The sample size used for content analysis is large for this kind of study, although not exceptionally so. However redundancy of data is apparent-saturation was reached with fewer than the 40 participants. This repetition of data can be seen in the analysis or over analysis and further fragmentation of the transcripts. This is why principally the thick layer of data has been presented here. Strauss and Corbin warn against falling into an “analytic rut” but this seems to have happened in this study. Data as language is invisible-in this study the words are analysed but context may be lost, although memoing took place no conversation analysis was undertaken. This may be a limitation in so far as the work remains superficial.

The handling of data from respondents was done with a single reviewer (the researcher) and without the benefit of social science packages such as SPSS or NUD*ST. This is unlikely to be considered best practice in social science or anthropology as it is not given as a method in any recent literature, however it was standard practice in the past. The primary reason for this method of data manipulation was budgetary, the study was unfunded.

Direct comparisons of the data generated are challenging enough but the study also loses some of its power due to the lack of theoretical comparisons the researcher was able to accomplish. Theoretical comparisons are necessary particularly when direct comparison is not possible, to allow relationships to become apparent. This is a

limitation to the study as the study becomes less rich for the lack of depth of theoretical comparisons herein.

The researcher's reflection

After reading the thesis of others, particularly in the Steinberg Collection, I have noticed that many theses and books in the areas of medical sociology, nursing and anthropology are written in the first person. This thesis has grown from a direct comparative study, in the positivist tradition. I do not have the necessary background in philosophy and have been educated as a scientist (taught to value empiricism), what is required for this work is conceptual clarity of quality of life. It is not usual to write in the first person in academic science and therefore I have not done so in the rest of this work. As the interviews and indeed the whole experience was part of my own personal and professional experience, it could have been integrated into the work as reflection. As I have not used reflection to a great degree apart from examining my own practice as a CNS, there is a possibility that something is lost from the work. This might be considered a limitation.

My original notes from almost five years ago tell me my original aim was "to add richness-to understand the perception and experience in addition to quantitative quality of life data". Instead the richness of the experience of the respondents has become paramount with the quantitative EORTC QLQ 30 data only a facet of what a person with incurable lung cancer considers quality of life. This work has however profoundly influenced my own practice in caring for lung cancer patients and patients undergoing thoracic surgery. I have led service redesign and created a patient centred service as a result of this work (Leary and Corrigan 2005)

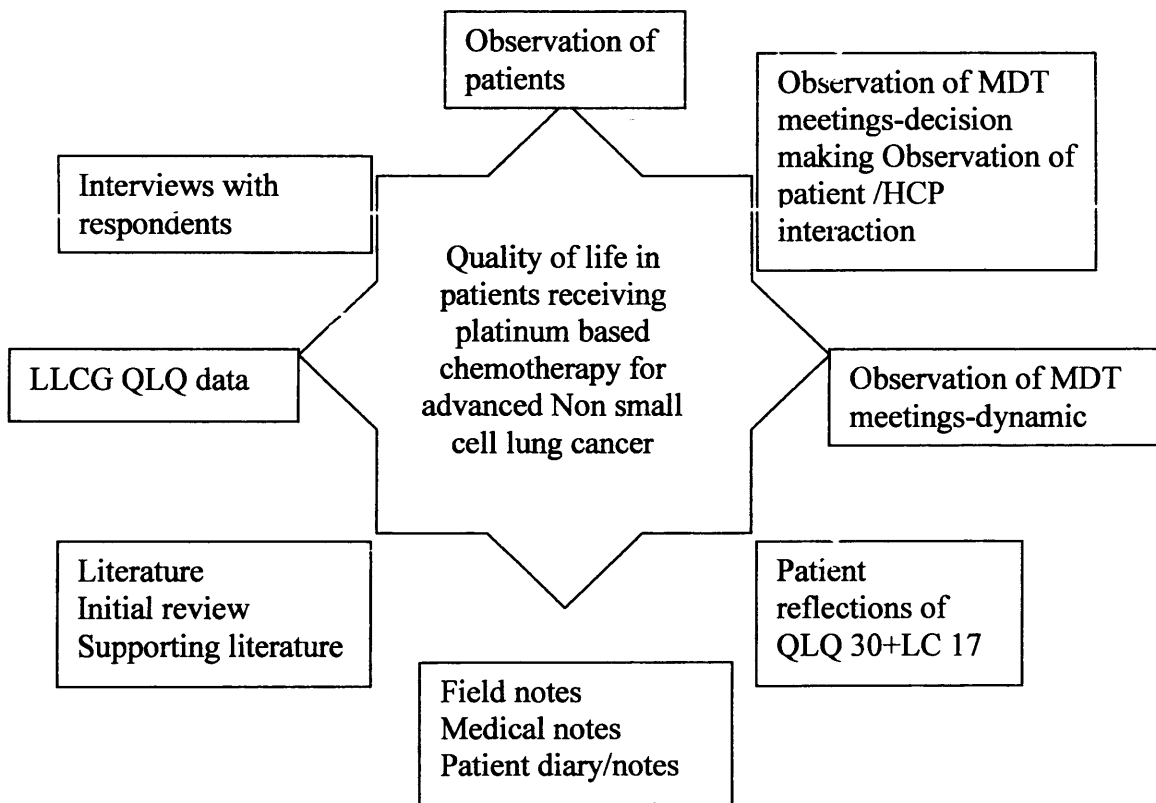
The work has also been influenced by two factors. Being a participant observer within the service to a degree has influenced my thinking (particularly the motivation for the study). The influences are shown in Figure 7.3 below

Influences

Data was collected from a variety of sources for comparative use to describe of quality of life in NSCLC.

Fig 7.3.Sources of data and influences that acted on the researcher.

Fig 7.3.Sources of data and influences that acted on the researcher.



In addition another influence, particularly in interpretation, could have been my own cancer experience from March 2004 onwards. This could be a limitation but reliability through tabulation should have countered this.

7.5 Areas for further study

This study generated huge amounts of data, which could be reviewed and re-processed as an independent study. Each theme could also be studied in more depth by experienced researchers who are skilled in drawing theoretical comparisons.

Each area elicited by this study could be examined in depth and using different methods, for example conversation analysis. More work is needed around a workable consensus for quality of life in clinical settings (it is unlikely the patient experience would appear in the social indicator movement in the well population) and more work needs to be done in terms of concept analysis and clarification from a nursing and/or sociological/philosophical perspective.

More work is needed around specific themes elicited such as the atrocity stories and negative experiences in the early illness trajectory. The focus of technical rationality (that professional activity is problem solving by application of rigorous scientific method-Donald Schon 1991) needs to be challenged if this aspect of care is to be improved but there is little evidence to support the value of work other than the technical. It has been shown that problem solving for these respondents involved much more than technical rationality but it can be seen from the stories and the lens of diagnosis that this is where the experience is located.

The experience from a family or significant other perspective would also be a valuable study. There has been some work in the experience of families and caregivers in the palliative setting, but these are mostly in the last days of life.

Work with healthcare professionals would also be of interest. Areas such as the emotional labour involved in a therapeutic relationship with patients with advanced NSCLC, the perceptions of staff with respect to diagnosis and atrocity stories, the perceptions of staff and the quality of life of their patients, how staff deal with issues in the context of the modernisation agenda and the Department of Health reforms, staff workload in lung cancer and issues around trust, truth telling and the experience of care would be interesting topics for further study and offer valuable insight.

7.6 Summary

This work has only begun to touch upon the conceptual confusion that surrounds quality of life, to draw upon some elements of the literature and compare these to the data generated by the study contained herein. This work does, however, contribute to the practice of caring for people undergoing platinum based chemotherapy for advanced non-small cell lung cancer. It does this by providing insight into the experience, by allowing the people undergoing the experience to speak and by drawing the attention of the practice community to the limitations of current methods of quality of life assessment and their possible, albeit unintentional, misuse. Any discussion of the quality of life in this group of patients should include the four core themes elicited from the respondents of patient experience, suffering, the experience of diagnosis and the worth of treatment *from the patient's perspective*.

The NHS Modernisation agenda covers many of these areas, certainly the patient experience but the flaw in the method of modernisation is that it remains target driven and yet from the interviews with respondents, quality is a important factor. It is difficult to quantify what patients want and need and therefore difficult to address these issues in a target driven culture. The two week wait stipulated in the Cancer Plan (DH 2000) between seeing a GP with the symptoms of cancer and seeing a specialist are only of benefit if the GP recognises the symptoms of cancer in the first place. They are only of benefit if the hospital specialist the patient has gone to see is professionally current.

The issues around quality have yet to be addressed. For example is the MDT in reality a team or do those members who are the most vocal or those who hold the positional

authority making the decisions? Are patients really involved in the decision making process? What mechanisms are in place to ensure a broad quality of service? Are quality assurance mechanisms such as the peer review process nomothetic in the same way that HRQoL is?

The way forward in quality of life assessment in advanced NSLCL may be to move away from the functionally dominant scales and questionnaires. A return to fundamental measures of which quality of life questionnaires are derivative may be the answer here.

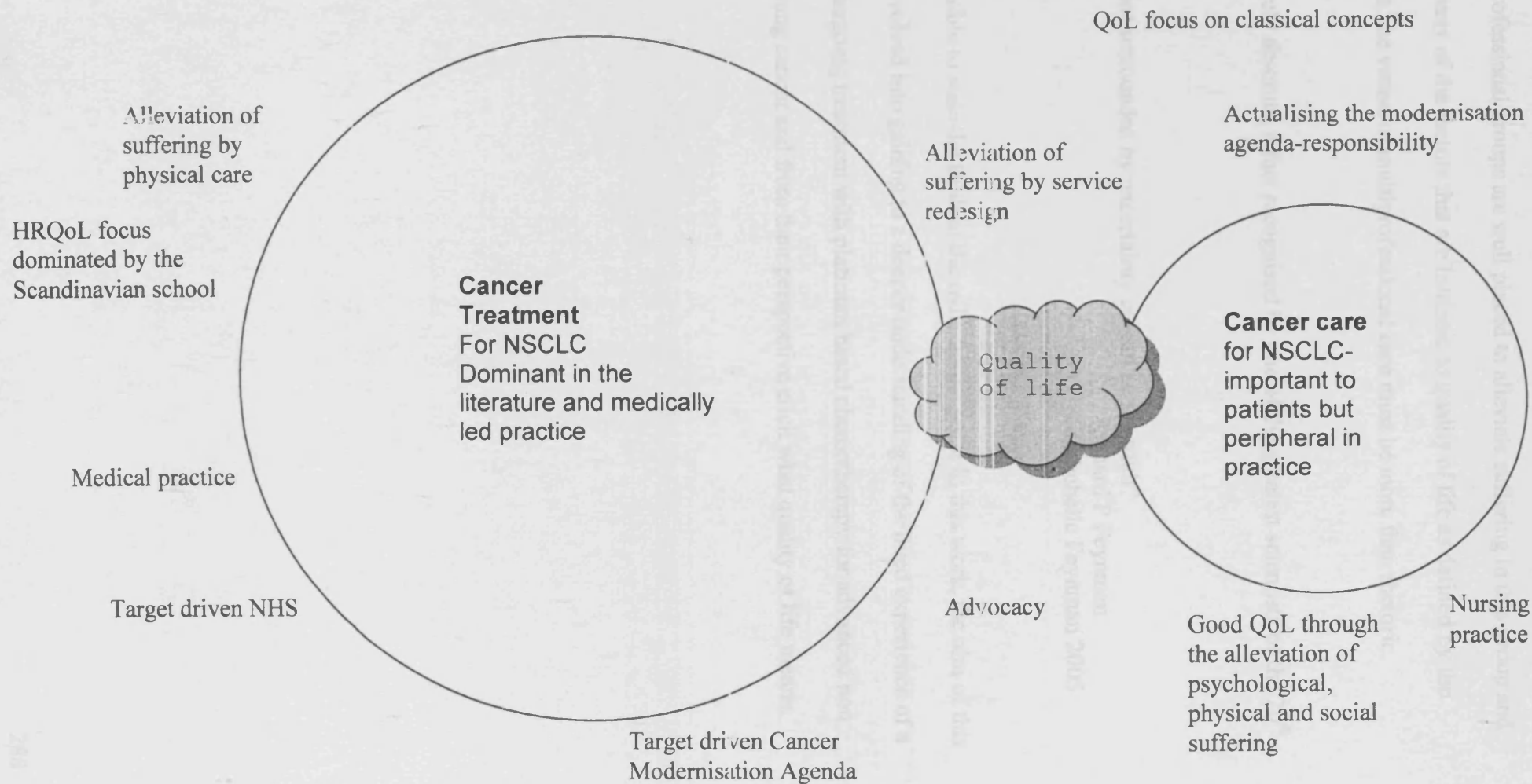
If quality of life is a psychological construct it may be more appropriate to use psychological tools, for example the Hospital Anxiety and Depression (HAD) scale. Unlike the QLQ 30+LC 17, which are derived from factor analysis, HAD is based on clinical experience. From these data it seems likely the quality of life is a psychological construct, and as was discussed in Chapter 6, Cummins argues that since the seminal studies of Campbell et al (1976) the view that personal or subjective well-being is made up of affective or cognitive components have become accepted. This is referred to as subjective well-being. Should we measure this instead? Should clinicians who wish to examine the effects of palliative chemotherapy use fundamental measures? Derivation often leads to systematic error and this is never considered in the literature.

Quality of life is certainly an area, which has impact on of nursing practice. The contribution of the professions is highly valued in the context of quality of life as described by the respondents. The alleviation of suffering, whether physical,

emotional, spiritual social or psychological is central to the meaning of nursing. At a recent meeting attended by the researcher (November 2005) on the management of thoracic cancers, an international panel of speakers addressed issues such as combination chemotherapy, the future of radiotherapy and even the best way to calculate the glomerular filtration rate for optimum chemotherapy dosage. There was no discussion of quality of life other than the presentation of trial data in a group receiving palliative treatment.

Despite the fact that this group of patients are receiving palliative treatment, the observation of the MDT meetings, the quality of life questionnaires and the lung cancer clinical community still fail to address the psychological, social, spiritual and emotional needs of this group. In short-the dominance of medical ontology in this field fails to address the suffering of this group which has direct reference to quality of life. This is shown in Fig 7.4

Fig 7.4 QoL as an area of practice-good quality of life in the care of patients with non-small cell lung cancer through alleviation of suffering



As many professional groups are well placed to alleviate suffering in this group and deal with many of the factors that are intrinsic to quality of life as defined by the respondents, the vision of multiprofessional care must be more than rhetoric.

Truth is rarely absolute, a fact recognised by one of the greatest scientists of the 20th century.

“What is not surrounded by uncertainty cannot be the truth”

Richard P Feynman
In Michelle Feynman 2005

It is impossible to state the truth in the reductionist sense in this work, the aim of this work has evolved into gaining to a deeper understanding of the lived experience of a person undergoing treatment with platinum based chemotherapy for advanced non small cell lung cancer and from their perspective elicit what quality of life means.

Appendix A
EORTC QLQ 30 Version 3 with LC17 (LC13)
Lung cancer module



EORTC QLQ-C30 (version 3)

Appendix B
Study Patient Information Sheet

The University College London Hospitals
CLINICAL HAEMATOLOGY AND CANCER SERVICES
Clinical Trials Unit

Oncology Research Office,

MIC Vs GC Chemotherapy Quality of Life Study
Patient Information Sheet

You are being invited to take part in a research project. You have a type of cancer called Non-Small Cell Lung Cancer and we are interested in how your treatment for this has affected your quality of life.

What will this involve?

In addition to any questionnaires you may have already completed, we would like to ask you some additional questions about how you feel about the chemotherapy you have had. There are no right or wrong answers and we would like you to be as frank as possible. This would take no more than one hour and can be done at a time and place convenient to you.

Will this information be confidential?

Any information you give during this interview will be treated with the strictest confidence and will not be revealed even to the medical team treating you. We hope this will allow you to be as open as possible about your experience of treatment.

If you decide that you would like anything discussed in the interview to be brought to the attention of the medical team caring for you please do let us know.

Do I have to take part?

It is up to you to decide if you would like to take part. If you decide not to take part it will not affect your care in any way.

What are the possible benefits of taking part?

It is unlikely that the study will benefit you directly but information you give may benefit others in the future.

This research is being conducted by Alison Leary, Research Nurse, at UCLH Trust.
Telephone



Appendix C

Common Toxicity Criteria

**ECOG
COMMON TOXICITY CRITERIA**

		0	1	2	3	4
Leukopenia	WBC x 10 ³ Granulocytes/Bands Lymphocytes	<4.0 <2.0 ≥2.0	3.0 - 3.9 1.5 - 1.9 1.5 - 1.9	2.0 - 2.9 1.0 - 1.4 1.0 - 1.4	1.0 - 1.9 0.5 - 0.9 0.5 - 0.9	<1.0 <0.5 <0.5
Thrombocytopenia	Plt x 10 ³	WNL	75.0 - normal	50.0 - 74.9	25.0 - 49.9	<25.0
Anemia	Hgb	WNL	10.0 - normal	8.0 - 10.0	6.5 - 7.9	<6.5
Hemorrhage (Clinical)	-----	none	mild, no transfusion	gross, 1-2 units transfusion/episode	gross, 3-4 units transfusion/episode	massive, >4 units transfusion/episode
Infection	-----	none	mild, no active Rx	Moderate, localized infection requires active Rx	severe, systemic infection requires active Rx, specify site	life-threatening, sepsis, specify site
Fever in absence of infection	-----	none	37.1° - 38.0° C 98.7° - 100.4° F	38.1° - 40.0° C 100.5° - 104.0° F	>40.0° C (>104.0° F) for less than 24 hours	>40.0° C (104.0° F) for >24 hrs or fever with hypotension
<ul style="list-style-type: none"> Fever felt to be caused by drug allergy should be coded as allergy. Fever due to infection is coded under infection only. 						
GU	Creatinine	WNL	<1.5 x N	1.5 - 3.0 x N	3.1 - 6.0 x N	>6.0 x N
	Proteinuria	No change	1+ or <0.3g% or <3g/l	2-3+ or 0.3 - 1.0g% or 3 - 10g/l	4+ or >1.0g% or >10g/l	nephrotic syndrome
	Hematuria	neg	micro only	gross, no clots	gross + clots	requires transfusion
	*BUN	<1.5 x N	1.5 - 2.5 x N	2.5 - 5 x N	5.1 - 10 x N	>10 x N
<ul style="list-style-type: none"> Urinary tract infection should be coded under infection, not GU. Hematuria resulting from thrombocytopenia should be coded under hemorrhage, not GU. 						
GI	Nausea	none	able to eat reasonable intake	intake significantly decreased but can eat	no significant intake	-----
	Vomiting	none	1 episode in 24 hours	2-5 episodes in 24 hours	6-10 episodes in 24 hours	>10 episodes in 24 hrs or requiring parenteral support
	Diarrhea	none	increase of 2-3 stools/day over pre-Rx	increase of 4-6 stools/day, or nocturnal stools, or moderate cramping	increase of 7-6 stools/day or incontinence, or severe cramping	increase of ≥10 stools/day or grossly bloody diarrhea, or need for parenteral support
	Stomatitis	none	painless ulcers, erythema, or mild soreness	painful erythema, edema, or ulcers, but can eat	painful erythema, edema or ulcers, and cannot eat	requires parenteral or enteral support
Liver	Bilirubin	WNL	-----	<1.5 x N	1.5 - 3.0 x N	>3.0 x N
	Transaminase (SGOT, SGP-T)	WNL	≤2.5 x N	2.6 - 5.0 x N	5.1 - 20.0 x N	>20.0 x N
	Alk. Phos or 5-nucleotidase	WNL	≤2.5 x N	2.6 - 5.0 x N	5.1 - 20.0 x N	>20.0 x N
	Liver - clinical	no change from baseline	-----	-----	precoma	hepatic coma
<ul style="list-style-type: none"> Viral Hepatitis should be coded as infection rather than liver toxicity. 						
Pulmonary	-----	none or no change	asymptomatic, with abnormality in PFTs	dyspnea on significant exertion	dyspnea at normal level of activity	dyspnea at rest
	<ul style="list-style-type: none"> Pneumonia is considered infection and not graded as pulmonary toxicity unless felt to be resultant from pulmonary changes directly induced by treatment. 					
Cardiac	Cardiac dysrhythmias	none	asymptomatic, transient, requiring no therapy	recurrent or persistent, no therapy required	requires treatment	requires monitoring, or hypotension or ventricular tachycardia or fibrillation
	Cardiac function	none	asymptomatic, decline of resting ejection fraction by less than 25% of baseline value	asymptomatic, decline of resting ejection fraction by more than 25% of baseline value	mild CHF, responsive to therapy	severe or refractory CHF
	Cardiac-ischemia	none	non-specific T-wave flattening	asymptomatic, ST and T wave changes suggesting ischemia	angina without evidence for infarction	acute myocardial infarction
	Cardiac-pericardial	none	asymptomatic effusion, no intervention required	pericarditis (w/ chest pain, ECG changes)	symptomatic effusion, drainage required	tamponade, drainage urgently required

		0	1	2	3	4	
Blood Pressure	Hypertension	none or no change	asymptomatic, transient increase by >20 mm Hg (D) or to >150/100 if previously WNL. No treatment required	recurrent or persistent increase by >20 mm Hg (D) or to >150/100 if previously WNL. No treatment required	requires therapy	hypertensive crisis	
	Hypotension	none or no change	changes requiring no therapy (including transient orthostatic hypotension)	requires fluid replacement or other therapy but not hospitalization	requires therapy and hospitalization, resolves within 48 hours of stopping the agent	requires therapy and hospitalization for >48 hours after stopping the agent	
Skin	-----	none or no change	scattered macular or papular eruption or erythema that is asymptomatic	scattered macular or papular eruption or erythema with pruritus or other associated symptoms	generalized symptomatic macular, papular or vesicular eruption	exfoliative dermatitis or ulcerating dermatitis	
Allergy	-----	none	transient rash, drug fever <38°C, 100.4°F	urticaria, drug fever ≥ 38°C, 100.4°F, mild bronchospasm	serum sickness, bronchospasm, requires parenteral meds	anaphylaxis	
Phlebitis		none	arm	thrombophlebitis, leg	hospitalization	embolus	
Local		none	pain	pain and swelling with inflammation or phlebitis	ulceration	plastic surgery indicated	
Alopecia	-----	no loss	mild hair loss	pronounced or total hair loss	-----	-----	
Weight gain/loss	-----	<5.0%	5.0 - 9.9%	10.0 - 19.9%	≥ 20%	-----	
CNS/CENTRAL	Sensory	neuro - sensory	none or no change	mild paresthesias; loss of deep tendon reflexes	mild or moderate objective sensory loss, moderate paresthesias	severe objective sensory loss or paresthesias that interfere with function	-----
		neuro - vision	none or no change	-----	-----	symptomatic subtotal loss of vision	blindness
		neuro - hearing	none or no change	asymptomatic, hearing loss on audiometry only	tinnitus	hearing loss interfering with function but correctable with hearing aid	deafness, not correctable
	Motor	neuro - motor	none or no change	subjective weakness, no objective findings	mild objective weakness without significant impairment of function	objective weakness with impairment of function	paralysis
		neuro - constipation	none or no change	mild	moderate	severe	ileus >60 hours
	Psych	neuro - mood	no change	mild anxiety or depression	moderate anxiety or depression	severe anxiety or depression	suicidal ideation
	Clinical	neuro - cortical	none	mild somnolence or agitation	moderate somnolence or agitation	severe somnolence, agitation, confusion, disorientation or hallucinations	coma, seizures, toxic psychosis
		neuro - cerebellar	none	slight incoordination, dysadiadochesis	intention tremor, dysmetria, slurred speech, nystagmus	locomotor ataxia	cerebellar necrosis
		neuro - headache	none	mild	moderate or severe but transient	unrelenting and severe	-----
	Metabolic	Hyperglycemia	<116	116 - 160	161 - 250	251 - 500	>500 or ketoacidosis
Hypoglycemia		>84	55 - 84	40 - 54	30 - 39	<30	
Amylase		WNL	<1.5 x N	1.5 - 2.0 x N	2.1 - 5.0 x N	>5.1 x N	
Hypercalcemia		<10.8	10.8 - 11.5	11.6 - 12.5	12.6 - 13.5	≥ 13.5	
Hypocalcemia		>8.4	8.4 - 7.6	7.7 - 7.0	6.9 - 6.1	≤ 6.0	
Coagulation	Hypomagnesemia	>1.4	1.4 - 1.2	1.1 - 0.9	0.8 - 0.6	≤ 0.5	
	Fibrinogen	WNL	0.99 - 0.75 x N	0.74 - 0.50 x N	0.49 - 0.25 x N	≤ 0.24 x N	
	Prothrombin time	WNL	1.01 - 1.25 x N	1.26 - 1.50 x N	1.51 - 2.00 x N	> 2.00 x N	
	Partial thromboplastin time	WNL	1.01 - 1.60 x N	1.61 - 2.33 x N	2.34 - 3.00 x N	> 3.00 x N	

* denotes ECOG specific criteria

Appendix D
Protocol for Study 11
London Lung Cancer Group



LONDON LUNG CANCER GROUP

CRC & UCL CANCER TRIALS CENTRE

A Phase III Randomised Comparison of Gemcitabine/Carboplatin with Mitomycin, Ifosfamide and Cisplatin in Non-Small Cell Lung Cancer (Study 11)

November 1998 version 2
April 1999 version 3.1
June 1999 version 3.2



STUDY CONTACTS

Page	CONTENTS
1	Introduction
4	Trial Objectives
5	Eligibility Criteria
6	Trial Design
6	Chemotherapy Treatment Plan
6	Administration of Regimens
7	Anti-emetics
7	Prophylactic Antibiotics
7	Concomitant Medication
7	Dispensing Procedures
7	Radiotherapy
8	Patient Evaluation
8	Clinical Evaluation
8	Quality of Life
8	Toxicity
8	Response
9	Follow-up after Chemotherapy
9	Criteria for discontinuing protocol treatment
9	Therapy after protocol treatment stopped
9	Follow-up after stopping protocol treatment
10	Investigations
10	Initial Investigations
10	Assessments during treatment
10	Assessments at follow-up
11	Dose Modifications
11	Consent, Ethical and Regulatory Considerations
11	Serious Adverse Event Reporting
12	Statistical Considerations
13	Randomisation
13	Data Management
14	References
15	Appendix 1 WHO Toxicity Scores
17	Appendix 2 WHO Response Criteria
18	Appendix 3 ECOG Performance Scale
19	Appendix 4 Cockcroft & Gault formula
20	Appendix 5 EORTC QLQ C30 + LC 17
23	Appendix 6 Daily Diary Card
24	Appendix 7 Staging
26	Appendix 8 Statistical Methodology

All clinicians wishing to enter patients on this study should be able to comply with this protocol

1.0 INTRODUCTION

Non-small cell lung cancer (NSCLC) is inoperable at presentation in more than 80% of cases and with the exception of a small minority suitable for 'radical radiotherapy' the only realistic option for treatment aimed at prolonging survival is chemotherapy.

Several drugs have useful response rates of 20% or greater and combination chemotherapy produces higher response rates. One of the most active and most widely used regimens employs mitomycin, ifosfamide and cisplatin (MIC). This regimen has been shown in randomised trials to improve survival significantly in patients with extensive disease¹. In these patients the overall response rate to MIC was 31% (2% CR and 29% PR)¹. In this study WHO toxicity scores were not reported. In a study which compared three cisplatin containing regimens in patients with stage IIIb and IV NSCLC and found a response rate of 40% with MIC grades 3 and 4 toxicity were found for neutropenia in 21% and for thrombocytopenia in 10%.²

New drugs that have already shown both preclinical and clinical activity with low toxicity should be strong contenders for introduction as agents for initial treatment of NSCLC. In this respect gemcitabine [G] is an interesting new agent which could have a major impact in the treatment of NSCLC and therefore warrants further clinical investigation.

Gemcitabine (difluorodeoxycytidine) an analogue of cytosine arabinoside (ara-C) is a pyrimidine antimetabolite whose mechanism of action has been well characterised and is reviewed elsewhere.³ On a preclinical basis, gemcitabine is active in a variety of murine solid tumours and leukaemias, as well as several human tumour xenografts⁴. Clinically, gemcitabine has undergone extensive testing and has activity in many cancers including NSCLC and SCLC.

Extensive phase II single-agent and combination studies indicate that gemcitabine possesses significant activity in NSCLC. Single-agent studies from around the world have involved nearly 600 evaluable patients. Anderson et al⁵ reported on the results of four phase II trials in Great Britain and Denmark with gemcitabine given by short IV infusions weekly times 3 every 4 weeks in doses ranging from 800 to 1,250 mg/m² and involving 332 evaluable patients with advanced, inoperable NSCLC (54% stage IV). Objective responses were documented in 20% of patients, and toxic reactions were generally mild with WHO grade 3 or 4 neutropenia occurring in 25% of patients (clinical infections were rare), WHO grade 3 or 4 thrombocytopenia in 2%, WHO grade 3 or 4 elevations of hepatic transaminase levels in 12%, and transient rashes or lethargy in 20 to 24%. Negoro et al⁶ reported the results of two Japanese phase II trials involving 74 evaluable patients with NSCLC (41 with stage IV disease) using gemcitabine in doses of 1,000 to 1,250 mg/m²/week. Objective responses were reported in 20 patients, for an overall response rate of 27%. WHO grade 3 or 4 leukopenia was seen in <10% of patients.

Shepherd et al⁷ reported on a multinational trial involving 93 response-evaluable, chemotherapy-naive patients with inoperable NSCLC (60% stage IV), excluding large cell histology, treated with gemcitabine 1,250 mg/m²/week times 3, with cycles repeated every 4 weeks. Objective responses were seen in 20% of patients, with principal toxic reactions consisting of WHO grade 3 or 4 neutropenia in 6% of cycles and WHO grade 3 or 4 thrombocytopenia in <1% of cycles. Hepatotoxic reactions, manifesting as WHO grade 3 or 4 elevations in transaminase levels, occurred in <3% of cycles. Abratt et al⁸ from South Africa reported on 76 evaluable patients with locally advanced or metastatic NSCLC (41.7% with stage IV disease) who had not received previous chemotherapy. Gemcitabine was again given as a short IV infusion weekly times 3 and repeated at 4-week intervals in doses of 1,000 to 1,250 mg/m²/week. Objective responses were seen in 15 patients (including 2 CRs), for an overall response rate of 20%. Toxic reactions were again minimal, with WHO grade 3 or 4 leukopenia occurring in 1% of cycles and WHO grade 3 or 4 thrombocytopenia occurring in <0.1% of all cycles. Non-haematologic toxic reactions were generally mild and included peripheral oedema, asthenia, transient malaise, and elevations in hepatic transaminase levels.

Gemcitabine may modify the ability of the cancer cell to repair platinum induced DNA lesions and thereby modify resistance to platinum. Several trials have evaluated gemcitabine in combination with cisplatin in advanced NSCLC. Gemcitabine was administered on a weekly basis, while cisplatin schedules varied. One study administered gemcitabine weekly (days 1, 8 and 15) at 1 g/m² and cisplatin 100 mg/m² on day 2 of each 28 day cycle.⁹ This combination produced a dramatic increase in the overall response rate to 54%. Although 27% of patients experienced grade 4 thrombocytopenia, this was short lived and there were no clinical sequelae.

Carboplatin [C] is believed to share a common mechanism of chemical activation with cisplatin and it has advantages over cisplatin in terms of lower toxicity and being suitable for out-patient administration. There has been only one head-to-head randomised comparison of the two agents. The European Organization for Research and Treatment of Cancer (EORTC) Lung Cancer Working Party conducted a randomised trial comparing cisplatin 120 mg/m², day 1 and carboplatin 325 mg/m², day 1 in combination with etoposide 100 mg/m², days 1, 2, and 3 in advanced non-small-cell lung cancer (NSCLC)¹⁰. 228 patients were eligible for survival and 202 assessable for response. There were no significant differences in response rates or survival. The carboplatin arm, however, produced significantly less leucopenia, nausea, vomiting, and diarrhoea than the cisplatin arm.

When single-agent carboplatin was compared with several cisplatin-containing combination regimens in an ECOG prospective randomized trial¹¹, the single-agent carboplatin arm produced a lower objective response rate (9%) but significantly longer median survival (p=0.008) than the other arms in the trial.

The mitomycin, vinblastine, and cisplatin (MVP) combination is one of the most frequently used for NSCLC. Data from the Royal Marsden showed overall response rate of 32% (95%CI 24-42); 52% for stage IIIb and 25% for stage IV. The median response duration was 6 months and the median survival 5 months¹².

Paccagnella et al¹³ evaluated a combination similar to MVP, using carboplatin instead of cisplatin to render it more feasible in an outpatient setting. Inclusion criteria for this study included: inoperable patients or patients relapsing after previous surgery, with NSCLC. The chemotherapy regimen included carboplatin, 300 mg/m² on Day 1; mitomycin, 8 mg/m² on Day 1; and vinblastine, 4 mg/m² on Days 1, 8, and 15 (on Day 15 vinblastine was delivered only in the first cycle) (MVC) every 3 weeks for at least 3 cycles. 70 patients entered the trial with only 4 patients requiring hospitalisation for treatment delivery, the remainder being treated as out-patients. Overall response rate was 38% (95% CI 27-51%). Median duration of response was 9.8 months (range, 2-27 months) and the median survival 9.5 months. In Stage III patients the RR was 42% and in Stage IV patients it was 34%. The results using carboplatin were therefore at least as good as those expected from cisplatin in combination with vinblastine and mitomycin. The back calculation of carboplatin area under the curve (AUC) with Calvert's formula showed a median AUC value of 4 (range, 2-8). Haematologic toxicity was the major side effect; Grades 3 and 4 leukopenia were observed in 34% and 6% of patients, respectively, and Grades 3 and 4 thrombocytopenia in 25% and 4% of patients, respectively. Grade 2 infection occurred in 10% of patients, with only 1 case of sepsis; severe constipation and Grade 2 alopecia occurred in only 1 patient; and no case of higher than Grade 1 nephrotoxicity was observed. No pulmonary toxicity was observed.

Therefore, because of its nearly equivalent efficacy, more manageable toxicity, and ease of outpatient administration, carboplatin is a more attractive platinum analogue than cisplatin for outpatient treatment of NSCLC. Furthermore, an improved understanding of the pharmacokinetics and pharmacodynamics of carboplatin strongly suggests that its efficacy in NSCLC may have been underestimated in trials that used body surface area based dosing. Several investigators have found that carboplatin's pharmacokinetics (area under the plasma concentration time curve [AUC]) and pharmacodynamics (myelotoxicity) are more closely associated with an individual patient's glomerular filtration rate (GFR) than with BSA. Calvert et al¹⁴ have proposed the use of a simple formula in which the dose of carboplatin (in total milligrams) is determined by multiplying the calculated creatinine clearance (an estimate of GFR)

plus 25 by the desired carboplatin AUC (ie, carboplatin dose=AUC x [calculated creatinine clearance+25]). This approach would be expected to decrease the proportion of patients suffering severe toxic reactions when their dose based on BSA is much higher than it would be if based on GFR. Conversely, there would be a decrease in the proportion of patients receiving doses too low for therapeutic effect, because their carboplatin dose based on BSA is much lower than it would be if based on GFR.

A phase I study evaluated a combination of gemcitabine and carboplatin in 13 chemotherapy-naive patients with non-small cell lung cancer to determine the maximum tolerated dose of carboplatin in combination with gemcitabine.¹⁵ Gemcitabine at a dose of 1,000 mg/m² was administered on days 1, 8, and 15 of a 28-day cycle and carboplatin was given as a 30 minute infusion immediately before gemcitabine on day 1. Carboplatin dosing was escalated and determined using the Calvert formula, and three patients were treated at the initial predicted dose of area under the curve (AUC) 4 mg/mL/min. Subsequently the carboplatin dose was escalated to a predicted AUC 5.2 mg/mL/min. Pharmacokinetic studies were performed measuring gemcitabine and carboplatin (total platinum) concentrations. Responses were assessed following two cycles of treatment and patients with stable disease or objective responses proceeded to receive a maximum of six cycles. Dose-limiting myelosuppression was identified at a predicted carboplatin AUC 5.2 mg/mL/min, with two patients developing grade 4 neutropenia and two patients grade 4 thrombocytopenia. However, these grade 4 toxicities were not associated with any serious sequelae. In this preliminary study, four partial responses were observed and the median length of survival for all patients was 45 weeks. The authors commented that symptomatic toxicities were rare and outpatient treatment was easy.

These preliminary data suggest a response rate and survival from this combination comparable to that obtained with MIC. We propose to examine the role of gemcitabine in combination with carboplatin (GC) in NSCLC. We plan a randomised comparison with MIC which is the combination that has been used most widely for treatment of NSCLC in patients with inoperable stage IIIb – IV NSCLC. The aims will be to determine whether GC can achieve a response rate and survival advantage comparable to or better than that conferred by MIC but with less toxicity and greater quality of life advantage.

The four weekly schedule involving treatment on three occasions per four week cycle is less convenient for comparison with MIC which is a three weekly regimen, and the different timing considerably complicates comparison of quality of life. Gemcitabine has most frequently been used at a doses of 1000 mg/m² on days 1, 8 and 15 of a four weekly cycle, ie a dose intensity 750 mg/m²/week. To maintain a comparable dose intensity using gemcitabine on days 1 and 8 of a three weekly cycle a dose of 1200 mg/m² is appropriate. A regimen using gemcitabine 1250 mg/m² and carboplatin AUC 6 based on measured EDTA clearance has been used in 19 patients with advanced lung cancer. A total of 62 cycles have been administered with a maximum number of 6 cycles per patient. Grade 4 thrombocytopenia was observed following 8% of cycles and the regimen was generally well tolerated. (Dr Sederholm, Sweden, personal communication). Because experience with this regimen is limited the design of the study incorporates early stopping rules based on response and toxicity data after the first 40 patients have been treated with GC.

Ideally any measure of QOL should be 'self-reported' and multi-dimensional, encompassing the domains of psychological, social and physical functioning as well as disease related symptoms and relating toxicities. The EORTC QLQ-C30 with additional lung cancer module (LC17) has been well validated and appears to achieve these requirements. Daily diary cards are better than interval questionnaires at demonstrating daily fluctuations and these are particularly relevant when comparing chemotherapy regimens given at similar intervals and over the same total period. The LLCG diary card has been validated for use in SCLC¹⁶ and has been used in several previous studies, eg ¹⁷, and will therefore be used in addition.

2.0 TRIAL OBJECTIVES

- 2.1 To compare survival following GC and MIC.
- 2.2 To determine the response rate to GC x 4 courses in patients with NSCLC and compare it with MIC x 4 courses.
- 2.3 To compare toxicities of GC and MIC.
- 2.4 To compare QOL in patients with NSCLC receiving GC and MIC. The dimensions which will be assessed are: physical (including lung cancer symptoms and treatment side effects), social and cognitive functioning, as well as global quality of life.

3.0 ENTRY CRITERIA

3.1 ELIGIBILITY CRITERIA

- 3.1.1 Histologic or cytologic proof of non-small cell carcinoma of the lung.
- 3.1.2 Stage IIIb or IV disease (See appendix 7).
- 3.1.3 Measurable or evaluable disease.
- 3.1.4 Renal function adequate for chemotherapy: ie, EDTA clearance greater than 60 ml/min.
In cases where EDTA is not possible, measured creatinine clearance or calculated (Cockcroft formula) should be greater than 50 ml/min
- 3.1.5 Age 18 or over.
- 3.1.6 If female and of child bearing potential using adequate contraception for the duration of chemotherapy.
- 3.1.7 Willing to give written informed consent.

3.2 CRITERIA OF INELIGIBILITY

Patients will not be eligible for entry into the trial under any one of the following conditions:

- 3.2.1 Prior treatment with radiotherapy or chemotherapy.
- 3.2.2 A life expectancy of less than 8 weeks.
- 3.2.3 A history of prior malignant tumour, unless the patient has been without evidence of disease for at least 3 years or the tumour was a non-melanoma skin tumour.
- 3.2.4 White cell count less than 3,000/ mm³.
- 3.2.5 Platelet count less than 100,000/ mm³.
- 3.2.6 Haemoglobin less than 10.0 g/ dL
- 3.2.7 A medical condition that excludes the use of chemotherapy.
- 3.2.8 Symptomatic brain metastases.

4.0 TRIAL DESIGN

4.1 OVERALL DESIGN

A multicentre randomised, phase III, open label, study to compare 4 cycles of GC with 4 cycles of MIC with respect to response rate, survival and QOL.

4.2 CHEMOTHERAPY TREATMENT PLAN

4.2.1 GC – 3 weekly regimen

Gemcitabine 1200mg/m² IV Day 1 and 8

Carboplatin (AUC 5). Dose in mg calculated according to formula:

Dose = Target area under curve x (Creatinine clearance + 25) IV day1.

***NB: where possible, EDTA should be used to calculate GFR** as it is most accurate measure of renal clearance. [Measured (creatinine) clearance gives closer approximation to EDTA. Calculated (Cockcroft) underestimates by about 10%].

Thus, the formula for dose of Carboplatin is:

5 (EDTA/creatinine clearance + 25) mg **OR** 6 (calculated (Cockcroft) clearance + 25) mg

4.2.2 MIC – 3 weekly regimen

Mitomycin 6 mg/ m² IV Day 1

Ifosfamide 3 g/m² IV Day 1

Cisplatin 50 mg/m² IV Day 1

4.3 ADMINISTRATION OF REGIMENS

GC – Gemcitabine and Carboplatin

Day 1 Gemcitabine 1200mg/m² IV in 250 ml N saline over 30 minutes

*Carboplatin mg=AUC 5 IV in 500 ml dextrose over 30 minutes

Day 8 Gemcitabine 1200mg/m² IV in 250 ml N saline over 30 minutes

MIC – Mitomycin, Ifosfamide and Cisplatin

Day 1 Mitomycin 6 mg/m² iv bolus into fast running drip

Ifosfamide 3 g/ m² in 1 L N saline over 3 hours and Mesna 1.5 g/ m²

Frusemide 40 mg po

Cisplatin 50 mg/m² in 500 ml N saline over 1 hour

Mesna 1.5 g/ m² in 1 L N saline with 20 mmol KCl over 4 hours.

4.4 ANTI-EMETICS

Suggested anti-emetics:

- Granisetron 3 mg iv and dexamethasone 8 mg iv before each chemotherapy except gemcitabine day 8 for which metoclopramide 20mg iv should be adequate.
- Metoclopramide 20 mg 8 hourly prn after.
- This may be varied according to local practice and patient needs.

4.5 PROPHYLACTIC ANTIBIOTICS

All patients will receive prophylactic trimethoprim (or locally preferred equivalent) from day 8 to day 21 of each cycle to minimise the risk of neutropenic sepsis and respiratory infection.

4.6 CONCOMITANT MEDICATION

Other medication, including steroids, may be administered at the discretion of the clinician. The commonest indication for steroids would be as part of standard anti-emetic regimen.

4.7 DISPENSING PROCEDURES

Dispensing procedures will follow usual local pharmacy practice.

4.8 RADIOTHERAPY

If palliative radiotherapy is considered necessary before chemotherapy has been completed this will be considered evidence of progressive disease and the patient will not receive further chemotherapy.

4.9 PATIENT EVALUATION

4.9.1 CLINICAL EVALUATION

- Patients will be evaluated for response at the start of each cycle of chemotherapy by chest radiograph.
- In cases in which disease is measurable or evaluable only by CT scan of the thorax this will be repeated after each second cycle.
- Patients will also be assessed at 3 week intervals by history, physical examination, chest radiograph and laboratory tests as indicated in Section 5.2. Scans will be repeated if clinically indicated.
- Toxicity to chemotherapy will be assessed after each treatment. ie, toxicity scores at each cycle should relate to the previous course

4.9.2 QUALITY OF LIFE

- The EORTC QLQ-C30 with additional lung cancer questions (LC17) (Appendix 5) will be completed by all patients after consent but before knowledge of randomisation to prevent any influence of treatment allocation on baseline information.
- The EORTC QLQ-C30 + LC17 will also be completed before each cycle of chemotherapy and at the first two follow-up visits.
- Each questionnaire refers to how the patient has felt over the past week. The questionnaire should be given out and collected at each visit, preferably by the same person and then returned to the trials office on completion. The forms will be completed by the patient without conferring.
- The daily diary cards (DDC) will be completed on a baseline day to represent pre-treatment levels and then every evening from the first day of chemotherapy until 3 weeks after the last course.

4.9.3 TOXICITY

Toxicity will be assessed according to NCIC Common Toxicity Criteria. (Appendix 1)

4.9.4 RESPONSE

Response will be assessed according to WHO criteria (Appendix 2)

Survival time is the interval between date of randomization and death.

4.10 PATIENT FOLLOW-UP AFTER CHEMOTHERAPY

Patients should be seen every 4 weeks for the first year and thereafter at 8 weekly intervals. At these visits the date and site(s) of progressive disease and any further treatment should be recorded on follow-up forms.

4.11 CRITERIA FOR DISCONTINUING PROTOCOL TREATMENT

Once patients are randomised they remain part of the study until death.

- Protocol treatment may, however, be stopped in the following instances:
- Tumour progression
- Unacceptable toxicity
- Intercurrent illness which, in the clinician's opinion would require discontinuation of protocol therapy.
- If subsequent histological / cytological review is contrary to the original diagnosis.
- Patient wish.

4.12 THERAPY AFTER PROTOCOL TREATMENT HAS STOPPED

Subsequent therapy after discontinuation of protocol treatment will be left to the discretion of the clinician.

4.13 FOLLOW-UP AFTER STOPPING PROTOCOL TREATMENT

After stopping protocol treatment, all patients should be followed up in the usual way – see section 4.10.

5.0 INVESTIGATIONS

5.1 INITIAL INVESTIGATIONS

- History and physical examination
- Weight, height, surface area and record of performance status (ECOG scale as in Appendix 3)
- Haemoglobin, white blood cell count, differential count and platelet count
- Creatinine, blood urea, electrolytes
- AST/ALT, alkaline phosphatase, bilirubin, calcium
- Assessment of renal function in accordance with local practice but preferably by EDTA
- Chest X ray PA
- CT or US abdomen
- CT brain scan if clinically indicated
- Isotope bone scan if clinically indicated.
- EORTC-QLQ C30 + LC 17

5.2 ASSESSMENTS TO BE FOLLOWED DURING TREATMENT

Prior to each cycle:

- Weight
- ECOG performance status
- Full blood count and differential
- Biochemistry
- Chest xray (PA)
- Scans (where clinically indicated)
- Toxicity since last visit
- EORTC QLQ-C30 + LC17
- Daily Diary Card
- Assessment of renal function as indicated

5.3 ASSESSMENTS AT FOLLOW-UP

- Full blood count and differential
- Biochemistry
- Chest xray (PA)
- Scans (where clinically indicated)
- EORTC QLQ-C30 + LC17

6.0 DOSE MODIFICATIONS

Dose reductions are based on pre-treatment blood tests and/or renal function.

6.1 ALL DRUGS ON PRE-TREATMENT COUNTS

WBC x 10 ⁹ /l		Platelets x 10 ⁹ /l	
> 3	And	> 100	Full dose
1.5 – 2.99	Or	50 - 99,9	75% dose
< 1.5	Or	< 50	Delay 1 week

6.2 GEMCITABINE (Day 8) DOSE MODIFICATION

Day 8 Total WBC (x 10 ⁹ /l)		Day 8 Platelets (with no evidence of bleeding) (x 10 ⁹ /l)	Gemcitabine
≥ 2.0	And	≥ 50	Full dose
< 2	Or	< 50	omit gemcitabine

6.3 CISPLATIN AND GEMCITABINE DOSE MODIFICATION FOR RENAL FUNCTION

Calculated Creatinine Clearance (ml/ min)	Cisplatin dose	Gemcitabine dose
> 60	100%	100%
40 – 60	50%	50%
< 40	Omit	Omit

(NB: for any serious unexpected drug reactions during treatment with Gemcitabine/Carboplatin, please complete a Serious Adverse Event form - see 7.0)

7.0 INFORMED CONSENT AND ETHICAL CONSIDERATIONS

Written informed consent will be obtained according to the local institutional ethical committee requirements. Due to differing requirements, a standard consent form for the trial will not be provided. Multi-Centre Research Ethics Committee approval will be applied for. It will be the responsibility of the local participating investigators to obtain the necessary Local Research Ethics Committee approval. A DDX certificate for the trial has been obtained as Carboplatin is not licensed for use in non-small cell lung cancer. **The DDX is also conditional on all serious unexpected adverse reactions being reported promptly to the Committee on Safety of medicines, and all centres must take the appropriate steps to ensure that this reporting mechanism is in place.**

8.0 STATISTICAL CONSIDERATIONS

The aim is to recruit 387 patients. The basis for this is as follows. We hope that GC may be less toxic with better QOL but we need to be reasonably confident that it will not be less effective in terms of survival. Therefore patient numbers have been calculated to allow reasonable exclusion of a clinically significant survival decrement with GC. With MIC in stage IIIb-IV disease one year survival is 28%¹.

With the entry of 387 patients there would be only a 20% chance that the 95% CI on the hazard ratio at the end of the trial would include survival differences of 10% or greater in favour of MIC at 1 year (see reference 18 or Appendix 8 calculated with $a=0.05$, $b=0.20$, d - the difference in log hazard ratio = 0.298). Thus, with 387 patients entered, and the two treatments being really equivalent, we are likely (with an 80% chance) to be able to conclude at the end of the trial that there are not more than 10 percentage points difference in survival in favour of MIC.

The statistical methodology for these results is given in detail in a paper submitted for publication.¹⁹ See also Appendix 8. The method in outline consists of examining the confidence limits on the hazard ratio from a survival comparison (usually at the end of the trial), and setting the sample size sufficiently large that the lower confidence limit on the hazard ratio gives a % survival difference which is less than some pre-chosen value, at a particular time of interest. Thus at the end of the trial, when the survival comparison is performed and confidence limits are calculated on the hazard ratio, the numbers entered will have been sufficiently large to ensure that the lower confidence limit excludes a survival difference of more than x%, where x has been specified in advance (eg in this trial $x=10\%$).

The trial will continue to completion only if response rate and toxicity of GC in the first 40 patients receiving GC are regarded as acceptable. Criteria for acceptability will be:

1. With MIC the response rate in this group of patients is 34% (95%CI 26-42) (MIC2 Cullen, personal communication). So if the true response rate is 26% then the chances of seeing 5 or fewer responses in the first 40 (GC) patients is just less than 5% (exact probability = 3.2%). Therefore if there are 5 responses or fewer in the first 40 (GC) patients the study will be terminated.

2. In the MIC2 trial the proportion of courses 2, 3 and 4 delayed was 8.6% (95%CI 5.7-12.2%) mainly due to haematological toxicity and infection (Cullen et al). Some increase in haematological toxicity would be acceptable if GC had other advantages, however. Hence, the lower end of the 95% CI for the proportion of courses delayed (ie courses 2, 3 and 4) due to haematological toxicity or infection shall not exceed 20%, (around twice that expected with MIC). In the MIC2 trial 60% of courses 2, 3 and 4 were actually administered, others not being administered because of progressive disease, patient refusal or other reasons. If patients were eligible for 60% of courses 2, 3 and 4 of GC, the total number of courses 2-4 in 40 patients would be 72. Hence, the proportion of courses 2-4 delayed because of toxicity should not exceed 29% (95%CI 20 - 40%).

The planned study size would have only a modest chance of detecting anything less than a major survival advantage for GC over MIC if that existed. If analysis of the data were to suggest the possibility of a survival advantage for GC which had not reached statistical significance because of inadequate numbers consideration would be given to extending the study to a total of 631 patients which would confer 80% power to detect a 10% survival difference significant at the 5% level (2-sided test).

For the EORTC QLQ results, the main comparisons will be at 6 weeks, ie after two cycles, 3 weeks after the last cycle of chemotherapy (whenever that is for the individual patient) and at 6 months from randomisation. These time points have been chosen as representative of rapidity of relief of symptoms of cancer and initial tolerance of chemotherapy, an assessment of relief of symptoms and tolerance at the end of treatment, and an assessment of durability of relief of symptoms of cancer. On the DDC scores of 1-4 are obtained for each symptom (1 well - 4 ill)

daily. These are analysed by comparing the proportion of patients whose replies fall into each category over the period of observation using non-parametric methods. Graphical presentations demonstrate the time course of adverse effects of chemotherapy.

Assuming that approximately 40% of patients fail to complete sufficient QoL assessments to be evaluable and that adequate data are obtained from 232 patients, QoL comparisons will have approximately 90% power to detect a difference between treatment groups of 20% or greater, eg difference between 15% and 35%, in the proportion of patients crossing a threshold score on a QoL measure.

9.0 RANDOMISATION METHOD

Patients are enrolled after completion of pre-treatment evaluation. They are stratified according to study centre, stage, ie IIIb or IV, and according to ECOG performance status. The purpose of stratification is to balance the groups by these prognostic factors. Computer generated randomisation using the minimization technique will be administered by the London Lung Cancer Group Trials Office.

10.0 DATA MANAGEMENT

Trial forms will be returned to the London Lung Cancer Group trials centre for computerisation and statistical analysis.

10.1 DOCUMENTATION - Study forms

Eligibility checklist	- to be checked and then faxed or phoned to the Trials Office.
Chemotherapy	- <u>complete all details</u> on form with each course of chemotherapy AND for every delay.
Post chemotherapy	- <u>complete all details</u> after final course of chemotherapy and radiotherapy (if given).
Follow up	- <u>complete all details</u> on form every month after the completion of chemotherapy for 1 year, and every two months thereafter.
Quality of Life	- complete EORTC QLQ-C30 and LC-17 before patients' knowledge of treatment allocation, before each cycle of chemotherapy and at first two follow-up visits. - daily diary cards to be completed by patients and collected at each visit from randomisation until 3 weeks after the last course of chemotherapy
Final Form	- on death of patient
Serious Adverse Event	- complete form for all cases of serious unexpected adverse reactions during Gemcitabine/Carboplatin treatment

11.0 REFERENCES

1. Cullen MH, Woodroffe CM, Billingham LJ, Chetiyawardana AD, Joshi R, Ferry D, Connolly CK, Bessell E. Mitomycin, ifosfamide and cisplatin (MIC) in non-small cell lung cancer (NSCLC): 2. Results of a randomised trial in patients with extensive disease. *Lung Cancer* 1997;18(S1):5.
2. Crino L, Clerici M, Figoli F, Carlini P, Ceci G, Cortesi E, et al. Chemotherapy of advanced non-small-cell lung cancer: a comparison of three active regimens. A randomized trial of the Italian Oncology Group for Clinical Research (G.O.I.R.C.). *Ann Oncol* 1995;6:347-53.
3. Hertel, LW, Kroin, JS, Misner, JW et al .Synthesis of 2-deoxy-2'.2'-difluoro-D-ribose and 2-deoxy-2'.2'- difluoro-D-ribofuranosyl nucleosides. *J Org Chem.* 1988, 53: 2406 -2409.
4. Hertel, LW, Boder, GB, Kroin, JS et al. Evaluation of the antitumour activity of gemcitabine (2'.2'-difluoro-2'- deoxycytidine). *Cancer Res* 1990, 50: 4417 - 4422.
5. Anderson H, Thatcher N, Walling J, et al. Gemcitabine and palliation of symptoms in non-small cell lung cancer. *Proc Am Soc Clin Oncol* 1994;13:367.
6. Negoro S, Fukuoka M, Kurita Y, et al. Results of phase I studies of gemcitabine in non-small cell lung cancer (NSCLC). *Proc Am Soc Clin Oncol* 1994;13:367.
7. FA, Gatzemeier U, Gotfried M, et al. An extended phase II study of gemcitabine in non-small cell lung cancer (NSCLC). *Proc Am Soc Clin Oncol* 1993;12:330
8. Abratt RP, Bezwoda WR, Falkson G, et al. Efficacy and safety profile of gemcitabine in non-small cell lung cancer: a phase II study. *J Clin Oncol* 1994; 12:1535-40.
9. Crino, L, Scagliotti, G, Marangolo, M et al. Cisplatin - gemcitabine combination in advanced non-small cell lung cancer: a Phase II study. *J Clin Oncol* 1997;15:297 – 303.
10. Klastersky J, Scullier JP, Lacroix H, Dabouis G, Bureau G, Libert P, Richez M, Ravez P, Vandermoten G, Thiriaux J. A randomized study comparing cisplatin or carboplatin with etoposide in patients with advanced non-small-cell lung cancer: European Organization for Research and Treatment of Cancer Protocol 07861. *J Clin Oncol* 1990;8:1556-1562.
11. Bonomi PD, Finkelstein DM, Ruckdeschel JC, et al. Combination chemotherapy versus single agents followed by combination chemotherapy in stage IV non-small cell lung cancer: a study by the Eastern Cooperative Oncology Group. *J Clin Oncol* 1989; 7:1602-13.
12. Ellis PA, Smith IE, Hardy JR, Nicolson MC, Talbot DC, Ashley SE, Priest K. Symptom relief with MVP (mitomycin C, vinblastine and cisplatin) chemotherapy in advanced non-small-cell lung cancer. *Br J Cancer* 1995;71:366-370.
13. Paccagnella A, Favaretto A, Oniga F, Festi G, Lauro S, Morabito A, Ossana L, Sartore F, DePoli F, Fiorentino MV. Mitomycin C, vinblastine, and carboplatin regimen in patients with nonsmall cell lung cancer. A phase II trial. *Cancer* 1996;78:1701-1707.
14. Calvert AH, Newekk DR, Gumbrell LA, et al. Carboplatin dosage: prospective evaluation of a simple formula based on renal function. *J Clin Oncol* 1989; 7:1748-56
15. Carmichael J, Allerheiligen S, Walling J. A phase I study of gemcitabine and carboplatin in non-small cell lung cancer. *Semin Surg Oncol* 1996;23:55-9.
16. Geddes DM, Dones L, Hill E, Law K, Harper PG, Spiro SG et al. Quality of life during chemotherapy for small cell lung cancer: assessment and use of a daily diary card in a randomised trial. *Eur J Cancer* 1990;26:484-92.
17. Gower NH, Rudd RM, Ruiz de Elvira MC, Spiro SG, James LE, Harper PG, Souhami RL. Assessment of 'quality of life' using a daily diary card in a randomised trial of chemotherapy in small-cell lung cancer. *Ann Oncol* 1995;6:575-580.
18. Gregory, W.M. Theory and tables for the numbers of patients required to demonstrate non-inferiority in a clinical trial using the logrank test. 1998. Submitted for publication

NCIC CTC expanded Common Toxicity Criteria
(revised 1994)

Grade	0	1	2	3	4
Allergy	none	transient rash, fever < 38° c	urticaria, fever ≥38°c mild bronchospasm	serum sickness, bronchospasm, req. parenteral medication	anaphylaxis
Fever felt to be caused by drug allergy should be coded as allergy. Non allergic drug fever (eg: as from biologics) should be coded under 'flu like symptoms. If fever is due to infection, code infection only					
Other	none	mild	moderate	severe	life threatening
Cardiac					
Dysrhythmias	none	asymptomatic, transient, req. no therapy	recurrent or persistent, no therapy req.	req. therapy	req. monitoring; or hypotension; or ventricular tachycardia,; or fibrillation
Oedema	none	1 + or dependent in evening only	2 + or dependent throughout day	3+	4+, generalized anasarca
Other (includes sinus tachycardia & palpitations)	none	mild	moderate	severe	life threatening
Flu like symptoms					
Arthralgia	none	mild	moderate	severe	-
diaphoreses	none	mild	moderate	severe	-
Fever in absence of infection (includes drug fever)	none	37.1 – 38.0° c	38.1 – 40.0° c	> 40.0° c for < 24 hours	> 40.0° c for > 24 hours or fever accompanied by hypotension
Fever felt to be caused by drug allergy should be coded as allergy. Non allergic drug fever (eg: as from biologics) should be coded under 'flu like symptoms. If fever is due to infection, code infection only					
Lethargy	none	mild – fall of 1 level in perf. status	moderate – fall of 2 levels of perf. status	severe – fall of 3 levels in perf. status	-
Myalgia	none	mild	moderate	severe	-
Rigors/chills	none	mild or brief	pronounced and/or prolonged	cyanosis	-
Other	none	mild	moderate	severe	life threatening
Gastro-Intestinal					
Diarrhoea	none	increase of 2-3 stools/day	increase of 4-6 stools/day	increase of 7-9 stools/day	increase of ≥ 10 stools/day
Nausea	none	able to eat reasonable intake	intake significantly decreased, but can eat	no significant intake	-
Vomiting	none	1 episode in 24 hrs	2-5 episodes in 24 hrs	6-10 episodes in 24 hrs	>10 episodes in 24 hrs or requiring parenteral support
Stomatitis/oral	none	painless ulcers, erythema or mild soreness	painful erythema, oedema or ulcers but can eat	painful erythema, oedema or ulcers and cannot eat	mucosal necrosis and/or req. parenteral or enteral support. Dehydration
Anorexia	none	mild	moderate	severe	dehydration
Other	none	mild	moderate	severe	life-threatening

NCIC CTC Expanded Common Toxicity Criteria. (revised 1994) (contd)

Grade	0	1	2	3	4
Haematology					
Hb	WNL	10 - Normal	8.0-9.9	6.5-7.9	<6.5
WBC	≥ 4.0	3.0 - 3.9	2.0 - 2.9	1.0 - 1.9	<1.0
Plats	WNL	75.0 - Normal	50.0 - 74.9	25 - 49.9	<25.0
Neuts	≥ 2.0	1.5 - 1.9	1.0 - 1.4	0.5 - 0.9	<0.5
Hepatic					
Alk Phos	none	≤ 2.5 x N	2.6 – 5.0 x N	5.1 – 20.0 x N	> 20.0 x N
ALT/AST	none	≤ 2.5 x N	2.6 – 5.0 x N	5.1 – 20.0 x N	> 20.0 x N
Bilirubin	none	-	< 1.5 x N	1.5 – 3.0 x N	> 3.0 x N
Liver- clinical	no change from baseline	-	-	pre-coma	hepatic coma
LDH	normal	< 2.5 x N	2.6 – 5.0 x N	5.1 – 20.0 x N	> 20.0 x N
Other	none	mild	moderate	severe	life threatening
viral hepatitis should be coded as infection rather than liver toxicity					
Infection	none	mild, no active	moderate, localized infect. req. active. trt.	severe, systemic infect., req. parenteral trt., specify site	life threatening sepsis specify site
febrile neutropenia	none	-	-	present	-
Fever felt to be caused by drug allergy should be coded as allergy. Non allergic drug fever (eg: as from biologics) should be coded under Flu like symptoms. If fever is due to infection, code infection only					
Neurological					
Sensory	none or no change	mild paresthesia, loss of deep tendon reflexes (incl. tingling)	Mild or moderate objective sensory loss; moderate parasthesia	sensory loss or parasthesias that interfere with function	-
Constipation	none or no change	mild	moderate	severe	ileus ≥ 96 hours
Renal (CTC Genitourinary Group)					
Haematuria	negative	micro. only	gross, no clots	gross + clots	req. transfusion
Creatinine	WNL	< 1.5 x N	1.5 – 3.0 x N	3.1 – 6.0 x N	>6.0 x N
Skin					
Alopecia	no loss	mild hair loss	pronounced or total head hair loss	total body hair loss	-
Skin Changes	none	hyperpigmentation	atrophy	subcut. fibrosis	ulceration or necrosis
Desquamation	none	dry desquamation	moist desquamation	confluent moist desquamation	-
Rash/Itch (not due to allergy. Includes recall reaction)	none or no change	scattered macular or papular eruption or erythema that is asymptomatic	scattered macular or papular eruption or erythema with pruritus or other associated symptoms	generalized symptomatic macular, papular, or vesicular eruption	exfoliative dermatitis or ulcerating dermatitis
Other	none	mild	moderate	severe	life threatening

RESPONSE CRITERIA (WHO)

Complete response (CR): total disappearance of all known disease for at least 4 weeks.

Partial response (PR): at least 50% reduction in the sum of products of diameters of measured lesions and no new disease, maintained at least 4 weeks.

Stable disease (SD): partial response cannot be established and neither can a 25% increase in tumour size be demonstrated.

Progressive disease (PD): greater than 25% increase in tumour size or the appearance of any new lesion.

Evaluable but not measurable disease will be assessed as PR if there is substantial improvement but not complete resolution of all known disease.

PERFORMANCE SCALE (ECOG)

GRADE

- 0 - Fully active, able to carry on all predisease performance without restriction (Karnofsky 90-100).
- 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work (Karnofsky 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 (Karnofsky 50-60).
- 3 - Capable of only limited self-care, confined to bed or chair more than 50% of waking hours (Karnofsky 30-40).
- 4 - Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair (Karnofsky 10-20).

COCKCROFT & GAULT FORMULA

If creatinine measured in $\mu\text{mol/l}$:

Males:
$$\frac{1.23 \times (140 - \text{age}) \times \text{weight}(\text{kg})}{\text{serum creatinine } (\mu\text{mol/l})}$$

Females:
$$\frac{1.05 \times (140 - \text{age}) \times \text{weight}(\text{kg})}{\text{serum creatinine } (\mu\text{mol/l})}$$

If creatinine measured in mg/%

Males:
$$\frac{(140 - \text{age}) \times \text{wt}(\text{kg})}{72 \times \text{serum creatinine}}$$

Females:
$$\frac{(140 - \text{age}) \times \text{wt}(\text{kg}) \times 0.85}{72 \times \text{serum creatinine}}$$



EORTC QLQ-C30 (version 3)

APPENDIX 6

DAILY DIARY CARD

PLEASE ANSWER THE FOLLOWING QUESTIONS.
WRITE DOWN THE NUMBER OF YOUR ANSWER
IN THE APPROPRIATE BOX OPPOSITE THIS PAGE.

	WEEK 1							WEEK 2							WEEK 3							WEEK 4						
	Mon	Tues	Wed	Thur	Fri	Sat	Sun	Mon	Tues	Wed	Thur	Fri	Sat	Sun	Mon	Tues	Wed	Thur	Fri	Sat	Sun	Mon	Tues	Wed	Thur	Fri	Sat	Sun
DID YOU FEEL SICK TODAY? 1. Not at all 2. Occasionally 3. A lot 4. All the time																												
DID YOU VOMIT TODAY? 1. Not at all 2. Once 3. Twice 4. More than twice																												
HOW GOOD HAS YOUR APPETITE BEEN TODAY? 1. Good 2. Fair 3. Poor 4. Bad																												
HOW MUCH PAIN HAVE YOU HAD TODAY? 1. None 2. A little 3. Quite a lot 4. A lot																												
HOW DID YOU SLEEP LAST NIGHT? 1. Very well 2. Quite well 3. Badly 4. Not at all																												
HOW HAPPY HAVE YOU BEEN TODAY? 1. Happy 2. Fairly happy 3. Unhappy 4. Very unhappy																												
HOW ARE YOU FEELING GENERALLY? 1. Well 2. Fair 3. Poor 4. Very poor																												
WHAT DID YOU DO TODAY? 1. Stayed in bed 2. Got up - did nothing 3. Light work/House work 4. Fully active																												

APPENDIX 7

TNM AND STAGING DEFINITIONS

STAGING

Stage	T	N	M
Occult	X	0	0
0	IS	0	0
Ia	1	0	0
Ib	2	0	0
IIa	1	1	0
IIb	2	1	0
	3	0	0
IIIa	3	1	0
	1-3	2	0
IIIb	Any	3	0
	4	Any	0
IV	Any	Any	1

Ref: Mountain CF - "Revisions in the international system for staging lung cancer", Chest 1997, vol:111(6) P:1710-1717.

DEFINITIONS

Primary tumour (T)

- TX Tumour proven by the presence of malignant cells in bronchopulmonary secretions but not visualized by roentgenography or bronchoscopy, or any tumour that cannot be assessed in retreatment staging.
- T0 No evidence of primary tumour.
- TIS Carcinoma in situ.

contd.

- T1 A tumour that is 3.0 cm or less in greatest dimension, surrounded by lung or visceral pleura, and without evidence of invasion proximal to a lobar bronchus at bronchoscopy*
- T2 A tumour more than 3.0 cm in greatest dimension, or a tumour of any size that either invades the visceral pleura or has associated atelectasis or obstructive pneumonitis extending to the hilar region. At bronchoscopy, the proximal extent of demonstrable tumour must be within a lobar bronchus or at least 2.0 cm distal to the carina. Any associated atelectasis or obstructive pneumonitis must involve less than an entire lung.
- T3 A tumour of any size with direct extension into the chest wall (including superior sulcus tumours), diaphragm or the mediastinal pleura or pericardium without involving the heart, great vessels, trachea, oesophagus, or vertebral body, or a tumour in the main bronchus within 2.0 cm of the carina without involving the carina.
- T4 A tumour of any size with invasion of the mediastinum or involving heart, great vessels, trachea, oesophagus, vertebral body, or carina or with presence of malignant pleural effusion.**

Nodal Involvement (N)

- N0 No demonstrable metastasis o regional lymph nodes.
- N1 Metastasis to lymph nodes in the peribronchial or the ipsilateral hilar region, or both, including direct extension.
- N2 Metastasis to ipsilateral mediastinal lymph nodes and subcarinal lymph nodes.
- N3 Metastasis to contralateral mediastinal lymph nodes, contralateral hilar lymph nodes, or ipsilateral or contralateral scalene or supraclavicular lymph nodes.

Distant Metastasis (M)

- M0 No known distant metastasis.
- M1 Distant metastasis present – specify site(s)

* The uncommon superficial tumour of any size whose invasive component is limited to the bronchial wall and that may extend proximal to the main bronchus is classified as T1.

** Most pleural effusions associated with lung cancer are due to tumour. There are however, some few patients in whom cytopathologic examination of pleural fluid (on more than one specimen) is negative for tumor and the fluid is nonbloody and is not an exudate. When these elements and clinical judgment dictate that the effusion is not related to the tumour, the cases should be staged T1, T2 or T3, with effusion being excluded as a staging element.

'NON-INFERIORITY TRIALS' – METHODOLOGY AND EXAMPLES

Background

It is becoming more common to design clinical trials where a new treatment is hoped to be equally effective as the standard treatment but with less toxicity; so called 'non-inferiority' or 'equivalence' trials. Statistical methods for calculating sample sizes for such trials have been developed where response is the endpoint.¹ There is no comparable method for such trials where survival is the endpoint. Actuarial survival times are continuous data and therefore contain more information than response data which are categorical in nature. Therefore the analysis is more efficient and less patients are required. For conventional (positive) trials, where the aim is to show a *benefit* for the new treatment, methods have been developed for both types of data^{2,3} and the numbers required are considerably less when survival is the endpoint. A new method is presented which enables these calculations to be performed for non-inferiority trials, with a similar reduction in required numbers.

Methodology

The method follows a generally similar line of reasoning to that employed by Makuch and Simon¹, and will now be described in detail.

Suppose the two treatments give rise to survival rates P_1 and P_2 at some chosen time point. Suppose further that the ratio of the hazards (i.e. risks of death) in the two groups does not change with time and is $\theta:1$. Then $\theta = \log_e(P_1)/\log_e(P_2)$. The hazard ratio is approximately log-normally distributed⁴, so let $\log_e(\theta) = \zeta$.

For a particular trial for each event (failure or death) we can calculate the expected number of events, given that the two treatments are equivalent, and compare it with that actually observed. These can then be summed over the whole trial to produce total observed and expected numbers of events in each group. Suppose these totals are O_1 and E_1 respectively. ζ can then be estimated for the particular trial as $(O_1 - E_1)/V$ - see reference 5, where V is the variance of $O_1 - E_1$. Let this estimate be denoted η . Denote the standard error of ζ by σ . Thus σ can also be estimated as $1/\sqrt{V}$ (see below). (Note that $(O_1 - E_1)^2/V$ is the log-rank statistic, which has a χ^2 distribution).

Of course η is also related to P_1 and P_2 by

$$\eta = \log_e(\theta) = \log_e\{\log_e(P_1)/\log_e(P_2)\} \quad [1]$$

Based upon the patients studied η is the best estimate of the log hazard, which represents the treatment efficacy. This observed efficacy is subject to random fluctuation however. Thus when the sample sizes are small, even a small value for η is consistent with a large true difference in hazards (large θ and thus large ζ). An approximate upper $100 \cdot (1 - \alpha)\%$ confidence limit for the true log hazard, ζ , is $\eta + z_{\alpha} \cdot \sigma$, where z_{α} is the upper α tail point of the standard normal distribution (eg, $z_{0.05} = 1.645$).

This confidence statement can be written

$$\Pr(\zeta > \eta + z_{\alpha} \cdot \sigma) = \alpha \quad [2]$$

The confidence limit depends upon the observed log hazard, η (and thus upon P_1 and P_2 - see [1]), and the confidence level α , together with the true log hazard ratio, ζ , and the corresponding sample sizes (which affect V and thus σ). For infinite sample sizes the observed log hazard η is an exact estimate of the true log hazard ζ , since V approaches ∞ , and σ approaches 0. In calculating the confidence limit at the end of the study, one can approximate σ to estimate the unknown true log hazard, ζ , as follows :

Arguing conditionally on the set of patients at risk before each event and letting ϕ_i denote the ratio of patients at risk in the two groups before event i ($i=1,\dots,d$ where the total number of events is d), then²

$$V = \sum_{i=1}^d \frac{\phi_i}{1+\phi_i} \quad [3]$$

(and $\sigma = 1/\sqrt{V}$, see above).

The confidence limit is a random variable, since it involves P_1 and P_2 . It is reasonable therefore to set the sample sizes sufficiently large so that, with a high probability $(1-\beta)$, the confidence limit will not exceed some value δ . This can be written

$$\Pr(\eta + z_\alpha \sigma > \delta) = \beta \quad [4]$$

So that

$$\Pr [(\eta - \zeta)/\sigma > (\delta - \zeta)/\sigma - z_\alpha] = \beta \quad [5]$$

Which implies

$$(\delta - \zeta)/\sigma - z_\alpha = z_\beta \quad [6]$$

where z_β represents the upper β tail point of the standard normal distribution (eg, $z_{0.20} = 0.84$). If there is no difference in treatment efficacy then $\zeta=0$, and if the numbers in the two arms of the trial are equal then we can make the simplifying assumption that $\phi_i=1$ ($i=1,\dots,d$).

Then $V=d/4$, and thus $\sigma = 2/\sqrt{d}$, so that, from [6]:

$$d = 4 \{ (z_\alpha + z_\beta)/\delta \}^2 \quad [7]$$

This last equation specifies the required number of events (in both arms together) to ensure with probability $(1-\beta)$ that the upper $100(1-\alpha)\%$ confidence limit for the true log hazard ratio does not exceed δ . For planning purposes δ is estimated as follows:

Suppose the survival in the standard arm of the trial is known from previous studies etc. to be approximately P_s . A new trial with less toxicity or complications will be considered acceptable if it can be demonstrated with $100 \cdot (1-\alpha)\%$ confidence that it is at worst $x\%$ inferior to the standard treatment. Then

$$\delta = \log_e \{ \log_e(P_s) / \log_e(P_s - [x/100]) \} \quad [8]$$

Having estimated the number of events, d , the total number of patients required in the trial can be estimated by²

$$n = d / (1 - P_s) \quad [9]$$

assuming again equal numbers in the two groups.

Applications: The SCLC and NSCLC Lung trials

SCLC:

It is assumed that PE gives a 20% one year survival ($P_s=.20$) and we want the 95% confidence limit on the hazard at the end of the trial to exclude the possibility that GC is more than 10% worse at one year. We are content to accept a 20% chance of falsely concluding that GC does confer a 10% or more reduction in survival at 1 year.

Thus $z_\alpha=1.645$, $z_\beta=.84$. From [8] $\delta = .358$, and therefore from [7], $d=193$. From [9] $n=241$.

So the trial requires the entry of 241 patients.

NSCLC:

It is assumed that MIC gives a 28% one year survival ($P_s=.28$) and we want the 95% confidence limit on the hazard at the end of the trial to exclude the possibility that GC is more than 10% worse at one year. We are content to accept a 20% chance of falsely concluding that GC does confer a 10% or more reduction in survival at 1 year.

Thus $z_\alpha=1.645$, $z_\beta=.84$. From [8] $\delta = .298$, and therefore from [7], $d=279$. From [9] $n=387$.

So the trial requires the entry of 387 patients.

Simulations

To check the accuracy of the formula a series of simulations were carried out. A value was chosen for β , and the value for the total number of patients required in the trial (n) was derived from [7]. Survival was assumed to follow a negative exponential distribution, with parameter chosen to give the required % at the time under consideration (eg 20% surviving at 1 year). Random samples were then drawn from this distribution for each arm of the trial, to a total number, n . Survival times greater than 1 year were censored at 1 year. The log hazard was calculated for the survival comparison of the two groups and a 1-sided upper $100(1-\alpha)\%$ confidence limit was calculated for the log hazard, as described above. As above, let x be the % below the standard which is still considered acceptable for the new treatment. For different values of P_s and x (and therefore δ) this process was repeated 1,000,000 times, and the proportion of times that the upper $100(1-\alpha)\%$ confidence limit exceeded δ was recorded. This was compared with the chosen value of β .

For the two values used for the lung trials, namely $P_s=.2$ and $P_s=.28$ (with $x=10\%$), the proportions were .205 and .202 respectively. This is very close to the theoretical β of .20. The values estimated for the variance, V , were also very close to those actually seen.

Additional comments

The trial-size estimates for the lung trials are somewhat conservative. Equation [9] which estimates the total number of patients required from the number of events required, assumes that times are censored at the chosen time of 1 year. However, patients continue to die with this disease after 1 year, with only a very small proportion of patients surviving more than 2 years. Thus the total number of *patients* required is in fact very close to the total number of *events* required, and an estimate of 203 patients in total, for the SCLC case, is probably more accurate. This depends to some extent on the time point at which the trial is analyzed. The estimate of 203 assumes that patients are entered over a period of about 3 years, and the trial is analyzed about 1 year after the last patient is recruited. This figure is derived by noting that survival in SCLC is about 2% at 2 years⁶. Thus if analysed 1 year after the entry of the last patient two-thirds of

the patients entered will be at or beyond 2 years, and have a survival rate of about 2%, while the remaining one-third will vary between 2% and 20%, perhaps averaging about 11%. Thus the average survival at the time of analysis will be approximately 5%. The total number to be entered will therefore be $d \cdot (100/95) = 203$.

Under similar assumptions, with a 2-year survival estimate of 5%⁷ for NSCLC, an estimate of about 302 patients required in total is reasonable for the NSCLC case.

References

- 1 Robert Makuch and Richard Simon. *Sample size requirements for a conservative therapy*, Cancer Treatment Reports, 1978, 62: 1037-1040.
- 2 L.S. Freedman. *Tables of the number of patients required in clinical trials using the logrank test*, Statistics in Medicine, 1982, 1: 121-129.
- 3 Pocock S.J. *The size of a clinical trial*. In: *Clinical Trials. A Practical Approach*, John Wiley, 1991, pp 123-141.
- 4 R. Simon. *Confidence intervals for reporting results of trials*, Ann Intern Med., 1986, 105: 429-435.
- 5 D.G. Altman. In: *Practical Statistics for Medical Research*, Chapman and Hall, 1991, pp 375-385.
- 6 R.L. Souhami & K. Law. *Longevity in small cell lung cancer*, Br. J. Cancer, 1990, 61: 584-589.
- 7 M.H. Cullen, L.J. Billingham, C.M. Woodroffe et al, *Mitomycin, ifosphamide and cisplatin in unresectable non-small cell lung cancer: Effects on survival and quality of life*. Submitted, 1998.

Appendix E

Scales of performance status referred to in the text

- ECOG
- WHO (simplified ECOG)
- Karnofsky Performance Status

ECOG PERFORMANCE STATUS*

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

- As published in Am. J. Clin. Oncol.:
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

WHO Performance Status (simplified ECOG score)

- 0 Asymptomatic
- 1 Symptomatic, fully ambulatory
- 2 Symptomatic in bed <50% day
- 3 Symptomatic in bed >50% day
- 4 Bedridden
- 5 Dead

Karnofsky Performance Status

- 100 Normal, no complaints, no evidence of disease
- 90 Able to carry on normal activity: minor symptoms of disease
- 80 Normal activity with effort: some symptoms of disease
- 70 Cares for self: unable to carry on normal activity or active work
- 60 Requires occasional assistance but is able to care for needs
- 50 Requires considerable assistance and frequent medical care
- 40 Disabled: requires special care and assistance
- 30 Severely disabled: hospitalization is indicated, death not imminent
- 20 Very sick, hospitalization necessary: active treatment necessary
- 10 Moribund, fatal processes progressing rapidly
- 0 Dead

References

- Aaronson NK, Bullinger M, & Ahmedazi S 1988, "A modular approach to quality of life assessment in cancer clinical trials," in *Recent Results in Cancer Research*, Springer-Verlag, Heidelberg.
- Aaronson NK, Ahmedazi S, & Bullinger M 1991, "The EORTC quality of core questionnaire. Interim results of an international field study," in *Effect of Cancer on Quality of Life*, Osoba D, ed., CRC Press, California.
- Aaronson NK, Ahmedazi S, Bergman B, & et al 1993, "The EORTC QLQ-30 A quality of life instrument for use in international trials in clinical oncology", *Journal of the National Cancer Inst*, vol. 85, pp. 365-376.
- Addington Hall J & Kalra L 2003, "Who should measure quality of life?," in *Quality of Life*, Carr A, Higginson I, & Robinson PG, eds., BMJ, London, pp. 54-62.
- Ahmedzai S 1993, "Quality of life in Palliative Care, philosophy science or pontification?", *Progress In Palliative Care*, vol. 1, pp. 6-10.
- Anderson H, Hopwood P, Stephens RJ, Thatcher N, Cottier R, Nicholson M, & et al 2000, "Gemcitabine plus best supportive care (BSC) Vs BSC in inoperable non small cell lung cancer-a randomised trial with quality of life as the primary outcome", *British Journal of Cancer*, vol. 83, pp. 447-453.
- Andrews FM & Withey SB 1976, *Social Indicators of Well-being: American's perception of life quality* Plenum Press, New York.
- Arman M & Rehnsfeldt A 2003, "The hidden suffering amongst breast cancer patients. A qualitative metasynthesis", *Qualitative Health Research*, vol. 13,no. 4, pp. 510-527.
- Bakker W, V. A., Aaronson NK, & et al 1986, "Vindistine, Cisplatin and Bleomycin combination chemotherapy in Non Small Cell Lung Cancer", *European Journal of Cancer*, vol. 22, pp. 963-970.
- Ballard A, Green T, McCaa A, & Logsdon CM 1997, "A comparison of the level of hope in patients with newly diagnosed and recurrent cancer", *Oncology Nursing Forum*, vol. 24,no. 5, pp. 899-904.
- Barkauskas VH, Baumann LC, & Darling-Fisher CS 2002, *Health and Physical Assessment*, 3rd ed, Mosby, St Louis.
- Baruch G 1981, "Moral Tales, Parents stories of their encounters with health professionals", *Sociology of Health and Illness* , vol. 3,no. 3, pp. 275-295.
- Beadle GF, Yates PM, Najman JM, Clavarino A, Thomson D, & et al 2004, "Beliefs and practices of patients with advanced cancer-implication for communication", *British Journal of Cancer*, vol. 91, pp. 254-257.

Beck A, Ward C, Mendelson M, Mock J, & Erbaugh J 1961, "An Inventory for measuring depression", *Archives General Psychiatry*, vol. 4, pp. 561-571.

Beck AT, Steer RA, Kovacs, M, & Garrison G 1985, "Hopelessness and eventual suicide: A ten year prospective study of patients", *American Journal Of Psychiatry*, vol. 142, pp. 559-563.

Belbin M 2003, *Management Teams-Why they succeed or fail*, 2nd ed, Butterworth-Heinemann, Oxford.

Bell J 1999, *Doing your research project-A guide for first time researchers in education and social science*, Third ed, Open University Press, Milton Keynes.

Benit L, Sandman P, & Rasmussen BH 2005, "On becoming dependent on mechanical home ventilation", *Journal of Advanced Nursing* , vol. 49,no. 1, pp. 33-42.

Benner P & Wrubel J 1989, *The Primacy of Caring* Addison Wesley Publishing Company, Woking.

Bennett MI & Bennett BC 1984, "The uses of hopelessness", *American Journal Of Psychiatry*, vol. 141, pp. 559-562.

Berckman KL & Austin JK 1993, "The causal attribution and perceived control and adjustment in patients with lung cancer", *Oncology Nursing Forum*, vol. 20, pp. 20-30.

Berelson B & Lazarsfeld PF 1948, *The analysis of communication content* University of Chicago Press, Chicago.

Bergman B, Aaronson NK, Ahmedazi S, & et al 1994, "The EORTC QLQ 30 + LC 13 a modular supplement to the EORTC core quality of life questionnaire for use in lung cancer clinical trials", *European Journal of Cancer*, vol. 30A, pp. 635-642.

Bergner M, Bobbitt RA, & Carter WB 1981, "The Sickness Impact Profile: Development and revision of a health status measure", *Medical Care*, vol. 19, pp. 787-805.

Bernhart J, Gusset H, & Hurney C 1995, "Quality of life in cancer clinical trials", *Supportive Cancer Care*, vol. 3,no. 1, pp. 66-71.

Bertero C & Ek A 1993, "Quality of life in adults with acute Leukemia", *Journal of Advanced Nursing*, vol. 18, pp. 1346-1353.

Binnie A & Titchen A 1999, *Freedom to Practice-The Development of Patient Centered Nursing* Butterworth-Heinemann, Oxford.

Blaxter M & Paterson E 1982, *Mothers and Daughters* Heinemann Educational Press, London.

Boas ML 1983, *Mathematical Methods in the Physical Sciences*, 2nd ed, Wiley & Son, New York.

Bokkel-Huinik WW, Bergman B, Chemaaisani A, Dornoff W, Drings P, & et al 1999, "Single agent Gemcitabine: an active and better tolerated alternative to standard cisplatin based chemotherapy in locally advanced or metastatic non small cell lung cancer", *Lung cancer*, vol. 26, pp. 85-94.

Bourke SJ & Brewis RAL 2000, *Respiratory Medicine*, 5th ed, Blackwell Scientific, London.

Bowling A 1995, *Measuring Disease*, 1st ed, Open University Press, Buckingham.

Bowling A 1997, *Measuring Health*, 2nd ed, Open University Press, Buckingham.

Bowling A 2001. *Measuring Disease: A review of disease specific quality of life measurement scales*, 2nd ed, Open University Press, Bucks.

Bowling A 2003, "Current state of the art in quality of Life measurement," in *Quality Of Life*, Carr A, Higginson I, & Robinson PG, eds., BMJ, London, pp. 1-18.

Bowling A, Gabriel Z, Dykes J, Marriott-Dowding L, Evans O, Fleissig A, Bannister D, & Sutton S. Lets Ask Them: A national survey of definitions of quality of life and its enhancement among people aged 65 and over. *International Journal of Aging and Human Development* 56[4], 269-306. 2003.
Ref Type: Journal (Full)

Boyle P, Gandini S, & Grey N 2000, "Epidemiology of Lung Cancer: A century of great success and ignominious failure," in *Textbook of Lung Cancer*, Hansen H ed, ed., Martin Dunitz, London.

Bradburn NM 1969, *The structure of psychological well-being* Aldine, Chicago.

Brown J, Thorpe H, Napp V, Fairiamb DJ, Gower NH, Milroy R, Parmar MK, Rudd R, Spiro S, Stephens RJ, Waller D, West P, & Peake M 2005, "Assessment of Quality of Life in the supportive care setting of the Big Lung Trial in Non Small Cell Lung Cancer", *Journal of Clinical Oncology*, vol. 23,no. 30, pp. 7417-7427.

Buckman R 1996, "Talking to patients about cancer", *British Medical Journal*, vol. 313, pp. 699-700.

Bullinger M, Anderson R, Cella DF, & Aaronson NK 1993, "Developing and evaluating cross-cultural instruments-from minimum requirements to optimum models", *Quality of Life Research*, vol. 2, pp. 451-459.

Burgess C, Morris T, & Pettingale KW 1988, "Psychological responses to a cancer diagnosis II. Evidence for coping styles", *Psychosomatic Research*, vol. 32,no. 3, pp. 263-272.

Burman E 1986, *The Templars Knights of God Aquarian*, Northants.

Burriss HA, Moore MJ, Andersen J, Green MR, Rothenbery ML, & et al 1997, "Improvements in survival and clinical benefit with Gemcitabine as first line therapy for patients with advanced pancreas cancer: A randomised trial", *Journal of Clinical Oncology*, vol. 15,no. 6, pp. 2403-2413.

Byock IR 1994, "When Suffering Persists", *Journal of Palliative Care*, vol. 10,no. 2, pp. 8-13.

Byrne M 1992, "Cancer chemotherapy and quality of life", *British Medical Journal*, vol. 304. pp. 1523-1524.

Campbell A, Converse PE, & Rodgers WL 1976, *The quality of American life: Perceptions, Evaluations and Satisfactions* Sage, New York.

Campbell DT, Converse P, & Rogers WL 1976, *The quality of American life: Perceptions, Evaluations and Satisfactions* Russell Sage, New York.

Cancer Research UK. Incidence by age and sex/lung cancer. CRUK . 2004. 5.
Ref Type: Electronic Citation

Cancer Research UK. Cancer Statistics (UK). Cancer Research UK . 2005. 6.
Ref Type: Electronic Citation

Cancer Services Collaborative 2001, *Service Improvement Guide (lung)*, HMSO, London.

Cardenal F, Lopez-Cabrerizo MP, Anton A, Alberola V, Massuti B, Carrato A, & et al 1999, "Randomised phase III study of Gemcitabine-cisplatin versus etoposide-cisplatin in the treatment of locally advanced or metastatic non small cell lung cancer", *Journal of Clinical Oncology*, vol. 17, pp. 12-18.

Carlens E & Darhlstrom G Nou E 1970, "Comparat5ive survival of lung cancer patients after diagnosis", *Scandinavian Journal of Respiratory Disease*, vol. 51, pp. 268-275.

Carr A, Thompson P, & Kirwan J 1996, "Quality of life measures", *British Journal of Rheumatology*, vol. 35, pp. 275-281.

Carr A, Gibson B, & Robinson PG 2001, "Is quality of life determined by expectation or experience?", *British Medical Journal*, vol. 322, pp. 1240-1243.

Cassell EJ 1985, "The theory of doctor-patient communication," in *Talking with patients*, vol. 1 Cassell EJ, ed., MIT Press, Cambridge MA.

Cassell EJ 1992, "The nature of suffering: physical, psychological, social and spiritual aspects," in *The hidden dimensions of illness; human suffering*, Stark PL & McGovern JP, eds., National League for Nursing Press, New York, pp. 1-10.

Cassell EJ 2004, *The nature of suffering and the goals of medicine*, 2nd ed, Oxford University Press, Oxford.

Cawkwell G trans 1972, *Xenophon The Persian Expedition* Penguin, Harmondsworth.

Cella DF. Functional assessment and quality of life: Current views on measurement and intervention. American Cancer Society. First National Conference on Cancer Nursing Research. 1-12. 1989. Atlanta.
Ref Type: Generic

Cella DF 1992, "Quality of life-the concept", *Journal of Palliative Care*, vol. 8,no. 3, pp. 8-13.

Cella DF, Tulsky DS, & Gray G et al 1993, "Functional Assessment Cancer Therapy Scale: Development and validation of the general measure", *Journal of Clinical Oncology*, vol. 11, pp. 570-579.

Cella DF, Bonomi AE, Lloyd SR, & et al 1995, "Reliability and validity of the Functional Assessment of Cancer Therapy-Lung (FACT-L) quality of life instrument", *Lung cancer*, vol. 12, pp. 199-220.

Cella DF 1998, "Quality of Life," in *Psycho-oncology*, Holland JC, ed., Oxford University Press, New York.

Cella DF, Chang CH, Lai, JS, & Webster K 2002, "Advances in quality of life measurement in oncology patients", *Seminars in Oncology*, vol. 29,no. June, pp. 60-68.

Chapple A, Ziebland S, & McPherson A. Stigma, shame and blame experienced by patients with lung cancer: qualitative study. *British Medical Journal BMJ*, doi:10.1136/bmj.38111.639734.7c. 2004.
Ref Type: Electronic Citation

Chaturvedi SK 1991, "What's important for quality of life to Indians-In relation to cancer", *Social Science and Medicine*, vol. 33,no. 1, pp. 91-94.

Chief Medical Officers Expert Advisory Group on Cancer 2004, *A Policy framework for commissioning cancer services (commonly know as The Calman-Hine Report)*, Department of Health, London.

Christman NJ 1988, "Uncertainty and adjustment during radiotherapy", *Nursing Research*, vol. 39,no. 1, pp. 17-20.

Cicero & Grant M trans 1971, *On the Good Life* Penguin, Harmondsworth.

Clegg A, Scott DA, Sidhu M, Hewitson P, & Waugh N 2001, *A rapid and systemic review of the clinical effectiveness and cost effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine in non small cell lung cancer*, HMSO, Vol 5, 32.

Cohen G, Forbes J, & Garraway M 1996, "Can different patient satisfaction survey methods yield consistent results?", *British Medical Journal*, vol. 313, pp. 841-844.

Coleman MP, Rachet B, & Woods L 2004, "Trends and socioeconomic inequalities in cancer survival in England and Wales to 2001", *British Journal of Cancer*, vol. 90,no. 7, pp. 1367-1373.

Cooley ME 1998, "Quality of life in persons with non small cell lung cancer-a concept analysis", *Cancer Nursing*, vol. 21,no. 3, pp. 151-161.

Corbin J & Strauss A 1988, *Unending work and care* Jossey Bass, San Francisco.

Corner J & Wilson-Barnett J 1992, "The newly registered nurse and the cancer patient: an educational evaluation", *International Journal of Nursing Studies*, vol. 29,no. 2, pp. 177-190.

Corner J. Beyond Survival rates and side effects: cancer nursing as therapy. The Robert Tiffany Lecture. *Cancer Nursing* 20[1], 3-11. 1997.
Ref Type: Journal (Full)

CRC 2001, *Public Opinion (Lung Cancer)*, MORI.

Crino L, Scaglotti GV, Ricci S, De Marinis F, Rinaldi M, Gridelli C, & et al 1999, "Gemcitabine and cisplatin Vs mitomycin, ifosfamide and cisplatin in advanced non small cell lung cancer: a randomised phase II study by the Italian Lung Cancer Project", *Journal of Clinical Oncology*, vol. 17, pp. 3522-3530.

Crook A Duffy A, Girling DJ, Souhami B, & Parmar MK. Survey on the treatment of NSCLC in England and Wales. *European Respiratory Journal* 10, 1552-1558. 1997.
Ref Type: Journal (Full)

Crooker KJ and Near JP 1998, "Happiness and satisfaction: measures of affect and cognition?", *Social Indicators Research*, vol. 44, no. 2, pp. 195-224.

Cullen MH 1993, "The MIC Regemin in Non Small Cell Lung Cancer", *Lung cancer*, vol. 9, p. 581.

Cummins RA 1997, "Assessing quality of life," in *Quality of life for people with disabilities: Models, Research and Practice*, 2nd ed, Brown RI, ed., Stanley Thomas, Cheltenham.

Cummins RA, Gullione E, & Lau ALD 2005, *A model of subjective being in homeostasis: the role of personality* Kluwer Academic, Dordrecht.

Notes: In Press

Cunningham AJ 1986, "Information on health in the many levels of man: toward a more comprehensive theory of health and disease", *Advances*, vol. 1, no. 1, pp. 32-45.

Dark GG & O'Brien MER 2001, "The evidence base for palliative chemotherapy," in *The Effective Management of Lung Cancer*, Muers MF et al., eds., Aesculapius, London.

Dawson J, Fitzpatrick R, & Carr A 1996, "Questionnaire on the perceptions of patients about total hip replacement", *Journal of Bone and Joint Surgery*, vol. 78, no. B, pp. 185-190.

de Haes JC & Van Knippenberg FCE 1985, "Quality of life of cancer patients: A review of the literature", *Social Science and Medicine*, vol. 20, no. 8, pp. 809-817.

De Sorbiere S 1672, "Advice to the young physician," in *The silent world of doctor and patient*, Katz J, ed., Free Press, New York.

Deitmier SB, Muller MG, & et al 2002, "The role of health related quality of life in palliative chemotherapy treatment decisions", *Journal of Clinical Oncology*, vol. 15, no. 20, pp. 1056-1062.

Department of Health 2000, *The NHS Cancer Plan: A plan for investment, a plan for reform*, HMSO, London.

Notes: 2000a

Department of Health 2000, *The Nursing Contribution to Cancer Care*, HMSO.

Notes: 2000b

Department of Health 2003, *The NHS Cancer Plan-Maintaining the momentum*, HMSO.

Diamond J 2005, *Collapse. How societies choose to fail or survive* Penguin, London.

Dick R. Resource Papers in Action Learning. scu.edu.au . 2005. 2005.
Ref Type: Electronic Citation

Dingwell R 1977, *The Ceremonial order of the clinic* Ashgate, Aldershot.

Dingwell R 2001, *Aspects of illness*, 2nd ed, Ashgate, Aldershot.

Doll R & Hill AB 1950, "Smoking and carcinoma of the lung", *British Medical Journal*, vol. ii, pp. 739-748.

Doll R & Hill AB 1952, "A study of the aetiology of carcinoma of the lung", *British Medical Journal*, vol. ii, pp. 1271-1286.

Doll R & Hill AB 1954, "The mortality of doctors in relation to their smoking habits", *British Medical Journal*, vol. ii s, pp. 1451-1455.

Donaldson GW & Moinpour CM 2005, "Learning to live with missing Quality of Life data in advanced-stage disease trials", *Journal of Clinical Oncology*, vol. 23,no. 30, pp. 7380-7384.

Downie RS 1999, "The Value and Quality of Life", *Journal of the Royal College of Physicians of London*, vol. 33,no. 4 July/Aug, pp. 378-381.

Dranitsaris G, Cottrell W, & Evans W. Cost-effectiveness of chemotherapy for non small lung cancer. *Current Opinion in Oncology* 14[4], 375-383. 2002.
Ref Type: Journal (Full)

Drenowski J 1974, *On Measuring and Planning Quality of Life*, Morton de Gruyter, The Hague.

Ekberg-Aronsson M Nilsson PM, Nilsson JA, Pehrsson K, & Lofdahl CG 2006, "Socio-economic status and lung cancer risk including histologic subtyping-a longitudinal study", *Lung cancer*, vol. 50,no. 1, pp. 21-9.

Ellis PA, Smith IE, Hardy JR, & et al 1995, "Symptom relief with MVP chemotherapy in advanced non small cell lung cancer", *British Journal of Cancer*, vol. 71, p. 366.

Ellis PA & Tattersall MH 1999, "How should doctors communicate the diagnosis of cancer to patients?", *Annals of Medicine*, vol. 31,no. 5, pp. 336-341.

Engel G 1977, "The need for a new medical model: A challenge for biomedicine", *Science*, vol. 196, pp. 129-136.

EORTC. EORTC QLQ 30 validity. European Organization for Research and Treatment of cancer . 2005. 6.
Ref Type: Electronic Citation

Erikson R & Uusitalo H. *The Scandinavian Approach to Welfare Research*. 1987. Stockholm, Swedish Institute for Social Research. Reprint Series 181.
Ref Type: Serial (Book, Monograph)

Erikson R 1993, "Descriptions of Inequality-The Swedish Approach to Welfare Research," in *The Quality of Life*, Nussbaum M & Sen A, eds., Clarendon Press, Oxford.

Ersek M 1992, "The process of maintaining hope in adults undergoing bone marrow transplantation for leukaemia", *Oncology Nursing Forum*, vol. 19, pp. 883-889.

Fagerstrom L & Bergbom I 1998, "Measuring the unmeasurable-A caring science perspective on patient classification", *Journal of Nursing Management*, vol. 6, pp. 165-172.

Fargerstom L, Eriksson K, & Bergbom EI 1998, "The patients' perceived caring needs as a message of suffering", *Journal of Advanced Nursing*, vol. 28, no. 5, pp. 978-987.

Notes: 1998a

Faull C & Woof R 2002, *Palliative Care* Oxford University Press, Oxford.

Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, & Bottomley A 2001, *The EORTC QLQ 30 Scoring Manual*, 3rd ed, European Organisation for Research and Treatment of Cancer, Brussels.

Ferrans CE & Powers MJ 1990, "Quality of Life Index: Development and psychometric properties", *Advances in Nursing Science*, vol. 8, pp. 15-24.

Feynman RP 2005, *Don't you have time to think?* Penguin, London.

Fife BL 1995, "The measurement of meaning in illness", *Social Science and Medicine*, vol. 40, no. 8, pp. 1021-1028.

Finkelstein DM, Cassileth BR, & Bonomi PD 1988, "A pilot study of the Functional Living Index-Cancer (FLIC) scale for the assessment of quality of life", *American Journal of Clinical Oncology*, vol. 11, pp. 630-633.

Fitzpatrick R, Davey C, Buxton MJ, & Jones DR 1998, *Evaluating patient based outcome measures for use in clinical trials*, NCCHTA, 2(14).

Forjaz MJ & Guarnaccia CA 2001, "A comparison of Portuguese and American patients with hematological malignancies: a cross cultural survey of health related quality of life", *Psycho-oncology*, vol. 10, no. 3, pp. 251-258.

Fowler JK Rickman JG 1898, *Diseases of the Lungs* Longman Greene & Co, London.

Frankl V 1984, *Man's search for meaning* Washington Square Press, New York.

Frauman JF, Devessa SS, Hoover RN, & Kinlen LJ 1993, "Epidemiology of Cancer," in *Cancer Principles and Practice of Oncology*, DeVitta VT, Hellman S, & Rosenberg SA, eds., Lippencott, Philadelphia.

Fredriksson L 1998, "The caring conversation-talking about suffering", *International Journal of Human Caring*, vol. 1, pp. 24-32.

Fredriksson L & Eriksson K 2001, "The patient's narrative of suffering-A path to health?", *Scandinavian Journal of Caring Sciences*, vol. 15,no. 1, pp. 3-11.

Frisbie R. The use of microcomputer programs to improve reliability and validity of content analysis. Purdue ICS . 1986. 6.

Ref Type: Electronic Citation

Galante JM, Bowles TL, Khatri VP, & et al 2005, "Experience and attitudes of surgeons toward palliation in cancer", *Archives of Surgery*, vol. 140,no. 9, pp. 873-878.

Geddes DM, Dones L, Hill E, Law K, Harper PG, & Spiro S 1990, "Quality of life during chemotherapy for small cell lung cancer: Use of the daily diary card in a randomised trial", *European Journal of Cancer*, vol. 26, pp. 484-492.

Georgoulis V, Papadakis E, Alexopolous A, Tsaifaki X, Rapti A, & et al 2001, "Platinum based and non platinum based chemotherapy in advanced non small cell lung cancer: A randomised multicentre trial", *Lancet*, vol. 357, pp. 1478-1484.

Gerhardt U. Qualitative research on chronic illness, the issue and the story. *Social Science and Medicine* 30[11], 1149-1159. 1990.

Ref Type: Journal (Full)

Girzadas PM, Counte MA, & Glandon G 1993, "An analysis of elderly health and life satisfaction", *Behav Health Aging*, vol. 3, pp. 103-117.

Goldbeck R 1997, "Denial in physical illness", *Journal of Psychosomatic Research*, vol. 43,no. 6, pp. 575-593.

Goldstraw P 2000, "Staging, Classification and Prognosis," in *Textbook of Lung Cancer*, Hansen H ed, ed., Martin Dunitz, London.

Goldstraw P & Crowley JJ 2006, "The International Association for the Study of Lung Cancer International Staging Project on Lung Cancer", *Journal of Thoracic Oncology*, vol. 1,no. 4, pp. 281-286.

Gralla RJ 1994, "Measuring quality of life in patients with lung cancer", *Lung cancer*, vol. 11, pp. 70-71.

- Grassi L, Giraldi T, Messina EG, & et al 2000, "Physicians attitudes to, and problems with, truth telling to cancer patients", *Supportive Care in Cancer*, vol. 8,no. 1, pp. 40-45.
- Gregory DM 1994, "The Myth of Control, Suffering in Palliative Care", *Journal of Palliative Care*, vol. 10,no. 2, pp. 18-22.
- Grilli R, Oxman AD, & Julian JA 1993, "Chemotherapy for advanced non small cell lung cancer: How much benefit is enough?", *Journal of Clinical Oncology*, vol. 11, pp. 1866-1872.
- Gurin G, Verloff J, & Field S 1960, *Americans views of their mental health* Basic Books, New York.
- Hardy JR, Noble T, & Smith IE 1989, "Symptom relief with moderate dose chemotherapy (mitomycin C, vinblastine and cisplatin) in advanced non small cell lung cancer", *British Journal of Cancer*, vol. 60, pp. 429-430.
- Haura FB 2001, "Treatment of advanced non small cell lung cancer: A review", *Cancer Control Journal*, vol. 8,no. 4.
- Hawthorne MH & Hixon ME 1994, "Functional status, mood disturbance and quality of life in patients with heart failure", *Progress in Cardiovascular Nursing*, vol. 9, pp. 22-32.
- Hayry M 1991, "Measuring Quality of Life", *Theoretical Medicine*, vol. 12, pp. 97-116.
- Hayry M 1999, "Measuring the Quality of Life: Why, How and What?," in *Individual Quality of Life*, 1st ed, Joyce CRB, O'Boyle CA, & McGee H, eds., Harwood Academic Press, Amsterdam.
- Helsing M 1998, "Quality of life and survival", *European Journal of Cancer*, vol. 34,no. 7, pp. 1036-1044.
- Hewitson P 1973, *Health and Illness* Academic Press, London.
- Hilton BA 1988, "The phenomenon of uncertainty in women with breast cancer", *Mental Health Nursing*, vol. 9, pp. 217-238.
- Hinton J 1975, "The influence of previous personality on reactions to having terminal cancer", *Omega*, vol. 6, pp. 95-111.
- Hippocrates, Chadwick J, & Mann WN 1983, *Hippocratic Writings (The Hippocratic Corpus abridged)* Penguin, London.

Holland JC. Psycho-oncology; Where are we at and where are we going?
Journal of psychosocial oncology 10[2], 103-112. 1992.
Ref Type: Journal (Full)

Holland JC 1998, *Psycho-oncology* Lippencott, Philadelphia.

Hollen PJ, Gralla RJ, Kris MG, & et al 1993, "Quality of life assessment in individuals with lung cancer, testing the Lung Cancer Symptom Scale (LCSS)", *European Journal of Cancer*, vol. 29 a, no. s 1, p. s51-s58.

Hollen PJ, Gralla RJ, Kris MG, Cox C, Belani CB, & et al 1994, "Measurement of Quality of Life in patients with lung cancer in multicenter trials of new therapies", *Cancer*, vol. 73,no. 8, pp. 2087-2098.

Hollen PJ & Gralla RJ 1996, "Comparison of quality of life instruments in patients with lung cancer", *Seminars in Oncology*, vol. 23,no. s5, pp. 31-40.

Hollen PJ, Gralla RJ, Cox C, Eberly SW, & Kris MG 1997, "A dilemma in analysis: Issues in the serial measurement of quality of life in patients with advanced lung cancer", *Lung cancer*, vol. 19,no. 2, pp. 119-136.

Hollen PJ, Gralla RJ, Kris MG, Eberly SW, & Cox C 1999, "Normative data and trends in quality of life from the Lung Cancer Symptom Scale (LCSS)", *Supportive Cancer Care*, vol. 7,no. 3, pp. 140-148.

Holsti OR 1969, *Content Analysis for the Social Sciences and Humanities* MIT, Reading, Mass. USA.

Hopwood P & Thatcher N 1990, "Preliminary experience with quality of life evaluation in patients with lung cancer", *Oncology*, vol. 4, pp. 158-162.

Hopwood P 1992, "Progress, problems and priorities in quality of life research", *European Journal of Cancer*, vol. 28a, pp. 1748-1752.

Hopwood P 1996, "Quality of Life assessment in chemotherapy trials for non small cell lung cancer: Are theory and practice significantly different?", *Seminars in Oncology*, vol. 5,no. Suppl 10, pp. 60-64.

Houldin AD 2000, *Patients with cancer* Lippincott, Philadelphia.

Hyland ME 1999, "A reformulation of quality of life for medical science," in *Individual Quality of Life*, Joyce CRB, O'Boyle CA, & McGee H, eds., Harwood Academic Press, Amsterdam.

IARC. Eurocare 3: Cancer survival in Europe. IARC . 2003. 6.
Ref Type: Electronic Citation

IASLC 2000, *Textbook of Lung Cancer* Martin Dunitz, London.

Ihde DC 1992, "Chemotherapy for lung cancer", *New England Journal of Medicine*, vol. 327, pp. 1434-1441.

Janis IL 1967, "Effects of fear arousal on attitude change," in *Advances in Experimental Social Psychology*, Berkowitz L, ed., Academic Press, New York.

Jassem J, Krzakowski M, Roszkowski K, Ramlau R, Slominski JM, Szczesna A, & et al 2002, "A phase II study of gemcitabine plus cisplatin in patients with advanced non small cell lung cancer: Clinical outcomes and quality of life", *Lung cancer*, vol. 35,no. 1, pp. 73-79.

Jones PW, Baveystock CM, & Littlejohns PJ 1989, "Relationship between general health measured with the Sickness Impact Profile and respiratory symptoms, physiological measures and mood in patients with chronic airflow limitation", *American Review of Respiratory Disease*, vol. 140, pp. 1538-1543.

Kaasa S & Mastekaasa A 1988, "Psychosocial well-being of patients with inoperable NSCLC: The importance of treatment and disease related factors", *Acta Oncologica*, vol. 27, pp. 829-835.

Kahn, DL, & Steeves RH 1986, "The experience of suffering: conceptual clarification and theoretical definition", *Journal of Advanced Nursing*, vol. 11, pp. 623-631.

Kahn DL & Steeves RH 1995, "The significance of suffering in cancer care", *Seminars in Oncology Nursing*, vol. 11,no. 1, pp. 9-16.

Karamanoukian HL Soltoski PR & Salerno TA 2001, *Thoracic Surgery Secrets*, 4th ed, Hanley and Belfus, Philadelphia.

Karnofsky DA, Abelman WH, Craver LF, & Burchenal JH 1948, "The use of Nitrogen Mustard in the palliative treatment of carcinoma, with particular reference to bronchogenic carcinoma", *Cancer*, vol. 1, pp. 634-656.

Kegan R 1982, *The evolving self-problems and process in human development* Harvard University Press, Cambridge MA.

Kim MK & Alvi A 1999, "Breaking the bad news of cancer-the patient's perspective", *Laryngoscope*, vol. 109,no. 7, pp. 1064-1067.

King RJB. *Cancer Biology*. 2000. England, Pearson.
Ref Type: Generic

Klagsbrun C 1994, "Patient, family and staff suffering", *Journal of Palliative Care*, vol. 10,no. 2, pp. 14-17.

Klatersky J & Paesmann SM 2001, "Response to chemotherapy quality of life, benefits and survival in non small cell lung cancer", *Lung cancer*, vol. 4, pp. 95-101.

Knutsdon P & Suzuki D 1992, *Wisdom of the elders* Stoddart & Co, Toronto.

Koller M, Lorentz W, Wagner K, Neil A, Trott, D, & et al 2000, "Expectations and quality of life of cancer patients undergoing radiotherapy", *Journal of the Royal Society of Medicine*, vol. 93,no. 12, pp. 609-610.

Koller M & Lorentz W 2002, "Quality of life a deconstruction for clinicians", *Journal of the Royal Society of Medicine*, vol. 95, pp. 481-488.

Kong SX & Gandhi SK 1997, "Methodological assessments of Quality of Life measures in clinical trials", *Annals of Pharmacotherapy*, vol. 31, pp. 830-836.

Kosmidis P 1996, "Quality of life as a new endpoint", *Chest*, vol. 109, pp. 110s-112s.

Krippendorff K 2004, *Content Analysis-an introduction to its methodology*, 2nd ed, Sage Publications, Thousand Oaks CA.

Krishnasamy M & Wilkie E 1999, *Lung Cancer: Patients', families and professionals perceptions of health care need. A national needs assessment study* London.

Kruijver IP, Kerkstra A, Bensing JM, & van der Wiel HB 2000, "Nurse-patient communication in cancer care-A review of the literature", *Cancer Nursing*, vol. 23,no. 1, pp. 20-31.

Kuppelomaki M & Lauri S 1998, "Cancer patients reported experience of suffering", *Cancer Nursing*, vol. 21,no. 5, pp. 354-369.

Landis BJ 1996, "Uncertainty, spiritual wellbeing and psychosocial adjustment to chronic illness", *Issues in Mental Health Nursing*, vol. 17,no. 3, pp. 217-231.

Lasswell HD 1965, *Studies in quantitative semantics* MIT Press. Cambridge, Mass.

Lazarus RS 1983, "The costs and benefits of denial," in *The Denial of Stress*, Breznitz S, ed., International University Press, New York.

Lazarus RS & Folkman S 1984, *Stress appraisal and coping* Springer, New York.

Leary A & Corrigan P. Redesign of thoracic surgical services-using an oncology focus to inform change. *European Journal of Oncology Nursing* . 2005. Ref Type: In Press

Leary A 2005, "Education in the acute setting", *Cancer Nursing Practice*, vol. 4,no. 7, pp. 22-23.

Levathal H, Nerenz DR, & Levanthal E 1982, "Feelings of threat and dehumanization in the medical care system," in *Advances in Environmental Psychology*, Baum A & Singer JE, eds..

Lin CC 1999, "Disclosure of the cancer diagnosis as it relates to the quality of pain management among patient's with cancer", *Journal of Pain and Symptom Management*, vol. 18,no. 5, pp. 331-337.

Lindholm L & Eriksson K 1993, "To understand and alleviate suffering in a caring culture", *Journal of Advanced Nursing*, vol. 18, pp. 1354-1361.

Lindley CM & Hirsch JD 1994, "Oncology nurses attitudes, perceptions and knowledge of QoL in assessment of patients with cancer", *Oncology Nursing Forum*, vol. 21,no. 1, pp. 108-110.

LLCG. Protocol Study 11. 1999
Ref Type: Unpublished Work

Lutz ST, Huang DT, Fergusson CL, Kavanagh BD, Tercilla OF, & Lu J 1997, "A retrospective quality of life analysis using the Lung Cancer Symptom Scale in patients treated with palliative radiotherapy for advanced non small cell lung cancer", *International Journal of Radiation Oncology*, vol. 1,no. 37, pp. 117-122.

Macbeth F 1996, *Lung Cancer A Practical Guide to Management* Harwood Academic.

Macbeth F 2000, "All evidence was considered when COIN guidelines were drawn up", *British Medical Journal*, vol. 320, p. 640.

MacDowell L & Newell C 1987, *Measuring health: A guide to rating scales and questionnaires* Oxford University Press, Oxford.

Macintyre A 2005, *Seven Traits for Designing Our Descendents*, Hastings Center Report, 9.

Marcus Tullius Cicero & Grant M (trans) 1971, *Cicero-On the Good Life* Penguin, London.

Marino P, Pampallona S, Preatoni A, Canatoni A, & Invernezzi F 1994, "Chemotherapy Vs Best supportive care in advanced non small cell lung cancer: results of a meta-analysis of the literature", *Chest*, vol. 106, pp. 861-865.

Maslow A 1954, *Motivation and Personality* Harper, New York.

- Mast ME 1998, "Adult uncertainty and illness: A critical review of the literature", *Scholarly Inquiry for Nursing Practice*, vol. 9,no. 1, pp. 3-29.
- Mathiesen CM & Stam HJ 1995, "Re-negotiating identity: cancer narratives", *Sociology of Health and Illness*, vol. 15,no. 3, pp. 283-306.
- McCann TV & Clarke E 2003, "Grounded Theory in Nursing Research", *Nurse Researcher*, vol. 11,no. 2, pp. 19-29.
- McMillan SC & Mahon M 1994, "Measuring Quality of Life in hospice patients using the newly developed Hospice Quality of Life Index", *Quality of Life Research*, vol. 3, pp. 437-447.
- McMillan SC 2000, "Quality of Life Assessment in Palliative Care", *Cancer Control Journal*, vol. 3,no. 3, pp. 1-9.
- Meeberg GA 1993, "Quality of life: A concept analysis", *Journal of Advanced Nursing*, vol. 18, pp. 32-38.
- Meeks D & Favard-Meeks C 1999. *Daily Life of the Egyptian Gods*, 2nd ed, Pimlico, London.
- Meyerowitz BE 1993, "Quality of Life in breast cancer patients: The contribution of data to the care of patients", *European Journal of Cancer*, vol. 29a,no. S1, pp. 559-562.
- Middleton MR, Thatcher N, & Hopwood P 2000, "Palliative Chemotherapy," in *Lung Cancer Principles and Practice*, 2nd ed, Pass H et al., eds., Lipincott, Williams and Wilkins, Philadelphia.
- Mishel MH 1990, "Reconceptualisation of the uncertainty in illness theory", *Image: The Journal of Nursing Scholarship*, vol. 22, pp. 256-262.
- Mishler GE 1996, *Research Interviewing-Context and Analysis*, 3rd ed, Harvard, Cambridge.
- Molzahn AE. Quality of life: What is it? 1990. Alberta Canada, University of Alberta.
Ref Type: Serial (Book, Monograph)
- Montazeri A, Milroy R, Gillis CR, & McEwan J 1996, "Quality of life, perception of lung cancer patients", *European Journal of Cancer*, vol. 32A,no. 13, pp. 2284-2289.
- Montazeri A, Gillis C, & McEwen J 1998, "Quality of life in patients with lung cancer: A review of the literature from 1970-1995", *Chest*, vol. 113,no. 2, pp. 467-481.

MORI 2000, *Lung Cancer Research for the Cancer Research Campaign*, MORI and Cancer Research Campaign, London.

Morrow GR, Lindke J, & Black P 1992, "Measurement of quality of life in patients: Psychometric analysis of the Functional Living Index-Cancer", *Quality of Life Research*, vol. 1, pp. 287-296.

Morse J & Johnson P 1991, *The illness experience, the dimension of suffering* Sage, Newbury Park.

Moser CA, K. G. 1971, *Survey methods in social investigation* Heinemann, London.

National Audit Office 2005, *Tackling Cancer-Improving the patient journey*, NAO for the House of Commons, London, HC288 2004/5 Session.

Notes: 2005a

National Audit Office 2005, *The NHS Cancer Plan: A progress report*, HMSO, London, 2005b.

Neal A & Hoskins P 1994, *Clinical Oncology* Hodder, London.

Ness DE & Ende J 1994, "Denial in the medical interview", *JAMA*, vol. 273, pp. 1777-1781.

NICE: National Institute for Clinical Excellence & National Collaborating Centre for Acute Care 2005, *The Diagnosis and Treatment of Lung Cancer*.

Noll H. Social Indicators and Social Reporting-An International Experience. ccsd.ca . 2000. 2004.

Ref Type: Electronic Citation

Novack DH, Plummer R, Smith RI, & et al 1979, "Changes in physicians attitudes toward telling the cancer patient", *JAMA*, vol. 241, pp. 897-900.

NSCLCCG 1995, "Chemotherapy in NSCLC: A meta-analysis using updated data on individual patient data from 52 randomised clinical trials", *British Medical Journal*, vol. 311, pp. 899-909.

O'Brien MER & Cullen MH 2000, "Managing patients with lung cancer. Guidelines must bring us into line with European standards", *British Medical Journal*, vol. 320, p. 1604.

Oberst MT & Scott D 1985, "Going home: Patient and spouse adjustment after cancer surgery", *Topics in Clinical Nursing*, vol. 7, no. 1, pp. 46-57.

Oken D 1961, "What to tell cancer patients", *JAMA*, vol. 175, pp. 1120-1128.

Omer H & Rosenbaum R 1997, "Diseases of hope and the work of despair", *Psychotherapy*, vol. 34,no. 3, pp. 227-245.

ONS Office of National Statistics. The Office of National Statistics General Household Survey and Lung cancer datasets. ONS . 2006. 6.
Ref Type: Electronic Citation

Opong JR Ironside RG Kennedy LW 1987, *Perceived Quality of life in a centre: periphery framework*, Dept of Sociology, University of Canada, Alberta Canada.

Osoba D, Murray N, & Gelmon K 1994, "Quality of life and weight change in patients receiving dose-intensive chemotherapy", *Oncology*, vol. 8, pp. 61-65.

Packa DR 1989, "Quality of life in adults after heart transplant", *Journal of Cardiovascular Nursing*, vol. 3,no. 2, pp. 12-22.

Padilla GV, Presant C, & Grant MM 1983, "Quality of Life Index for Patients with Cancer", *Research, Nursing and Health*, vol. 83, pp. 117-126.

Parker PA, Baile WF, de Moor C, & et al 2001, "Breaking bad news about cancer", *Journal of Clinical Oncology*, vol. 19,no. 7, pp. 2049-2056.

Parsons T 1951, *The Social System* Free Press, New York.

Patrick DL & Deyo RA 2004, "Generic and disease specific measures in assessing health status and quality of life", *Medical Care*, vol. 27, p. S217-S232.

Payne S 1997, "Selecting approach and design in qualitative research", *Palliative Medicine*, vol. 11, pp. 249-252.

Perng RP, Chen YM, Ming LJ, Tsai CM, Lin WC, Yang KY, & et al 1997, "Gemcitabine versus the combination of cisplatin and etoposide in patients with inoperable non small cell lung cancer in a phase II randomised study", *Journal of Clinical Oncology*, vol. 15, pp. 2097-2102.

Peto R, Darby S, Deo H, Silcocks P, Whitely E, & Doll R 2000, "Smoking, Smoking cessation and Lung Cancer in the UK since 1950: combination of national statistics with two case control studies", *British Medical Journal*, vol. 321, pp. 323-329.

Pill R & Scott N 1982, "Concepts of illness causation and responsibility: Some preliminary data from working class mothers", *Social Science and Medicine*, vol. 16, pp. 43-52.

Post-White J, Ceronsky C, Kreitzer MJ, Nickelson K, Drew D, Mackay KW, Koopmeiners L, & Gutknect S 1996, "Hope, spirituality, sense of coherence and quality of life in patients with cancer", *Oncology Nursing Forum*, vol. 23,no. 10, pp. 1571-1579.

Public Accounts Committee 2006, *Office of the Comptroller General: Report on the Cancer Plan for England and Wales*, HMSO.

Quinn ME, Fontana AF, & Reznikoff M 1986, "Psychological distress in reaction to lung cancer as a function of spousal support and coping strategy", *Journal of psychosocial oncology*, vol. 4, pp. 79-90.

Rapley M 2003, *Quality Of Life Research* Sage, London.

Rehnsfeldt A 1999, *The encounter with the patient with a life changing process (English summary)*, PhD, Vasa University, Finland.

Reutter LI & Northcott HC 1994, "Achieving a sense of control in the context of uncertainty. Nurses and AIDS", *Qualitative Health Research*, vol. 4, no. 1, pp. 51-71.

Richer M & Ezer H. Understanding beliefs and meanings in the experience of cancer: A concept analysis. *Journal of Advanced Nursing* 32, 1108-1115. 2000.
Ref Type: Generic

Rodgers B 1989, "Concepts, analysis and the development of nursing knowledge-The evolutionary cycle", *Journal of Advanced Nursing*, vol. 14, pp. 330-335.

Rodgers B & Knafk K 1993, *Concept Development in Nursing* W B Saunders, Philadelphia.

Rodgers B & Cowles KV 1997, "A conceptual foundation for human suffering in nursing care and research", *Journal of Advanced Nursing*, vol. 25, pp. 1048-1053.

Rosenberg A 2000, *Philosophy of Science* Routledge, London.

Roy Castle Foundation & Leary A. Update on Roy Castle Data from Clegg 2000. 2003.

Ref Type: Personal Communication

Roy Castle Foundation & Baird J. Are patients with lung cancer being offered chemotherapy? 2005.

Ref Type: Personal Communication

Roy Castle Foundation. Lung Cancer Patient's Charter. Roy Castle Foundation . 2006. 6.

Ref Type: Electronic Citation

Rudd R, Gower NH, Spiro S, Eisen TG, Harper PG, Littler JAH, Hatton M, Johnson PWM, Martin WMC, Rankin EM, James LE, Gregory WM, Qian W, & Lee SM 2005, "Gemcitabine plus Carboplatin Vs Mitomycin, Ifosfamide and

Cisplatin in patients with stage IIIb or IV Non small cell lung cancer: A phase III randomised study of the London Lung Cancer Group", *Journal of Clinical Oncology*, vol. 23,no. 1, pp. 142-153.

Ryan L "Quality of life and lung or colon cancer: A prospective study to determine the impact of an experimental treatment", Houston, Texas.

Ryan LS 1996, "Psychosocial issues and lung cancer: A behavioral approach", *Seminars in Oncology Nursing*, vol. 12,no. 4, pp. 318-323.

Sacks H 1989, "Lecture 5," in *Lectures in Human Studies*, Jefferson G, ed., University of California, San Francisco, pp. 211-215.

Sandler AB, Nemunaitis J, Denham C, von Pawl J, Cornier Y, Gatzmeier U, & et al 2000, "Phase III trial of gemcitabine and cisplatin Vs cisplatin alone in patients with locally advanced or metastatic non small cell lung cancer", *Journal of Clinical Oncology*, vol. 18, pp. 623-631.

Sarna L 1993, "Fluctuations in physical functioning in persons with Non Small Cell Lung Cancer", *Journal of Advanced Nursing*, vol. 18, pp. 714-724

Sarna L 1993, "Correlates of symptom distress in women with lung cancer", *Cancer Practice*, vol. 1, pp. 21-28.

Sarna L, Lindsey AM, Dean H, Brecht ML, & McCorkle R 1993, "Nutritional intake, weight change, symptom distress and functional status over time in adults with lung cancer", *Oncology Nursing Forum*, vol. 20, pp. 481-489.

Saunders TJ trans 1970, *Plato: The Laws*, 12 ed, Penguin, Harmondsworth.

Saunders TJ trans 1987, *Early Socratic Dialogues (Plato)* Penguin, Harmondsworth.

Scambler G 1991, *Sociology as applied to medicine*, 3rd ed, Balliere Tindall, London.

Scarry E 1985, *The body in pain-making and unmaking the world* Oxford University Press, Oxford.

Schipper H, Clinch J, McMurray A, & et al 1984, "Measuring Quality of Life in Cancer Patients The Functional Living Index-Cancer", *Journal of Clinical Oncology*, vol. 2,no. 472, p. 483.

Schipper H, Clinch J, & Powell V 1990, "Definition and conceptual issues," in *Quality of life assessments in clinical trials*, Spiker B, ed., Raven Press, New York.

Schon D 1991, *The Reflective Practitioner*, 2nd ed, Arena, Aldershot.

Schou KC & Hewison J 1999, *Experiencing Cancer*, 1st ed, Open University Press, Buckingham.

Schutz A & Luckman T 1974, *The Structures of the Lifeworld* Heinemann, London.

Selby P, Chapman JAW, Etazadi-Amoli J, & et al 1984, "Development of a method for assessing quality of life of cancer patients", *British Journal of Cancer*, vol. 50, pp. 13-22.

Seo M, Tamura K, Shijo H, Morioka E, Ikegame C, & Hirasako K 2000, "Telling the diagnosis to cancer patients in Japan: Attitude and perception of patients, physicians and nurses", *Palliative Medicine*, vol. 14, no. 2, pp. 105-110.

Shimosato Y 2000, "Pathology: Revised classification of epithelial tumours of the lung," in *Textbook of Lung Cancer*, Hansen H ed, ed., Martin Dunitz, London.

Shin DC & Johnson DM 1978, "Avowed happiness as an overall assessment of the quality of life", *Social Indicators Research*, vol. 5, pp. 475-492.

Siiverman D 2003, *Interpreting Qualitative Data*, 2nd ed, Sage, London.

Silvestri GA, Pritchard R, & Gilbert Welch H 1998, "Preferences for chemotherapy in patients with advanced non small cell lung cancer: descriptive study based on scripted interviews", *British Medical Journal*, vol. 317, pp. 771-775.

Slevin ML, Plant H, & Lynch D 1988, "Who should measure quality of life-doctor or patient?", *British Journal of Cancer*, vol. 57, pp. 109-112.

Smith IE 1994, "Palliative chemotherapy for advanced non small cell lung cancer", *British Medical Journal*, vol. 308, pp. 429-430.

Somerfield M & Curbow B 1993, "Methodological issues and research strategies in the study of coping with cancer", *Social Science and Medicine*, vol. 34, no. 11, pp. 1203-1216.

Sontag S 1977, *Illness as metaphor*, 1991 ed, Penguin, London.

Souhami B & Tobias J 2005, *Cancer and its management*, 4th ed, Blackwell, Oxford.

Souquet PJ, Chavin F, Boissel JP, Cellerino R, Cornier Y, & Ganz PA 1993, "Polychemotherapy in advanced non small cell lung cancer: A meta analysis", *Lancet*, vol. 342, pp. 19-21.

Speigel D 1997, "Psychosocial aspects of breast cancer treatment", *Seminars in Oncology*, vol. 24, no. 1 s1, p. s1.36-s1.47.

- Spencer J, Davidson H, & White V 1997, "Helping clients develop hope for the future", *American Journal of Occupational Therapy*, vol. 51,no. 3, pp. 191-198.
- Spiro SG, Rudd R, Souhami RL, Brown J, & Fairlamb DJ 2004, "Chemotherapy versus supportive care in advanced non small cell lung cancer: improved survival without detriment to quality of life", *Thorax*, vol. 59, pp. 828-836.
- Spiro SG & Silvestri GA 2005, "One hundred years of lung cancer", *American Review of Respiratory Critical Care Medicine*, vol. 172,no. 5, pp. 523-529.
- Splinter TAW 1993, "Chemotherapy in advanced lung cancer", *European Journal of Cancer*, vol. 26, pp. 1093-1096.
- Stacey J 1997, *Teratologies-A cultural study of cancer* Routledge, London.
- Stegbauer CC 1994, *Expanding a grounded theory: The latent theory of quality of life in older men with non small cell lung cancer*, PhD, University of Texas.
- Steginga SK, Dunn J, Dewar AM, McCarthy A, Yates P, & Beadle G 2005, "impact of an intensive nursing education course on nurses knowledge, confidence, attitudes and perceived skills in the care of patients with cancer", *Oncology Nursing Forum*, vol. 32,no. 2, pp. 375-381.
- Stephens RJ & Hopwood P 2000, "Standards of reporting quality of life in clinical trials", *Journal of Clinical Oncology*, vol. 18,no. 8, pp. 1800-1807.
- Stetz KM, Haberman HR, Holcombe J, & Jones S 1995, "Oncology Nursing Society research priority survey", *Oncology Nursing Forum*, vol. 22, pp. 785-790.
- Strang P 2000, "Qualitative Research Methods in Palliative Medicine and Palliative Oncology", *Acta Oncologica*, vol. 39,no. 8, pp. 911-917.
- Strauss A & Glaser BG 1975, *Chronic Illness and Quality of Life* Mosby, St Lois.
- Strauss A, Fagerhaugh S, Suczek B, & Weiner C 1985, *Social organisation of medical work* Chicago University Press, Chicago.
- Strauss A & Corbin J 1998, *Basics of qualitative research*, 2nd ed, Sage, London.
- Tamburini M, Casali PG, & Miccinesi G 2000, "Outcome assessment in cancer management", *Surgical Clinics of North America*, vol. 80,no. 2, pp. 4712-486.
- Tartar RE, Erb S, Biller PA, & Switala J Van Thiel DH 2003, "Quality of Life following liver transplantation", *Gastroenterology clinics of North America*, vol. 17,no. 1, pp. 207-217.

Testa MA & Simonson DC 1996, "Assessment of quality of life outcomes", *New England Journal of Medicine*, vol. 334, pp. 835-840.

The A-M, Hak T, & Koeter G, v. d. W. G. 2000, "Collusion in doctor-patient communication about imminent death-an ethnographic study", *British Medical Journal*, vol. 321, pp. 1376-1381.

Thomsen OO, Wulff HR, Martin A, & Singer PA 1993, "What gastroenterologists in Europe tell cancer patients", *Lancet*, vol. 341, pp. 473-476.

Tishelman C, Degner LF, & Mueller B 2000, "Measuring symptom distress in patients with lung cancer", *Cancer Nursing*, vol. 2, pp. 82-90.

Tywcross R 1987, "Quality before Quantity: A note of caution", *Palliative Medicine*, vol. 1, pp. 65-72.

Tywcross R 1997, *Introducing Palliative Care*, 2 ed, Radcliffe Medical Press, Oxford.

UK Lung Cancer Coalition. Lung Cancer Awareness Survey UK Lung Cancer Coalition . 2005. 6.

Ref Type: Electronic Citation

Velikova G, Wright P, Smith AB, & et al 2001, "Self reported quality of life of individual cancer patients", *Journal of Clinical Oncology*, vol. 19,no. 7, pp. 2064-2073.

Waldron D & O'Boyle CA 1999, "Individual quality of life in Palliative Care," in *Individual Quality of Life*, Joyce CRB, O'Boyle CA, & McGee H, eds., Harwood Academic, Amsterdam.

Warren WH & Faber LP 2000, "Extended resections for locally advanced non small cell lung cancer," in *Lung Cancer Principles and Practice*, 2nd ed, Pass H et al., eds., Lipincott, Williams and Wilkins, Philadelphia.

Waters A. What is nursing? *Nursing Standard* 17[3], 20-22. 2003.

Ref Type: Journal (Full)

Wineman NM, Schwetz KM, Goodkin DE, & Rudick RA 1996, "Relationships among illness, uncertainty, stress, coping and emotional well-being at entry into a drug trial", *Research, Nursing and Health*, vol. 9,no. 2, pp. 53-60.

Wong C & Bramwell L 1992, "Uncertainty and anxiety after mastectomy for breast cancer", *Issues in Mental Health Nursing*, vol. 15, pp. 363-371.

Zaner R 1988, *Ethics and the clinical encounter* Prentice Hall, Englewood Cliffs, NJ.

Zautra A & Goodhart D 1979, "Quality of life indicators, A review of the literature", *Mental Health Review*, vol. 4, pp. 1-10.

Zebrack B 2000, "Cancer survivors and quality of life: A critical review of the literature", *Oncology Nursing Forum*, vol. 27, no. 9, pp. 1395-1401.

Zubrod CG, Schnedierman M, Frei E, & et al 1960, "Appraisal of methods for the study of chemotherapy of cancer in man. Comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramidate", *Journal of Chronic Diseases*, vol. 11, pp. 7-33.