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Quality of Life in Patients with Lung Cancer:
An Epidemiological Study

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Thesis submitted to the Faculty of Medicine of University of Glasgow for the degree of Doctor of Philosophy (Ph.D.)
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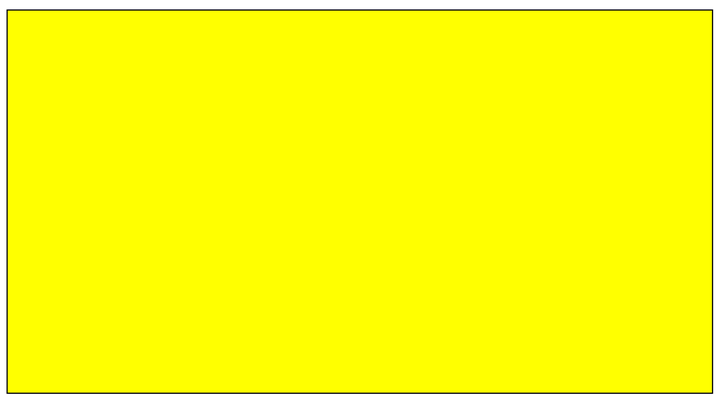
In the name of God

... Dedicated to my parents, my wife, and my children
and
In memory of my beloved brothers Reza and Elyas

Declaration

This thesis is submitted in fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Glasgow, Faculty of Medicine, Department of Public Health. Unless stated otherwise, the work is that of the author.



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List of publications

The following publications originated from this project and have been used in this thesis.

A. Papers

1. Montazeri A, Milroy R, Macbeth F, McEwen J, Gillis CR (1996) Understanding patients: let's talk about it. A study of cancer communication. *Supportive Care in Cancer*, 4, 97-101.

2. Montazeri A, McEwen J, Gillis CR (1996) Quality of life in patients with ovarian cancer: current state of research. *Supportive Care in Cancer*, 4, 169-179.

3. Montazeri A. A descriptive study of a cancer support group. *European Journal of Cancer Care* 1996; 4: 32-37.

4. Montazeri A, Gillis CR, McEwen J (1996) Measuring quality of life in oncology: is it worthwhile? Part I. Meaning, purposes, and controversies. *European Journal of Cancer Care*, 5, 159-167.

5. Montazeri A, Gillis CR, McEwen J (1996) Measuring quality of life in oncology: is it worthwhile? Part II. Experiences from the treatment of cancer. *European Journal of Cancer Care*, 5, 168-175.

6. Montazeri A, Milroy R, Gillis CR, McEwen J (1996) Interviewing cancer patients in a research setting: the role of effective communication. *Supportive Care in Cancer*, 4, 447-454.

7. Montazeri A, Milroy R, Gillis CR, McEwen J (1996) Quality of life: perception of lung cancer patients. *European Journal of Cancer*, 32A, in press.

8. Montazeri A, Gillis CR, McEwen J (1997) Tak Tent. Studies conducted in a cancer support group, *Supportive Care in Cancer*, 5, in press.

B. Abstracts and presentations

1. Montazeri A, McEwen J, Gillis CR (1995) Can we add life to years not years to life? *Proceedings of the Organisation of European Cancer Institute (OECI) Conference on Cancer and Quality of Life.*
The paper presented at the OECI's Conference on Cancer and Quality of Life, 12-14 May 1995, Bled, Slovenia.

2. Montazeri A (1995) Quality of life and cancer. Department of Public Health, University of Glasgow, Glasgow, 25 October.

3. Montazeri A, Milroy R, Gillis CR, McEwen J (1996) Interviewing cancer patients in a research setting: does communication matter? *Supportive Care in Cancer*, 4, 233.
The paper has been accepted for presentation at the 8th Symposium of the Multinational Association of Supportive Care in Cancer (MASC), 19-22 June 1996, Toronto, Canada.

4. Montazeri A, Milroy R, McEwen J, Gillis CR (1996) Feasibility of conducting a double blind case-control study of quality of life in patients with lung cancer. *Proceedings of the XIV International Scientific Meeting of the International Epidemiological Association (IEA)*, p. 209.
The paper has been accepted for presentation at the XIV International Scientific Meeting of the IEA, 27-30 August 1996, Nagoya, Japan.

5. Montazeri A (1996) Quality of life in patients with lung cancer. To be presented at the West of Scotland Health Services Research Network joint meeting with the West of Scotland Oncological Organisation, Royal College of Physicians & Surgeons of Glasgow, 12 November.

6. Montazeri A (1996) Measuring quality of life in patients with lung cancer. To be presented at the Department of Public Health, University of Glasgow, Glasgow, 20 November.

7. Montazeri A, Milroy R, Gillis CR, McEwen J (1996) Quality of life in patients with lung cancer: an important prognostic factor. *Thorax*, 51 (Suppl. 3), A8.
(accepted for presentation at the British Thoracic Society Winter Meeting, London, 9-11 December).

8. Milroy R, Montazeri A, Gillis CR, McEwen J (1996) Quality of life in patients with lung cancer: does treatment matter? *Thorax*, 51 (Suppl. 3), A56.
(accepted for presentation at the British Thoracic Society Winter Meeting, London, 9-11 December).

C. Short Contributions

1. Montazeri A (1994) Is improving survival worthwhile? a study of the quality of life in patients with ovarian cancer. *HSR News* (West of Scotland Health services Research Network), No. 12, 4. (research proposal)

2. Montazeri A (1996) Clinical oncology information network: is the need urgent? *Clinical Oncology*, 8, 132. (letter).

D. Submitted papers

1. Montazeri A, Gillis CR, McEwen J (1996) Quality of life in patients with lung cancer: 25 years on. Part I. Lung cancer in general.

2. Montazeri A, Gillis CR, McEwen J (1996) Quality of life in patients with lung cancer: 25 years on. Part II. Small and non-small lung cancer.

Key to the thesis

A.	**Title indications**
1.	**Titles**
1.1.	**Sub-titles**
1.1.1.	***Sub-sub-titles***
B.	**Abbreviations and phrases**
Assessment	Assessment of quality of life
Baseline	Prior to diagnosis
CT	Chemotherapy
Cum	Cumulative
EORTC	European Organisation for Research and Treatment of Cancer
Follow-up	Three months after treatment
LC	Lung cancer
n	Sample size
NHP	Nottingham Health Profile
No.	Numbers
NSCLC	Non-small cell lung cancer
Obs.	Observer
P	P value (Probability)
Phyns.	Physicians
PS	Performance status
PT	Palliative treatment
Pt(s).	Patient(s)
(%)	Percentage
QLQ-C30	Quality of Life Cancer Core 30-item Questionnaire
QLQ-LC13	Quality of Life Lung Cancer 13-item Questionnaire
QOL (QL)	Quality of life
RT	Radiotherapy
SC	Supportive care
SCLC	Small cell lung cancer
SD	Standard Deviation
Vs.	Versus

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Finally, I wish to express my heartfelt gratitude to my parents, my wife and children, whose sacrifices and support made this study possible. I hope I should be able to reciprocate these in the future.

Abstract

A population-based study of quality of life in patients with lung cancer cases and chronic respiratory disease controls was carried out at Stobhill Hospital in Glasgow between January 1995 and April 1996. A study-specific questionnaire was administered in addition to three standard instruments (the Nottingham Health Profile- NHP; the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire- EORTC QLQ-C30; and its Lung Cancer complementary questionnaire- QLQ-LC13) used to measure quality of life. The aim was to carry out baseline assessments of quality of life following referral by General Practitioners but before diagnosis was made by consultants. The researcher and patients were blind to the diagnosis. Follow-up assessments were scheduled only for lung cancer patients but not controls three months after initial treatment. Two-hundred and thirty-eight patients were interviewed both at their homes and in the clinic. Of these, 129 patients had lung cancer and 109 were patients with chronic respiratory disease. There were no significant differences between the characteristics of cases and controls except for age (mean age = 67.5 ± 9.1 and 64.6 ± 10.4 years respectively). The majority of cases and controls were married (56%), retired (56%), with a low level of education (95%), from severely deprived areas (60%). The main results may be summarised as follows:

- There were no significant differences between quality of life in cases and controls except for pain and loss of appetite.
- Patients with different socio-economic status had different quality of life. The poorer reported a lower level of quality of life.

- Social support systems, social networks, and socio-demographic status of the patients were found to predict baseline quality of life prior to diagnosis.
- Non-medical factors (Deprivation Category and marital status) were found to be significant predictors of patients' global quality of life at follow-up, whereas medical factors (cell type and treatment modalities) were not.
- Global quality of life prior to diagnosis was a clear predictor of survival.
- Treatment regimens were found to be ineffective regardless of cell type and stage of disease when comparing baseline and follow-up assessments of quality of life in patients with lung cancer.
- Patients' reactions to the study indicated that they did not find the study intrusive. However, they preferred to be interviewed at home rather than to fill in a questionnaire in the clinic.
- Patients' perceptions of quality of life were found to differ from those of health professionals.

In the light of study findings it is concluded that conducting a robust epidemiological study of quality of life in patients with lung cancer is feasible. It is essential that such an assessment be carried out in the context of their socio-economic status. The results suggest that quality of life is a real and useful prognostic factor. It predicts survival and it is important to include quality of life measures in future studies of outcomes in lung cancer care.

The above forms the basis of recommendation to improve lung cancer care and to provide guidelines for further work.

Entrance of Stobhill Hospital NHS Trust

A General District and Teaching Hospital in the Northern Sector of Glasgow

The study setting

Introduction to the study

Lung cancer is an important public health problem and the most common cause of cancer deaths among men and ranked fifth in females world-wide (Parkin et al., 1993).

Based on comparable data, Scotland is among countries with the highest recorded incidence of lung cancer in the world. Within Scotland, the West of Scotland has an even higher rate as compared to the Scottish average. More importantly, since 1990 the age standardised incidence of lung cancer in females in Glasgow has over taken that of breast cancer (Gillis et al., 1992).

The efficacy of treatment for lung cancer remains poor and most lung cancer patients die with a relative survival rate of approximately 20% at one year after diagnosis (Black et al., 1993). With such a low level of cure on one hand, and because the disease and its treatment have severe effects on patients' physical and psychological well-being on the other hand, quality of life is the most relevant issue in lung cancer care.

Quality of life issues in lung cancer patients are discussed from two broad perspectives: first, in clinical decision-making for individual patients including decisions to treat patients with curative or palliative intent, and secondly, in the evaluation of new treatment modalities in group of patients. Yet, the question remains, what are the factors that determine quality of survival for lung cancer patients? It is important to assess these factors prospectively in order to identify, not only the existence of physical signs or symptoms but also the factors that predispose to them at a much earlier stage. This question which has not received enough attention in previous work is the subject of this project.

Definition of quality of life

Quality of life has been defined in many ways. One of the most recent and acceptable definitions has been offered by the World Health Organisation Quality of Life Group (1994):

"Quality of life is an individual's perception of his/her position in life in the context of the culture and value system in which he/she lives, and in relation to his/her goals, expectations, standards, and concerns".

This definition is the basis on which this study is built. In this respect, studying quality of life in the context of the socio-economic characteristics of patients becomes essential. Thus, this study addresses quality of life issues in patients with lung cancer and the extent to which social characteristics influence quality of life of patients with lung cancer.

Reasons for choosing lung cancer

Given the large number of cases of lung cancer in Glasgow, most of whom come from deprived areas, and the substantial resources which lung cancer cases consume; this is an issue which commands significant attention. In addition, there were two practical considerations which influenced the decision to undertake this research:

(a) The high incidence of disease which would facilitate efficient recruitment of patients.

(b) The rapid diagnosis and progression of the disease which would allow examination of what happened to the patients after diagnosis and treatment.

The setting

This project was undertaken in the Northern sector of Glasgow. This area of Glasgow was chosen because of local interest, facilities and a sufficient number of patients that would allow recruitment of an appropriate sample for the study. In addition, there is a clear contrast of social structure within the population. That structure reflects a range of socio-economic deprivation. On the basis of these considerations, Stobhill Hospital Trust, a large teaching and District General Hospital, was chosen as an ideal setting for this study. It has: an active Department of Respiratory Medicine, good relationships with General Practitioners (GPs) in the area, has been and is presently involved in other collaborative projects.

The study

There have been many published studies (about 170 reviews, papers, abstracts, and reports) on quality of life in lung cancer patients since 1970. This project is an advance on these because it comprises the following eight criteria that have not been brought together in other studies.

The eight criteria not previously brought together:

1. Quality of life as the main outcome measure.
2. An epidemiological population-based study rather than a clinical study.
3. A prospective case-control study.
4. At the baseline interview both patients and interviewer being blind to the final diagnosis.
5. A detailed investigation of socio-economic status of patients.
6. Assessment made using an interviewer-administered approach.
7. Data obtained either at patients' home or in the clinic.
8. Patients' attitudes toward the study examined.

These are all important issues both from a methodological point of view and as far as quality of life studies are concerned.

The thesis

It consists of eight chapters. In the first chapter the study background is presented in addition to a description of lung cancer and its management. The next two chapters are a review of literature. While Chapter two reviews the issue of quality of life in cancer patients in general, chapter three more specifically looks at studies of quality of life in patients with lung cancer. In this chapter a comprehensive review of literature from 1970 (when the first study of quality of life in lung cancer patients was published) to the end of 1995 is provided. Aims and objectives are listed in chapter four. The methodology is presented in chapter five. In this chapter the unique design of the study is explained. In addition, the instruments used to measure quality of life and study limitations are described. Chapter six presents the results. There are two main groups of results: the first, measuring quality of life in lung cancer patients and controls including comparing these outcomes based on their socio-economic characteristics and secondly, the initial quality of life in lung cancer patients compared with their follow-up quality of life measures. In chapter seven the study findings are discussed. Finally, in chapter eight conclusions, and recommendations are presented.

It is hoped that this project would provide an insight into quality of life in patients with lung cancer and identify areas for future improvement in lung cancer care.

CHAPTER ONE

1

STUDY BACKGROUND

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- Introduction

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3. Screening for lung cancer

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Summary

Lung cancer is one of the most fatal malignancies world-wide. To provide an introduction for this project, this chapter describes lung cancer, its treatment and symptoms. There are different types of lung cancers and they require different management policies. The survival outcome of treatment for lung cancer is poor and most patients die within one year of diagnosis with a median survival of less than six months. The disease and its treatment have severe effects on the physical and psychosocial well-being of the patients. There are several risk factors for developing lung cancer. Of these, smoking accounts for most cases of lung cancer. A section on aetiology of lung cancer and socio-economic deprivation is provided to explain why people in lower social classes develop more lung cancer as compared to affluent. The magnitude of the problem is demonstrated by lung cancer statistics from Scotland, the setting for this study. There were two preliminary investigations in conducting this research, experiences from a study on cancer communication, and a study on quality of life in patients with ovarian cancer; these are described. This chapter however, summarises the situation which a patient with diagnosis of lung cancer is likely to face, a situation which suggests that "quality of life" is one of the most relevant and important outcomes in lung cancer care.

Introduction

Cancer is a generic term applied to a variety of different diseases that have in common a deformity of cell development, leading to unregulated proliferation of cell growth that in turn results in invasion and metastases. The primary site and cell type of a cancer dictates many of its features including rate of development, response to cancer therapies, common sites of metastatic spread of the disease, symptoms, and consequent quality of life.

Studying outcome in lung cancer care requires a primary knowledge of the disease and its management. Similarly, studying quality of life needs initial information about the disease and the ways that its treatment is managed. Thus, to provide an introduction to this study and demonstrate the complex situation that patients with diagnosis of lung cancer and their clinicians are likely to face, this chapter gives a brief description of the disease and its management.

The situation for lung cancer patients is different from those which patients with other cancer types are may possibly confront (Gregor and Macbeth, 1995). First, most lung cancer patients come from lower socio-economic backgrounds. This is, therefore, against the formation of patient-led political pressure groups that have made so much political headway in treatment of other cancers. Thus, one may argue that a patient with a diagnosis of lung cancer and with an underprivileged life, might suffer from even much poorer quality of life in the future.

Secondly, despite advances in the treatment of other cancers, the treatment of lung cancer remains unsatisfactory and the outcome survival of the treatment for this cancer is short. This by itself raises the question of cost-benefit issues,

cost in terms of resources used and social costs and benefit in terms of health gain and the quality of life. For example, despite aggressive treatments for lung cancer, the survival benefit is sometimes a matter of living for a few extra weeks with major adverse side-effects. In such a situation therefore, the question for example, is: does staging make any differences in the outcome with outcome measured both in terms of survival and quality of life?

Thirdly, more than half the patients with lung cancer are never seen by an oncologist and also lung cancer specialisation within oncology is uncommon. This in turn may cause several problems including "nihilistic attitudes" towards treatment of lung cancer patients.

This chapter provides introductory information and basic facts about lung cancer that was necessary for the investigator, and that would perhaps be necessary for the readers of this thesis in order to appreciate the problem.

1. Global overview

"...a disease which, I am satisfied, is more common than it is supposed to be by the profession, and which, unless a careful examination be made, both of the history of the case, and of the physical signs attending it, is very apt to be mistaken for some other complaint."

Kilgour A. (1850)
[cited in: Thatcher and Spiro (1994) New Perspectives in Lung Cancer]

Lung cancer is the most common cancer of men and the fifth most frequent cancer of women world-wide (Parkin et al., 1993). It is a complex environmental disease involving the accumulation of several risk factors (Economou et al., 1994). The study of the epidemiology of lung cancer has been one of the rewarding aspects of medical research in the past 50 years and it has already taught us enough to ensure that lung cancer can be considered to

be the most common form of fatal yet preventable cancer throughout the world (Doll, 1994).

A world-wide lung cancer epidemic has occurred during the 20th century. Parkin et al. (1993) estimated that lung cancer was the most common cancer in the world in 1985, with 896,000 new cases, or 11.8% of the total, about 61% of which occur in developed countries. They calculated that this is a large increase (36%) since the 1980 estimate.

The highest incidence rates of lung cancer currently observed in men are in the Maori population of New Zealand (119.1 per 100,1000), and several black populations of the United States including New Orleans (115.9), San Francisco Bay area (107.4), Detroit (107.2), and Alameda county (106.9). The incidence rate in the West of Scotland remains very high (97.2). The lowest incidence rates in men at the present time are reported from Indian, African and South American populations ranging from 13.5 to 1 per 100,1000 respectively. In women, the highest incidence rate is found in the Maori population (62.2), Canada (51.8) and among black and white populations of the United States (36.5 and 37.9). The lowest rates occur in similar populations to those in men (Parkin et al., 1992).

Although the incidence of lung cancer is presently declining among middle-aged men in some countries, it is increasing among women in many developed countries (Gillis et al., 1992). For example, in the United Kingdom the Chief Medical Officer of the Department of Health reported that in England and Wales over the period of 1979-1990 age-adjusted rates of lung cancer decreased for males but for females increased. This report did not indicate the figures (Department of Health, 1995). Data from United States indicate that from 1973-1977 to 1983-1987, the age-adjusted rates of lung cancer increased

by 30%, with the gain markedly greater in women (70%) than in men (17%) (Travis et al., 1995).

The rise of smoking in developing nations will inevitably be followed by spread of the lung cancer epidemic. Epidemiological research has convincingly established that cigarette smoking is a cause of lung cancer (early studies such as: Wynder and Graham, 1950; Levin et al., 1950; Doll and Hill, 1950; 1952), accounting for the majority of lung cancer cases in most countries. The international variation in incidence rates of lung cancer is well explained by different current and past exposures to the main cause of lung cancer- cigarette smoking (Tomatis et al., 1990).

Overall risk of lung cancer for smokers depends on several factors including age at starting, number of cigarettes smoked, the products smoked and inhaling pattern. Other causes of lung cancer include exposure to occupational agents, environmental tobacco smoke (ETS), residential exposure to radon, radiation, diet, and alcohol consumption (Tomatis et al., 1990; Samet, 1993; 1994; Kabat, 1993).

Discussions about risk factors for developing lung cancer still continue to be topical in biomedical literature. For instance, in a recent study Gross (1995) after reviewing 32 studies world-wide (29 case-control and 3 cohort studies) involving exposed and unexposed male and female smokers concluded that a causal relationship between ETS and lung cancer is currently not supported by the data. In response, Leeuwen (1995) argued that epidemiological studies, provide strong evidence for a causal association between ETS and lung cancer risk.

However, since smoking is the main cause of lung cancer, it is argued that over 90% of lung cancer may be avoided simply through avoidance of cigarette smoking. There is a world-wide epidemic of smoking among young people, which will be translated into increasing rates of lung cancer cases in the coming decades. (Boyle and Maisonneuve, 1995).

2. Diagnosis of lung cancer

A chest X-ray is the initial test to establish diagnosis of lung cancer. Following abnormal X-ray, a pathological diagnosis is required. Sometimes this is established from sputum cytology. More clinicians prefer to have the greater accuracy and confidence by examining a piece of the tumour itself (a biopsy). This can be done by biopsy of an abnormal lymph gland (usually at the root of the neck) or a piece of the pleural lining of the chest (if there was pleural effusion, fluid between the lung and chest wall). More often, bronchoscopic biopsy is needed. This test allows the doctor to look into the airways and the lungs. By this test it is also possible to take a small piece of tissue for examination. However, if it is not possible to make a diagnosis by these tests, an exploratory operation (thoractomy) can be done to examine the lungs (Williams, 1992; Hancock and Coleman, 1996).

3. Screening for lung cancer

Two techniques were used for detecting lung cancer: the chest X-ray and sputum cytology. The intention is that the patients found on screening, will have a better chance of cure. Studies have shown that the benefit achievable by screening is limited both by the sensitivity of currently used methods for early lung cancer detection and by the cure probability associated with treatment of those patients who were found by screening techniques (Flehinger et al., 1994). Thus, population-based screening or large-scale

screening for those who are in risk of developing lung cancer, has not been recommended.

4. Types of lung cancer

Lung cancer is not one disease and there are several types of cancers that can develop in the lungs. Lung cancers have been divided into two major groups; small cell and non-small cell lung cancer. Table 1.1 presents the main types of lung cancer in a typical population.

Small cell lung cancer is a unique form of lung cancer characterised by rapid growth and dissemination at diagnosis (Hinson and Perry, 1993). Non-small cell lung cancer is the most common type of the disease and consists of three major histologic types: squamous cell carcinoma, adenocarcinoma, and large cell carcinoma.

Table 1.1 Main types of lung cancer

Type	Estimated incidence %
Small cell lung cancer (oat-cell)	25
Non-small cell lung cancer (squamous, adeno, and large cell carcinoma)	74 (34, 25, 15)
Mesothelioma (pleura)	1

Source: adapted from Williams (1992)

There was a long-standing belief that squamous and oat-cell carcinoma were smoking associated, but that adenocarcinoma was not. It now appears that adenocarcinoma and bronchioloalveolar carcinoma (a special type of adenocarcinoma) are both associated with smoking (Petersen, 1994).

5. Staging of disease

There are separate staging systems for small-cell and non-small cell lung cancer. The staging system of small cell lung cancer is very simple (Table 1.2).

Table 1.2 Staging system for small cell lung cancer

Limited disease The tumour is confined to one side of the chest and to the draining lymph nodes on that side.
Extensive disease The tumour is spread beyond the chest including distant lymph nodes, bone, liver, bone marrow, brain, etc.

Source: adapted from Williams (1992)

In non-small cell lung cancer the staging system is more complex and is based on tumour size, lymph nodes and metastases (TNM) system. The various T, N, M categories are organised into stage groupings: stage I, II, IIIa IIIb, and IV (Table 1.3)

While in small cell lung cancer the distinction between limited and extensive disease is more important in understanding patient's attitude towards treatment, in non-small cell lung cancer staging is part of the treatment procedure and the importance of such staging system is in selecting those patients who will benefit from an operation.

Table 1.3 Simplified staging system for non-small cell lung cancer

	Stage	Description
Limited disease	Stage I	Tumour size less than 3 cm, no spread to lymph nodes, no metastasis.
	Stage II	Tumour size more than 3 cm, spread to the first group of lymph nodes, no metastasis.
Extensive disease	Stage IIIa, Stag IIIb	Locally advanced, tumour with any size spread to other respiratory organs, no distant metastasis.
	Stage IV	Advanced, tumour with any size, distant metastasis found.

Source: adapted from Mountain (1986)

6. Treatment of lung cancer

Treatment of lung cancer continues to be one of the greatest challenges in oncology today. In the following sections a brief description of different treatment policies in management of lung cancer is presented.

6.1. Small cell lung cancer

6.1.1. *Surgery*

Most patients are not candidates for curative surgical resection due to their tumour extent or coexistent disease (Ginsberg, 1989). Therefore, surgery is usually considered only an as addition to chemotherapy in small cell lung cancer.

6.1.2. *Radiotherapy*

Small cell lung cancer is quite sensitive to radiation therapy and historically it was managed with radiotherapy (McLennan and Roder, 1989). The results of radiation when used as the main treatment for small cell lung cancer, have proved to be similar to surgery. However, chemotherapy was subsequently introduced as an adjunct to radiotherapy, and is now routinely administered to patients with limited disease (Pignon et al., 1992). Radiotherapy does not appear to have any benefit in patients with extensive disease except for symptom palliation.

6.1.3. *Chemotherapy*

Although small cell lung cancer remains largely incurable, considerable progress has been made over the past 20 years in the development of combination chemotherapy regimens that significantly improve patient survival and quality of life. The chemotherapy of small cell lung cancer includes many active single and combinations agents. In limited disease it is not uncommon to see response rates of greater than 80 per cent to

combination chemotherapy, and even in extensive disease, response rates of over 50 per cent can be achieved (Natale, 1995).

For patients with limited disease the current standard of care is chemotherapy plus thoracic radiation therapy. Patients with extensive disease initially receive combination chemotherapy. Radiation therapy is not used for most patients with extensive disease, since their disease has spread to distant parts of the body.

It is argued that ultimately to provide the maximum palliative benefit for patients with extensive small cell lung cancer, the therapeutic benefit must be balanced against the costs (physical, psychological, and financial) of treatment (Loehrer, 1995).

6.2. Non-small cell lung cancer

6.2.1. *Surgery*

In case of stage I and II non-small cell lung cancer surgical resection is considered to be the treatment of choice, but the problem is that two thirds of the patients present with a late stage of the disease and therefore are not suitable for surgery. After surgery, long term survival is seen in approximately 70 per cent of patients with stage I and in 40 to 50 per cent of patients with stage II disease (Friedland and Comis, 1995).

6.2.2. *Radiotherapy*

For inoperable non-small cell lung cancer, radiotherapy used to be the standard treatment in most institutions (Palmer et al., 1990). Effective radiotherapy of locally advanced non-small cell lung cancer remains a challenge. Distant relapse is the main cause of failure of radiotherapy to

control disease (Koukourakis et al., 1995). Radiotherapy has a major role in patients with non-small cell lung cancer for the palliation of symptoms.

6.2.3. *Chemotherapy*

Chemotherapy, sometimes combined with radiotherapy, can be administered before surgery (neoadjuvant chemotherapy) or after surgery with or without radiotherapy (adjuvant chemotherapy). The role of neoadjuvant and adjuvant chemotherapy in non-small cell lung cancer remains undetermined, although there are some encouraging results (Milroy and Macbeth, 1995).

Previously there was considerable pessimism about the role of chemotherapy in the treatment of non-small cell lung cancer, but a recent meta-analysis of the 52 randomised clinical trials concluded that chemotherapy may have a role in treating this disease (Stewart and Pignon, 1995). Meta-analysis suggests that modern combination chemotherapy regimens may provide absolute benefits of about 5 per cent with surgical treatment, 2 per cent with radical radiotherapy, and 10 per cent from supportive care-all at five years. Comparing modern combination chemotherapy with single agent chemotherapy, again the literature suggests that combination chemotherapy does improve the probability of survival of patients with non-small cell lung cancer (Marino et al., 1995).

Therefore, it is argued that non-small cell lung cancer can no longer be regarded as resistant to chemotherapy and that chemotherapy can produce a small but modest survival benefit (Thatcher et al., 1995).

6.2.4. *Supportive care*

This refers to no active treatment policy and sometimes is called "Best supportive care". The best supportive care is usually used for symptom relief

and includes one or more analgesic treatment, palliative radiotherapy and psychological support. Patients with poor performance status or elderly patients in advanced stage of disease are the most appropriate candidates for supportive care.

The results of a recent meta-analysis, which also included a review of individual patient data, comparing chemotherapy versus supportive care in advanced non-small cell lung cancer suggests that chemotherapy is superior to supportive care. However, the authors conclude that the results have to be considered in the light of their actual clinical relevance and of the balance between quality of life, toxicity and costs of chemotherapy and best supportive care (Marino et al., 1994)

7. Symptoms of lung cancer

There are two major categories of symptoms: disease- and treatment-related symptoms. Often, it is difficult to differentiate between these two, but generally speaking, disease-related symptoms are those that patients report at the time of diagnosis of the disease and treatment-related symptoms (side-effects) are those appearing after receiving treatment.

7.1. Disease-related symptoms

The most common symptoms for lung cancer patients are: cough, coughing up blood (haemoptysis), breathlessness (dyspnoea), chest discomfort and pain, chest infection and obstruction, hoarseness, swelling of the neck or face caused by pressure on large veins in the chest, symptoms caused by tumour in the brain or tumour pressing on a nerve. Mures et al. (1993) studied symptoms in a group of non-small cell patients and observed that patients at presentation reported the following symptoms (Table 1.4). They graded symptoms as severe, moderate, and mild.

However, patients with metastatic disease, for example with brain or spinal cord metastases, may suffer from additional symptoms. Common symptoms are: severe headache, nausea and vomiting, weakness of parts of the body usually both legs, disturbances in balance and of vision, and change in mood.

Table 1.4 Some common symptoms at presentation

Symptoms	All grades No. (%)	Severe No. (%)	Moderate No. (%)	Mild No. (%)
Cough	228 (79)	12 (4)	101 (35)	116 (40)
Haemoptysis	101 (35)	4 (1)	30 (10)	67 (23)
Breathlessness	216 (75)	23 (8)	95 (33)	98 (34)
Chest pain	107 (37)	9 (3)	40 (14)	58 (20)
Hoarseness	32 (11)	6 (2)	6 (2)	20 (7)
Anorexia	130 (45)	10 (3)	47 (16)	73 (25)
Malaise	136 (47)	6 (2)	43 (15)	87 (30)

Source: adapted from Mures et al. (1993)

7.2. Treatment-related symptoms (side-effects)

7.2.1. *Potential complications of surgery*

Despite careful selection of patients for surgery on the lungs, a very small proportion die soon after operation and this is usually due to heart problems in older patients. The potential complications of surgery include excessive bleeding, change in heart rhythm, persistent leakage of air into the chest, collapse or infection in the other lung, and infection in the chest between the lung and the chest wall.

7.2.2. *Side-effects of radiotherapy*

Common side-effects include cough caused by the inflammation of the lung, pain on swallowing, tiredness, nausea and loss of appetite, sleepiness and loss of concentration and memory, reddening and soreness of the skin.

7.2.3. *Side-effects of chemotherapy*

Common side-effects include tiredness, loss of appetite (anorexia), hair loss, feeling sick, vomiting, constipation, diarrhoea, sore mouth or tongue, tingling hands or feet, anaemia, and susceptibility to infection.

In a typical sample (100 patients) of the general lung cancer population receiving different treatment regimens, Krech et al. (1992) found that the most common and severe symptoms were pain (86), dyspnoea (70) and anorexia (68). There were no difference between males and females. The following common symptoms are reported (Table 1.5).

However, apart from physical symptoms, psychological morbidity has often been reported after diagnosis of cancer. This is an additional symptom which may reinforce physical morbidity as well as affecting their family and social life. These will be discussed in more detail in chapter 3.

Table 1.5 Some common treatment-related symptoms in lung cancer patients

Symptom	All grades No. %	Severe No. %	Moderate No. %	Mild No. %	No rating No. %
Pain	86	32	38	16	0
Dyspnoea	70	12	35	17	6
Anorexia	68	13	33	16	6
Constipation	52	9	26	12	5
Fatigue	52	6	29	11	6
Cough	47	0	17	26	4
Weakness	47	8	27	6	6
Sleep problem	43	2	24	16	1
Weight loss	39	39	0	0	0
Depression	34	7	18	5	4
Anxiety	27	1	17	8	1

Source: adapted from Krech et al. (1992)

8. Lung cancer in Scotland

"This is the only case of cancer of the lung which I have ever met with; so I presume the disease rarely attacks this organ in Scotland".

Bennett J. H. (1849, in Edinburgh)
[cited in: Thatcher and Spiro (1994) New Perspectives in Lung Cancer]

Now lung cancer is the most common cancer both in men and females in Scotland. In 1980 lung cancer ranked first in males and third in females. From 1981 to 1990 the incidence of lung cancer declined by 15.9% in men and increased by 25.5% in females. This has resulted in lung cancer becoming the second most common cancer in Scottish females in 1990 (Sharp et al., 1993). This may be partly explained by the changes in smoking habit among males and females in Scotland. Smoking has declined in recent years amongst men, and there is evidence that morbidity rates for lung cancer have fallen in Scottish men under 50 years. In women, where the numbers smoking are increasing, the lung cancer rates are also increasing (Gillis, 1987, Gillis et al, 1992).

Within Scotland, the West of Scotland has an even higher rate as compared to the Scottish average. The West of Scotland is among countries with the highest recorded incidence rate of lung cancer in the world; with incidence of 97.2 per 100,000 for males and 33.6 per 100,1000 for females (Parkin et al., 1992). Greater Glasgow has more than 30% higher incidence than the Scottish average (Sharp et al., 1993). With a population of 1,000,000; each year there are more than 1000 new case in Greater Glasgow. More importantly, since 1990 the age standardised incidence of lung cancer in females in Glasgow has overtaken that of breast cancer (Gillis et al., 1992).

The most recent figures available indicate that 33% of adult males (over 16 years) and 35% of adult females are smokers (Scottish Health Statistics,

1992). In young adults (16-24 years) the corresponding figures are 28% for males and 38% for females. The level of smoking in Scottish males has steadily declined since 1972 but in females there was an increase between 1984 and 1988 (Scottish Forum for Public Health Medicine, 1994).

Gillis and his colleagues (1988a; 1988b) in their two most cited works showed that the risk of lung cancer did not increase significantly with increasing amounts of tobacco exposure above an average consumption of 20 cigarettes per day. They argued that:

"...it is not just the West of Scotland smoker who is at an increased level of risk compared with his equal smoking counterpart elsewhere but also the West of Scotland non-smoker who may also experience a higher than expected lung cancer risk."

These findings however, led the authors to investigate other possible risk factors including environmental tobacco smoke (Hole et al., 1989), occupational exposure (de vos Irvine et al., 1993), and socio-economic deprivation (Hart et al., 1996). These will be described in the following section.

It has been reported that the five year relative survival rate for males is 6.6% and for females the figure is 6.4%. In 1994 there were 4,237 deaths from lung cancer in Scotland (Registrar General for Scotland, 1995).

9. Lung cancer and socio-economic deprivation

It is often found that lung cancer is inversely related to socio-economic status of individuals (Baquet et al., 1991). Socio-economic deprivation is usually regarded as an indicator for lifestyles such as smoking, and exposures to

occupational carcinogens that have been recognised as possible risk factors for lung cancer (Firth et al., 1993). There is evidence that differences in smoking partially are responsible for the difference in lung cancer risk (Levi et al., 1988). In most divided societies smoking has been found to be more prevalent among lower social classes (Rosen et al., 1990) and therefore they are more likely to have lung cancer as compared to the more affluent.

Although not a direct cause, it is argued that in aetiology of lung cancer poverty plays a role. For example, it has been suggested that unemployed men and their families have increased mortality experience, particularly from suicide and lung cancer (Wilson and Walker, 1993). In the United States of America data from the Western Collaborative Group Study, a prospective cohort study with a 22-year follow-up, showed that after adjustment for other risk factors, having lower income did increase the relative risk for lung cancer mortality (Bucher and Raglend, 1995).

Austoker et al. (1994) argued that smoking is undoubtedly associated with the problems of poverty, unemployment, and other kinds of socio-economic deprivation. They pointed out that in the United Kingdom men and women in social class V are nearly four times more likely to be smokers than are those in social class I. Working class men are three times more likely to die of lung cancer than are those in middle class occupations. Among females, death rates from lung cancer increased in social class IV and V and decreased in social class I and II.

A Danish study found substantial social inequalities in the risk of lung cancer. They found that the people in lower social classes had a higher risk for lung cancer even after adjustments were made for form of smoking, amount smoked, whether inhalation took place, number of pack-years and age. In

contrast to the findings from other studies, the effect of these adjustments was small. They, therefore, concluded that these inequalities in lung cancer risk in Denmark are only to a minor degree explained by social class differences in tobacco smoking (Hein et al., 1992).

A recent prospective cohort study of 58,279 men from Netherlands concluded that there is an inverse association between highest level of education and lung cancer even after adjustment for all other possible socio-economic related risk factors including age, smoking habit, dietary intake of vitamin C, beta-carotene and retinol. They also found that lower white collar workers had a significant lower lung cancer risk as compared to the blue collar workers that could partially be explained by their smoking habits (Loon et al., 1995). Similar findings were previously reported from Italy where in a case-control study it was observed that the men in the lowest level of education had increased risk of lung cancer, but not females. There was also an inverse association between risk for lung cancer and housing tenure for both sexes (Faggiano et al., 1994).

There is a strong deprivation gradient in the incidence of lung cancer in Scotland, with some 80% higher incidence in the most deprived areas (Sharp et al., 1993). Studies have shown that in 1980-1982 the standardised mortality rate of carcinoma of the lung and bronchus for patients with most deprived backgrounds was 120% greater than that for affluent patients but was 170% greater by 1990-1992 (McLoone and Boddy, 1994). This may be attributed to several factors including smoking habit in lower social class and exposure to occupational hazards. Studies of incidence of mesothelioma and asbestos related lung cancer in Glasgow and the West of Scotland clearly suggest that part of the excess of lung cancer in these groups of people may be explained by occupational exposure to asbestos (Gillis et al., 1990; de vos Irvine et al.,

1993). Other studies from Scotland found a less clear pattern of association between lung cancer and social class (Williams and Lloyd, 1991). They only observed a negative correlation in social class II and a positive correlation in social class V. This finding could not be generalised since the method of statistical analysis was based on the percentages of the districts' populations with each group of social class not based on each individual characteristics.

A recent study by the West of Scotland Cancer Surveillance Unit (Hart et al., 1996), comparing three prospective cohort studies in the UK including a male cohort population from the Renfrew/Paisley general population study (a typical population of the West of Scotland) found that there is a difference in cancer risk between social classes in addition to the effect of smoking. Social class was measured by the Registrar General's classification based on occupation. They concluded that this may help to explain why the West of Scotland, an area of high socio-economic deprivation and levels of smoking, has such high lung cancer mortality.

To sum up it is clear that socio-economic status as measured by educational level, occupational social class, house ownership, and level of income all play important roles in the aetiology of lung cancer.

10. Preliminary investigations

To set the stage for the main study of quality of life in patients with lung cancer two practical investigations were conducted. The first was a study of a cancer support group, Tak Tent, and the second involved a preliminary investigation to set up a study of quality of life in ovarian cancer patients. The objectives were:

I. To understand issues in communication with cancer patients in general.

II. To develop the study protocol

III. To test the study-specific questionnaire

In the following sections brief description are presented.

10.1. Communication with cancer patients: Tak Tent study

To have a better understanding of cancer patients, and to practice interviewing skills, it was decided to participate in a cancer support group known as "Tak Tent"-Old Scots for "Take Care" (Appendix I). Permission was asked from the Tak Tent Executive Committee and on several occasions the researcher took part in activities of the six branches of Tak Tent in the West of Scotland. Following visits to, and conversations with, patients and their relatives a descriptive study was carried out by means of a structured interview. Patients and their families were asked about their demographic and socio-economic status, support they were receiving, their concerns and problems, and their general health status and global quality of life.

The study had several results:

I. It was shown that interviewing cancer patients was feasible and that they were pleased to talk about their concerns and quality of life issues.

II. A purposed-designed questionnaire was tested and it was found that the questionnaire could be used in the main project.

III. A paper for publication was prepared.

Full details of the study can be found in Appendix II.

10.2. Quality of life in patients with ovarian cancer

The West of Scotland Cancer Surveillance Unit originated and carried out a series of investigations on variation in the care of ovarian cancer in the West of Scotland and demonstrated significant differences in outcome of therapy between hospitals inside and outside Glasgow (Gillis, 1991). Their recent study showed that improvement in survival is significantly associated with

multi-disciplinary therapy and optimal treatment (Junor et al., 1994). Thus, based on these clear-cut findings, the researcher was interested in a fundamental question: does optimal treatment result in better quality of life? This was the subject of the research proposal submitted to the Department of Public Health, University of Glasgow.

To set up the study, several visits, including meetings with a leading gynaecologist in Glasgow, were held. These provided an opportunity to discuss the proposed project and to evaluate the practicality of the research.

After careful consideration it was realised that it would be difficult to conduct this research study. First, because of time constraint, since during one year it would only be possible to collect or interview a very small number of the patients even in the whole of Glasgow because the incidence of the disease is very low. Secondly, it was unrealistic to assume that the researcher alone could catch all possible cases in Glasgow during a particular period. Therefore, because of insufficient numbers of patients for the study and time constraint, this led to the submission of a new proposal on quality of life in lung cancer patients.

Several lessons were learned. First, all experiences gained during the setting up of the ovarian cancer study were applied to the present study. Secondly, a comprehensive literature review on quality of life in ovarian cancer was carried out. This, by itself led to interesting results:

I. A recommendation for an international study on quality of life in ovarian cancer patients was made.

II. It was learned that relying solely on standard measures of quality of life is not enough. Based on this understanding it was decided when studying quality

of life in lung cancer patients, that socio-economic status of patients be taken into account.

III. The main study protocol had been developed.

IV. A similar method of literature search was used in the lung cancer study.

V. The review has been published (Montazeri et al., 1996a).

11. Conclusion

Against these backgrounds the study set out to investigate quality of life in patients with lung cancer with the hope that the results would contribute to existing knowledge in lung cancer care.

This chapter summarises the situation which a patient with a diagnosis of lung cancer is likely to face. A situation which will change the patient's and his or her family's life. The effects of disease and its treatment, the short survival time, and the psychological morbidity all suggest that there is nothing more important than the "quality of life" in lung cancer patients, although improving survival should not be neglected. The question is- at what price? This is why it is argued that "quality of life" in oncology is essential. In the following two chapters the literature on "quality of life" in cancer patients in general and in lung cancer patients in particular will be reviewed to give a better perspective on the subject.

CHAPTER TWO

2

MEASURING QUALITY OF LIFE: EXPERIENCES FROM THE TREATMENT OF CANCER

Contents

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1. Outcome: measuring health, "hard" and "soft" data

2 Quality of life: meaning and purposes

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5. New directions

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Summary

This chapter examines some of the fundamental issues in health related quality of life measurement with particular attention being given to assessment of quality of life in patients with cancer, thus helping to focus the direction and methodological rigour required in future investigations. Three relevant topics are discussed to illustrate the importance of quality of life measures in cancer therapy. A perspective on the meaning of "outcome" and "quality of life" is presented to demonstrate the controversies that exist in the field. Some experiences from the treatment of cancer are discussed, relevant literature is reviewed and new directions in measuring quality of life are highlighted. It is argued that in a chronic condition, adding life to years instead of years to life is an important task. Adding years to life may prolong survival, but whether this is to the benefit of patients is debatable. Considering patients' views may improve the quality of care and at the same time, reduce the psychological distress and physical discomfort in patients with cancer. It is concluded that quality of life measures have considerable potential in this challenging issue.

Introduction

The issues of measuring health are always surrounded by a number of uncertainties, strengths and weaknesses. Four distinctive components or approaches related to the measurement of health and outcome can be identified: quantity of life, health related quality of life, satisfaction with care, and process based outcome measures (Long et al., 1993). Studies in the outcome of clinical treatment have concentrated increasingly on subjective health-related measures. There is, however, a long standing debate on the topic- sometimes called "unresolved issues" (Patrick and Bergner, 1990). This chapter attempts to examine general aspects of quality of life measurement and in particular, as it relates to oncology. Since quality of life can be viewed primarily as an outcome measure, issues relating to "outcome" are described in order to demonstrate the place and role of perceived health assessment in the health care system. Difficulties in measuring health status are also discussed.

1. Outcome: measuring health, "hard" and "soft" data

There is no single definition for outcome, but perhaps Donabedian's (1985) is the most familiar one. He defines outcome as "those changes either favourable or adverse in the actual or potential health status of persons, groups or communities that can be attributed to prior or concurrent care". But as Gulliford (1992) notes:

> *health care is only one of the factors which determines the outcome of disease. Age, gender, ethnicity, psychological factors, the social and physical environment, and the nature of underlying and associated conditions also combine to influence the prognosis. A clear distinction should therefore be maintained between the general term "outcome" and the specific term "health care outcome".*

Alternatively in examining measured "outcomes" the factors which might have contributed to the "outcome" should be ascertained and identified.

There is also concern about the distinction between the notions, "impact" and "outcome". The former can be taken to refer to short term, while the latter refers to long term consequences of health care interventions (McCallum, 1993). Metcalfe (1990) defines outcome as the output of medical intervention, and he argues that outcome cannot be measured unless the medical intervention is correctly explained so that the end point can be judged.

In fact, the term "outcome" means different things to different people. Clinicians are concerned with the results of their practice; patients seek relief and satisfaction; carers have an interest in improving services; managers are concerned with resource utilisation to provide a more effective and efficient service; and there is a concern that patients should be treated as individuals and given choice, respect and dignity (Austin and Clark, 1993). It is suggested that in assessing medical outcomes five key aspects should be considered. These include the facts that: outcomes are multidimensional; most outcomes are qualitative; assessment of outcomes will be affected by timing; subgroups of disease may have differing outcomes; and outcomes may not be attributable to specific treatments (Orchard, 1994).

However, a number of systematic ways exist to measure health care outcomes. In some ways “hard” data such as morbidity and mortality statistics are outcomes, but these are not always enough (Spitzer et al., 1981) or relevant (Ebrahim, 1990). First, they have their own limitations in the context of completeness and validity and secondly, for chronic illnesses such as malignancy, they may not be very useful measurements. It is understood that

for cancers "in which treatment has improved mortality, statistics must be interpreted with care" (Coggon and Inskip, 1994).

As Bardsley and Coles (1992) pointed out in the case of chronic conditions, it is necessary that outcomes be considered as changes in the patient's health status whether improvement or deterioration. When the aim of clinical treatment is to control disease or its progression and associated symptoms, outcome should be expanded "from objective evidence of the effect of disease and treatment to the subjective or personal perception of patients" (Warner and Williams, 1987). In other words, outcome measures in chronic situations must also rely on other sources of information, namely "soft" data. Information which is more cognitive, perceptual, or filtered by human judgement is likely to be considered soft (Read, 1993). In this respect, there are several other reasons to judge outcomes based on "soft" data. These are: objective standards of assessment with cut-off points indicating desirable outcomes are limited, objectively defined disease is not always a causal association with subjectively experienced illness, and finally certain forms of objectively defined disease may be so prevalent that they are rarely viewed as illness by people who are experiencing them (Jenkinson, 1994a). Therefore, outcome measures, for example, may rely on individuals' judgements, whether patients' or clinicians' views (Donovan et al., 1993). In oncology (and other chronic diseases) this judgement is seen as lying beyond the scope of survival and traditional measurements (Ware, 1984) and usually refers to terms such as quality of life (Najman and Levine, 1981) or more accurately, health related quality of life, or health status measures.

2. Quality of life: meaning and purposes

Although the concern over health related quality of life is relatively recent (Olweny, 1993) quoting Heroditus- 450 BC-, Rosser (1993) believes that the

issue had been investigated in early medical care in Egypt. As she explains, "in the second millennium the tombs in the valley of the kings and those of nobles at Thebes showed an anticipation that the quality of life after death would be desirable"! More generally, McEwen (1993) argues that the efforts to measure health began in the 1930s when Stouman and Falk (1936) introduced the concept of health indicators, but that it was in the 1970s that the explosion of interest began.

The history of quality of life measures in cancer generally, goes back to the use of Karnofsky's Index in the 1940s as a key measure of performance status (Spitzer, 1986). However, as Strain (1990) points out quality of life had its earlier roots in the political and social arena rather than the medical one. Psychologists, and sociologists carried out most of the early empirical social research on quality of life studies with an intention to estimate well being, satisfaction or happiness (Bowling, 1995a). It is argued that the "social indicators movement" of the 1960s and 1970s actually initiated quality of life studies before current research interest on the subject emerged (Andersen et al., 1994). In this instance, it is believed that Breslow (1972) and some other social scientists conceptualised quality of life research, adopting the World Health Organisation definition of health focusing on physical, mental and social well-being. According to such a view, quality of life encompasses all aspects of life including literacy, leisure activities, housing, employment, the physical environment, etc. (e.g. Campbell et al., 1976). Thus, it is not far from reality to say that measuring quality of life is an emerging science in health and medicine.

Quality of life can be defined in two ways: conceptual and operational. Conceptually, it refers to well-being, quality of survival, human values and the satisfaction of needs (van Knippenberg et al., 1988). It has also been described

as the "complete life". Calman (1987) refers to Oliver Wendell Holmes (1860) and quotes:

> *The longer I live the more I am satisfied of two things. First that the truest lives are those that are cut rose-diamond fashion, with many facets. Second that society is always trying in some way or another to grind us down to a single flat surface.*

Fallowfield (1990) states that "quality of life is not a unitary concept, but rather a complex amalgam of satisfactory functioning in essentially four core or primary domains"; these are: psychological, social, occupational, and physical. She argues that this was recognised by Herophilus in 300 BC:

> *To lose one's health renders science null, art inglorious, strength effortless, wealth useless and eloquence powerless. (Quoted by Sextus Empricus in Adversus Ethicus, XI.50.)*

Operationally, quality of life refers to patients' evaluation of their own life as compared to what they expect to be possible or ideal (Cella and Tulsky, 1990). It can also be seen as a measurement of difference between the hopes and expectations of the individuals (Calman, 1984). Quality of life sometimes has been explained in a form of formula: $QL = NE \times (H+S)$ where NE is the patient's natural endowment, and H and S are the efforts made on behalf of patient by his or her family, and society (de Haes and van Knippenberg, 1985). It is argued that many people talk about quality of life, but nobody knows precisely what it is or what to do about it (Campbell et al., 1988). Being abstract as it is, Aaronson et al. (1988) suggest that quality of life should be defined and broken into its components, but they did not attempt to

demonstrate how to achieve a unique agreement about its component parts. This is the focus of the following section.

It seems that to overcome the problem of definition, specially on operational grounds, it should be understood that quality of life as a global term is usually not relevant and can not be used. But as far as health is concerned it should be regarded as perceived health and a self-rated measure, and therefore it should be lay-defined. However, there are considerable variations in the purposes of quality of life studies. Table 2.1 illustrates some suggested areas.

Table 2.1. Examples of variations in purposes of quality of life studies

Katz's (1987) suggested list	Application of quality of life measures by **Fitzpatrick et al.** (1992)	Three general reasons for measuring quality of life in patients with cancer by **Cella et al.** (1993)
To measure well-being	Screening and monitoring of psychosocial problems	Assessment of rehabilitation needs
To improve treatment and care for chronic illnesses	Perceived health investigation	As an end point of health care outcome
To provide data for policy-making and planning	Medical audit	As predictor of response to future treatment
To provide information about risk factors	Evaluation of health services	
To develop new and cost-effective methods of health care	Cost-utility analyses	
	Clinical investigation	

There are two main gaps in quality of life measures, whatever the purposes are. First, the comparison between studies with different objectives are difficult (Gelber et al., 1993) and sometimes impossible (Fallowfield, 1993; 1994). This is due to several facts including: variations in methodology, sampling procedures, and instruments used. Secondly, there is a gap between the expectation of patients from such studies and researchers' achievement. Patients are concerned about their immediate needs of relief from symptoms

whereas psychologists, sociologists, clinicians and other contributors to quality of life studies concentrate on their study objectives. In a study on quality of life in lung cancer patients, Bernhard et al. (1995) reported that " an unexpected and more difficult problem was that some patients thought that their individual response would be the basis for further treatment decisions and a worse level of self-estimation was to be avoided". These may therefore, not only influence quality of life studies in the context of external validity but also in reliability.

3. Quality of life: Controversies

There are several useful reviews of quality of life measures (e.g. Fallowfield 1990; Bowling, 1991; Wilkin et al., 1992; Walker and Rosser, 1993; Patrick and Errickson, 1993; Jenkinson, 1994a; Bowling, 1995a) and these provide an excellent insight into the issue. Considerable literature also exist in the area of cancer therapy (e.g., Clark and Fallowfield, 1986; Aaronson and Beckmann 1987; Donovan et al., 1989; Osoba, 1991; Selby, 1993). Full discussion of all these works is beyond the scope of this chapter, but some of the key issues have been selected.

3.1. The use of objective health measures

Although quality of life measures are today more acceptable than at their earlier stages, Donovan et al. (1993) in their paper "assessing the need for health measures", heavily criticised the use of subjective health-related measures. They argued that "it is not clear what would be gained from the health status questionnaire material that might not be found more economically from routinely available statistics". They concentrated on the Nottingham Health Profile (NHP) as an example and pointed out that these measures do not "allow people to express what they really feel". They observed that several people with serious disease assigned themselves as

being relatively healthy because their symptoms had become part of their normal life. However, they pointed out that the extent to which these measures would in practice modify the interpretation of conventional measures of health need are not clear, although some assessment of perceived health might in principle be desirable.

Their discussion is limited. First, they de-emphasise the fact that people's feelings are subject to changes overtime. If therefore, there are differences between data obtained by a questionnaire at a particular time and an interview sometime later, this could be true for any subsequent new interviews as well. People's views may change with time. Although interview is a better way of providing in-depth information, this is not a sound basis for judging the measurement of people's perceived health status as worthless. Secondly, it is not clear what the outcome for chronic diseases should be- a situation in which the power of medicine to cure is limited and the main objectives of health care are relief of symptoms and/or reduction of side effects of treatments. Thirdly, it is not a systematic approach to extract data from tape and come to a general conclusion about health measures or even about that particular instrument. There is supporting evidence for the applications of these measures in well designed studies (e.g., Kind and Gudex, 1994; Visser et al., 1994; Westlake and George, 1994), although the limitation of the NHP is recognised both by its own pioneers (McEwen, 1993) and others (Kind and Carr-Hill, 1987). In a recent paper there is a critical review of international assessments of health-related quality of life including the NHP. The authors stated that "the NHP has performed well in the role for which it was developed: to measure distress in functional status and estimate major needs for health services in populations from major disabling health conditions" (Anderson et al., 1993).

3.2. Definitions of quality of life

Quality of life is not well defined. The literature reveals that much effort has been made to define quality of life, but there is no "common rules and language" (Aaronson, 1990) to bring into agreement all contributors to the quality of life studies.

However, there should be at least a clear distinction between conceptual and operational definitions, and secondly, different approaches to quality of life assessment should be recognised. Fries and Spitz (1990) pointed out that in clinical studies quality of life does not mean happiness, satisfaction, living standards, climate or environment, but rather it can be defined as those dimensions of life that might be influenced positively or negatively in clinical studies and in the clinical situation. Five basic approaches to definition of quality of life have been recognised (Schipper et al., 1990). These are:

(i) The psychological approach and this refers to the fact that measuring quality of life means distinction between illness and disease as perceived by patients (Kleinman, 1986).

(ii) The time trade-off or utility concept which refers to the desirability or preference that individuals exhibit for a particular condition, for example preferring quality of life instead of survival or vice versa (Torrance, 1987).

(iii) Ware's concept of quality of life which emphasis five concepts as minimal standards for the content validity of health measures: physical health, mental health, general health perceptions, social functioning, and role functioning (Ware, 1984; 1987).

(iv) The reintegration to normal living concept which has been defined as "the reorganisation of physical, psychological, and social characteristics of an individual into a harmonious whole so that one can resume well-adjusted

living after an incapacitating illness or trauma" (Wood-Dauphinee and Williams, 1987).

(v) Calman's Gap Theory which defines quality of life as a measurement of difference between the hopes and expectations of individuals (Calman, 1984).

It appears that these are all different, but at the same time, the same. In other words, all are discussing a subjective impression perceived by the patients or a normal population about their own health status, but with different names and different usage. Thus, expending much more time on definition is no longer a beneficial practice.

3.3. Differing approaches

A decade ago quality of life was "a glimmer in the eye of a small number of psychologists and sociologists", but the issue " at best rarely entered the clinician's mind. At worst it was an anathema" (Schipper, 1990). It is argued that there are two different approaches to quality of life measures: a pragmatic clinical point of view, and the methodologist's point of view (Greer, 1987). The former refers to clinicians who believe in simple instruments of direct use in their speciality. The latter refers to those who are more concerned with methodological aspects of quality of life instruments. These are reliability, validity and responsiveness, namely psychometric properties of quality of life measures (Hays et al., 1993).

However, it is recommended that "the gap between these two points of view must be closed if we are to create a sound methodology of quality of life evaluation which will be both useful and used in the clinical realm". Similarly, Tchekmedyian and Cella (1990) highlighted that there is a gap in information and communication between social scientists and clinicians and that this gap should be filled. In other words, social scientists should realise that in a practical setting, for example in a clinic or in a clinical trial, it is very difficult

to consider all methodological aspects, and in contrast, clinicians require to accept that any instrument for measuring quality of life should be valid and reliable. Such considerations by both sides, however, may make the issue easier and reduce conflicts.

3.4. Use of general or specific measures

There are several names for different classifications of health measures, although some of these categories are the same. Two basic types of instruments have been identified: disease specific and generic (Fletcher et al., 1992). The former refers to the measures which are used for one disease or narrow range of illnesses while the latter refers to those which can be used for a wide range of purposes. Donovan et al. (1993) identify health status instruments as falling into seven basic categories: general health measures, measures of physical function, pain measures, social health measures, psychological measures, quality of life measures, and specific disease measures. As it is clear, there is no need for such a classification, because many of these instruments fall into the same category.

In cancer literature, these categories are mostly described in two ways. In their review van Kinppenberg and de Haes (1988) distinguished three types of instruments: ad hoc instruments constructed for a specific study, general instruments, and instruments specifically designed for measuring quality of life of patients with cancer. Aaronson (1989) describes four categories: generic, disease-specific, ad hoc, and disease-cluster that "have a somewhat narrower focus, while still maintaining a generic element".

Advantages and disadvantages of these measures are discussed in the literature. There is "a spectrum of opinions from those who discourage generic measures preferring diagnostic- or individual-specific measures through to

those still look for a single index for use at the top level of government decision making" (Rosser, 1993). It is argued that "generic measures should not be expected to completely capture the particular effects of disease or treatment" (Ware, 1987). In contrast, it is suggested that, because generic measures contain many health related dimensions, these are more likely to detect unexpected effects (Fletcher et al., 1992). It is argued that generic measures make the comparison between studies possible, while specific approaches have the advantage of detecting specific disease related quality of life problems.

However, there are no simple answers to the question, rather it depends on which dimension of quality of life is under study, for which type of people it is used e.g. ill or general population, and to what type of disease it is going to be applied.

Several instruments have been used for the measurement of quality of life of cancer patients. Maguire and Selby (1989) reviewed all available measures with regard to their clinical application, ease of administration, scoring, and reliability and validity (20 instruments). They concluded that the "best- bet" instrument is the Rotterdam Symptom Checklist. Sometime later Selby (1993) concluded that no single measurement method for quality of life in cancer patients is yet satisfactory. In examining item content of these measures, it appears that many concepts measured are generic rather than cancer-specific.

A recent review of measures widely used in oncology (10 instruments) addressed the problem (Cella, 1995a) showing that there is little attention to underlying factors which contribute to the quality of life in cancer patients such as social and family life. Since patients with cancer need more support,

for example, the issues of family and caregivers become very vital to patients' daily life.

Progress has been made in synthesising a single modular assessment strategy which provides a combination of general and disease-specific measures. The European Organisation for Research and Treatment of Cancer questionnaire (EORTC Quality of Life Questionnaire) is a product of such an approach (Aaronson, 1989) and the final stages of development and validation of their instrument was recently reported (Aaronson et al., 1993). Similarly, Fletcher et al. (1992) argued that "a common recommendation is to include both disease specific and generic measures in a study". In addition, it seems that in each study it would be beneficial to consider a set of study specific questions to cover all quality of life related problems of the subjects under study.

It is difficult to indicate the best available instrument, but to meet the major principles that quality of life measures require, the EORTC QLQ-C30 (cancer core questionnaire) seems to be one of the best developed measures across different European and North American languages and cultures (Cella, 1995a). In a comprehensive review of more than 30 instruments used in oncology settings Bowling (1995a) concludes that the best developed measure for use with cancer patients is currently the EORTC QLQ.

However, an ideal selection depends on the objectives of the study and the current emphasis is on supplementation with other measures. For example, the EORTC, now has developed a modular supplement (QLQ-LC13) to the core questionnaire (QLQ-C30) for use in lung cancer clinical trials (Bergman et al., 1994). Another example of such a development is the Functional Assessment of Cancer Therapy-Lung quality of life questionnaire (FACT-L). The FACT-L has been developed after the FACT-G (general cancer core questionnaire,

34-item version 2) and its reliability and validity have recently been published (Cella et al., 1995). Yet, a major question remains: to what extent does the initial quality of life and socio-economic status of patients contribute to their recent quality of life?

3.5. Major dimensions to be included

From the literature review it appears that a quality of life instrument should at least contain four areas as important dimensions: physical, psychological, social, and performance. It is argued that physical function, mood, symptoms and social support are the key predictors of the assessment of the quality of life and should be monitored from diagnosis, through treatment to terminal illness (Mor, 1987). Although quality of life measures only include a few items related to the social aspect of quality of life, many researchers emphasis that social well-being should be considered as an important part of these instruments. In their review de Haes and van Knippenberg (1985) suggest that social aspects of quality of life "may account for some of the unexplained variance in the indicators of well-being".

However, there have been different ideas about major dimensions to be included in a quality of life measure. Some argue a minimum of four components should be contained in a quality of life instrument: physical functional status, disease symptoms and treatment side-effects, psychological status, and social functioning (Aaronson, 1990). After consideration of 30 different categories for component parts of quality measures applied by various authors, Cella and Tulsky (1990) distinguished ten dimensions: physical concern (symptoms; pain), functional ability (activity), family well-being, emotional well-being, spirituality, treatment satisfaction (including financial concerns), future orientation (planning; hope), sexuality/intimacy (including body image), social functioning, and occupational functioning.

This problem (including different items and domains by different researchers) may explain why there are so many instruments. Some of these are not truly quality of life measures (e.g. Karnofsky Performance Status), some are generic measures (e.g. Sickness Impact Profile) and a few are cancer-specific (e.g. Functional Living Index-Cancer). In addition, including several dimensions in an instrument may cause other problems such as administrative difficulties and an excessive burden on patients. Different people, perceive quality of life differently. For example, in a study on quality of life in lung cancer patients including a sample of patients with chronic respiratory disease it was found that patients defined quality of life as "good health" (42%), "enjoyment of life" (25%), "good family life" (24%), "happiness" (21%), "ability to do what one wants to do/work" (16%), "financial security " (16%), "good social life/leisure activities" (13%), and "living longer" (5%) (Montazeri et al., 1996b). There is no way to include all these dimensions in an instrument. Again, it is very unlikely to find an instrument which covers all these items.

On the other hand, the development of new instruments is not a solution to the limitations of existing quality of life measures. Simply, to create a new specific measure will result in subsequent similar criticisms of not meeting another defined need. Sometimes behind the development of these new instruments there is a lack of logical reasoning and theoretical justification. The establishment of any new measurement requires to be justified. It may be preferable to use existing measures and improve their application to reduce confusion in the field.

3.6. Who should measure

The next question is, who should measure quality of life, patients or clinicians? It has been suggested that there are three possible options for

measuring quality of life: measurement by outside observer, by the patient, and by measuring objective parameters e.g. physiological ones (van Knippenberg and de Haes, 1988). All are different however, and all require different approaches and measuring instruments. Several studies have shown that assessment of quality of life by doctors and nurses correlated poorly with those rated by the patients themselves (Slevin et al., 1988).

In contrast, in a study of quality of life measurement in breast cancer patients, Bell et al. (1985), using a physician as an independent observer, reported that in general there is good agreement between patients self-rating and independent observer assessment of quality of life. Hunt and McKenna (1992) pointed out that "since quality of life is assumed to encompass psycho-social elements which are not normally accessible to doctors, it is possible to argue that the patient is the best judge of quality of life and that it is the patient's self-report which should carry most weight".

However, in palliative care, in which sometimes the patients may not be able to speak for themselves, proxy rating (observer rating on behalf of the patient) must be considered. This also is crucial in assessing quality of life in cognitively impaired individuals (Cella, 1995b). Since the proxy assessments reflect the caregivers' concerns (family or health professionals) rather than the patients' feelings, then, the challenge is how reliable are these measures?

Finally, sometimes clinicians are rather reluctant to judge outcomes based on quality of life measures. Thus, it is difficult to ask them to measure patients' quality of life as outside observer. This is due to several reasons (Feld, 1995; Montazeri et al., 1996c):

1. The benefits of these measures are not clear relative to standard endpoints.

2. In a busy clinic it is not possible or it is very difficult to administer these measures. In other words, in a clinical setting measuring quality of life is not the first priority.

3. Some clinicians are concerned about burden on patients in such assessments.

4. There are some uncertainties about how to measure quality of life and how to analyse the information obtained and how to interpret them. This is true even for some researchers, especially those who are dealing with analysing these data. Difficulties in analysing quality of life data include the multidimensional nature of data, attrition, and missing information (Hopwood et al., 1994).

However, difficulties which arise from theoretical concepts through to operational practices all demonstrate the limitations rather than possibilities. For example, since each individual has his or her own values and norms even within a study it is difficult to compare quality of life scores among study subjects; or from a more radical point of view it is difficult to judge on quality of life scores of the same individual through time in the same study. Jenkinson (1994b) argued that, to date, the benefits of including health status measures routinely in clinical practice are far from conclusive.

Criticism about quality of life measures continues, since it is argued that these measures are subjected to measurement of many variables which are often neglected. This means that quality of life does not, to some extent, reflect a sound scientific approach where the basis of any measurement is the perception of individuals which changes over time either due to change in their own values or because they are human beings. In addition, experiences of illness change because people learn, adjust, or accommodate over the course of illness (Liang et al., 1990).

In contrast, it is argued that despite so many shortcomings in measuring quality of life; it can do more good than harm if the basic principles are considered. Measuring quality of life may help to build up a more realistic picture of patients' feelings, and their needs. In the following section experiences from the treatment of cancer may help to justify the application of these measures.

4. Experiences from the treatment of cancer

In assessing the outcome of clinical treatment it is important to identify whether treatment results in a better quality of life- if not a longer life (Katz, 1987). It is argued that if the patient would not be able to enjoy his or her own time, survival for a few extra months is meaningless. This will only cause the patient to suffer more. A patient with cancer experiences a "living-dying" situation and this is "the intolerable incompatibility of life and death" (Muzzin et al., 1994). For example, 30-40% of patients with cancer "experience periods of depression or anxiety or both" (Higginson, 1993), and psychosexual morbidity is one of the most important problems in women with gynaeocologic malignancies (Crowther et al., 1994).

Three reasons have been mentioned to justify considering quality of life as an important part of cancer treatment (Slevin, 1992). First, a patient with cancer has no control over his or her disease. Secondly, the cause of illness cannot be explained. The explanation can only create confusion and sometimes there is no answer even for experts. Thirdly, patients are often told "there is nothing we can do for you".

it is therefore not surprisingly that patients with cancer often feel more miserable and despondent than patients with other potentially fatal illnesses and that quality of life is a much bigger issue in cancer than it is in other equally life threatening disease.

In addition, others observed that in cancer therapy it is difficult to describe whether a patient has benefited overall from a treatment or not (Rees, 1991), because the side-effects of treatment have also a major contribution to the quality of life. Surgery can seriously damage a patient's body, radiotherapy may cause physical and emotional discomfort, and chemotherapy can often be toxic (de Haes and van Knippenberg, 1985). Quality of life studies, however, have several advantages in cancer treatment. A few examples are given to demonstrate why measuring quality of life is so important.

4.1. Quality of life and survival

Quality of life measures can be used as an end point in clinical trials to compare different treatments, to measure outcome of health care or as a predictor of survival (Weeks, 1992). Quality of life studies may influence decisions about the effectiveness of therapies, enhance supportive care, and identify the patient's reaction towards treatment.

In a prospective clinical trial of different treatment protocols for advanced breast cancer, Coates et al. (1992) found that there is a significant association between scores obtained from quality of life measures and changes in scores on survival duration. To explore the relationship between quality of life and subsequent survival, studying lung cancer patients it was found that nonmedical factors such as quality of life assessment and marital status play a role in survival and that they should be evaluated and described as potential predictors of survival in cancer patients in clinical trials (Ganz et al., 1991).

In addition, survival is not patients' only consideration towards treatment. In a study of attitudes towards the quantity and quality of life in a group of healthy volunteers, presented with hypothetical options for treatment of advanced laryngeal cancer, it was found that 20 per cent of volunteers preferred to trade

off their life expectancy so that they can retain speech (McNeil et al., 1981). This is true even in trade off between two different treatments. When survival for two different regimens are the same, it will be useful to judge outcomes based on the quality of life which is perceived by the patients. If survival for one treatment is better, but the quality of life is decreased, the patient may contribute to the process of decision-making. In this situation offering a choice of treatment, when it is possible, may help to overcome some problems related to the treatment. It is argued that patients with cancer in choosing between two treatments, when disease is likely to be cured, may be willing to accept a treatment that effects their quality of life in a negative way; but if the chance of survival is small, then the quality of life becomes the main concern (Slevin et al., 1990; Kiebert et al., 1994).

The literature suggests that several contextual factors may affect the patients' choices between survival and quality of life; for example age, sex, marital and domestic status of the patients, and probability of survival (Coates et al., 1983; O'Conner, 1989). To explore the issue further, in a study by Kiebert et al. (1994) it was found that having a partner, having children, the nature of side effects of treatment, and baseline quality of life were all of considerable importance in choosing between quality of life and survival. This is why it has been argued that survival and quality of life are not competing predictors of outcome measures, but rather complement each other in decision making. The initiative to combine length of survival and quality of life into a single end point to provide quality-adjusted life years is an example (Olschewski et al., 1994).

Quality-adjusted life years (QALYs) measure the health gain which combine the survival time and quality of life. Quality of life is usually measured on a scale from zero (death) to one (full health). Thus, to calculate QALYs, first

the change in both survival and quality of life from a particular treatment should be estimated, then QALYs can be calculated as: change in survival multiplied by change in quality of life (Petrou and Renton, 1993). The two proposed applications for QALYs are as a measure to be used in the allocation of resources and second as a measure to determine which individuals should receive the available treatment (Goodinson and Singleton 1989). On this basis the use of QALYs has been criticised in many ways. For example, it is argued that QALY-based analysis will tend to discriminate against elderly people and those with shorter life expectancies because greater QALY benefits can be obtained by treating younger patients and those with longer survival (Spiegelhalter et al. 1992; Selai and Rosser 1993).

A more acceptable model of such an approach is Time Without Symptoms and Toxicity (TWiST). This model of quality-adjusted survival analyses the length of survival without symptoms of disease and toxicity of treatment can be used as an outcome to describe patient's quality of life (Gelber et al., 1986).

4.2. Contribution to development of cancer treatment

There is an extensive body of literature on the role of quality of life studies in clinical trials and development of cancer treatment.

Barofsky and Sugarbaker (1990) demonstrated that quality of life assessment can lead to improved cancer treatment in two ways: when it is an integral part of the treatment development process (single step), and when it contributes to improvement through a multistep procedure.

To explain these two procedures they discuss the development of soft tissue sarcoma and breast cancer treatment. For example in the case of the extremity

soft-tissue sarcoma it was found that the limb-sparing surgery procedure did not produce better quality of life than amputation. Then, other studies modified the limb-sparing surgery and radiotherapy that patients received. Subsequently, new evidence shows that compared with the previous method, the modified procedure can lead to a better quality of life. At last, the modified limb-sparing method was confirmed and accepted as the new protocol.

4.3. Identification of psychological needs

Modern therapies in medicine have become increasingly effectual and, at the same time, more likely to produce harmful side effects (Greer, 1984). Thus, with regard to the psychological morbidity associated with cancer medicine, it is recommended that clinical trials should contain measures of psychological adjustment to enable clinicians to base their decisions not only on survival but also on the quality of that survival.

In this instance, studies of quality of life measurements in breast cancer provide an interesting experience. While it was thought that lumpectomy would reduce psychological morbidity in women who underwent breast conservation it was found that there are no significant differences in the incidence of anxiety and depression between women who underwent mastectomy and those who have had breast conservation (Fallowfield et al., 1986; 1990). Morris and Ingham (1988) showed that choice of surgery treatment, independent of the type of operation, is attributed to better psychological outcomes. This finding, however, was not supported by a recent study on which patients with stage I or II breast cancer were offered choice of surgery. The patients were followed up for 3 years after their treatment and the results showed that there is no evidence to support the notion that choice prevents psychological morbidity (Fallowfield et al., 1994).

It is, however, suggested that quality of life of patients with breast cancer may be improved by a good communication style (Fallowfield, 1993). A prospective randomised trial indicated that adjuvant psychological therapy can lead to a reduction in psychological distress (Greer et al., 1992). This adjuvant psychological therapy is a "cognitive behavioural treatment programme" in six sessions, focusing on an individual's personal strengths to overcome psychological morbidity related to cancer (Greer et al., 1991).

4.4. Quality of life and alternative therapy

Use of alternative therapy or complementary medicine for the treatment of cancer has increased in recent years (Hauser, 1993). It is argued that these therapies may lead to a better quality of life. A study on survival of patients with breast cancer attending the Bristol Cancer Help Centre (BCHC), offering alternative treatment, showed that "patients choosing to attend the BCHC do not gain any substantial benefit. Whether quality of life is enhanced is yet to be answered" (Bagenal et al., 1990), although subsequent debate revealed that this study suffered from design flaws, since patients attending BCHC had more advanced disease (Morris et al., 1992).

Another study on survival and quality of life among a group of patients with cancer receiving unproven cancer therapy as compared with a group of patients receiving conventional treatment showed no difference between the two patient groups in length of survival. On the other hand, the same study shows that quality of life is better among conventionally treated patients (Cassileth et al., 1991).

Recently the *BMJ* (Downer et al., 1994) reported a study on use of complementary therapies by cancer patients receiving conventional treatment. Overall, a high proportion (82%) of those using complementary treatments

along side the conventional therapies indicated that they are either satisfied or very satisfied. They specified that the benefits are both physical and psychological. The psychological benefits, included feeling more optimistic and hopeful about the future. This indicates that patients with cancer need more support and help which may make life more meaningful to people with an incurable disease (Taylor, 1993).

4.5. Obtaining additional information

A critical review on quality of life in patients with ovarian cancer shows that there is much to learn from such studies (Montazeri et al., 1996a). For example, studies have shown that psychological factors, experience of pain, gastrointestinal symptoms and experience of fatigue and malaise all contribute to quality of life of patients with ovarian cancer (de Haes et al., 1990). Thus, measuring quality of life in this way may help to identify people in need and provide interventions required, especially psychological support to enhance the quality of life in these groups of patients who are affected by life threatening disease.

However, interpretation of results concerning studies of quality of life is not an easy task. van Knippenberg et al. (1992) reported on a study of quality of life in patients with resected oesophageal cancer and showed that quality of life of surgically treated patients can be assessed in two opposite ways- depending on the indicator chosen: from a medical point of view patients were considered to have been adequately treated, but when other variables such as physical symptoms and the effect on activity level are taken into account quality of life had deteriorated.

Furthermore, social and cultural contexts also affect one's perceptions of health and illness. Thus, patients' feelings and problem contexts are also

essential in understanding health status and quality of life (Albrecht, 1994; Fitzpatrick, 1994).

5. New directions

Several lessons have been learned from measuring quality of life in oncology. These include: quality of life is multidimensional; observers are poor judges of how patients feel about their quality of life; symptoms are associated with quantifiable disruptions in quality of life; and pre-treatment quality of life may be predictive of on-treatment quality of life and survival (Osoba, 1994). Yet, several challenges remain. One such challenge is how should the values and preferences of patients be integrated into quality of life measures?

It is argued that since quality of life is a uniquely personal perception, most measurements of quality of life in the medical literature seem to aim at the wrong target. Reviewing 75 randomly selected original quality of life articles, Gill and Feinstein (1994) observed that in 87% of the articles, patients were allowed to respond only to a list of items previously selected by experts and were not invited to add any individual responses. This is a serious problem which questions the face validity of these instruments.

Recently, there have been interesting attempts to identify the components of quality of life as perceived by individuals. Two examples of these are the Schedule for the Evaluation of Individual Quality of Life (SEIQoL), and the Patient Generated Index (PGI).

The SEIQoL was developed using the judgement analysis technique in a semi-structured interview form and provides a list of five areas that individuals judge to be the most important to their quality of life. It also indicates the relative weights of importance attached to the components of quality of life

nominated by the individuals (McGee et al., 1991; O'Boyle et al., 1992; O'Boyle, 1992).

The PGI was developed using the priority evaluator method (to take account of the preferences) and designed as a self-completed questionnaire. It is very similar to the SEIQoL and allows patients to define quality of life and to value the relative importance of improvement in their chosen areas of life (Ruta and Garratt, 1994; Ruta et al., 1994). A similar method was used by Guyatt et al. (1987) when they developed a questionnaire that asks patients to specify the five most important areas of their lives affected by their condition, or to choose the five most important from a list of 20 items.

Using the SEIQoL, in a limited sample of healthy individuals (42) it was found that a variety of areas of life were nominated as being important to their overall quality of life. Considerable variability was also found in the relative importance attached by participants to the various aspects of their quality of life. For example, those who nominated health as an important factor, weighted health varying from 3 to 59 out of a possible 100 score. A similar study with a sample of 40 patients indicated that leisure, family and work were significantly more important components of quality of life for the patients than for the healthy comparison sample, while fewer patients referred to health than did members of the healthy group (McGee et al., 1991). Although this method has been reported to be valid, the bias of introducing life domains by showcards to those who have no idea about nominated areas, remains to be resolved.

Two recent publications by Farquhar (1995) and Bowling (1995b) are the most advanced in these series of investigations. While the former aimed to identify lay definitions of quality of life among people aged 65 and over living

in three different areas (204 subjects), the latter aimed to provide population norms on the dimensions of life that people perceive to be important in relation to their quality of life based on a large sample (2033) of the general public. The former study (Farquhar, 1995) using a set of simple questions highlights how quality of life varies among different age groups of the elderly population living in different geographical areas. The study conclusions also indicate that social contacts appear to be as valued as health status. The latter study (Bowling, 1995) which used a method very similar to the SEIQoL found that relationship with family or relatives, the respondents' own health, the health of someone close, and finances (good or bad) were the most important things in respondents' lives.

However, considering the patient's viewpoint, validity of quality of life measures must become the central measure of efficacy for a quality of life instrument. To achieve this research into the best ways of measuring and assessing quality of life must continue to seek individual values and preferences. These methods now are being applied in assessment of quality of life in cancer patients. Examples of such instruments are the Functional Assessment of Cancer Therapy, FACT (Cella et al., 1995), the Subjective Quality of Life Profile, SQLP (Dazord, 1995), and an Italian instrument the GIVP- individual ranking of values and preferences (Belli et al., 1996).

5. Conclusion

Since health and illness are not confined to a biomedical model of well being, quality of life is a potential perspective of individuals' judgement about their own values and expectations. The recent definition by the WHO Quality of Life Group confirms this where they state that quality of life is "an individual's perception of his/her position in life in the context of the culture

and value systems in which he/she lives, and in relation to his/her goals, expectations, standards, and concerns" (WHOQOL Group, 1994).

There are several practical and acceptable measures, to all sides (clinicians, patients, social scientists, psychologists), and these should be used. Methodological limitations are no longer an excuse for not measuring quality of life. We cannot wait for a "gold standard". As Ganz (1994) reminds us, "although quality of life was once described as being subjective, unmeasureable, and poorly defined, this is no longer the case".

Cancer has become a new public health priority (BMJ, 1994) and the information which is available from quality of life studies may have a central role in providing additional data for the development of cancer control and its treatments. The autonomy of patients is one of the main features of these types of assessment that may contribute to their participation in informed decision-making (Payen, 1992).

Patients with cancer need cure, prolongation of survival, and improvement of quality of life. These may not be achievable unless we provide a good partnership between social sciences, medical science, complementary health care, and faith (Morris et al., 1992).

Quality of life measures may help in adding life to years instead of years to life. Adding years to life may prolong survival time, but it should not be the cause of suffering, deterioration in health status, and the quality of life of patients with cancer. Cancer patients may refuse further treatment, not because they want to die, but because treatment leads to a life not worth living, a situation which would result in a health status worse than death (Kiebert et al., 1994).

Experiences from the treatment of cancer indicate that quality of life measures could be used in different ways. For example, these measures may be used to assess the overall outcome of a particular regimen or procedure, to compare different treatments, to predict survival, to examine health care outcome, and to use these measures as screening tools to identify patients' particular needs in the context of their social and cultural status.

Patients with cancer need, more than any thing, hope (Slevin, 1992; Downer et al., 1994) and quality of life studies may bring this to them by considering their own views and preferences. That is the way forward: adding life to years to make patients' life, even short, happy and enjoyable.

CHAPTER THREE

3

QUALITY OF LIFE IN PATIENTS WITH LUNG CANCER

Contents

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-. Introduction

1. Quality of life in lung cancer patients in general

2. Quality of life in patients with small and non-small lung cancer

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Summary

A review of the literature was carried out covering the last 25 years (1970-1995) by searching through the MEDLINE and manually. The review consists of two companion parts. The first includes studies of quality of life in lung cancer patients in general, while the second part is restricted to defined samples of small and non-small cell lung cancer patients. Excluding non-English and review papers, in total 150 citations were identified and all have been reviewed. Over fifty instruments were used to measure quality of life in lung cancer studies. Of these, the European Organisation of Research and Treatment of Cancer Quality of Life Lung Cancer Questionnaire (EORTC QLQ-LC13) in conjunction with the core cancer questionnaire (QLQ-C30) was found to be the best developed instrument, although there were two other lung cancer specific measures with good reliability and validity. Several topics in this chapter have been highlighted including the importance of regularly measuring quality of life in lung cancer patients. Progress and achievements in areas such as performance status as a proxy of quality of life measure, psychological morbidity and symptom distress as predictive factors of quality of survival, and communication problems in quality of life studies of lung cancer patients have been emphasised and their implications in lung cancer care discussed. It is argued that palliation of symptoms, psychosocial interventions, and understanding patients' feelings and concerns all contribute to improving quality of life in lung cancer patients. It is concluded that the future challenge in treatment of lung cancer lies not only in improving the survival, but mainly the patients' quality of life regardless of cell type. Clinical trial and epidemiological population-based outcome studies are recommended to provide this and to allow a better understanding of the contribution of the socio-economic characteristics of the patients to their pre- and post-treatment quality of life.

Introduction

For the purpose of this study, this chapter reviews the literature on quality of life studies in lung cancer patients and gives an insight into the improvement achieved and highlights the problems and deficiencies. In the following sections two topics will be covered; firstly studies on quality of life in patients with lung cancer covering more general aspects and secondly, studies of small and non-small cell lung cancer including more specific issues. This distinction was made due to the fact that in the former studies either the cell type was not identified or different histologic types were included in the studies whereas in the latter studies only small cell lung cancer or non-small cell lung cancer patients were included in the studies.

There are several papers on the subject. Of these, most are commentaries, one is a symposium agenda, one is a report, and one is a paper that examines different ways of analysing the quality of life data. The remaining papers are reviews. Table 3.1 gives a summary of all these papers. The review papers mainly focus on two issues: review of instruments used and, the effect of disease and its treatment on quality of life of lung cancer patients. All papers suggest that assessment of quality of life should be included in evaluating treatment outcomes. Of these, only two papers include a summary of quality of life studies in lung cancer patients (Bergman, 1992; Bergman and Aaronson, 1995). Some of these review papers have a narrow focus on clinical trials and none were carried out in a systematic way. The method of review and the criteria for including papers are not identified. In addition, these reviews did not include all published papers at the time they were carried out.

Two methods of investigations were carried out: MEDLINE search, and a manual search. The year 1970 was chosen because the first study of quality of

life in patients with lung cancer was published in 1970. For MEDLINE search the key words "quality of life" and "lung cancer" were used. This provided the initial database for the review. The initial search was carried out in 1994 and up-dated twice in 1995 and once at the end of January 1996.

In the second procedure, using the initial database, the papers cited in the literature were examined for possible additional existing papers. There were no specific criteria for inclusion of papers in the review, but they were excluded if the language was not English. A similar method of investigation was used in reviewing quality of life in patients with ovarian cancer (Montazeri et al., 1996a).

A total of 150 citations were identified and reviewed. Of these, 67 citations were not restricted to specific cell type of lung cancer, but the remaining were restricted to define samples of small and non-small cell lung cancer patients. Thus, the review consists of two parts.

1. Quality of life in lung cancer patients in general

Excluding non-English and review papers a total of 67 citations were identified, 47 citations on quality of life in lung cancer patients in general (Table 3.2), and 20 citations on quality of life in cancer patients including that of lung (Table 3.3). Out of 67 citations, 18 were in abstract form (Tables 3.2 and 3.3) and there were studies which appeared both in an abstract form and in a complete publication form. This means that some studies were counted twice (once in an abstract form and once in form of a complete publication). In addition there were identical studies from the same author(s) that had been published at different stages of the studies or with different findings. These were also counted as many times as they appeared in the literature. In fact,

there were 51 studies with 67 citations (35 lung cancer studies and 16 including samples of lung cancer patients).

However, out of 67 citations, 16 citations (in fact, 14 actual studies) were validation studies and one was a feasibility study (Tables 3.2 and 3.3). The rest were studies with different objectives including investigations of quality of life in lung cancer clinical trials, descriptive studies measuring clinical outcomes, and supportive care.

1.1. Instruments

Over 50 instruments were used to measure quality of life or some dimensions of life quality in patients with lung cancer. Some of these instruments were used rarely, some were used only for validation purposes, and some were not true quality of life measures. The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ C-36 or C-30), the Rotterdam Symptom Checklist (RSCL), the Hospital Anxiety and Depression Scale (HADS), the Functional Living Index-Cancer (FLI-C), and the Daily Diary Card (DDC) were among the most popular instruments used and their applications in studies of quality of life is well documented.

The Daily Diary Card (DDC) is one of the widely used instruments in the UK context. The instrument was developed by the Medical Research Council (MRC) Lung Cancer Working Party and has been used in many randomised trials. Although its sensitivity is well documented, it has been criticised because compliance with DDC is low, and it has a limited focus on treatment related side-effects.

There were three site-specific (lung cancer) measures: the Lung Cancer Symptom Scale (LCSS), the Functional Assessment of Cancer Therapy-Lung (FACT-L), and the EORTC QLQ LC-13.

The LCSS focuses on the physical and functional dimensions of quality of life measuring major lung cancer symptoms and their effect on activity status. It consists of two instruments; one for patients and one for health professionals as observers. The patient scale consist of nine items: six measuring major symptoms for lung cancer (loss of appetite, fatigue, cough, dyspnoea, haemoptysis, and pain) and three summation items related to total symptomatic distress, activity status, and overall quality of life all using visual analogue scale. The observer scale is a 5-point ordinal level scale similar in content to the patient scale measuring the intensity of six major lung cancer symptoms.

The LCSS is a very limited measure of quality of life because it does not contain many of the important components of the quality of life and in addition, in its introductory statement contains the word "lung cancer" which might be seen as a limiting factor.

The FACT-L (version 3) is a 44-item self-reported instrument and consists of two parts. Part one is a 34-item measure of general health related quality of life (FACT-G) covering five dimensions; physical, social and family, emotional, and functional well-being and relationship with doctor. Part two (Lung Cancer Subscale, LCS) is a 10-item measure of quality of life with emphasis on lung cancer symptoms.

The problem with the FACT- L is that it mostly covers lung cancer related and not the treatment-related symptoms. The most important feature of the

FACT-L is due to the fact that it measures the relative weight of importance attached to the components of quality of life.

However, both the LCSS and the FACT-L have been validated and show a high level of reliability and validity including good internal consistency, content validity, and responsiveness (Hollen et al., 1993a; Cella et al., 1995).

A full description about the EORTC QLQ-C-36, QLQ-C30, and QLQ-LC13 can be found in chapter five section 3.2 and 3.3. Table 3.4 summarises the instruments cited in quality of life studies in lung cancer patients.

However, these are the most useful instruments and can provide information additional to the clinical data. With such a relatively good number of measures it appears that there is no excuse for not measuring quality of life in lung cancer patients. Such information has an important role in clinical decision making and ensuring effective care for lung cancer patients.

1.2. General findings

1.2.1. *Performance status*

The frequent use of performance status as a proxy of quality of life is not uncommon. In lung cancer patients it is an important prognostic factor and predictor of survival (Buccheri and Ferrigno, 1994a). The history of quality of life studies in lung cancer patients goes back to 1970 when the first paper was published by Carlens et al. (1970) using the "vitagram index". It consisted of two dimensions: x-axis (survival) and y-axis (every month of survival as judged on a scale of performance status ranging from -20 to 20). They found that patients undergoing radical operations had a substantially better survival and performance status. Subsequent studies confirmed that performance status is a good predictor of quality of life or there is a significant correlation

between performance status and psychological, physical and symptomatic distress (Nou and Aberg, 1980; Eguchi et al., 1992; Aaronson et al., 1993; Buccheri et al., 1995). Although the use of performance status has been controversial, correlation between performance status and global quality of life is well established (Osoba et al., 1994a; 1994b). It has also been shown that the number and severity of symptoms increases with worsening performance status (Hopwood and Stephens, 1995). In addition it has been suggested that psychiatric disorder in lung cancer patients is significantly associated with poorer performance status (Cody et al., 1993). Schag et al. (1994) studied 57 lung cancer disease free survivors and reported that the Karnofsky Performance Scale (KPS) was the best predictor of quality of life. In contrast, studying 139 lung cancer patients receiving palliative treatment, quality of life was found to be a much broader concept than the KPS and there was a weak association between the KPS and the quality of life as measured by the European Organisation of Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C30) (Schaafsma and Osoba, 1994). Contradictory to these findings, Osoba et al (1994b) found that performance status as measured by the ECOG (European Cooperative Oncology Group) performance status strongly correlated with several domains of quality of life as measured by the EORTC QLQ-C30.

However, although performance status is not a true measure for quality of life and there is inconsistency in findings, it should be seen as an important predictor of survival and quality of life. This implies that physicians, especially oncologists, should record the performance status of the lung cancer patients in the case notes. They can use either the KPS or the ECOG performance status. Although the ECOG is superior to the KPS, both are valid, easy to score and take a few seconds to rate (Buccheri and Ferrigno, 1994b). As Osoba (1994) pointed out multidimensional instruments provide

much more information about quality of life than do unidimensional instruments. Therefore, a distinction should be made between the comprehensive measurement of quality of life and the measures that only have one or two components.

1.2.2. *Quality of life as a prognostic factor*

One of the most interesting findings in quality of life studies of lung cancer patients is that initial quality of life was found to be the strongest prognostic factor for survival. This was confirmed by studies carried out by Ruckdeschel and Piantodosi (1989; 1991; 1994) and Ganz et al. (1991). Using the Functional Living Index-Cancer (FLI-C), it was found that FLI-C score was an independent predictor of survival even after correcting for initial performance status, weight loss, stage of disease, number of metastatic sites, and type of treatment.

These findings have shown that non-medical factors such as quality of life assessment play an important role in predicting survival and they should be evaluated. For example, Buccheri et al. (1995) in a study of 128 lung cancer patients using the Therapy Impact Questionnaire (TIQ) found that in addition to the stage of disease some aspect of quality of life such as difficulty at work and doing household jobs are prognostic factors of improved survival.

1.2.3. *Psychosocial issues*

It has been shown that a diagnosis of lung cancer by itself is a cause of depression. An early study of 134 lung cancer patients and controls (consisting of chest disease, patients with hernia and healthy population), it was found that depression was higher in lung cancer patients than controls even before the diagnosis was confirmed. A past history of psychiatric illness and the presence of metastatic disease were the most significant correlates of

depression (Hughes, 1985a). The follow-up study of a sub-group of the same lung cancer patients (50 patients) showed that depression was associated with severe physical disability and the anticipation of a fatal outcome (Hughes, 1985b). Therefore, regardless of tumour type, there is a significant correlation between psychological disorder and physical symptoms (Goldberg et al., 1984) which leads to a lower quality of life in lung cancer patients. Similarly in a study of 136 lung cancer patients it has been suggested that a diagnosis of lung cancer is associated with considerable psychiatric morbidity. Furthermore, initial psychiatric illness was a predictor of psychiatric disorder at follow-up and significantly associated with physical symptoms, pain, past psychiatric history, and female gender (Cody et al., 1993).

These, however, confirm that there is a need for more comprehensive interventions including psychosocial support. For example, in a study of 87 lung cancer patients, it was found that there were significant associations between overall quality of life and four factors including health, socio-economic, psychospiritual and family criteria. The personal and contextual factors together accounted for 30% of the variance in quality of life of the patients under the study (Hinds, 1990). A study of 50 lung cancer patients indicated that they described their leisure as the domain where they are the most dissatisfied (Dazord, 1995).

These clearly suggest that standard clinical quality of life measures are very limited in nature. It is necessary to consider a broader concept of quality of life and to include areas of life which are important to patients, such as family or social life.

1.2.4. *Symptom distress*

There in no doubt that lung cancer and its treatment affects patients' physical ability and consequently causes several physical and, as discussed earlier, psychosocial problems. Hopwood and Stephens (1995) argued that it is important to have a better understanding of the symptoms lung cancer patients suffer from to provide an effective treatment. In this respect, they studied 650 lung cancer patients using the Rotterdam Symptom Checklist (RSCL) and found that the most frequently reported symptoms at presentation included tiredness, lack of appetite, worry, anxiety, cough, and shortness of breath. Early studies of quality of life in cancer patients receiving chemotherapy have shown that lung cancer patients experienced more problems with vomiting, sleeping, loss of weight, and anxiety over treatment than other cancer patients (Coates et al., 1983a). It has been reported that the most troublesome symptoms in patients receiving chemotherapy were anorexia, alopecia, pain, and constipation (Ahmedzai et al., 1984). Similarly it was found that after radiotherapy distress as measured by the Symptom Distress Scale (SDS), was the most important predictor of survival after adjusting for age, functional status, and patient's personality (Kukull et al., 1986). The same finding was reported in a study of 434 cancer patients including 82 lung cancer patients where higher distress was found in lung cancer patients and this was a significant predictor of survival (Degner and Sloan, 1995). Interviewing 30 lung cancer patients, Benedict (1989) reported that 15 patients suffered from the disease process by itself producing disability, pain, anxiety, changed daily activities, weakness and fatigue which were the causes of greatest suffering. In a study of 61 lung cancer patients receiving palliative radiotherapy it was reported that males and females experienced treatment related symptoms equally including chest pain, rigor, fever, sweat, and difficulties in normal activity (Omand and Meredith, 1994). On the other hand, it has been shown that there is significant link between symptoms and loss of physical

functioning (Ballatori et al., 1993). It was found that there was a significant association between symptom distress and disruption in quality of life in females (Sarna, 1993a; 1993b; 1994). In a validation study of a quality of life instrument it was demonstrated that there was a high correlation between quality of life and nausea and vomiting, but low correlation concerning hair loss and lack of appetite (Kaasa et al., 1988a).

Thus, assessment of a wider range of symptoms both before and after treatment may help clinicians to increase their knowledge of patients' feelings and concerns and justify any further decisions, especially when the intention is palliation and there is no survival benefit.

1. 3. Communication

Communication problems between patients and their physicians and their contribution to the quality of life in lung cancer patients have been investigated by several researchers. Early studies on the subject showed that psychological adjustment in lung cancer patients might be improved if patients were given opportunities to ask questions about their disease and participate in decisions about treatment (Hughes, 1985b). Berglund and Sjoden (1987) noticed that communication problems with medical staff were strongly associated with anxiety and with anticipatory nausea and vomiting. Studying 94 lung cancer patients, 74% wanted to be told about their diagnosis. On the other hand, in those who did not want to know about the disease, their quality of life was found to have deteriorated as measured by psychological, social and financial factors (Sakai et al., 1994a).

However, these indicate firstly the importance of the communication issues, and secondly that studying quality of life requires a straightforward communication with patients themselves. Relying on other sources of

information such as relatives or physicians, may not reflect the exact nature of the patients' feelings and concerns. Interviewing 40 lung cancer patients and their relatives showed that relatives rated symptoms higher and mood lower than patients (Ahmedzai et al., 1988a). Significant differences were found between 71 lung cancer patients, their relatives and physicians. Physicians were more optimistic, relatives were more pessimistic. Physicians were most reliable at rating treatment tolerance by patients (Buccheri et al., 1992; 1993). Two British randomised clinical trials, revealed high levels of agreement between clinicians and patients in reporting symptoms, but increasing disagreement with increasing severity of symptoms. They also found that physicians underestimated the level of severity of the patient's symptoms (Stephens, 1994).

2. Quality of life in patients with small and non-small lung cancer

In the following sections the literature on quality of life in patients with firstly small and secondly non-small cell lung cancer is considered. This is the first systematic review on the subject, since previously there have only been two commentaries on the subject (Feld, 1987; Fayers, 1992). The method of investigation has already been described in the introduction to this chapter.

Excluding non-English and review papers, 83 citations were identified. Of these, 41 were on quality of life in patients with small cell lung cancer (Table 3.5), and 42 studies of non-small cell lung cancer (Table 3.6). Out of 83 citations, 30 were abstracts (Tables 3.5, and 3.6), three validation studies (Aaronson et al., 1987; Hurny et al., 1988; Hollen et al., 1994a), and two feasibility investigations (Hurny et al., 1992; Monars et al., 1985). Most studies were clinical trials with survival time and quality of life as end points.

2.1. Small cell lung cancer

Combination chemotherapy with or without radiotherapy is the treatment of choice in small cell lung cancer. Thus, most studies, both randomised trials and descriptive ones evaluated chemotherapy and its effects on quality of life. In reviewing quality of life studies in patients with small cell lung cancer the following results could be identified.

2.1.1. *Tumour response*

Not surprisingly early studies of quality of life showed that patients with good performance status and who responded to chemotherapy had a better quality of life (Lau, 1988; Flechtner et al., 1988). In a study of 321 patients with small cell lung cancer (of those 195 patients were entered into the quality of life study) quality of life was found to be dependent on tumour stage and tumour response (Wolf et al., 1991). Using the Sickness Impact Profile (SIP) in measuring quality of life in 62 patients, Bergman et al. (1991) found that tumour response correlated with SIP summary scores and anxiety. The same authors with the same patients using the European Organisation of Research and Treatment of Cancer quality of life questionnaire (EORTC QLQ-C36) reported that there were good correlation between changes of the QLQ-C36 scores over a given time period and clinical variables as measured by tumour response and performance status (Bergman et al., 1992).

These findings, however indicate that early detection of lung cancer is an important issue. Detection of disease at an early stage would allow better management and thus increase the chance of cure. Benefit achievable by screening is limited (Flehinger and Melamed, 1994). Early detection mainly depends on referrals by General Practitioners (GPs). Figures from the Yorkshire Cancer Registry (England) 1988-91 showed that the median delay

was 12 days (range 6-20) between referral and first hospital visit and 22 days (range 11-40) between this hospital visit and the start of treatment (Muers, 1994).

2.1.2. *Intensive versus less intensive therapy*

The challenge to improve survival and quality of life led some investigators to study different ways of managing small cell lung cancer. Most studies have shown that conventional (scheduled, planned) policies, although intensive, are providing a better quality of life (less nausea and pain, better sleep, mood and general well-being) than less intensive (experimental, as required, unplanned) regimens (Geddes et al., 1988; Spiro et al., 1988; Earl et al., 1991). Comparing standard chemotherapy with a palliative regimen, Wolf et al. (1994) studied 221 patients and found no significant difference in survival between these two regimens. However, patients receiving the standard regimen had a better tumour response and improvement of quality of life than patients receiving palliative treatment, but the former group had more severe side effects. In a similar study (standard versus palliative chemotherapy) a significantly better survival was observed in patients receiving standard treatment, despite its greater toxicity. Assessment of quality of life using the EORTC 42-item QLQ, demonstrated no significant difference in most areas measured. Less mucositis and alopecia were reported by the patients receiving palliative treatment while patients in the standard group had better values for sleep disturbance, fatigue, and psychological distress (Joss et al., 1995a). It is argued that regular chemotherapy, although producing unpleasant side effects, also could be palliative and may control the effects of the progression of cancer (Fayers, 1992). Several studies have shown that different management policies resulted in no major survival benefit. Studying early versus late alternating chemotherapy in a group of 127 patients showed that there was no significant survival difference between treatment groups, but patients

receiving early alternating chemotherapy had a better quality of life as measured by the EORTC QLQ questionnaire (Joss et al., 1995b).

On the other hand some studies suggested that the less intensive the treatment, the better the quality of life. The result of a recent randomised trial comparing conventional versus intensive chemotherapy showed a better quality of life in favour of conventional chemotherapy (Gower et al., 1994; 1995). In a randomised trial of 12 (maintenance) versus 6 (no maintenance) courses of chemotherapy with addition of radiotherapy in both regimens it was shown that there were no significant differences in survival. Both assessments of the quality of life as measured by patients using the Daily Diary Card (DDC) and as measured by physicians indicated a better quality of life in favour of 6 courses of treatment (Bleehen et al., 1989a). However it was reported that no maintenance chemotherapy patients experienced a gradually deteriorating quality of life as compared to the more severe effects in the maintenance group (Hopwood, 1991a). Using the same method of measurement Geddes et al. (Geddes et al., 1990) in a study of 8 versus 4 courses of chemotherapy reported that there was no significant survival difference between these two regimens. The study results indicated that each successive cycle of chemotherapy had a negative impact on the patients' quality of life, especially in patients receiving 8 courses of chemotherapy. In a series of randomised trials comparing alternating versus response-dependent chemotherapy, carbo- versus cis-platinum, and treatment for extensive versus limited disease, it was noticed that intensive treatment of more than 4 cycles resulted in an overall marked negative effect on patients' quality of life (Flechtner et al., 1993).

Although these findings are not consistent, the results suggest that when there is no clinical benefit, for example in survival time or tumour response, perceptions and attitudes of patients toward different treatment policies could

provide additional information. Therefore, measuring quality of life becomes essential and it seems that it is the most reasonable way of judging the clinical outcomes. As Hopwood and Cull (1994) remind us there is no guarantee that adding quality of life measures makes the choice of treatment policy easier, but it does serve to clarify the potential trade-offs that need to be discussed with patients. There is evidence that physical functioning, treatment side-effects, disease-related symptoms, psychological distress, fatigue and malaise are the most relevant aspect of quality of life in patients receiving chemotherapy (Bernhard et al., 1988). Furthermore, fatigue and malaise were found to be global indicators of quality of life (Hurny et al., 1993). Using such findings may provide a better understanding of clinical achievements. It is argued that it is important to ascertain what patients feel about the trade-offs between improved quality of life and toxicity where there is a significant potential for long-term side effects that may result in less than an optimum quality of life (Osoba, 1994).

2.1.3. *Radiotherapy*

Little is know about the effect of radiotherapy on patients' quality of life. The International Association for the Study of Lung Cancer (IASLC) workshop on quality of life reported that local radiation in addition to chemotherapy in small cell lung cancer showed a significant advantage in median and long term survival. Randomised trials of prophylactic cranial irradiation (PCI) have failed to demonstrate survival advantage (Abratt, 1994). Recent meta analysis of thoracic radiotherapy for small cell lung cancer has also confirmed the view that radiotherapy can have survival benefits (Pignon et al., 1992).

Studying 53 patients receiving therapeutic or elective brain irradiation, it was found that patients receiving elective irradiation had both better survival and quality of life as measured by Karnofsky Performance Status (Rosenman and

Noah, 1982). The role of chemotherapy in addition to radiotherapy has been studied and it was shown that patients receiving immediate chemotherapy plus radiotherapy had better survival as compared to groups of patients who received palliative treatment. In terms of quality of life physicians reported a better "condition" in favour of immediate chemotherapy plus radiotherapy, but patients reported a better quality of life in favour of palliative treatment. Both groups reported the same "overall condition" and anxiety (Bleehen et al., 1989b). Recently Cull et al. (1994) have reported the results of a retrospective study on 52 patients who had received PCI. They observed that anxiety and depression in these patients were lower than patients recently receiving active treatment. However, it was found that a high proportion of patients still experienced treatment-related symptoms, but not functional impairment.

These studies highlight the palliative effect of the radiotherapy in the management of small cell lung cancer. Radiotherapy is a common treatment, but there are few studies that investigate the quality of life in patients receiving radiation treatment. The need to conduct such studies is essential.

2.2. Non-small cell lung cancer

There are various policies in the management of non-small cell lung cancer and aspects of the treatment related to quality of life outcome are discussed.

2.2.1. *Chemotherapy*

As Thatcher et al. (1995) pointed out non-small cell lung cancer can no longer be regarded as resistant to chemotherapy. Early studies of quality of life in patients receiving chemotherapy suggested that treatment-related toxicity and the deterioration of patient's well-being offset any potential survival advantage for the majority of the patients (Bakker et al., 1986). In a more systematic assessment of quality of life, change in quality of life scores as

measured by Functional Living Index-Cancer (FLI-C), correlated with performance status change and weight loss, but not with treatment regimen, side-effects of treatment or change of pain (Finkelstein et al., 1988). Consequent studies pointed out that after chemotherapy patients had marked relief of symptoms (Moreno et al., 1988; Fernandez et al., 1988). Recent studies, however have shown that improved or stable quality of life mainly depends on tumour response. For example, Pujo et al. (1994) in a study of 54 patients found a stable quality of life in responders as compared to those who had not responded to treatment. Another explanation is that baseline quality of life not only predicts the likelihood of response and survival, but also has greater impact than most known prognostic factors (treatment types, performance status, gender, and age). Gralla et al. (1995) in a multi-centre randomised trial of a combination chemotherapy regimen studied 673 patients using the Lung Cancer Symptom Scale (LCSS) and found that baseline quality of life was the best predictor of both response to the treatment and survival. Using the same instrument (LCSS), Hollen et al. (Hollen et al., 1994b) found that physical and functional dimensions were the most important predictors of quality of life in patients receiving chemotherapy.

2.2.2. *Chemotherapy and best supportive care*

Comparing chemotherapy versus supportive care alone Buccheri et al. (1989) studied 74 patients and found that there was no significant difference in depression and performance status between treatment arms. As expected, while a better treatment tolerance was reported in favour of supportive care, a better physical status has been found in favour of the chemotherapy group. In another study, by Ganz et al. (1986; 1989) due to poor compliance with quality of life assessment it was impossible to examine differences between treatment arms (supportive care versus supportive care plus chemotherapy). However, they found that there was a positive correlation between quality of

life scores as measured by the Functional Living Index-Cancer (FLI-C) and performance status as measured by the KPS. In a retrospective study in which patients had received chemotherapy or supportive care, it was found that chemotherapy produced a temporary benefit in quality of life as measured by improvement in performance status (Weeks et al., 1989).

In terms of quality of life there is no single answer to the question, as to whether the best supportive care or chemotherapy could produce a better quality of life, but there is evidence that chemotherapy is less expensive than supportive care. This is due to the fact that chemotherapy produces tumour control, requires shorter hospital stay, and thus is less expensive (Jaakkimainen et al., 1990).

2.2.3. *Radiotherapy*

The value of radiotherapy in controlling specific cancer related symptoms is undisputed and can be achieved with unsophisticated and undemanding schedules (Gregor, 1995). Yet, more research is needed in order to answer the critical issues of role of radiotherapy in the treatment of non-small cell lung cancer (Damstrup and Poulsen, 1994). As far as quality of life studies are concerned there are several studies to help answer some of these issues. Kaasa et al. (1988b; 1988c) randomised 95 patients to receive either radiotherapy or chemotherapy. They found significant differences in psychosocial well-being and global quality of life in favour of radiotherapy. There were no significant group differences in physical functioning and daily activities. A British study has shown that conventional and experimental radiotherapy policies are the same both in survival time and quality of life. The study suggested that dysphagia and reduction in physical activities were the most important side-effects of the radiotherapy (Bleehen et al., 1991). Considering these side effects which affects the patients' quality of life, consequent studies indicated

that there were no survival benefits with multi or even 2 fractions as compared with single fraction radiotherapy. The quality of life assessment as measured by the Daily Diary Card (DDC), the Hospital Anxiety and Depression Scale (HADS) and the Rotterdam Symptom Checklist (RSCL) showed that disease-related symptoms improved, anxiety improved, depression was unchanged and there was less dysphagia in favour of single fraction (Hopwood 1991b; Bleehen et al., 1992). In their recent study comparing short versus aggressive radiotherapy, they found that survival improved slightly in favour of the aggressive regimen, but in other respects (palliation of main symptoms, adverse effects, response, appearance of metastases) the two regimens were very similar (Hopwood and Stephens 1994c).

2.2.4. *Adjuvant chemotherapy with radiotherapy*

A recent meta analysis of randomised trials of combined chemotherapy and radiotherapy in non-small cell lung cancer concluded that cisplatin-based chemotherapy and radiotherapy are superior to the other regimens, but these results must be considered in the light of the balance between quality of life, toxicity, and costs of chemotherapy (Marino et al., 1955). There are a few studies that examine the quality of life. Early studies used the KPS as the proxy of quality of life and had shown different results. Arcangeli et al. (1985) reported that chemotherapy plus radiotherapy improved patients' performance status markedly, while Minet et al. (1987) in a randomised trial comparing radiotherapy alone versus radiotherapy along with chemotherapy found that there was no significant difference between treatment arms in both survival and quality of life. In a study where patients were randomised to receive either radiotherapy alone, radiotherapy plus chemotherapy or palliative treatment, the results suggested that the patients who received radiotherapy or radiotherapy plus chemotherapy had fewer physical and psychological

problems as compared with those who received palliative treatment (Ahmedzai et al., 1988b).

2.2.5. *Surgery*

Surgery is the treatment of choice for stage I and II non-small cell lung cancer. The only study that has been reported so far is the one that carried out by Dales et al. (1993; 1994). They studied 117 patients, 92 patients with and 25 patients without a confirmed post-operative diagnosis of lung cancer. They found that pre-operatively, the prevalence of dyspnoea was 4 times higher in the cancer group, but other global quality of life indicators were similar. Dyspnoea worsened in both groups at 1 and 3 months post-operatively. Quality of life deteriorated post-operatively in those with cancer and returned to pre-operative levels at 6-9 months, but showed no deterioration post-operatively in those without cancer even at 1 and 3 months. They concluded that surgery resulted in deterioration in the quality of life during the first 3 months post-operatively in those with final diagnosis of cancer, but improvement back to baseline can be expected thereafter.

3. Discussion and conclusions

Survival in lung cancer patients is poor and has improved little over time. Despite the increasing research, there remains among many physicians a high degree of pessimism about the gains made in clinical care (Aisner and Belani, 1993), especially when one considers the side-effects of treatments and the costs involved. On the other hand there are those who believe that using both traditional outcomes (survival, and tumour response) and patient-based quality of life assessment may offer a more comprehensive approach to evaluating the relative risks and benefits associated with treatment (Bergman and Aaronson, 1995). It is argued that if there is no gain in survival time from clinical investigations, there are several other ways to improve health care delivery for

lung cancer patients and add quality to their life. Strategies for supportive care or inclusion of quality of life measures as an endpoint in clinical practice are a few examples of such proposals.

The review highlights both the progress and the shortcomings of the research activities on the subject. Despite 25 years of investigations and existence of nearly 150 papers and reviews, discrepancies are obvious. Many studies are built on common sense conclusions. For example, in a study of 455 patients it was found that performance status and extent of disease had a significant association with reported distress as measured by Profile of Mood States (POMS). The study concluded that the extent of disease can be seen as a risk factor for distress (Cella et al., 1987). When there is no insight into the patients' daily experiences nor to their living conditions, little is gained from studying such limited aspects of quality of life. In addition, as shown in Tables 3.2, 3.3, 3.5, and 3.6 many researchers included a restricted sample of patients in their studies. In these studies, mostly, there is generally no explanation of why the other patients were not included. It is not possible to be sure that these investigations are unbiased. Again, as these tables show, studies have used ad hoc instruments to measure quality of life and the findings in such assessments should be interpreted with caution. However, the achievements of researchers in this field should not be underestimated, especially the efforts of the clinicians and the oncologists who enthusiastically conducted the research.

Although clinical findings in these studies are important and have been discussed, the emphasis of this review was on general aspects of the findings concerning the quality of life. These findings constitute a crucial role in the treatment of lung cancer patients and reflect a wide spectrum of issues which should be integrated into clinical practice.

Several topics in this chapter have been highlighted. First, that quality of life assessment can be a prognostic factor and predictor of survival. Secondly, the need for psychosocial interventions in treatment of lung cancer patients has been emphasised. Since most lung cancer patients live for a short time, the need for palliation of symptoms is the first priority. Data from clinical studies of lung cancer clearly indicate that, for example, out of 100 lung cancer patients, 86 suffer from pain, 70 have dyspnoea, and 68 have anorexia (Krech et al., 1992). These findings suggest that to improve the quality of life in lung cancer patients, resources should be directed to palliative care and this has implications for lung cancer care purchasers.

As discussed earlier several recent meta-analyses have shown promising clinical achievements in the management of small and non-small cell lung cancer (e.g. Damstrup and Poulsen, 1994; Marino et al., 1995; Stewart and Pignon, 1955). These findings suggest that for patients with advanced and metastatic small and non-small cell lung cancer survival alone should not be considered as the only outcome, rather the best way forward is through further clinical trials looking at new drug schedules and using as end points cost effectiveness and validated quality of life measures (Smith, 1994).

The problem is that in these meta-analyses it is not possible to study quality of life. Thus, individual clinical trials need to address quality of life in an agreed manner and find out whether the progress in survival could lead to better quality of life or not? In addition to the clinical trials it is worthwhile to conduct population-based outcome studies to have a better understanding of patients' pre- and post-treatment quality of life. In such evaluations patients' socio-economic characteristics may play an important role. Variation in quality of life among patients with small and non-small cell lung cancer may be explained by other factors such as patients' socio-economic background

rather than just disease- or treatment-related side effects. Since little is known about the role of these factors, further investigation in this area is recommended.

The psychological symptoms after diagnosis of lung cancer should not be underestimated. Patients may not want to show their distress, but the reality is that these people are suffering from a lot of pain and physical and psychological symptoms including anxiety and depression. It is argued that many cancer patients will not disclose emotional distress unless specifically questioned in a systematic way or given an opportunity to describe their feelings. Thus, it is reasonable to recommend that in future all clinical investigations should include measures of psychological adjustment before and after treatment (Greer, 1984). Recent evidence has shown that the clinicians underestimate the distress in their patients (Ford et al., 1994). There is need to assess these symptoms carefully and necessary actions such as psychosocial interventions be taken. Such interventions should not be seen as an optional extra but as an integral part of every patient's management plan (Fallowfield, 1995).

In addition creation of a supportive environment may help patients overcome their problems. Relatives, clinicians, social work departments, and cancer support groups all have an important role to play in this matter. Of these the role of clinicians in recognising these symptoms and referring patients to appropriate care is very crucial. This can be achieved by simple measures of quality of life, for example the Hospital Anxiety and Depression Scale (HADS) which is a good screening tool to identify patients in need.

While there are still deficiencies in both quality of life measurement and research design, this review clearly shows that during the last 25 years there

have been promising developments in many areas of quality of life related research. For example, there now are several valid instruments to measure quality of life, quality of life is increasingly becoming integrated as part of clinical trials, and that quality of life by itself is becoming an issue of interest both for patients and clinicians. Patients themselves have expressed a wish for more emphasis on research into quality of life issues (Goodare and Smith, 1995). In contrast, the explosion of so many new instruments without critical appraisal, poor presentation of their data in published papers, complex statistical analyses, and lack of guidelines all can be seen as major causes of confusion. However, these recent developments should not prevent clinicians and oncologists from using the new instruments provided that they have evaluated them critically.

The most difficult problem in studies of quality of life come from the many methodological issues such as data collection, analysis and barriers to the interpretation of the results. Since these could be counter productive, there is an urgent need to provide simple and constructive guidelines to help researchers and clinicians in administering these measures.

The role of family, relatives, social life, economic, and leisure time received less attention in quality of life investigations. Focusing only on disease- or treatment-related symptoms makes quality of life studies very limited. There is an urgent need to investigate these issues more comprehensively, since lung cancer patients have indicated that family or leisure times are as important as their health.

Patients are the best source of information for any assessment of quality of life except in a terminal situation. Clinicians should take advantage of this, since most patients seem to want to please their doctors. A study of cancer patients

receiving radiotherapy showed that verbal communication especially from the physicians was the most popular choice for receiving information before treatment (Hinds et al., 1995). This, however means that communication between clinicians and patients needs to be improved (Montazeri et al., 1996c). Understanding lung cancer patients' feelings and concerns may help to improve the quality of care and the quality of life. There is evidence that patients do not necessarily share clinicians' priorities or place the same emphasis on different types of morbidity (Turner et al., 1996).

In conclusion, while research into quality of life has made substantial progress in a relatively short period of time, there is an urgent need to include a broader concept of quality of life in future studies despite the methodological difficulties. At present comprehensive lung cancer care requires a cyclical process that includes prevention, early detection, specific therapy, improvement in survival and supportive care strategies. In future the real challenge in the management of lung cancer lies in improving quality of life.

4. Summary Tables

Six summary tables are provided:

1. Review papers of quality of life studies in patients with lung cancer.
2. Quality of life studies in patients with lung cancer (in general).
3. Quality of life studies in patients with cancer including lung cancer.
4. Quality of life measures used in lung cancer studies.
5. Quality of life studies in patients with small cell lung cancer.
6. Quality of life studies in patients with non-small cell lung cancer.

To use tables the following notes should be considered.

(i) Those indicated with asterisk are abstracts.

(ii) The full name of measures are presented in Table 3.4.

(iii) In Tables 3.2, 3.5, and 3.6 numbers in the parentheses are actual samples that participated in quality of life assessments. In Table 3.3 numbers in the parentheses are the numbers of lung cancer patients in each study.

(iv) Abbreviations are listed below:

QL = quality of life, LC = lung cancer, SCLC = small cell lung cancer, NSCLC = non-small cell lung cancer, Pt(s) = patient(s), Phyns = physicians, PS = performance status, CT = chemotherapy, RT = radiotherapy, PT = palliative treatment, SC = supportive care.

Table 3.1 Summary of review papers of quality of life studies in patients with lung cancer

Study	Type	Scope	Conclusions
Bakker (1986)	Review	QL in LC pts.	Importance of measuring QL in LC pts and its contribution to the clinical decision making.
Yarnold (1986)	Commentary	Optimal QL for LC pts.	Need for development of simple measures of physical and psychological aspects related to the management of lung cancer patients.
Silberfarb (1986)	Commentary	Optimal QL for LC pts from psychiatry perspective	More research is needed regarding psychological factors in the setting of clinical treatment trials for LC pts.
Feld (1987)	Commentary	NSCLC and CT	Need for assessment of quality of life emphasised.
Hurny and Bernhard (1989)	Commentary	Problems in assessing QL in LC pts in clinical trials	Descriptive analysis is more appropriate than hypothesis testing. Need for carefully designed studies.
Feld (1989)	Commentary	QL assessment in LC pts	Need for improving survival and quality of life.
Kaasa (1989)	Review	Psychosoical assessment of pts with LC in controlled clinical trials	Need for evaluation of patients' subjective experience of their lives and situations in a broad area in psychosocial oncology in close co-operation with oncologist and lung cancer clinics.
Bernhard and Ganz (1991a; 1991b)	Review	Psychosocial issues in LC pts	Need for integrating the evaluation of psychosocial issues into the routine medical care of LC patient.
Hopwood and Thatcher (1991)	Review	Measurement of QL in LC pts	Need for QL assessment during and after treatment. QL measures should improve both the value of current LC treatments and influence future treatment protocols.
Geddes (1991)	Commentary	QL in LC	Measurement should concentrate on a few areas and be simple and frequent. For routine clinical practice outside clinical trials KPS is recommended.
Fergusson and Cull (1991)	Review	Measuring QL in pts undergoing treatment for LC	Sufficient progress has been made to suggest that assessment of QL should be included in the audit of clinical practice and evaluating treatment outcomes in clinical trials. Information could be used for decision making and resource allocation.
Bergman (1992)	Review	Review of QL studies in LC pts	Need for enhanced methodological issues, e.g. systematic use of standardised tools. EORTC QLQ-C30 constitutes a promising candidate for future studies.
Fayers (1992)	Review	Review of instruments used in studies of QL in SCLC patients	EORTC, RSCL, HADS, and DDC are recommended. Need for presentation of information of clinical relevance about differences between treatment groups.
Houston and Kendall (1992)	Commentary	Psychosocial implications of LC	The focus of care for families and patients living with lung cancer should be on care rather than cure.

Table 3.1 continued

Schmitt (1993)	Commentary	QL in LC and symptom management	Health care professionals can play a vital role in the identification and management of common symptoms and side-effects in treatment of LC and help to improve QL.
Hopwood et al. (1994a)	Analytic	Analysis of QL data	QL data should be analysed in a number of different ways, and conclusions reached only when consistency is seen.
Hopwood and Cull (1994)	Review	Review of instruments and studies of QL in LC	Lack of a working definition for QL and of instruments to measure it no longer valid excuses for failing to include QL end points in clinical trials. The challenge lies in its application to be integrated fully into clinical practice.
Abratt (1994)	Report	Report of workshop on improving QL and the SC of pts with LC	Methodological and psychological aspects, problems, QL in NSCLC and SCLC, and ethical issues were discussed.
Burke (1994)*	Presentation	QL and clinical trials	Methodological problems have been highlighted
Ganz (1994)*	Presentation	QL issues in LC treatment and research	Clinicians and researchers should familiarise themselves with tools and procedures for measuring QL assessment for evaluating the treatment, symptoms, or quality of care of LC pts.
Gralla (1994a)*	Presentation	Measuring QL in pts with LC	Several acceptable QL tools allow greater detail concerning specific aspects of QL.
Gralla (1994b)*	Symposium agenda	QL and LC	How to measure QL in LC clinical trials, and how to analyse data obtained in longitudinal assessment over the course of a trial.
Bergman and Aaronson (1995)	Review	QL and cost-effectiveness assessment in LC	Future efforts should be directed toward achieving higher levels of compliance with clinical trial-based QL studies, and the development of techniques for integration QL and clinical outcomes for purposes of cost-effectiveness evaluations.
Bernhard and Ganz (1995)	Review	Psychosocial issues in LC	Identifies a number of areas that need further investigation, and emphasises the importance for integrating psychosocial issues into the routine medical care of LC pts.

Table 3.2 Summary of quality of life studies in patients with lung cancer

Study	Design	Treatment	Sample	Quality of life measure	Results/Conclusions
Carlens et al. (1970)	Descriptive	Surgery, RT, RT + CT, No treatment	115	Vitagram index (assessing quality of survival in terms of performance status)	Small difference in survival and PS for all pts except substantial difference in favour of radically operated pts.
Nou (1979a)	Randomised	CT *vs* RT *vs* No treatment	48 extensive disease	Vitagram index	No significant difference in survival and quality of survival between treatment arms, but better survival in favour of RT.
Nuo (1979b)	Randomised	CT *vs* RT *vs* No treatment	54 limited disease	Vitagram index	No significant difference in survival and quality of survival between treatment arms, but better prognosis in favour of 'no treatment'.
Nou and Aberg (1980)	Descriptive	Surgery (three different procedures)	69	Vitagram index	Overall, low survival and poor PS in all surgically treated pts, but better PS in survivors. Better survival and PS in non-resectional treated pts.
Thatcher et al (1984)	Descriptive	CT	39	KPS, RS	PS and dyspnoea improved with the treatment.
Goldberg et al. (1984)	Descriptive	RT	21 pts, 18 relatives	KPS, POMS, PAIS	Depression decreased by time in both pts and relatives, but no significant change in PS and social interaction. Physical status related to depressive symptoms in pts, but not in relatives. Depression in relatives related to involvement in the social environment.
Ahmedzai et al. (1984)*	Descriptive	CT	162	Interview (symptoms, mood, disease awareness, treatment satisfaction)	Most troublesome symptoms were anorexia, alopecia, pain, and constipation. CT improved QL in SCLC in short term, but did not benefit NSCLC.
Hughes (1985a)	Descriptive	No treatment	134 cases,3 control groups (71,42,51)	KPS, ad hoc psychiatric assessment	Association was found between depression and LC diagnosis.
Hughes (1985b)	Descriptive	CT or RT or No treatment	50	KPS, ad hoc psychiatric assessment	Pts receiving no treatment more depressed. Depression was associated with severe physical disability. Psychological adjustment in cancer pts might be improved if pts were given opportunities to ask questions about their conditions and participate in decisions about treatment.

Table 3.2 continued

Kukull et al. (1986)	Descriptive	RT	65 (53)	SDS, ICC, ESDS, POMS, AIS, PFQ, EPQ	Post-diagnosis symptom distress was found to be the most important predictor of survival after adjusting for age, functional status, and personality.
Ahmedzai et al. (1988)*	Descriptive (retrospective)	CT	40 pts, 40 relatives	Interview (including questions on awareness of disease, problems in the last month of life), LGSAD	Relatives scored symptoms higher and mood lower and reported more frequently awareness of imminent death than the pts. Commonest problem in the last month reported were pain, loss of independence and weakness.
Kassa et al. (1988a)	Descriptive	CT or RT or CT + RT	31	29 items on psychological well-being, treatment and disease related symptoms, daily activities and PS	Validity study. A high degree of validity for the majority of the items. High correlation between QL and nausea and vomiting, but low concerning hair loss and lack of appetite.
Bachiocco et al. (1988)*	Descriptive	Surgery	94	MMPI, STAI, EPQ	Post-surgical pain significantly correlated with pts' personality. Those who are emotional and tough-minded suffer more.
Higgs et al. (1989)*	Descriptive	CT	40	FLI-C	QL deteriorated with increasing time.
Benedict (1989)	Descriptive	CT, RT, Surgery	30	Ad hoc structured interview	50% suffering very much due to disease. Disability, pain, anxiety, changed daily activities, weakness and fatigue the sources of greatest suffering.
McCorkle et al. (1989)	Randomised	Oncology home care *vs* Standard home care *vs* Regular home care	166 (78)	SDS, MPQ, ICC, POMS, ESDS, GHRI	No difference in pain, mood disturbance and concerns among the three groups. The two home nursing care group had less distress, and greater independence, but worse health perception.
Hinds (1990)	Descriptive	Various	87	Ad hoc (information preference, family functioning, self-control and overall QL)	High correlation between the overall QL and items related to health, socio-economic, psychospiritual and family criteria.
Aaronson et al. (1991)	Descriptive	CT or RT	537	EORTC QLQ-C36, ECOG	Validation study. Satisfactory to excellent psychometric properties. Able to distinguish between subgroups of pts with different clinical health status. Based on findings, slight modification has been made.

Table 3.2 continued

Ruckdeschel and Piantadosi (1989*; 1991; 1994)	Randomised	Pre-operative therapy + surgery or Surgery + post-operative therapy	437	FLI-C, KPS	Baseline QL was the strongest prognostic factor for survival. FLI-C sensitive to clinical status and predictor of survival even after correcting for initial PS, stage and treatment.
Ganz et al. (1991)	Descriptive	Palliative RT + SC, CT +SC	40	FLI-C	Initial QL was found as an independent predictor of survival.
Eguchi et al. (1992)	Descriptive	CT	64 cases, 50 controls	FLI-C (modified version), Designed questionnaire (derived from EORTC), YGQ	Significant correlation between PS and psychological, physical and symptomatic scores, but not for social aspects.
Buccheri et al. (1992*; 1993)	Descriptive	None, Surgery, RT, CT	71 pts. and their relatives and phyns.	Ad hoc (most Italian translation of EORTC) + 3 items for three groups: tolerance, physical feeling, depression, KPS, ECOG	Significant difference among pts, phyns, and relatives. Phyns were more optimistic, relatives were more pessimistic. Phyns were most reliable raters of treatment tolerance.
Aaronson et al. (1993)	Descriptive	CT or RT	354 (305)	EORTC QLQ-C30, ECOG	Validation study. Strong correlation between physical and role functioning and fatigue. Pts with a better PS and less weight loss, showed significant higher level of physical, role and cognitive functioning, overall QL, and lower symptoms. No significant change over time.
Hollen et al. (1993a)	Descriptive	CT or RT or Surgery or No treatment	121 cases, 52 observ	LCSS	Validation study. LCSS demonstrated good reliability and content validity.
Cody et al. (1993)	Descriptive	Various	136	RSCL, HADS, MACS, CLC	Baseline psychiatric illness predictor of psychiatric disorder at follow-up and significantly associated with physical symptoms, poorer PS, pain, psychiatric history and female gender. Tumour type did not predict psychiatric morbidity. LC is associated with considerable psychiatric disorder.
Sarna (1993a; 1993b; 1994)	Descriptive	Various	69 females	CARES-SF, SDS, KPS, PFS	Significant relationship between symptom distress and disruption in QL. Greater disruption in QL in women with recurrent disease, younger, and low income.

Table 3.2 continued

Bergman (1994)*, Bergman et al. (1994)	Descriptive	CT or RT	a. 537 (430) b. 346 (305)	ECOG a. EORTC QLQ C-36, and QLQ-LC13 b. EORTC QLQ-C30, QLQ-LC13	EORTC QLQ-LC13 was found to be valid and useful tool for measuring disease and treatment specific symptoms in LC pts receiving CT or RT, when combined with EORTC core QL questionnaire.
Schaafsma and Osoba (1994)	Descriptive	PT	162 (139)	EORTC QLQ-C30, KPS	Cross validation study. The QL found to be much broader concept than the KPS. The weak association between KPS and EORTC QLQ-C30. Difficulty in breathing has strongest negative impact on QL, and the fatigue the least.
Macbeth et al. (1994)*	Randomised	Megestrol Acetate (MA) *vs* Prednisol (P)	72	RSCL	Significant better QL in pts receiving MA, but poorer survival.
Omand and Meredith (1994)	Descriptive	Palliative RT	61	Ad hoc (pain, rigor, fever, sweat, normal activity)	No significant difference between males and females in experience of treatment related symptoms. 38% had chest pain, 8% rigor, 11% fever, 18% sweat, and 25% difficulties in normal activity.
Nakada et al. (1994)*	Descriptive	CT	50	Personality test, STAI, QL checklist (24 questions on somatic, social and psychological factors)	QL of LC pts should be evaluated after due consideration of their personality.
Sakai et al. (1994a)*	Descriptive	Various	94	EORTC QLQ-C30 (Japanese version), Ad hoc (questionnaire about telling diagnosis)	Most pts. wanted to be told about the diagnosis (74%). When the truth about diagnosis was told to the pts. who did not want the truth , their QL found to be get worse in psychological, social and financial factors.
Buccheri and Ferrigno (1994)*	Descriptive	Various	471	KPS, ECOG	Validation study. KPS and ECOG are both valid, but the ECOG is superior.
Cella et al. (1994)*	Descriptive	Various	58	FACT-L, ECOG	Validation study. Good internal consistency and sensitive to change in PS.
Cella et al. (1995)	Descriptive	Various	116	FACT-L, FLI-C, B-POMS, M-CSDS, ECOG	Validation study. FACT-L was found to be reliable, valid and sensitive to change.

Table 3.2 continued

Stephens (1994)*, Hopwood and Stephens 1994a*; 1995)	Descriptive (main studies randomised)	a. Two CT policies b. Two RT policies	a. 310 SCLC (232), b. 509 NSCL (423)	Phyns.: physical symptoms Pts.: RSCL + (3 LC specific questions), WHO-PS	High levels of agreement between phyns. and pts., but increasing disagreement with increasing severity of symptoms, and also phyns. underestimating the level of severity of the patients' symptoms. Overall pattern of symptom prevalence very similar for two disease. NSCLC patients reported higher levels of chest pain, coughing up blood. SCLC pts reported on average 17.4 symptoms, but NSCLC pts reported 14.3. In both disease number and severity of symptoms increases with worsening PS.
Maiwand et al. (1995)*	Descriptive	Cryotherapy	312 (100)	RSCL	Improvement in overall QL and in symptoms of fatigue, depression and physical activity.
Buccheri et al (1995)	Descriptive	Various	128	TIQ, ECOG	QL variables correlated well with each other, but poorly with clinical and demographic variables. Good correlation between working capacity and PS. Stage of disease, difficulty at work and doing housework prognostic indicators of survival.
Abratt and Viljoen (1995	Descriptive	Various	40	Ad hoc (2 subscales on outlook and social support), QL-I, HADS, RSCL	Outlook correlated with psychological status and QL but support correlate only with psychological status. 30% had psychological morbidity. Poor QL in 25%

Table 3.3. Summary of quality of life studies in patients with cancer including lung cancer

Study	Design	Treatment	Sample	Quality of life measure	Results/Conclusions
Coates et al. (1983a)	Descriptive	CT	99 (16)	Ad hoc (physical and non-physical side-effects of CT)	LC pts reported more problems with vomiting, sleeping, loss of weight, thought of treatment.
Coates et al. (1983b)	Descriptive	CT + RT	81 (42)	LASA (5 items on general well-being, mood, pain, nausea, and vomiting), ECOG	Validation study. Change in general well-being correlated with PS. High correlation between LASA scores for general well-being, mood and appetite. General well-being better during CT than RT.
Berglund and Sjoden (1987)	Descriptive	CT	40 (20)	CIPS, KPS	Communication problems with medical staff strongly associated with anxiety and with anticipatory nausea and vomiting.
Cella et al. (1989)	Descriptive	Various	a. 45 (15) b. 90 (30)	3 disease-specific measures (FACT-lung, breast and colorectal)	Development study. a) Pts. identified nine domains in order of priority: physical function, family life, emotional function, spirituality, treatment satisfaction, future orientation, intimacy/sexuality, social life, and work. b) Pts. rated the importance of each item to their own QL.
Ganz et al. (1992)	Descriptive	No active treatment, CT, RT	729 (214)	CARES	There are direct relationship between global CARES score , summary scale scores and extent of disease. CARES can differentiate between different cancer sites and stage of disease and it is responsive to change.
Ballatori et al. (1993)	Descriptive	CT	140 (60)	Ad hoc (49-item VAS), ECOG	Validation study. Need for self-assessment questionnaire. Strong interaction between physical condition and the psychological aspects.
Ovesen et al. (1993a; 1993b)	Descriptive	CT	104 (38)	QL-I, GHQ	No significant difference in survival in pts who received nutritional counselling and control group. QL was affected significantly in weight-loosing pts. Moderate weight loss is associated with psychological distress and lower QL.

Table 3.3 continued

Vijayakumar et al. (1993)	Randomised	RT + recombinant human eryrthropoietin *vs* RT alone	26 (11)	LASA (3 items on energy, daily activities, overall QL)	QL more stable in control group except for the overall QL. No improvement in QL of treatment group.
Kurtz et al. (1993)	Descriptive	CT, RT, Surgery, Combination therapy	279 (53)	SDS, loss of physical functioning derived from MOS, co-morbidity)	Physical functioning associated with symptoms and age. Co-morbidity correlated both with symptoms and loss of function for younger pts. Significant link between symptoms and loss of physical functioning.
Johnson et al. (1994a*; 1994b)	Descriptive	RT	19 (9)	QOL-RTI, FPQLIC	Validation study. QOL-TRI a quality of life measure for patients receiving RT.
Osoba et al. (1994a)	Randomised	Dose-intensive CT *vs* dose-intensive CT + SC	30 (20)	EORTC QLQ-C30 + 4-item enjoyment checklist, ECOG, appetite grade, weight change	PS, enjoyment level, physical functioning correlated with global QL. No significant association between appetite and weight change. Appetite significantly correlated with global QL, but weight change was not.
Osoba et al. (1994b; 1994c*)	Descriptive	Anti-emetics trials	535 (160)	EORTC QLQ-C30, ECOG	Validation study. Worse QL in metastatic pts. Strong correlation between PS and several domains of QLQ-C30.
Schag et al. (1994)	Descriptive	No active treatment	278 (57) disease free survivors	CARES, KPS	No difference in QL in LC pts with respect to their period of survival. KPS best predictor of QL. All cancer survivors had significant rehabilitation problems, but LC survivors had more problems than the other cancer survivors.
Degner and Sloan (1995)	Descriptive	RT, CT, surgery	434 (82)	SDS	Higher distress in LC pts. Symptom distress was a significant predictors of survival in LC pts.
Dazord et al. (1994)*, Dazord (1995)	Descriptive	Unknown	? (50)	SQLP, KPS	LC pts described their leisure as the domain where they are the most dissatisfied. A clear correlation between KPS and the pts' satisfaction related to their daily activities.
Kaasa et al. (1995)	Descriptive	Palliative RT	247 (79)	EORTC QLQ-C30, GHQ, Pain (frequency and severity)	Validation study. EORTC QLQ-C30 is found to be practical and valid in measuring QL in pts with advanced disease.

Table 3.4 Quality of life measures used in lung cancer studies

Instruments	Items	Dimensions
1. Performance status		
Vitagram index	2 axis	Quality of survival regarding the performance status
Karnofsky Performance Scale (KPS)	11	Performance status
Eastern Co-operative Oncology Group Performance Scale (ECOG)	5	Performance status
World Health Organisation (WHO) Performance Scale	5	Performance status
2. Functional status		
Rand Physical Functioning Scale (PFS)	10	Functional status (self-care, mobility, physical activity
Enforced Social Dependency Scale (ESDS)	10	Functional status (personal and social competence etc.)
3. Generic measures		
Sickness Impact Profile (SIP)	136	Physical and psychological status, sleep and rest, work, home management, recreation and pastimes.
Medical Outcome Study-Short Form 20 (MOS-SF 20)	20	Physical and social functioning, role limitations, mental health, energy, pain, general health perception
Medical Outcome Study-Short Form 36 (MOS-SF 36)	36	Physical and social functioning, role limitations, mental health, energy, pain, general health perception
General Health Rating Index (GHRI)	22	Health perception
Subjective Quality of Life Profile (SQLP)	33	Functional life, social life, material life, spiritual life, unforeseen domains, global assessment
Ferrans and Powers Quality of Life Index Cancer (FPQLIC)	46	Physical and functional ability, family well-being, spirituality, future orientation, sexuality, social and occupational functioning
Linear Analogue Self assessment Scale (LASA)	1	General well-being
4. Psychological		
Mental Adjustment to Cancer Scale (MACS)	?	?
General Health Questionnaire (GHQ)	30	Psychosocial assessment
Leeds General Scales for Anxiety and Depressio (LGSAD)	?	Anxiety and depression
Profile of Mood States (POMS)	65	Tension, depression, anger, vigour, fatigue, confusion
Brief Profile of Mood States (B-POMS)	?	Psychosocial well being
Mood Adjective Checklist (Bf-S well being scale)	28	Anxiety, depression
Hospital Anxiety and Depression scale (HADS)	14	Anxiety, depression
Beck Depression Inventory (BDI)	21	Cognitive Symptoms of depression
Psychosocial Adjustment to Illness Scale (PAIS)	46	Psychosocial adjustment to illness (seven domains)
Symptom Checklist-90 (SCL-90)	90	Nine sub-scales: depression, anxiety, somatisation, obsessive-compulsive, interpersonal sensitivity, hostility, phobic anxiety, paranoid ideation and psychotics
Personality Factor Questionnaire (PFQ)	?	?
Eysenck Personality Questionnaire (EPQ)	?	Personality assessment
Yatabe-Guilford questionnaire (YGQ)	39	Patients' personalities
Cancer Locus of Control (CLC)	?	?
Inventory of Current Concerns (ICC)	72	Current concerns under seven psychosocial categories
Awareness of Illness Scale (AIS)	18	How patients referred to their condition, their death and how describe their future and purpose of their treatments
Minnesota Multiphasic Personality Inventory (MMPI)	556	Ten major dimensions of emotional distress and personality disturbance
State Trait Anxiety Inventory (STAI)	40	Trait anxiety, and state anxiety
5. Pain and symptoms		
McGill Pain Questionnaire (MPQ)	78	Pain frequency, intensity and severity

Table 3.4 continued

Short Form McGill Pain Questionnaire (SM-MPQ)	15	As above
Symptom Distress Scale (SDS)	13	Cancer symptoms (appetite, nausea, sleep, elimination, pain, fatigue, breathing, cough, outlook, appearance, concentration)
Brief Symptom Inventory (BSI)	53	Psychological symptoms and symptomatic distress
6. Dyspnoea		
Clinical Dyspnoea Index (CDI)	?	Perceived dyspnoea (functional impairment at work or home)
Respiratory Status (RS)	5	Respiratory status
Pneumoconiosis Research Unit Index (PRU)	?	Perceived dyspnoea
American Thoracic Society Questionnaire (ATS)	29	Measuring pulmonary disease
7. Social functioning		
Duke-University North Carolina Social Support Scale	?	Social support
Short Form Marlowe-Crowne Social Desirability Scale (M-CSDS)	10	Social desirability
8. cancer-specific		
Spitzer Quality of Life Index (QL-I)	5	Activity, daily living, health, support, outlook
Daily Diary Card (DDC)	5	Overall condition, physical activity, vomiting, mood, anxiety
Functional Living Index-Cancer (FLI-C)	22	Physical symptoms, mood, physical activity, work, social interaction. It is a VAS
Rotterdam Symptom Checklist (RSCL)	38	Physical, psychological and functional status
Cancer Inventory of Problem Situations (CIPS)	131	Problem-oriented statements caused by cancer disease
Cancer Rehabilitation Evaluation System (CARES), early version called CIPS	139	Physical ,psychological, occupational, and sexual functioning, marital and medical interaction, family and social life,
Cancer Rehabilitation Evaluation System-Short Form (CARES-SF)	59	Physical, psychological and sexual functioning, medical and marital interaction
Time Without Symptoms and Toxicity (TWiST)	-	Quality-adjusted survival
European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QOL-C36)	36	Functioning (physical, role, emotional, social), cancer symptoms, financial impact, physical symptoms, overall health and quality of life
European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QOL-C30)	30	Functioning (physical, role, cognitive, emotional, social), global health and quality of life, dyspnoea, appetite loss, sleep disturbance, constipation, diarrhoea, perceived financial impact of the disease and treatment
Therapy Impact Questionnaire (TIQ)	11(36)	Psychological and functional status, social interaction, disease- and treatment-related symptoms (main instrument including physical symptoms and total of 36 items)
Quality of Life Radiation Therapy Instrument (QOL-RTI)	24	Functional status, emotional status, family and socio-economic status, general quality of life
9. site-specific		
European Organisation for Research and Treatment of Cancer Lung Cancer Quality of Lif Questionnaire (EORTC QOL-LC13)	44(13)	EORTC core questionnaire plus Lung cancer related symptoms and treatment side-effects (30 core items + 13-item lung cancer specific)
Lung Cancer Symptom Scale (LCSS)	15	Lung cancer related symptoms (patient- and observer-rated)
Functional Assessment of Cancer Therapy-Lung (FACT-L)	44(10)	Physical well-being, social/family well-being, relationship with doctor, emotional well-being, functional well-being, lung cancer symptoms (34 items general and 10 specific)

Table 3.5 Summary of quality of life studies in patients with small cell lung cancer

Study	Design	Treatment	Sample	Quality of life measure	Results/Conclusions
Rosenman and Noah (1982)	Descriptive	RT (therapeutic or elective brain irradiation)	53	KPS	Better survival and PS in favour of elective irradiation.
Silberfarb et al. (1983)	Randomised	CT (with *vs* without vincristine) +RT+PCI	77	POMS	No significant difference in tumour response between two regimens, but less depression and fatigue in without vincristine group.
Bakker et al (1984)	Randomised	Maintenance CT *vs* SC	23	KPS	No significant difference in survival. Pts who were randomised to stop treatment showed increase of their PS and body weight while patients who continued CT showed a decrease.
Aaronson et al. (1987)	Randomised	CT (12 *vs* 5 courses)	312 (80)	Early version of the EORTC qualityof life questionnaire	Validation study. The reliability and validity of the constructed instrument were found to be satisfactory.
Cella et al. (1987)	Descriptive	CT	455	ECOG, POMS	PS and extent of disease have a significant association with reported distress and can be considered risk factors for distress.
Bernhard et al. (1988)*	Randomised	Two combination CT	279	EORTC QLQ (41 items)	Physical functioning, treatment side-effects, disease-related symptoms, psychological distress, fatigue and malaise are most relevant aspects of QL.
Geddes et al. (1988)*	Randomised	CT(scheduled *vs* as required)	220 (80)	DDC	A better QL (less nausea and pain, better sleep, mood and general well being) in scheduled CT.
Spiro et al. (1988)*	Randomised	CT (Planned vs as required)	234	Unknown (8 variables)	A better QL in favour of planned treatment.
Lau (1988)*	Descriptive	CT	98	Ad hoc (somatic, social and psychological items), EPQ, BDI	Better QL in responders and those having good PS. Initial psychological status predicts QL.
Hurny et al. (1988)*	Descriptive (main study randomised)	Combination CT	74	General well-being (1 item), psychological distress (5 items), Bf-S	Validation study. Scales supposedly indicating similar QL are actually assessing different aspects.
Flechtner et al. (1988)*	Randomised	CT (alternating *vs* response-oriented)	334 (195)	EORTC QLQ C-36 (German version)	No significant difference between treatment arms, but significant difference between responders and non-responders. Except psychological distress, other subscales were significant prognostic factors for survival.

Table 3.5 continued

Bleehen et al. (1989a)	Randomised	CT (12 *vs* 6 courses), RT in limited disease	497 (109)	a. Pts: DDC b. Phyns: overall condition, physical activity, dyspnoea	No significant difference in survival. Both assessments showed a better QL in favour of 6 course CT regimen. Mood similar in both groups.
Bleehen et al. (1989b)	Randomised	CT *vs* PT, RT in limited disease	151 (50)	As above	Better survival in immediate CT + RT. Phyns reported a better condition in favour of immediate CT + RT, but pts reported a better QL in favour of PT. Overall condition and anxiety same in both groups.
Geddes et al. (1990)	Randomised	CT(8 *vs* 4 courses), prophylactic cranial irradiation	53 (31)	a. Pts: DDC b. Nurse: DDC, QL-I, EORTC QLQ (47 questions)	No significant difference in survival. Comparing two treatments, the study results indicated that each successive cycle had a worse impact on the pt's QL especially in patients receiving 8 courses CT.
Hopwood and Thatcher (1990)	Descriptive	CT	283 (274)	HADS	36% of pts showed psychological morbidity. No difference on depression between those on treatment and those not receiving treatment at the time of assessment. Depression in males and females were similar, but more anxiety and mixed anxiety-depression in females.
Hopwood (1991a)	Descriptive (main study randomised)	CT (4 *vs* 2 drug regimen)	?	HADS, RSCL, DDC	Psychological and disease symptoms reduced at first follow-up as compared to the pre-treatment scores. Despite increase in treatment-related symptoms, anxiety reduced markedly and depression a little.
Fayers et al. (1991)	Randomised	CT + RT(maintenance *vs* no maintenance)	369 (61)	a. Pts.: DDC, adverse reaction to treatment b: Phyns.: overall condition, activity	No significant difference in survival. Worse mood and better overall condition in no maintenance group, while those in maintenance group showed more sever adverse effects of chemotherapy. Anxiety similar in both groups.
Earl et al. (1991)	Randomised	CT (planned *vs* as required)	300 (62)	DDC	No significant difference in survival. More severe symptoms in as required group and less palliative effect seen.
Wolf et al. (1991)	Randomised	CT (continuous *vs* alternating)	321 (195)	EORTC QLQ-C36	No significant difference in survival. Continuous CT slightly superior. QL depended on tumour stage and tumour response. Overall, improvement in QL.

Table 3.5 continued

Bergman et al. (1991)	Descriptive	CT	62	SIP, HADS, and Lung Cancer questionnaire	Dyspnoea, cough improved significantly during treatment, but pain and appetite loss less substantially. Tumour response correlated with SIP summary indexes and anxiety. Non of SIP subscales changed significantly after 12 months, except items on sleep. Anxiety and depression significantly improved after 12 months.
Bergman et al. (1992)	Descriptive	CT	62	As above + EORTC QLQ-C36	No significant changes in EORTC scores except in social functioning (deteriorated) and emotional functioning (improved). Good correlation between changes of the EORTC scores and clinical variables (PS and tumour response), SIP and HADS.
Hueny et al. (1992; 1993)	Randomised	CT (early *vs* late alternation)	415 (188)	EORTC (core and lung including 42 items), Bf-S, a single LASA on general well-being	(a) Feasibility study. 68% completed at least one correctly questionnaire. Compliance and no compliance independent of medical or demographic variables. Institution significant predictor of compliance. (b) Fatigue and malaise found to be as a global indicator of QL.
Glimelius et al. (1992)	Descriptive	CT, cases received nutritional advice	58 (49) and two controls (22, 81)	CIPS, nutrition cardex	Global QL score better in study group. Treatment adverse effect less pronounced in study group. Nutritional care possibly contributing to the QL, but no major impact on either nutritional intake, nutritional status, or treatment outcome.
Rosenthal (1992)	Descriptive (retrospective)	CT	31	TWiST	Quality-adjusted survival study. No substantial difference from absolute survival. A reasonable QL may be achieved by intensive therapy for pts with limited SCLC.
Bleehen et al. (1993)	Randomised	CT (6 *vs* 3 courses of the same treatment *vs* 6 courses of different treatment)	485	Pts. : DDC Phyns. : overall condition, activity	No significant survival difference. All produced high and similar palliation of chest symptoms. QL stable over time. A minor advantage to the third treatment.
Anderson et al. (1993)	Randomised	CT (bolus *vs* continuous pump infusion)	159 (37, 40)	HADS, RSCL	No significant difference in survival and QL. Significant improvement in psychological symptoms.

Table 3.5 continued

Flechtner et al (1993)*	Randomised	a. CT (alternating *vs* response dependent), b. (carbo- *vs* cis-platinum), c. (treatment for extensive *vs* limited disease)	600	EORTC quality of life questionnaire	No significant difference between treatment arms in trial (a), but in trail (b) and (c) different. Intensive treatment more than 4 cycles results in overall marked negative effect on pts' QL.
Sufarlan and Zainudin (1993)	Descriptive	CT	17	KPS	A 30% overall improvement in the PS at the completion of CT.
Cull et al. (1994)	Descriptive (retrospective)	PCI	64 (52)	HADS, RSCL	Anxiety and depression lower than pts recently receiving active treatment. High proportion of pts still experiencing treatment-related symptoms, but not functional impairment.
Gower et al. (1994*, 1995)	Randomised	CT (intensive *vs* conventional)	75	DDC, ECOG	No significant difference in survival. Better QL in favour of conventional CT.
Hopwood and Stephens (1994b)*	Randomised	CT (4 drugs combination *vs* 2)	310	HADS, RSCL	No significant difference in survival. Better QL in favour of 4 drugs combination CT.
Hopwood et al. (1994b)*	Randomised	CT (alone *vs* with Lenograstim)	65 (62)	HADS, RSCL	Pts. receiving CT alone showed a reduction in anxiety and little change in depression or functional status, but pts. receiving CT + Lenograstim reported more impairment in physical symptoms and functional status with less improvement in anxiety.
Wolf et al. (1994)*	Randomised	CT (standard *vs* palliative)	221	Pre-validate quality of life questionnaire	No significant difference in survival. Pts. receiving standard regimen had a better tumour response and improvement of QL than pts. receiving palliative one, but more sever side effects were more frequent.
Jett et al. (1994)*	Randomised	CT (with *vs* without megestrol acetate)	237	FLI-C	Overall tumour response in favour of placebo arm, but anorexia, nausea and vomiting less in study group.
Joss et al. (1995a)	Randomised	CT (mild palliative *vs* standard)	59 (40)	Study specific (24 items derived from EORTC 42-item QLQ)	Survival significantly better in standard CT despite its more toxicity. No significant difference in most measures of QL, but mucositis and alopecia in favour of palliative CT. Standard CT group better values for sleep disturbance, fatigue, and psychological distress.

Table 3.5 continued

Joss et al. (1995b)	Randomised	CT (early *vs* late alternating), RT (in those with remission)	406 (127)	Study specific (derived from EORTC 42-item QLQ), Bf-S, LASA	No significant difference in survival. Better QL in pts receiving early alternating CT.
Bernhard et al. (1995)	Descriptive (main study randomised)	Two different combination CT	188	EORTC (42-item), Bf-S, LASA	QL assessment can be a supportive intervention by itself, increasing awareness to quality of life issues in both pats and clinical staff.
Eguchi et al. (1995)*	Descriptive (main study randomised)	CT (weekly *vs* alternative), Concurrent CT +RT *vs* CT +RT	459 (415)	EORTC QLQ (Japanese version, 42 items)	Significant improvement in physical, psychological, and global QL and decrease in relationship with family and friend in pats with limited disease. Pats with extensive disease improved in only physical domain.
Hickish et al. (1995)*	Descriptive	CT	50	EORTC QLQ-C30 and LC-13	Significant improvement in QL (emotional and cognitive functioning, global QL, pain, dyspnoea, and cough).

Table 3.6 Summary of quality of life studies in patients with non-small cell lung cancer

Study	Design	Treatment	Sample	Quality of life measure	Results/Conclusions
Lad et al. (1981)	Randomised	CT (conventional *vs* aggressive)	72	Ad hoc (housebound status, body weight, progression of tumour, death)	No significant difference between treatment arms in survival and QL.
Arcangeli et al. (1985)	Descriptive	RT + CT	31	KPS	Significant improvement in PS.
Monras et al. (1985)*	Descriptive	CT	20	VAS (common symptoms, anxiety, anorexia, QL), KPS	Feasibility study. Easy to use and relatively valid when comparing patient VAS with observer categorical rating.
Bakker et al. (1986)	Descriptive	CT	28	KPS + Questions on difficulties with CT + Change in body weight	Treatment-related toxicity and the deterioration of the patient's well-being offset any potential survival advantage for the majority of pts.
Monk et al. (1986)*	Descriptive (retrospective)	CT	349	KPS	QL as measured by KPS, was found to be a good predictor of increased survival alongside response to treatment and extend of disease (EOD). Response to treatment was not independent of PS and EOD. Long time survival had relatively good QL.
Minet et al. (1987)	Randomised	RT *vs* RT+ CT	81	KPS	No significant difference between treatment arms in survival and QL as measured by KPS.
Moreno et al. (1988)*	Descriptive	CT	47	VAS (disease-related symptoms)	Marked relief of symptoms after CT.
Javaid et al. (1988)*	Randomised	CT + anti-inflammatory drug (fenbufen) *vs* CT + placebo	22	Ad hoc (well-being, severity of pain, anxiety, PS, level of activity, social activities, appetite, mood, nausea)	Significant improvement in well-being and pain relief in favour of fenbufen. No significant difference between treatment arms in all other measures.
Ahmedzai et al. (1988b)*	Randomised	RT *vs* RT + CT *vs* PT	?	Ad hoc questionnaire (items on symptoms, mood, outlook, and treatment satisfaction rating by pts., phyns. or nurse)	Fewer physical and psychological problems in RT and CT + RT. Fewer problems in responders after 3 months. After 6 months no difference.
Finkelsteint et al. (1988)	Descriptive	CT	46	FLI-C	Change of FLI-C correlated with PS change and weight loss, but not with treatment regimen, side-effects of treatment or change of pain.

Table 3.6 continued

Kaasa et al. (1988b; 1988c)	Randomised	RT *vs* CT	95	Purposed questionnaire (assessing psychosocial well-being , physical functioning, treatment related symptoms, daily activity, global QL)	Significant difference in psychosocial well-being and global QL in favour of RT. No significant group differences in physical functioning and daily activity. Significant difference in treatment-related symptoms in favour of RT.
Kaasa and Mastekaasa (1988)	Randomised	RT *vs* CT	101	Purposed questionnaire (as above)	Significant correlation between psychosocial well-being and physical functioning and daily activity. Poor correlation between psychosocial well-being and biomedical variables. Significant correlation between symptoms related measures, but not RT and CT related measures.
Mattson et al. (1988), Maasilta et al. (1987*; 1990)	Descriptive	CT	55	VAS (11 items on performance and disease- and treatment related problems)	QL deteriorated during CT and was significantly dose-dependent. Worse nausea and vomiting, but general well-being unchanged.
Ganz et al. (1986*; 1989)	Randomised	SC *vs* SC + CT	48	FLI-C + KPS	Positive correlation between FLI-C and KPS. Due to poor compliance, studying difference between treatment arms was impossible.
Buccheri et al. (1989)	Randomised	CT *vs* SC alone	74	Ad hoc (3 items on treatment tolerance, physical well-being, depression) + KPS	No significance difference in depression and PS between treatment arms. Better tolerance in favour of SC, but better physical status in favour of CT.
Kaasa et al. (1989)	Randomised	RT *vs* CT	102	Purposed questionnaire (as above)	Psychosocial well-being found to be a good predictor of survival.
Fernandez et al. (1989)	Descriptive	CT	31	Ad hoc (11 VAS including lung cancer symptoms, treatment side-effects, physical activity, and global QL)	Disease-related symptoms reduced and QL improved. No correlation between KPS and global QL nor between physical activity and global QL.
Weeks et al. (1989)*	Descriptive (retrospective)	CT or SC	243 (56)	ECOG	CT produced a temporary benefit in QL as measured by PS.

Table 3.6 continued

Sarna (1990*; 1991)	Descriptive	CT	24	CIPS + Rand Physical Functioning Scale (PFS), KPS	Older adults had less psychosocial and marital problems than younger adults. Significant less decline in physical activities of treated pats as compared to an untreated cohort of NSCLC pts. Significant correlation between QL and measures of functional status.
Bleehen et al. (1991)	Randomised	RT (experimental *vs* conventional)	365	DDC	No survival difference. Dysphagia rose during treatment and fell after 2 weeks. Reduction in physical activity rose during treatment and fell after 5 weeks. Similar results for mood and overall condition. Findings similar in two groups.
Hopwood (1991b)*	Descriptive (main study randomised)	RT (two different regimens)	217	HADS, RSCL, Daily Diary Card	Disease-related symptoms improved, but dysphagia increased markedly. Anxiety improved, but depression unchanged.
Regan et al. (1991)	Randomised	Palliative RT (multi fractions *vs* 2)	40	ECOG + MRC scales of general condition and dyspnoea + EORTC QOL-C36	Good agreement between phyns and pts on change in specific physical symptoms and overall condition. Phyns were poor judges of QL at presentation, but able to identify improvement or deterioration.
Bleehen et al. (1992)	Randomised	Palliative RT (2 fractions *vs* single)	235 (145)	Pts. : DDC Phyns. : overall condition, WHO performance status, RS, symptoms	No survival difference. No significant differences in most areas that has been assessed, except less dysphagia in favour of single fraction arm.
Vinante et al. (1993)	Randomised	CT	28	KPS	PS improved in 46% and 38% had a complete symptom relief.
Sakai et al. (1994b)*	Descriptive	CT	61	Ad hoc (12 items on psychological, physiological, daily living, and general health)	QL might be strongly influenced by the effects of palliative CT.
Kosty et al. (1994)	Randomised	CT + hydrazine sulphate *vs* CT + placebo	266 (259)	Ad hoc (52 questions containing EORTC QOL-LC13 + Duck University Social Support Scale	No significant survival difference. Overall QL generally better in placebo-treated group. Increased toxicity by using adjunct agents (e.g. hydrazine sulphate) should be discouraged.

Table 3.6 continued

Loprinzi et al. (1994)	Randomised	CT + hydrazine sulphate *vs* CT + placebo	237	FLI-C	No significant median survival. No significant difference in QL. Study failed to provide any suggestion that (hydrazine sulphate) was beneficial in terms of QL or clinical measures. The drug is not recommended.
Pujo et al. (1994)	Descriptive	CT (fotemustine)	87 (54)	FLI-C + Five somatic variables (appetite, body weight, pain, sleep, fatigue)	QL stable for responders, but decreased for non-responders. Fotemustine is feasible as single-drug CT.
Moinpour et al. (1994)*, Moinpour (1994)	a. Randomised. b. Descriptive	a. CT (vinorelbine) *vs* CT (5-fluorouracil, leucovorin) b. CT (vinorelbine)	a. 211 (52) b. 162 (70)	Ad hoc (including MOS-SF 20, MOS-SF 36, SDS, LASA on global quality of life)	a. No significant differences for any QL measures, but better symptom status in vinorelbine treated pts. b. Better symptom distress and physical functioning associated with longer time on the study. Symptom distress stable over time.
Dales et al. (1993; 1994)	Descriptive	Surgery	117	1. Measures of perceived dyspnoea (including CDI, PRU). 2. Measures of perceived overall functioning (including QL-I, SIP)	General QL measures were not good predictors of morbidity. However, surgery deteriorates the QL during the first 3 months post-operatively in those with a final diagnosis of LC, but improvement back to baseline can be expected thereafter.
Hopwood and Stephens (1994c)*	Randomised	RT (short *vs* aggressive regimen)	500	RSCL, HADS	Survival slightly improved in favour of aggressive regimen, but in other respects (palliation of main symptoms, adverse effects, response, appearance of metastases) the two regimens were very similar.
Hollen et al. (1993b*; 1994a)	Descriptive	CT	a. 207 pts. b. 21 obs.	LCSS, KPS, BSI, SCL-90, SIP, POMS, ATS, SM-MPQ	Validation study. LCSS pts and observer scales was found to be reliable, valid and responsive to change.
Hollen et al. (1994b)	Descriptive	CT	144	LCSS	Physical and functional dimensions are important predictors of QL for LC pts.
Gralla et al. (1995)*	Randomised	CT (with *vs* without edatrexate)	673	LCSS	QL at baseline not only predicts for the likelihood of response and for survival, but also has greater impact than most known prognostic factors.

CHAPTER FOUR

4

AIMS AND OBJECTIVES

Contents

1. Aims

2. Objectives

3. Hypotheses

1. Aims

1. To understand the contribution of quality of life to lung cancer care.

2. To understand to what extent the socio-economic characteristics of lung cancer patients contribute to the outcome of their clinical management with outcome measured in terms of quality of life.

2. Objectives

1. To determine the social characteristics of patients with lung cancer and chronic respiratory disease in a geographically defined area.

2. To measure and compare quality of life in patients with lung cancer and chronic respiratory disease.

3. To examine the relative contribution of the socio-economic characteristics of patients to variation in their baseline quality of life.

4. To compare quality of life of patients in different settings these are: at home and in the clinic.

5. To compare baseline quality of life in patients who knew their cancer diagnosis and those who did not know their diagnosis.

6. To investigate the relationship between baseline quality of life and survival.

7. To compare quality of life in lung cancer patients before and after diagnosis and treatment.

8. To determine what predicts global quality of life at follow-up assessments.

9. To investigate how patients reacted to the study.

10. To study patients' perceptions of quality of life.

3. Hypotheses

1. There is no difference between the socio-economic characteristics of lung cancer cases and chronic respiratory disease controls.

2. There is no difference between the social networks and social support systems of patients with lung cancer and patients with chronic respiratory disease.

3. There is no difference between the baseline quality of life of patients with lung cancer and patients with chronic respiratory disease.

4. Socio-economic status and social support system variables do not contribute to the patients' quality of life.

5. Interview setting would not affect the outcome as measured in terms of quality of life.

6. Knowledge of having lung cancer diagnosis would not affect the outcome as measured in terms of quality of life.

7. The baseline quality of life is not a predictor of survival time.

8. Treatment will not improve quality of life in patients with lung cancer as compared to their baseline assessments.

9. Patients would prefer to fill in a questionnaire in the clinic rather than being interviewed at home.

10. Patients perceive quality of life in a similar way to health professionals.

These all were tested and the results are presented in chapter 6.

CHAPTER FIVE

5

MATERIALS AND METHODS

Contents

- Summary
- Introduction

1. Setting

2. Design

3. Patients

4. Materials

5. Data collection

6. Analysis

7. Limitations and difficulties

Summary

A prospective study was conducted to measure quality of life in patients with lung cancer. Data were collected during one complete calendar year-from 1st January to the 31st of December 1995 with the intention to interview all patients attending the chest clinic in Stobhill Hospital in the northern sector of Glasgow. Interviews were carried out at patients' homes or in the clinic both before and after treatment. Permission was obtained from the hospital ethical committee, general practitioners (GPs), clinicians, and the patients themselves. Quality of life was assessed at baseline and three months later using three standard questionnaires (the Nottingham Health profile, the EORTC quality of life core questionnaire, and the EORTC lung cancer questionnaire). In addition there was a study specific questionnaire to collect data on the socio-demographic status of the study subjects. Baseline assessments were scheduled after referral by GPs and before the diagnosis was made by the consultant in respiratory medicine. At this stage for each suspected case, one patient with chronic respiratory disease was interviewed as a control. The researcher was blind to this selection, the nature of the disease and diagnosis. At the time of the baseline interview patients did not know their confirmed diagnosis. All lung cancer patients were informed at a return appointment when the clinical tests were complete. Follow-up assessments were scheduled for those with a confirmed diagnosis of lung cancer three months later.

Introduction

To achieve the aims and objectives of the study, a prospective double blind case-control study was designed. In the following sections the method of investigation and the materials used are described.

1. Setting

1.1. Stobhill Hospital catchment area

The study was carried out in the Northern sector of Glasgow. Since one of the most important objectives of the study was to investigate the relationship between patients' socio-economic status and quality of life, it was thought that the area was an ideal setting. There is a clear contrast of social structure within the population in this area reflecting a range of deprivation categories from the least to the most deprived areas, and this would allow for a comparison of quality of life in different social groups. Thus, Stobhill Hospital NHS Trust, a large teaching and District General Hospital, serving the population of the Northern sector of Glasgow was chosen for the study.

The catchment area of Stobhill Hospital is shown in the following map. The map is divided into postcode sectors. These postcode sectors were in part, used to indicate patients' socio-economic status as described by Carstairs and Morris (1991). Using area-based analysis, and studying similar methods in the UK (for example the Jarman score (1983) which calculates "underprivileged area scores" in England and Wales), a Deprivation Category was established for each postcode sector in Scotland. These categories range from 1 (affluent) to 7 (deprived). Deprivation Category takes four variables into account: overcrowding, male employment, social class, and car ownership. Glasgow is fortunate to contain precise match of Deprivation Category and social class.

The catchment area is classified into two main divisions by the Stobhill Trust: "official" (the northern sector of Glasgow), and "unofficial" (a few fund holding general practitioners send their patients to Stobhill from these areas, see the map).

However, as mentioned above, the Stobhill catchment area contains a sharp contrast of social structure as indicated by postcode sectors. The composition of the area can be summarised as follow:

- Postcode sectors indicating Deprivation Category 1 and 2 (affluent) 19%,
- Postcode sectors indicating Deprivation Category 3, 4, and 5 (middle) 29%, and
- Postcode sectors indicating Deprivation Category 6 and 7 (deprived) 52%.

This structure is very similar to the distribution of Deprivation Category in Glasgow, but is fundamentally different from that of Scotland (Table 5.1)

Table 5.1 Population living at differing levels of Deprivation: Stobhill catchment area, Greater Glasgow, Scotland, and England and Wales

Deprivation Category	Stobhill catchment area+ %	Greater Glasgow* %	Scotland* %	England & Wales* %
Affluent (1&2)	19	18	20	52
Middle (3,4&5)	29	32	62	44
Deprived (6&7)	52	50	18	4

+ Source: 1991 census; * Source: Carstairs and Morris (1991)

To give an example of variation in people's living conditions, comparative statistics for postcode sectors from Stobhill catchment area are presented in Table 5.2.

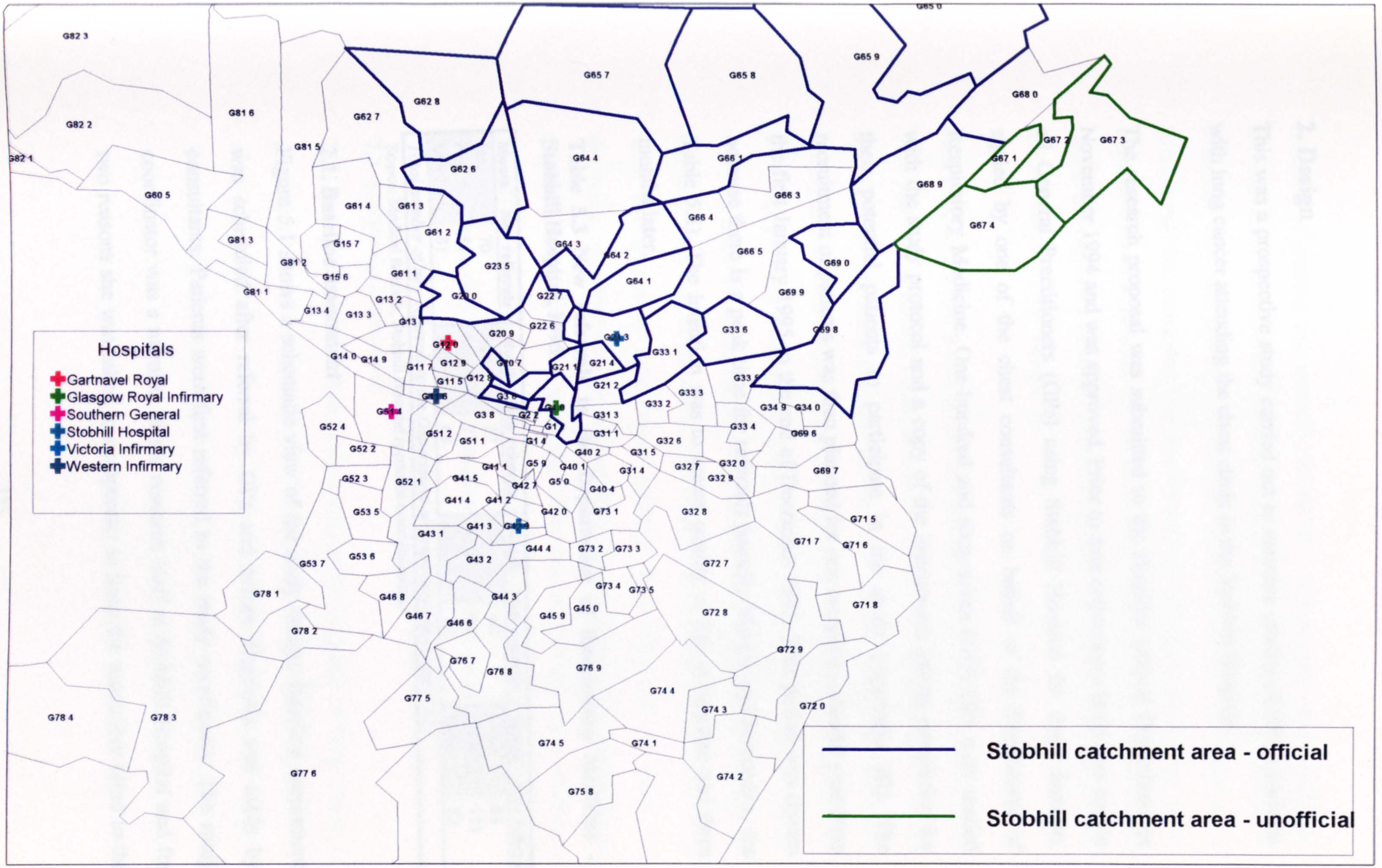
Table 5.2 Census 1991 statistics for selected postcode sectors from Stobhill catchment area

Postcode sector	Deprivation Category	% Home ownership	% Car ownership	% Population with l term illness	% Males unemployed
G64 3	1	95	85	8	5
G65 8	2	77	79	7	6
G64 1	3	75	70	9	8
G65 7	4	50	62	12	12
G66 2	5	34	46	17	15
G20 0	6	25	31	23	27
G21 3	7	18	25	27	32
Greater Glasgow	-	44	43	18	20

1.2. Department of Respiratory Medicine

Stobhill Hospital has an active Department of Respiratory Medicine which deals with all respiratory patients and there are no other chest specialists in this Hospital. The Department has six out-patient and one shared clinic every week run by two chest physicians and six registrars. There is the "Oncology Clinic" in which an additional oncologist participates (from the Beatson Oncology Centre) with one of the chest physicians for patients who are diagnosed as having lung cancer. There are also two "broncoscopy" clinics for examination of patients suspected of lung cancer. The Department has an in-patient ward for all respiratory patients including lung cancer patients connected to a "Day Unit" for management of patients who are receiving out-patient chemotherapy. Patients who need radiotherapy and surgery are referred to other hospitals, but after or during their additional care all return to the "Oncology Clinic" in Stobhill Hospital for further management.

For the purpose of this study the researcher was present at each clinic from Monday to Friday over the whole study period. The procedures for selection of patients and study design are described in the following sections.


Hospitals
Gartnavel Royal
Glasgow Royal Infirmary
Southern General
Stobhill Hospital
Victoria Infirmary
Western Infirmary
Stobhill catchment area - official
Stobhill catchment area - unofficial

2. Design

This was a prospective study carried out to measure quality of life in patients with lung cancer attending the chest clinic in the Stobhill Hospital.

The research proposal was submitted to the Hospital Ethical Committee on November 1994 and was approved. Prior to data collection a letter was sent to all General Practitioners (GPs) using Stobhill Hospital for chest diseases, signed by one of the chest consultants on behalf of the Department of Respiratory Medicine. One-hundred and sixty-seven (167) GPs were mailed with the study protocol and a copy of the instruments asking permission for their potential patients to participate in the study (Appendix III). The recruitment of patients was then planned for one complete calendar year-from the first January 1995 to the end of December 1995. This period was chosen because there is a peak time for referrals (usually March, and November, see Table 5.3). The intention was to assess quality of life at baseline and three months later.

Table 5.3 New referrals to the Department of Respiratory Medicine - Stobhill Hospital, 1995

Month	New referrals	Month	New referrals	Month	New referrals	Month	New referrals
Jan.	70	Apr.	27	Jul.	48	Oct.	64
Feb.	51	May	71	Aug.	64	Nov.	111
Mar.	81	Jun.	63	Sep.	24	Dec.	52
Total number of new referrals to the Department of Respiratory Medicine: 726							

Source: Medical Records, Stobhill Hospital (personal communication)

2.1. Baseline assessment

Figure 5.1 shows a schematic view of the study design. Baseline assessment was scheduled after referral by GPs and before diagnosis was made by consultants. Patients were first referred to the study coordinator. The study coordinator was a member of the research staff at Stobhill Hospital and for two reasons she was asked to co-operate: to keep the researcher blind to the

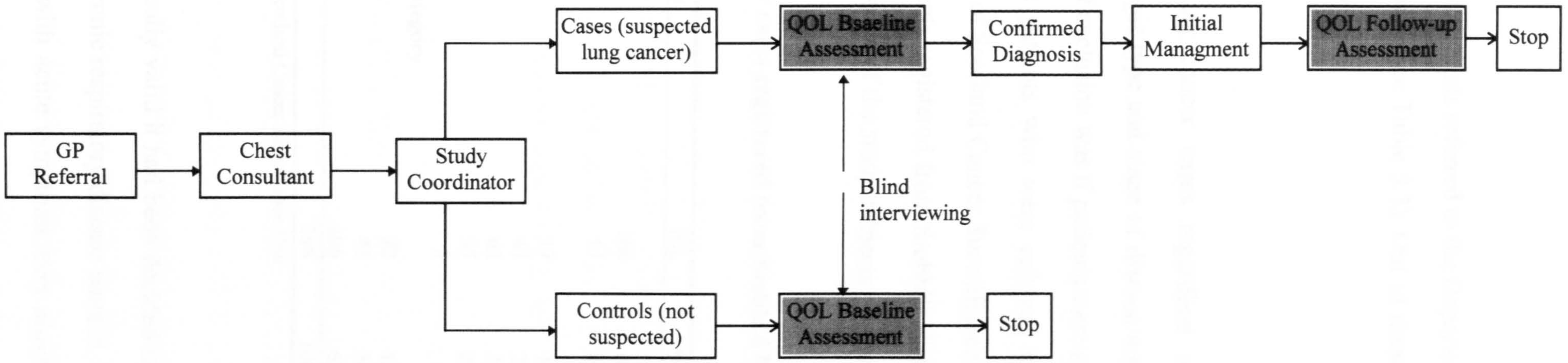
selection of patients and secondly, to ask GPs' and patients' permissions for the researcher to interview patients (Appendix IV). At this stage for each suspected case, one patient with chronic respiratory disease was interviewed as a control. The researcher was thus blind to the diagnosis. At the time of the baseline interview patients did not know their confirmed diagnosis. All lung cancer patients were informed of their diagnosis at a return appointment when the clinical tests were completed.

However, at baseline it was not always possible to carry out interviews blind. This was due to several practical reasons: it was not always feasible for the clinicians to introduce patients for interview before confirmed diagnosis; some patients were referred internally rather than by GPs and some patients were referred with short notice. Thus, to enter all cases to be included in the study on some occasions baseline assessments were scheduled after diagnosis but before the start of treatment. This means that at baseline assessment there were two groups of lung cancer patients: those who did not know the diagnosis, and those who knew about their disease. These later patients knew that they had lung cancer when they were entered into the study. However, this allowed the study to examine an additional question: does it matter if patients know their diagnosis at baseline assessment of quality of life?

2.2. Follow-up assessment

This was scheduled for those with a confirmed diagnosis of lung cancer at three months later, that is, after the completion of their initial management. This timing was based on the fact that the initial management (surgery, chemotherapy, or radiotherapy) takes at least three months to be completed.

Figure 5.1 A schematic view of the study design



3. Patients

In 1995 there were 726 new patients referred to the Department of Respiratory Medicine of Stobhill Hospital (see Table 5.3). Out of these, samples of cases and controls were selected.

3.1. Cases

All suspected primary lung cancer cases regardless of their sex, age, performance status, histologic type and stage of disease were entered into the study. The only criterion of exclusion was if patients were referred prior to the start of the study, that is patients who were referred in 1994. Based on information from the West of Scotland Cancer Surveillance Unit in 1994 there were 169 lung cancer patients registered from Stobhill Hospital. The data for 1994 gives an initial impression of the study subjects (Table 5.4).

Table 5.4 Lung cancer cases registered from Stobhill Hospital- 1994

Characteristics	No.	%
Gender		
Male	108	64
Female	61	36
Age Group		
41-54	17	10
55-64	47	28
65-74	62	36
75-84	35	21
85+	8	5
Deprivation Category		
Affluent	22	13
Middle	41	24
Deprived	106	63
Total	169	100

Source: West of Scotland Cancer Surveillance Unit

3.2. Controls

In this study to be scientifically valid it had been decided to match each lung cancer patients with one chronic respiratory disease control. The controls were selected if they presented with acute symptoms very similar to lung cancer

patients. To avoid any selection biases there were no matching for sex, age, performance status or other socio-demographic variables in the study.

4. Materials

Assessment of quality of life requires valid, reliable, and responsive instruments. To assess quality of life and social characteristics in lung cancer patients three main standard measures plus a study specific questionnaire were used. The selection of these measures was based on three main factors: their validity, recommendations from previous research, and the study objectives. Another consideration in such selection was related to the fact that these instruments do not contain any words indicating "cancer". In this project this was an important factor, since at baseline assessment the study design required that patients do not know they were suspected of having lung cancer.

In addition, from the study objectives there was a need to have a detailed assessment of social characteristics of patients. Thus, a study specific questionnaire was constructed. The inclusion of items were based on several factors including study objectives, pre-validated items from previous research works, and the pilot study. In the following sections each of these instruments is discussed.

4.1. Nottingham Health Profile (NHP)

This is a general health questionnaire and is used widely both within the UK and in other countries with a number of validated versions for countries including Sweden, Spain, France and Italy. The NHP is accepted as one of the recognised instruments associated with the extensive interest in quality of life. The main feature of the instrument is that it was developed through participation of members of the public. Thus, it is highly acceptable to respondents. Since the NHP does not ask directly if people have a health

problem, it is more likely to pick up people who are ill or at risk but who do not perceive their problems as being related to health. In addition, the measure is easy to complete and score, it has a very simple response format, and it takes a short time to complete (McEwen, 1993). The reliability and validity of the NHP are well established in a wide range of studies from individual clinical interviews to large scale postal surveys (McDowell and Newell, 1987; Bowling, 1991).

Specifically relating to this study, it has been suggested that while the NHP can be used in clinical trials for selected groups of patients, it is also a valuable measure in other clinical settings such as outcome studies in health of chronically ill patients, as an adjunct to the clinical interview, and in evaluating clinical intervention (McEwen and McKenna, 1996).

The NHP has also been used in an oncology setting measuring perceived health status in four groups of cancer patients including lung cancer patients. There appeared to be a positive relation between score at diagnosis and the end of therapy with those patients having more difficulties showing little improvement after treatment (cited in Hunt et al., 1993).

The NHP consists of two parts. Part I includes 38 items covering six areas: sleep (5 items), physical mobility (8 items), energy (3 items), pain (8 items), emotional reactions (9 items), and social isolation (5 items). Respondents are asked to answer "Yes" or "No" to problems identified “in general at the present time”. "Yes" answers carry one and "No" answers carry zero score. Each item on Part I has a weight. Therefore, the initial scores can be computed to obtain a weighted score for each area. The total score for each dimension (area) on Part I ranges from zero (no problem) to 100 (all problems are affirmed). Part II of the NHP consists of seven items relating to paid

employment, looking after the home, social life, family relation, sex life, hobbies and interests, and holidays. Items are scored one for affirmative and zero for a negative. Since in this study some of the items on Part II were not applicable to all respondents in this study e.g. work and sex life, as recommended by its authors, it was not used (Appendix V).

However, there have been some criticisms on the use of NHP, for example, suggesting that the items do not reflect the extent of severity of the problems (Kind and Carr-Hill, 1987; Jenkinson, 1994a). The severity of problems on the NHP means that some individuals with illness may not show up on the NHP. Although this also has been highlighted by the authors of the NHP themselves, it is argued that is not unusual for researchers to claim that the NHP lacks sensitivity in studies where it was not an appropriate measure or where the sample size were inadequate (McEwen and McKenna, 1996). Fallowfield (1990) argues that one of difficulties with using the NHP as a quality of life measure is the problem that it only looks at negative aspects of health, although very few statements cover positive health. However, in overall evaluation, she states that this well-researched instrument it worth considering as a quality of life measure in view of its acceptability, cheapness and easy scoring.

In conclusion, since all measures have their own limitations, the NHP is one of the best developed general health measures for administration, especially in the UK context. As it was discussed in Chapter One its international use also confirms such a conclusion.

The NHP is copyrighted to the authors. Permission to use the NHP was obtained from Professor James McEwen.

4.2. European Organisation fro Research and Cancer Treatment Quality of Life Questionnaire (EORTC QLQ-C30)

The first generation of the EORTC QLQ was developed in 1987. This was a 36-item questionnaire (EORTC QLQ-C36) designed to be cancer-specific, multidimensional, easy to complete, and applicable across a range of cultural settings. The QLQ-C36 was tested in an international field study in a sample of lung cancer patients (n = 537) drawn from 15 countries including most Western European countries, Australia, Canada, and Japan. Following this, a revision was carried out and there were minor changes in the wording of items, a few noninformative items were discarded, and due to inadequate reliability of the eight-item emotional functioning subscale it was substantially reviewed (Aaronson et al., 1991).

Table 5.5 Content of QLQ-C36 and QLQ-C30

Dimensions	QLQ-C36	QLQ-C30
Functional scale		
Physical	7	5
Role	2	2
Emotional	8	4
Cognitive	1	2
Social	2	2
Global quality of life	2	2
Symptom scales		
Fatigue	5	3
Nausea and vomiting	2	2
Pain	1	2
Dyspnoea	1	1
Sleep disturbance	1	1
Appetite loss	1	1
Constipation	1	1
Diarrhea	1	1
Financial impact	1	1
Total	36	30

Source: adapted from (Aaronson et al., 1996)

The second generation questionnaire, is known as the EORTC QLQ-C30. Table 5.5 demonstrates its differences from the QLQ-C36. It is a 30-item questionnaire and consists of five functional scales (physical, role, cognitive, emotional), three symptoms scales (fatigue, pain, and nausea and vomiting)

and a global health and quality of life scale. The remaining single items (six items) assess additional symptoms commonly reported by cancer patients including: dyspnoea, lack of appetite, sleep problem, constipation, and diarrhoea, as well as the perceived financial difficulties of the disease and treatment (Appendix VI).

The items on physical functioning have a dichotomous responses (yes or no). The sections on symptoms, anxiety, depression, and limitations have a 4-point response choices ranging from 1 (not at all) to 4 (very much). The global questions on general health and quality of life are a 7-point visual analogue scale ranging from 1 (very poor) to 7 (excellent). Apart from the physical functioning all items employ a 1-week time frame.

The EORTC QLQ-C30 has been validated in an international (Western Europe, North America, Australia, and Japan) field study of lung cancer patients and it was found to be a reliable and valid measure of the quality of life of cancer patients (Aaronson et al., 1993). In a recent study of quality of life in a group of cancer patients including a sample of lung cancer patients receiving radiotherapy it was found that the EORTC QLQ-C30 not only is a valid instrument in measuring quality of life in a cancer population in general, but also in patients with advanced disease (Kaasa et al., 1995). It is argued that the best developed quality of life measure for use with cancer patients is currently the EORTC QLQ-C30 (Bowling, 1995a), although it has been criticised as being too narrow in its focus with regard to ignoring much of the impact of cancer on social life (Siegrist and Junge, 1990). Currently the following proposed refinements are under test: an alternative role functioning scale which will include not only work and household jobs but also hobbies and leisure time activities and wider range of response categories; a revised physical functioning scale that employs four-point rather than dichotomous

response choice; and a revised overall health status/quality of life aspects of health (Aaronson et al., 1996).

4.3. EORTC QLQ Lung Cancer Questionnaire (The EORTC QLQ-LC13)

This is a tumour-specific questionnaire supplementary to the EORTC quality of life cancer questionnaire.

The EORTC QLQ-LC13 is a 13-item measure of lung-cancer related symptoms and treatment side-effects including: coughing (1 item), haemoptysis (1 item) , dyspnoea (3 items), sour mouth or tongue (1 item), trouble swallowing (1 item), tingling hands and feet (1 item), hair loss (1 item), experience of pain (3 items), and pain medication (2 items). With the exception of the first item on pain medication, which has dichotomous response categories (yes or no), all items are scored on a 4-point categorical scale ranging from 1 (not at all) to 4 (very much). All items employ a 1-week time frame (Appendix VI).

A recent publication by the EORTC Study Group on Quality of Life concluded that the results from international field testing, yielding a data base with over 700 lung cancer patients, lend support to the EORTC QLQ-LC13 as a clinically valid and useful tool for assessing disease- and treatment-specific symptoms in lung cancer patients, when combined with the EORTC core quality of life questionnaire. All symptom and toxicity scores changed significantly over time, with disease symptoms declining and treatment toxicities increasing during the treatment period. In a few cases, however, the questionnaire module could benefit from further refinements. In addition, its performance over a longer period of time still needs to be investigated (Bergman et al., 1994).

The use of both EORTC QLQ-C30 and QLQ-LC13 are subjected to copyright. The permission to use these instruments was provided by a written agreement from the EORTC Data Centre (Appendix VII).

4.4. Study specific questionnaires

4.4.1. *Socio-demographic questionnaire*

Different patients vary in their initial quality of life. Thus, relying solely on standard measures of health-related quality of life may not reflect the role of other variables which could be considered as possible confounders. For example, variables such as socio-economic status of patients or their family structure and social networks may account for great deal of variances in patients' quality of life. In this respect one may argue that patients' scores on one standard measure not only depend on disease- and treatment- related parameters but could also be affected by several other factors, namely patients' socio-economic background or lifestyle. Therefore, to adjust findings from standard measures of quality of life used in this study against patients' background, a proposed-questionnaire was constructed to provide this information. The variables were governed by a combination of previous research findings (Pill et al., 1995; Oostrom et al., 1995; Osler, 1995), the pilot study (see chapter one), and the desire to take advantage from face-to face interviewing the patients. In the following section these variables are described.

(a) Socio-demographic status: gender, age, martial status, and education level. Gender, martial status, and education level were categorical and age was recorded as a continuous variable.

Variables were categorised as follows:

- Educational level: no school leaving certificate (those who left school at age 14 or 15 which is very common for elderly people), school certificate, college, diploma, or university qualification.
- Marital status: married, widowed, separated, divorced, and single.

(b) Family structure: number of people in household, and number of children. All variables were numerical.

(c) Social network: visit frequency from children who had left home, visit frequency with other members of family and relatives, visit or contact frequency with neighbours. All variables were rated on a categorical basis.

- Visit frequency was categorised as follows:

Always (every day), almost always (2 or 3 times per week), sometimes (1 to 3 times per month), almost never (once a year), never (none).

(d) Social support: support and help received from children, family and relatives, and neighbours. This included any form of support such as financial, transport to shopping centres, or hospital, emotional support, shopping, cooking, cleaning, etc.

- Support was categorised as follows:

always, almost always, sometimes, almost never, never.

(e) Socio-economic status: employment status, home ownership, type of accommodation, persons per room, and car ownership.

Variables was categorised as follows:

- Employment status: employed, unemployed, housewife, and retired.
- Home ownership: owned, rented from private sector, rented from council or housing association.
- Type of accommodation: based on Scottish Housing Survey (1991), type of accommodation defined as flat, semidetached, 4 in a block, and terraced house, detached house, bungalow.
- Persons per room: number of rooms available divided by number of people at household. This was a numerical variable.

- Car ownership: having car, no car .

(f) Deprivation Category: was measured by Carstairs and Morris (1991) Deprivation Category index (Depcat) as described in this chapter section 1.1. It was used as an additional indicator of socio-economic deprivation of the respondents.

(g) Access to hospital: home distance from Stobhill Hospital, how transport to hospital is arranged.

The variables were rated as follows:

- Home distance from Stobhill Hospital were recorded in miles. These were numerical variables.

- Transport to hospital was categorised as follows: private car (own or relatives' car), public transport, walking, and hospital ambulance.

(h) Comorbidity: this was investigated by asking patients whether they were admitted to hospital during the last year prior to their recent illnesses (Appendix VIII).

4.4.2. *Acceptability questionnaire*

This was a 12-item short questionnaire to examine how the study population reacted to the study (Appendix IX). It included items on: easiness of understanding the questionnaires, relevance of the questions to the patients, preferences on how the patients would like to be assessed (that is, whether they prefer to be interviewed or to fill in a questionnaire by themselves), feelings about interview, and the preference on setting (that is, whether they prefer to be interviewed at home or in the clinic). These are important questions since many clinicians argue that assessing patients through interview is too upsetting particularly if it is conducted in the home environment (Montazeri et al., 1996c).

4.4.3. *Quality of life: patients' perceptions*

There were two open-ended questions to find out what quality of life means to the patients. Patients were asked what quality of life is. They did not receive any special instruction and were given freedom to mention as many areas or factors as they wanted. They were then asked what a good quality of life is for them and to rank nominated factors in order of importance.

4.5. Additional study measures

4.5.1. *Clinical variables*

These were extracted from case notes and only recorded for lung cancer patients not controls. These included:

- Histologic types of the disease: small cell lung cancer, non-small cell lung cancer, and unspecified or others such as mesothelioma (pleura).
- Stage of the disease: limited to chest, and extensive (metastatic disease identified outside chest)
- Weight loss: significant weight loss, weight steady, possible weight loss, no comments in case notes

Types of treatment received: surgery, chemotherapy, radiotherapy or no active treatment policy (best supportive care).

4.5.2. *ECOG Performance Scale*

This is an observer rating of physical ability developed by the Eastern Cooperative Oncology Group-ECOG (Zubrod et al., 1960). It is a 5-grade scale ranging from zero to 4. Zero indicates that patient is able to carry out all normal activities and 4 represents that the patient is completely disabled (Table 5.6).

5.6 ECOG Performance Status Scale

Score	Definition
0	Able to carry out normal activities without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out light work
2	Ambulatory and capable of all self-care but unable to carry out any work; up and about more than 50% of waking hours
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on self-care; totally confined to bed or chair

5. Data collection

After approval from Stobhill Hospital Ethical Committee and GPs' preliminary agreements, data collection began on 1st January 1995. Baseline assessment was finished by the end of December 1995 and the follow-up interviews ended by the 10th of April 1996. In this section the ways in which data were collected and interviews were carried out are described.

5.1. Baseline data collection

After GP referral and selection of patient by the chest consultant (either suspected lung cancer cases or chronic respiratory controls), they were referred to the study coordinator. Permission was first obtained from the patient's GP, and if there was no objection the patient was contacted to ask his or her permission and to arrange a convenient time for interview. At this stage, the patient was introduced to the researcher.

Interviews were carried out either in the clinic or at the patients' homes. There were two chest consultants. One of the consultants asked that his patients should only be interviewed in the clinic. The other consultant agreed for his patients to be interviewed either at home or in the clinic.

Home interviews usually were arranged before the patient was seen by the consultant, whereas in the clinic interviews took place after the patient had seen the consultant in a separate room. The procedure of data collection at baseline is shown in Figure 5.2.

5.3. Follow-up data collection

For follow-up interviews the patient's GP was first contacted to ask his or her permission and confirm that the patient was still alive and under the GP's care. Subsequently, a letter was sent to each lung cancer patient signed by one of the chest consultants (controls were not followed-up). They were asked if they were willing to be interviewed for the second time. There was a telephone number for patients to call the study coordinator and indicate if they do not wish to participate in the follow-up interview (Appendix X). If there was no reply, that was taken as a sign of the patient's agreement. Then, the patient was contacted and a convenient time was arranged for interview either at home or in the clinic. If a patient did not have a telephone number or his or her name was not listed in the telephone directory, a letter was sent by the researcher asking the patient to contact the researcher and indicate a convenient time for interview (Appendix XI). The procedure of data collection at follow-up is shown in Figure 5.2.

5.3. Interviewer-administered approach

Data were collected via a series of interviewer-administered approach. Although the NHP, the EORTC QLQ-C30, and the EORTC QLQ LC13 are designed as a self-administered questionnaire, the literature indicates that they can be administered in interview form as well. In the case of the NHP, the user's manual indicates that the questionnaire can be used as part of an interview (Hunt et al., 1993). For the EORTC questionnaires the authors reported that the mode of administration does not influence the patients'

responses (Aaronson et al., 1993). Thus, in this study these questionnaires were administered in interview form.

This method of data collection was used because one way of collecting high-quality data in quality of life studies is by interview (Cella, 1995a). It is argued that an interview is a more sensitive way of collecting accurate quality of life data as opposed to data collection by a self-administered questionnaire (Anderson et al., 1986). Relying solely on self-reporting questionnaires to assess quality of life can result in many problems such as missing data and inconsistent responses (Cella, 1995b). In addition, it is argued that self-administered instruments may cause some cognitive problems. In a study of quality of life in lung cancer patients, it was reported that elderly patients often had difficulties in understanding the different response formats. Patients with lower educational status also were sometimes afraid to make mistakes while filling in the questionnaire (Bernhard et al., 1995).

5.4. Time spent interviewing and traveling

The home interviews were not restricted to particular days or times and took place throughout the week, including evenings and weekends based on the patients' preferences. For each home interview the researcher traveled by means of a private car or bus and usually took two to three hours to conduct an interview. As described earlier, clinic interviews took place from Monday to Friday within the working hours. In the clinic, based on the patient's situation (consultant examination, medical tests, etc.) the researcher usually waited for one to two hours to carry out the interview. To set up the study and collect data about 1460 trips* to Stobhill Hospital or patients' homes were made, in total near 10,000 miles of travelling.

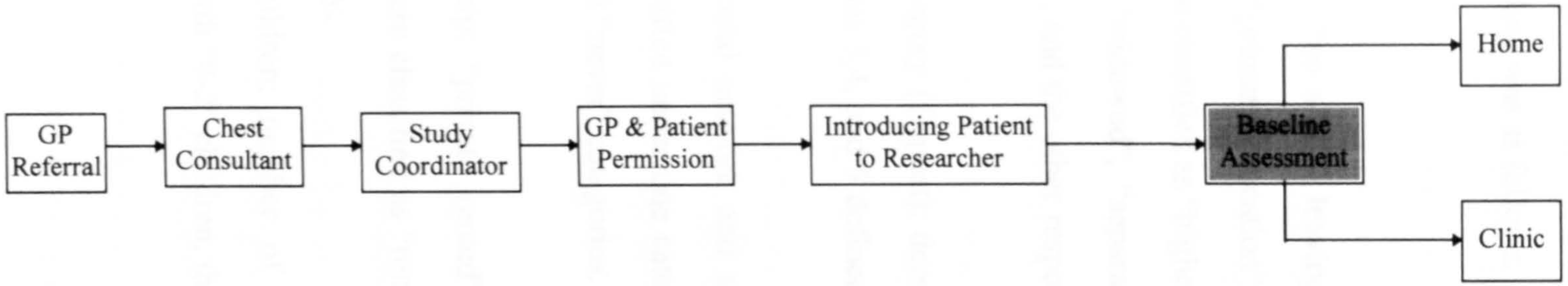
* Each trip defined as a journey from the Department of Public Health University Glasgow or the Ruchill Hospital (the researcher's base) to Stobhill Hospital, and patients' homes, and the return journey also was counted as one trip.

5.5. Other sources of identification of cases

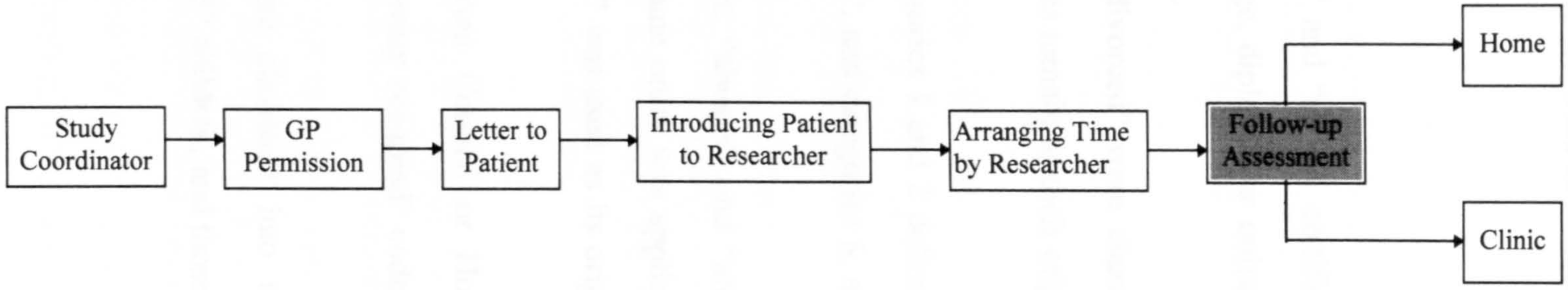
In the baseline interviews in addition to GP referrals, other sources of identification of possible cases were considered. These included: the "bronchoscopy" diary list, "pathology" results, internal referrals (referrals by other consultants in Stobhill Hospital to chest physicians where it was possible), the in-patient list in the Respiratory Medicine ward, and the Oncology Clinic.

Figure 5.2 The procedure of data collection

A. Baseline data collection (for both cases and controls)



B. Follow-up data collection (only for lung cancer cases)



6. Analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS) for Windows (Norusis, 1993). It was realised that for some response categories the numbers and frequencies were rather small, thus to be able to carry out tests of significance, some categorical variables were re-coded. The procedure of re-coding was as follows.

6.1 Coding

1. Education level: "no school leaving certificate" and "school certificate" were classified as "primary education", and "college, diploma, or university qualifications" were classified as "higher education".

2. Marital status: "widowed", "separated", and "divorced" were classified under one category, and the other response categories remain as their original coding.

3. Deprivation Category (Depcat): deprivation categories 1 and 2 defined as "affluent", categories 3,4, and 5 defined as "middle", and categories 6, and 7 as "deprived".

4. Variables on social network and social support: "always" and "almost always" were classified under one category. The same order was applied to "almost never" and "never" categories. "Sometimes" was used as its original coding.

5. Home ownership: "private rented", "rented from Council or Hosing Association" all were classified as "rented", and "owner occupied" coded as its original category.

6. Number of children: number of children were classified into three categories: those with "0-2" children, those with "3-5" children, and those "6-8" children.

7. Finally, according to the manual of the NHP and the EORTC questionnaires, patients' responses to these questionnaires were converted to a numerical basis to provide sub-scales as defined in this chapter ranging from zero (0) to 100. (Appendix XII and Appendix XIII)

6.2 Presentation of data and statistical tests

6.2.1 *Categorical data and Chi-square test*

For categorical data, numbers and percentages of responses for each response category of each variable were used. These were followed by Chi-square test where it was necessary to investigate associations or differences between different variables.

6.2.2 *Numeric data and non-parametric tests*

For numerical data, means and standard deviations (SD) were used as summary statistics followed by non-parametric tests for comparison. Parametric tests such as t-test were not used because parametric tests are based on the assumption that data are normally distributed (Bland, 1987). Since in this study the distribution of numeric data were rather skewed, non-parametric tests, where the analysis are based on free distribution, were used (Everitt, 1995). The following tests were performed for the analysis.

1. Mann-Whitney U test (also known as Wilcoxon-Mann-Whitney test or Wilcoxon Rank Sum test): is a distribution-free method used as an alternative to the t-test assessing whether there was a significant difference between scores of two independent samples (groups). The test does not use the actual values of the observations, but replaces them with ranks. The hypothesis is that the mean ranks are equal in two groups. If the mean ranks are equal, the groups are similar. In contrast, if the mean rank is substantially higher in one

group than the other, the difference is considered to be significant (Everitt, 1995).

2. Kruskal-Wallis test: this is a distribution-free method used as an alternative to the "one way analysis of variance" (ANOVA) assessing whether there were significant differences between scores of more than two independent samples. The test does not use the actual values of the observations, but replaces them with ranks (Everitt, 1995).

3. Wilcoxon Matched-Pairs Signed-Rank test: this is a distribution-free method used as an alternative to the paired t-test assessing whether there was a significant difference between scores of two dependent samples. The test does not use the actual values of the observations, but replaces them with ranks (Everitt, 1995).

6.2.3 *Logistic regression analysis*

A logistic regression analysis was performed to assess the relationship between outcome variables (dependent variables) and independent factors. The test predicts whether an event will or will not occur, as well as identifying the variables useful in making the prediction (Norusis, 1994).

To carry out the analysis, the dependent variables (outcomes) can only have two values (binary), but the independent variables may be numerical, categorical, ordered, etc. For example, to predict which variables (independent factors) predict patients' "global quality of life" (outcome variable), first patients should be classified in two groups. Those say with "very poor or poor" quality of life in one group, and those with "good or very good" quality of life in the second group. Then, input variables (independent factors) such as age, sex, social background, diagnosis, etc. may be used to

investigate which of these variables best predict the outcome, here the "global quality of life". The analysis indicates which variables significantly contribute to the outcome.

6.2.4. *Cox regression analysis*

The analysis was performed to investigate the relationship between survival and the baseline quality of life. In this analysis the survival is the dependent variable and other variable(s) both numerical or categorical could be used as independent or predictor factor(s). The Cox regression coefficient indicates the relative risk between each independent variable and the outcome variable (survival), adjusted for the effect of the independent variable(s). Cox regression is also called proportional hazard model indicating that the relationship between survival and hazard is proportional. Thus, the analysis not only indicates the probability of survival, but also shows the probability of an event occurring, for example dying (Dawson-Saunders and Trapp 1994; Norusis, 1994).

In this study the analysis was performed to investigate whether the baseline quality of life as measured by the NHP and the EORTC QLQ-C30 was a predictor of survival or not. In doing so, the survival was calculated and examined against patients' baseline aggregate scores on the NHP, and the EORTC-QLQ-C30.

6.2.5. *Content analysis*

This was performed to analyse qualitative data obtained from the open-ended questions used in the "acceptability questionnaire" and questions on perception of the patients about quality of life as described in this chapter in sections 4.4.2 and 4.4.3.

To carry out the content analysis, first all responses were extracted from the questionnaires. Secondly, to designate the units to be coded, the "theme" of each response was characterised by placing it in a given category and then Chi-square test was performed (Holsti, 1969).

6.3. Sample size and the power of the study

This was a prospective study, therefore it was not realistic to calculate sample size and the power of the study beforehand. However, based on the existing data already presented in this chapter (Tables 5.3 and 5.4), it was thought that for principal comparison between cases and controls at least a sample of 200 patients (100 cases and 100 controls) was necessary. A study of this size has a power of 90% to detect a difference of 20% between cases and controls at 5% significance level (Machin and Campbell, 1987). The actual sample obtained in this study was 238 (129 cases and 109 controls). This is fully presented in the result section.

7. Limitations and difficulties

Although the study was designed carefully to avoid any pitfalls, there were both limitations and difficulties in the research methodology.

7.1. Study design

The initial design of the study was to interview cases before diagnosis, but when the study started it was realised that this was not always possible. Therefore, the cases were interviewed either before confirmed diagnosis (intended design) or after confirmed diagnosis but before the start of treatment (alternated design). As mentioned earlier there were several practical limitations to the intended design. The most important consideration was to enter all cases with a confirmed diagnosis into the study in order to have a big

enough sample size. However, this allowed the study to examine an extra question, already described in section 2.1.

7.2. Follow-up of controls

Controls were not followed-up after their baseline interviews. Since this was a case-control study, it would have been better to have follow-up interviews for the controls as well, but time constraints and scarce resources did not allow this.

7.3. Interview settings

In the baseline interviews the primary intention was to visit patients either at their home or in the clinic. While most cases were interviewed in the clinic, most controls were interviewed at home. This meant that access to the cases' home environment was limited, and there was not enough data to compare cases and controls in this important aspect. This problem occurred for two main reasons: suspected cases were usually referred with short notice, and after referral, hospital appointments given very quickly. Thus, there was not enough time to arrange a home visit. In addition, as indicated before, one of the chest consultants did not agree to the researcher carrying out the baseline interview at his patients' home. However this problem, to some extent, was solved since in the follow-up interviews, most patients were interviewed at their home.

7.4. Blindness

Considering the above mentioned problem, there was a subjective impression that short notice referrals or those who received a quick hospital appointment, were suspected lung cancer cases. Although this was not always the case, the researcher had a feeling that in some instances he was not absolutely blind.

7.5. Sample

Comparing the number of cases to controls, the number of controls were less than cases. This was not identical to the study design. Since the selection of cases and controls was based on the decision of clinicians, a possible explanation is that there were not enough controls to match with suspected cases. This will be presented fully in the result section.

7.6. Missing cases

There were some cases missing. The reasons and the full picture of this will be presented in the result section. In summary, this was due to several factors: patients were referred through the internal referral system, not by GPs; sometimes the principal consultants were not in the clinic and therefore relying on junior doctors led to some cases being missed; on rare occasions the researcher was not in the clinic; and there was less than the expected number of cases from one of the chest clinicians.

7.7. Difficulties

The most difficult aspect of this study arose from interviewing patients at home or in the clinic. The advantages and disadvantages of interviewing patients at home or in the clinic are presented here.

The advantages of home interviews can be summarised as follows: (i) the interview had been arranged, therefore patients were expecting the researcher, (ii) there was enough time to carry out the interview, (iii) direct inspection of the home environment as part of research project was possible, (iv) patients felt the home interview was more conversational, (v) it was possible to arrange the interview for any time of the day and it was not restricted to the time of clinics, (vi) it was possible to interview patients before they were seen by consultants, while in the clinic it was usually not practical to interview

patients beforehand. The disadvantages of home interviews were: (i) getting permission was difficult and required several procedures including permission from GPs, patients, and sometimes their relatives, (ii) each interview took a long time including travelling time, and (iii) it was costly.

Interviewing a patient in the clinic had advantages and disadvantages. The advantages included: (i) the recruitment of patients was much easier than interviewing patients at home, which required further attempts to get permission from GPs and patients themselves, (ii) the patient saw the interviewer (researcher) as part of the clinical team and therefore felt more at ease, (iii) it saved time and reduced cost, and (iv) reduced the risk of refusal. The disadvantages of interviewing patients at the clinic were: (i) clinics were usually busy and thus, there was a risk of interference with clinical teams, (ii) patients had already waited for a long time to see clinicians, therefore the researcher was more under ethical pressure in the clinic, (iii) sometimes it created extra anxiety in patients, wondering what was the purpose of the interview despite a clear explanation at the beginning of the each interview.

CHAPTER SIX

6

RESULTS

Contents

- Introduction

1. Study population

2. Baseline assessments

3. Follow-up assessments

4. Evaluation of study acceptability

5. Patients' perceptions of quality of life

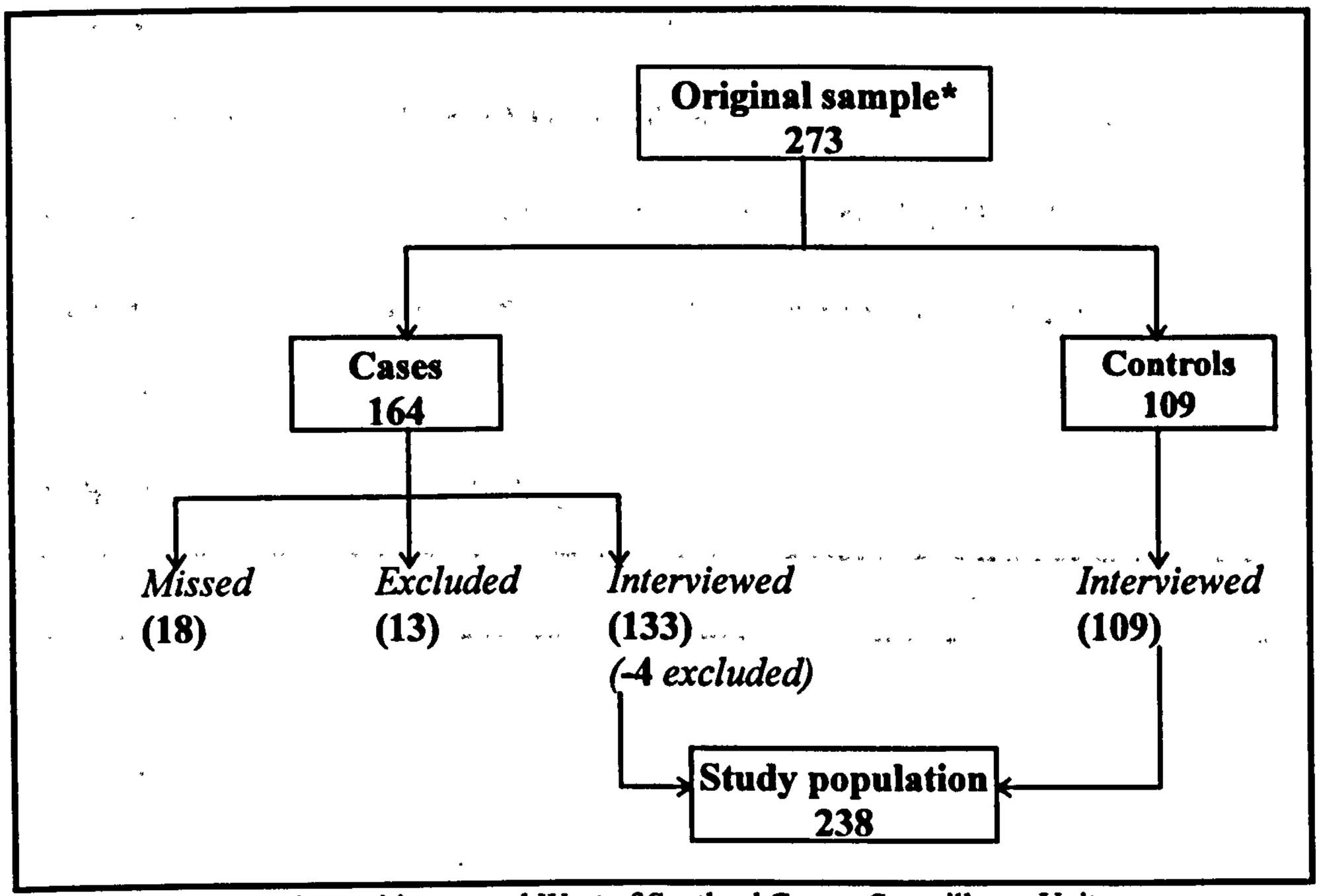
Introduction

Based on the study objectives the presentation of findings will follow in five distinct parts: study population, baseline and follow-up assessments, the evaluation of study acceptability, and finally patients' perceptions of quality of life.

1. Study population

Figure 6.1 is a schematic presentation of the patients recruited to the study. The study population consisted of 273 patients. Two hundred and forty-two interviews of patients were completed. Four lung cancer patients were excluded from the study. These 4 cases were excluded because they were referred and diagnosed in 1994 while the criteria for inclusion of the patients in the study was that they should have been referred and diagnosed in 1995. Thus, overall, data obtained from 238 patients were analysed. Of these, 129 patients had a confirmed diagnosis of lung cancer and 109 were chronic respiratory disease controls. However, the number of controls were less than cases. This was due to the selection of cases and controls not being under the researcher's direct control, and because the study design made the researcher blind to the diagnosis. He was thus, not able to inform clinicians about the numbers of cases and controls recruited to the study. Finally, the clinicians' outpatient department was very busy and in practice it was not possible for them to choose exactly one control per each case.

Figure 6.1 A schematic presentation of study samples



* From local General Practitioners and West of Scotland Cancer Surveillance Unit.

The response rate was 89% (238 of 273) and there were no refusals, but there were two other groups of cases: first, those who were excluded from the study before baseline interviews (13 patients-the first group), and second, those who were missed during the study period (18 patients-the second group). The main difference between these two groups lies on the fact that the patients in the first group were caught by the researcher, while the patients in the second group were not known to the researcher until their names were identified from the cancer registry database.

Since from the methodological stand-point this is an important issue, for the first group, the characteristics and the reasons why they were excluded are given in Table 6.1. For the second group (missing cases), this was extracted at

the end of April 1996 based on data provided from the West of Scotland Cancer Surveillance Unit. This was done by providing a list of cases who were registered from Stobhill Hospital in 1995 and then, the list was checked against the list of cases who participated in the study. The characteristics of these missing cases, and reasons why they were missed out are also given in Table 6.1.

Table 6.1.

Table 6.1 Excluded and missing cases

	Excluded cases (n = 13)	Missing cases (n = 18)
	No.	No.
Sex		
male	8	13
female	5	5
Lung cancer diagnosis		
non-small	6	4
small cell	0	4
unspecified	4	10
not available	3	0
Reasons why patients were excluded or missed		
Identified after the treatment	5	0
Internal referral	0	3
Emergency admission	1	9
Not well enough to be interviewed	4	0
Died before baseline interview	2	0
Mental illness	1	0
Clinicians did not introduce the patients to the researcher to be interviewed	0	6

1.1. Socio-demographic characteristics

The socio-demographic characteristics of the study population are shown in Table 6.2. There were no significant differences between cases and controls, except for age ($p = 0.02$) and comorbidity ($p = 0.02$). The controls tended to be slightly younger than cases and had more comorbidity.

Out of 238 patients, 134 (56%) were males and 104 (44%) females. Overall, the majority of cases and controls were in their 60s (mean age 66.1 years, sd = 9.8), married (56%), retired (56%), with a low level of education (95%), most from deprived areas (60%), and living in rented houses (66%). Classifications of patients' characteristics are fully described in the methods section.

Table 6.2 Socio-demographic characteristics of study population

	Cases (n = 129) No. (%)	Controls (n = 109) N0. (%)	Total (n = 238) No. (%)	P
Sex				
male	77 (60)	57 (52)	134 (56)	
female	52 (40)	52 (48)	104 (44)	
				0.3
Age				
mean (SD)	67.5 (9.1)	64.6 (10.4)	66.1 (9.8)	
range	40-87	38-83	38-87	
				0.02*
Marital status				
married	77 (60)	56 (51)	133 (56)	
single	7 (5)	10 (9)	17 (7)	
widowed/divorced/separated	45 (35)	43 (40)	88 (37)	
				0.3
Educational level				
primary	122 (95)	104 (95)	226 (95)	
higher	7 (5)	5 (5)	12 (5)	
				0.8
Employment status				
employed	17 (13)	17 (16)	34 (14)	
unemployed	8 (6)	14 (13)	22 (9)	
housewife	24 (19)	26 (24)	50 (21)	
retired	80 (62)	52 (48)	132 (56)	
				0.1
Deprivation category				
affluent	23 (18)	17 (16)	40 (17)	
middle	32 (25)	22 (20)	54 (23)	
deprived	74 (57)	70 (64)	144 (60)	
				0.6
Comorbidity				
yes	18 (14)	28 (26)	46 (19)	
no	111 (86)	81 (74)	192 (81)	
				0.02*
House ownership				
owned	48 (37)	33 (30)	81 (34)	
rented	81 (63)	76 (70)	157 (66)	
				0.3
Car ownership				
yes	37 (29)	25 (23)	62 (26)	
no	92 (71)	84 (77)	176 (70)	
				0.3

* Significant at 5% level.

1.2. Social network and social support

Table 6.3 shows the patients' social network and social support systems as indicated by frequency of visits from their children, families, support offered by their children, families, contact with neighbours, and support received from them. There were no significant differences for all the variables measured between cases and controls, except for support received from their children (p = 0.007). The controls reported that they received less support from their children as compared to the cases.

Overall, the majority of patients (n = 128, 54%) indicated that their children were visiting them "always/almost always", while a high proportion (n = 102, 43%) reported that they were not visited by their relatives at all. When patients were asked "how often do you contact your neighbours?", the majority (n = 123, 52%) again stated "almost never/never".

The pattern of responses to the variable on support from children, relatives, and neighbours was even worse. The majority (n = 122, 52%) stated that they did not receive any support from their children. Also most patients reported that they did not receive any support from their relatives (n = 187, 79%) and form their neighbours (n = 172, 72%).

Table 6.3 Patients' social network and social support

	Cases (n = 129) No. (%)	Controls (n = 109) No. (%)	Total (n = 238) No. (%)	P
Children's visit				
always/almost always	71 (55)	57 (52)	128 (54)	
sometimes	26 (20)	16 (15)	42 (18)	
almost never/never	32 (25)	36 (33)	68 (28)	
				0.3
Relatives' visit				
always/almost always	49 (38)	38 (35)	87 (37)	
sometimes	26 (20)	23 (21)	49 (20)	
almost never/never	54 (42)	48 (44)	102 (43)	
				0.9
Contact with neighbours				
always/almost always	45 (35)	35 (32)	80 (33)	
sometimes	22 (17)	13 (12)	35 (15)	
almost never/never	62 (48)	61 (56)	123 (52)	
				0.4
Receiving support from children				
always/almost always	63 (49)	33 (30)	96 (40)	
sometimes	7 (5)	13 (12)	20 (8)	
almost never/never	59 (46)	63 (58)	122 (52)	
				0.007*
Receiving support from relatives				
always/almost always	20 (16)	11 (10)	31 (13)	
sometimes	10 (8)	10 (9)	20 (8)	
almost never/never	99 (76)	88 (81)	187 (79)	
				0.45
Receiving support from neighbours				
always/almost always	23 (18)	18 (17)	41 (17)	
sometimes	13 (10)	12 (11)	25 (11)	
almost never/never	93 (72)	79 (72)	172 (72)	
				0.95

1.3. Housing, and family structure

Dwelling types and the patients' home distance from the Stobhill Hospital were investigated. There were no significant differences between cases and controls. These are shown in Table 6.4.

Accommodation was defined as in the Scottish Housing Survey (1991) classification. It was found that 97 patients (41%) lived in a "flat", 61 (25%)

* Significant at 5% level.

in "semi-detached" houses, 33 (14%) in "4 in a block" houses, and the remaining 47 (20%) in "terrace house/house/others". The mean distance from patients' homes to Stobhill Hospital was 4.2 miles (SD = 3.5). Only a small number of patients (n = 38, 16%) used the hospital ambulance, whereas 111 patients (47%) stated that they used their own or their relatives' car to travel to hospital for their first visit to the hospital outpatient clinic. The remaining 89 patients (37%) reported that they used public transport. There was significant difference between cases and controls (p = 0.002) indicating that controls used more public transport and less private car and hospital ambulance as compared to the cases.

The mean of "overcrowding", as measured by the ratio of people in the household to the number of available rooms, was 0.63 (SD = 0.27) person per room. One hundred and thirty-five patients (57%) had 0-2 children, 91 (38%) 3-5, and the remaining 12 patients (5%) had 6-8 children.

Table 6.4 Patients' housing and family structure

	Cases (n = 129) No. (%)	Controls (n = 109) No. (%)	Total (n = 238) No. (%)	P
Types of dwelling				
flat	53 (41)	44 (40)	97 (41)	
semidetached	35 (27)	26 (24)	61 (25)	
4 in a block	17 (13)	16 (15)	33 (14)	
terrace house/house/others	24 (19)	23 (21)	47 (20)	
				0.9
Home distance from Stobhill Hospital				
mean (SD)	4.3 (3.5)	4.1 (3.4)	4.2 (3.5)	
range	0.25-15	0.25-25	0.25-25	
				0.7
Means of travelling to Stobhill Hospital				
private car (own or relatives' car)	69 (54)	42 (38)	111 (47)	
public transport/by walking	35 (27)	54 (50)	89 (37)	
hospital transport	25 (19)	13 (12)	38 (16)	
				0.002*
Travelling problem				
yes	13 (10)	15 (14)	28 (12)	
no	116 (90)	94 (86)	210 (88)	
				0.4
Problems (n = 28)				
long walk/health	8 (62)	11 (73)	19 (68)	
time/travel fair	5 (38)	4 (27)	9 (32)	
				0.7
Number of children				
0-2	69 (54)	66 (60)	135 (57)	
3-5	53 (41)	38 (35)	91 (38)	
6-8	7 (5)	5 (5)	12 (5)	
				0.6
Number of people in the household				
one	41 (32)	45 (41)	86 (36)	
two	65 (51)	38 (35)	103 (43)	
three	16 (12)	16 (17)	34 (14)	
four/five	7 (5)	8 (7)	15 (7)	
				0.1
Overcrowding (persons per room)				
mean (SD)	0.64 (0.26)	0.62 (0.28)	0.63 (0.27)	
range	0.25-1.33	0.13-1.33	0.13-1.33	
				0.7

* Significant at 5% level.

Cigarette smoking the main cause of lung cancer

A female patient with lung cancer

Living alone at a residential home in a severely deprived area

1.4. Patients' characteristics, local and national figures

In Table 6.5 the study population's characteristics with reference to some national and local figures are given.

In general, there were a reasonable agreement between the characteristics of the study population with that of local and national statistics. However, car ownership and employment status in study population were very different from reference figures. Since a high proportion of the study population was a group of retired elderly patients, this was not unexpected.*

Table 6.5 Patients' characteristics compared with available local and national figures (all figures are percentages)

	Study population n = 238	Northern sector of Glasgow n = 169,016	Greater Glasgow He Board n = 916,600	Scotland n= 5,132,400
Sex				
male	56	48	48	48
female	44	52	52	52
Deprivation Category				
affluent	17	19	18	20
middle	23	29	32	62
deprived	60	52	50	18
House ownership				
owner occupied	34	46	45	33
rented	66	54	55	67
Types of dwelling				
flat	41	50	51	36
semidetached	25	14	12	20
4 in a block	14	14	12	27
detached/others	20	22	24	17
Car ownership	29	46	42	57
Unemployment	9*	20	20	13
Overcrowding mean (sd)	0.63 (0.27)	n/a	n/a	0.25 (0.11)

* Considering that only 56 patients (23%) of all study sample were able to work (see table 6.2), then the real figure for unemployment is 22 out of 56 which is 39%. This is much higher than the unemployment rate in the northern sector of Glasgow or Greater Glasgow.

2. Baseline assessments

The baseline assessments were made either at first presentation to the consultants in the outpatient clinic or after referral by the General Practitioners (GPs) and before consultant visit at patient's home. Quality of life was measured by the Nottingham Health Profile (NHP), and the European Organisation for Research and Treatment of Cancer, Core Quality of Life Questionnaire (EORTC QLQ-C30) and its supplementary Lung Cancer Questionnaire (EORTC QLQ-LC13).

2.1 The Nottingham Health Profile (NHP)

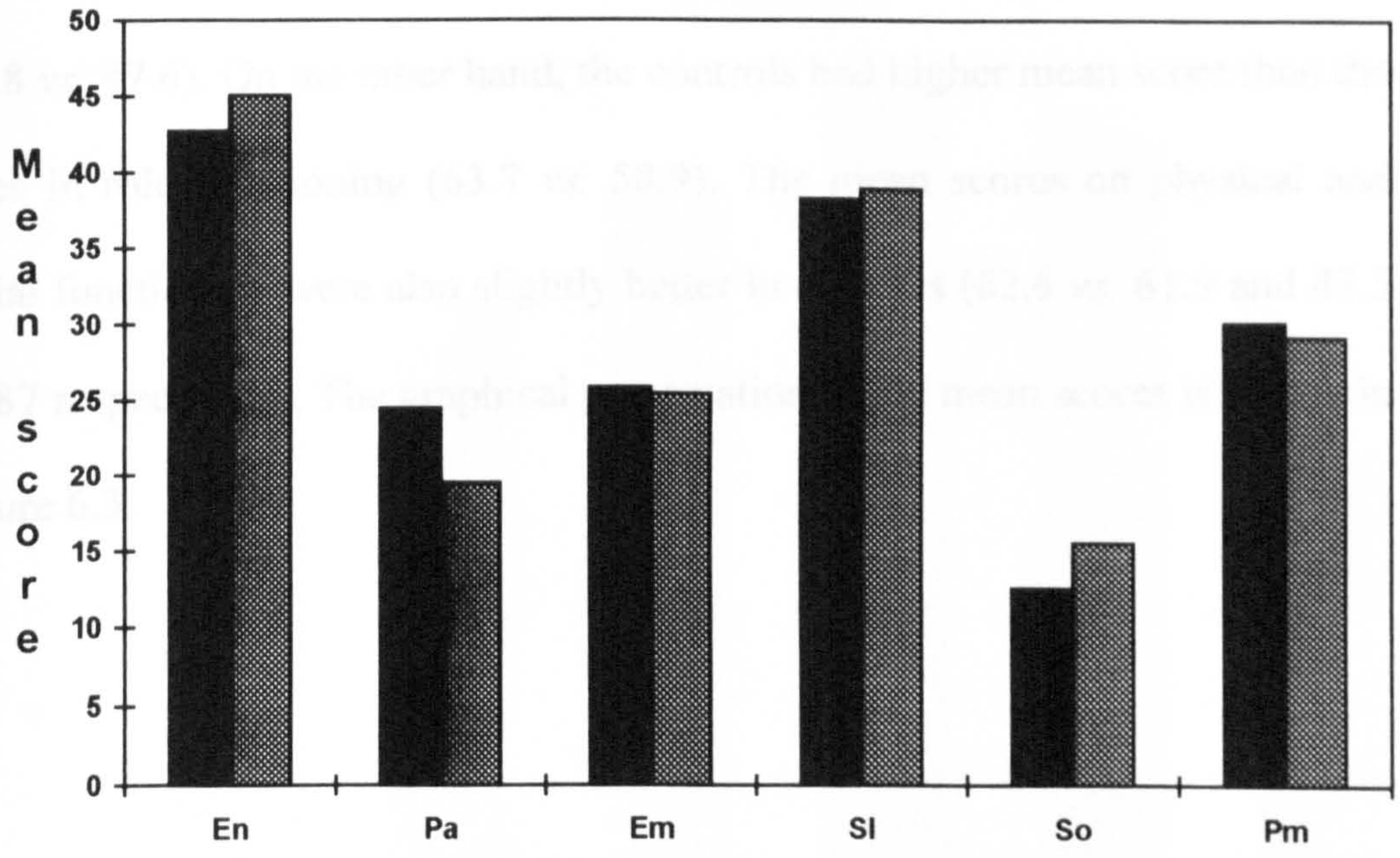
Table 6.6 presents results obtained from the analysis of the baseline assessment of the NHP-Part I for the cases and controls. The higher values indicate more perceived health problems. There were no significant differences between cases and controls in all areas measured, these were, energy, pain, emotional reactions, sleep difficulties, social isolation and physical mobility. However, in some areas the mean scores of controls were higher than cases indicating that they had more perceived problems. These were: energy (45.1 *vs.* 42.7), and social isolation (15.6 *vs.* 12.6). In contrast, the cases had more perceived problems than controls in pain (mean score 24.5 *vs.* 19.5), and physical mobility (32.2 *vs.* 29.3). The differences between mean scores on emotional reactions and sleep were very small: 25.8 in cases *vs.* 25.4 in controls (for emotional reactions), and 39 in controls *vs.* 38.3 in cases (for

sleep). The mean scores on the NHP by cases and controls are shown graphically in Figure 6.2.

Table 6.6 Baseline scores on NHP-Part I by cases and controls (the higher values indicate more perceived health problems, min.: 0, max.: 100)

	Cases (n = 129) Mean (SD)	Controls (n = 109) Mean (SD)	P+
Energy	42.7 (41.6)	45.1 (39.9)	0.6
Pain	24.5 (29.2)	19.5 (26.7)	0.1
Emotional reactions	25.8 (24.2)	25.4 (23.9)	0.9
Sleep	38.3 (32.5)	39.0 (31.6)	0.8
Social isolation	12.6 (22.0)	15.6 (22.2)	0.2
Physical mobility	32.2 (28.0)	29.3 (27.3)	0.8

Figure 6.2 NHP-Part I by Cases and Controls



En = Energy, Pa=Pain, Em=Emotional reactions, Sl=Sleep, So=Social isolation, Pm=Physical mobility

+ 2-tailed probability based on Mann-Whitney U test.

2.2 The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ-C30 and QLQ-LC13)

2.2.1. *Functioning and global quality of life*

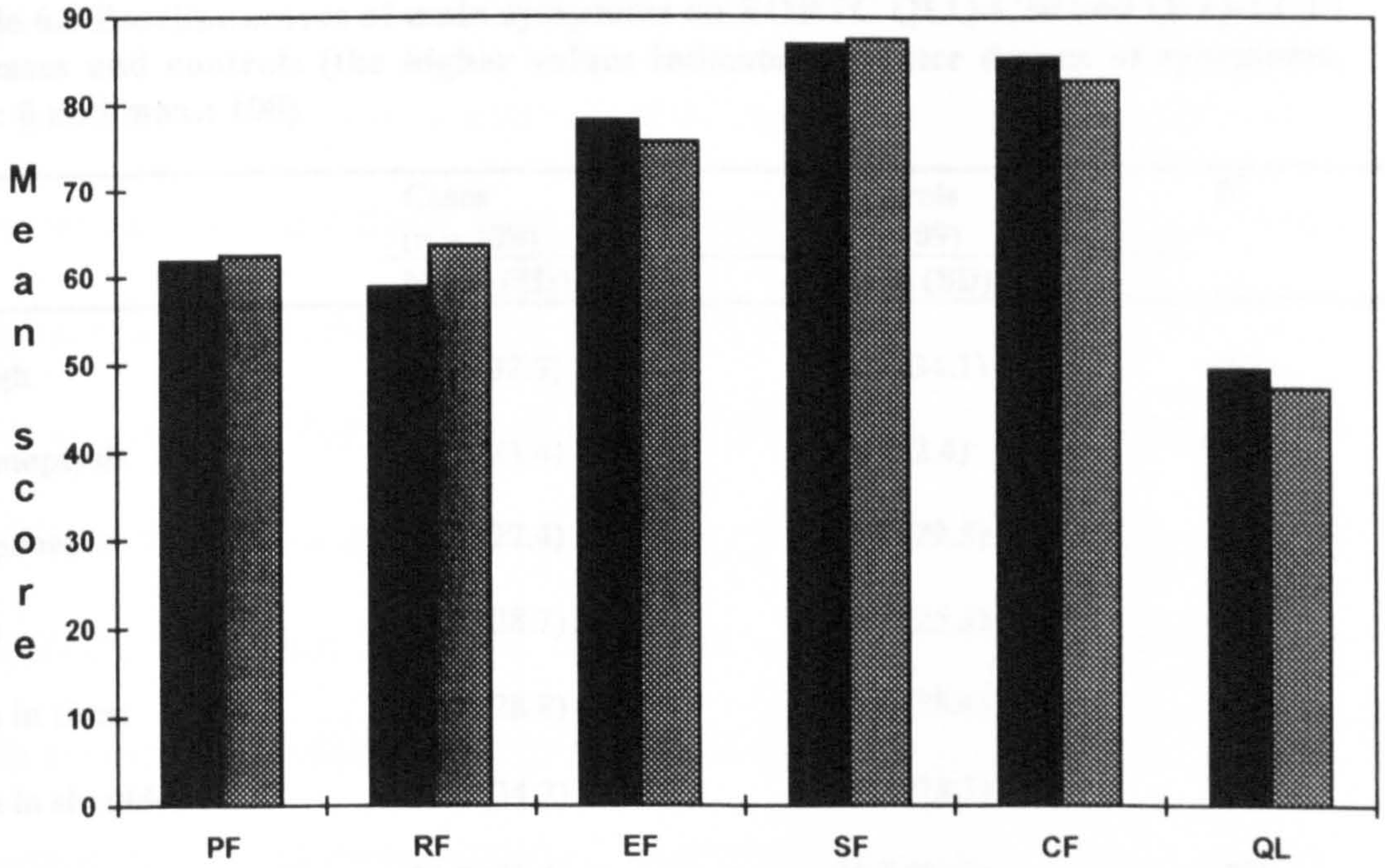
Table 6.7 presents the results obtained from the EORTC QLQ-C30 by cases and controls. This table includes scores on 5 functioning scales (physical, role, emotional, social, cognitive) and the global quality of life. The higher values indicate higher level of functioning and a better global quality of life.

There were no significant differences between cases and controls. However, the cases had higher mean scores than the controls in emotional functioning (78.4 *vs.* 75.9), cognitive functioning (85.5 *vs.* 82.9), and global quality of life (49.8 *vs.* 47.6). On the other hand, the controls had higher mean score than the cases in role functioning (63.7 *vs.* 58.9). The mean scores on physical and social functioning were also slightly better in controls (62.6 *vs.* 61.9 and 87.5 *vs.* 87 respectively). The graphical presentation of the mean scores is shown in Figure 6.3.

Table 6.7 Baseline functioning and global quality of life scores on EORTC QLQ-C30 by cases and controls (the higher values indicate a higher level of functioning and quality of life, min.: 0 and max.: 100)

	Cases (n = 129)	Controls (n = 109)	P+
	Mean (SD)	Mean (SD)	
Physical functioning	61.9 (27.6)	62.6 (26.1)	1.0
Role functioning	58.9 (37.2)	63.7 (33.9)	0.4
Emotional functioning	78.4 (21.5)	75.9 (23.2)	0.5
Social functioning	87.0 (23.2)	87.5 (22.4)	1.0
Cognitive functioning	85.5 (20.9)	82.9 (24.2)	0.6
Global quality of life	49.8 (23.1)	47.6 (24.7)	0.5

Figure 6.3 EORTC QLQ-C30 by Cases and Controls



+ 2-tailed probability based on Mann-Whitney U test.

2.2.2. *Main symptoms*

Tables 6.8 presents the mean scores of main symptoms on the EORTC QLQ-30 and QLQ-LC13. The higher values indicate a greater degree of symptoms. There were no significant differences between cases and controls except in pain (p = 0.04) and loss of appetite (p = 0.001). The cases reported significantly more problems in these symptoms. Although not significant, the mean scores of the cases also were higher than the controls for the following symptoms: pain in shoulder (27.4 *vs.* 20.2), sleep difficulties (30.7 *vs.* 27.2), fatigue (37.3 *vs.* 34.6). In contrast, the mean scores of the controls were higher for cough (51.7 *vs.* 46.8), dyspnoea (43 *vs.* 37.7), and haemoptysis (10.1 vs. 8.6).

Table 6.8 Baseline scores of main symptoms on EORTC QLQ-C30 and QLQ-LC13 by cases and controls (the higher values indicate a greater degree of symptoms, min: 0 and max.: 100)

	Cases (n = 129) Mean (SD)	Controls (n = 109) Mean (SD)	P+
Cough	46.8 (32.7)	51.7 (34.1)	0.2
Haemoptysis	10.1 (23.4)	8.6 (22.4)	0.3
Dyspnoea	37.7 (27.4)	43.0 (29.3)	0.2
Pain	27.1 (28.7)	19.7 (25.3)	0.04•
Pain in chest	21.7 (28.8)	21.1 (28.9)	0.8
Pain in shoulder	27.4 (34.7)	20.2 (28.3)	0.2
Pain elsewhere	24.8 (33.4)	24.8 (31.2)	0.8
Sleep difficulties	30.7 (37.2)	27.2 (35.2)	0.5
Fatigue	37.3 (29.2)	34.6 (29.3)	0.5
Appetite loss	34.4 (34.3)	21.1(30.1)	0.001•

+ 2-tailed probability based on Mann-Whitney U test.
• Significant at 5% level.

2. 3. Baseline quality of life and socio-economic deprivation

The relationship between baseline quality of life and socio-economic deprivation, as measured by the Carstairs and Morris (1991) Deprivation Category was investigated. Since there were no significant differences in mean scores between cases and controls, the following are results from pooled data. In fact, when the same analysis was performed separately for lung cancer patients and the controls the findings were similar to the findings from pooled data. Thus, to avoid repetition, only the pooled results are reported here.

2.3.1. *The NHP by Deprivation Category*

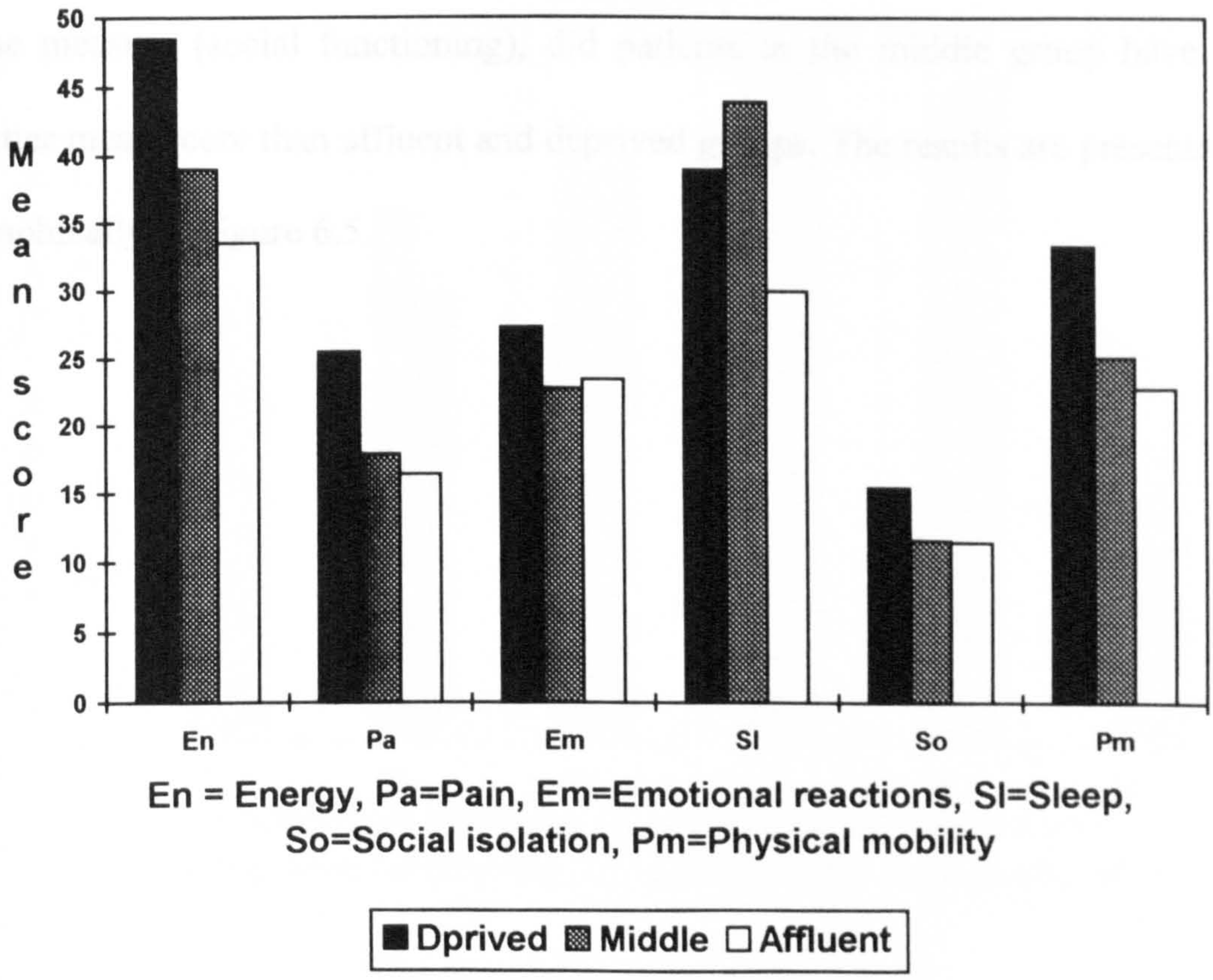
Table 6.9 presents baseline scores of all patients on the NHP-Part I by Deprivation Category (Carstaris and Morris, 1991), namely: affluent, middle, and deprived. The "one way analysis of variance" (ANOVA) was carried out to investigate whether there were statistically significant differences among mean scores of these three groups on the NHP-Part I or not. Except for mean scores on pain ($p = 0.03$) and physical mobility ($p = 0.03$) which indicated a significant difference among three groups, the other mean scores were not significantly different. However, there was a clear pattern of differences in mean scores among these three groups indicating that people of lower socio-economic status had more perceived health problems compared to the more affluent group. Only in one measure (sleep) did the middle group of patients have more perceived problems than the affluent and the deprived groups.

Figure 6.4 presents the mean scores on the NHP-Part I by Deprivation Category.

Table 6.9 Patients' baseline scores on NHP-Part I by Deprivation Category (the higher values indicate more perceived health problems, min: 0 and max.: 100)

	Affluent (n = 40)	Middle (n = 54)	Deprived (n = 144)	P[+]
	Mean (SD)	Mean (SD)	Mean (SD)	
Energy	33.5 (39.4)	39.0 (42.2)	48.5 (40.2)	0.07
Pain	16.4 (25.0)	17.9 (26.4)	25.5 (29.4)	0.03*
Emotional reactions	23.4 (25.1)	22.7 (21.9)	27.3 (24.4)	0.3
Sleep	30.0 (27.3)	44.0 (30.4)	39.0(33.5)	0.1
Social isolation	11.6 (23.1)	11.7 (20.5)	15.5 (22.4)	0.2
Physical mobility	22.9 (26.3)	25.2 (25.3)	33.4 (28.4)	0.03*

Figure 6.4 NHP-Part I by Deprivation Category



[+] Probability based on Kruskal-Wallis one way analysis of variance corrected for ties.
* Significant at 5% level.

2.3.2. *The EORTC by Deprivation Category*

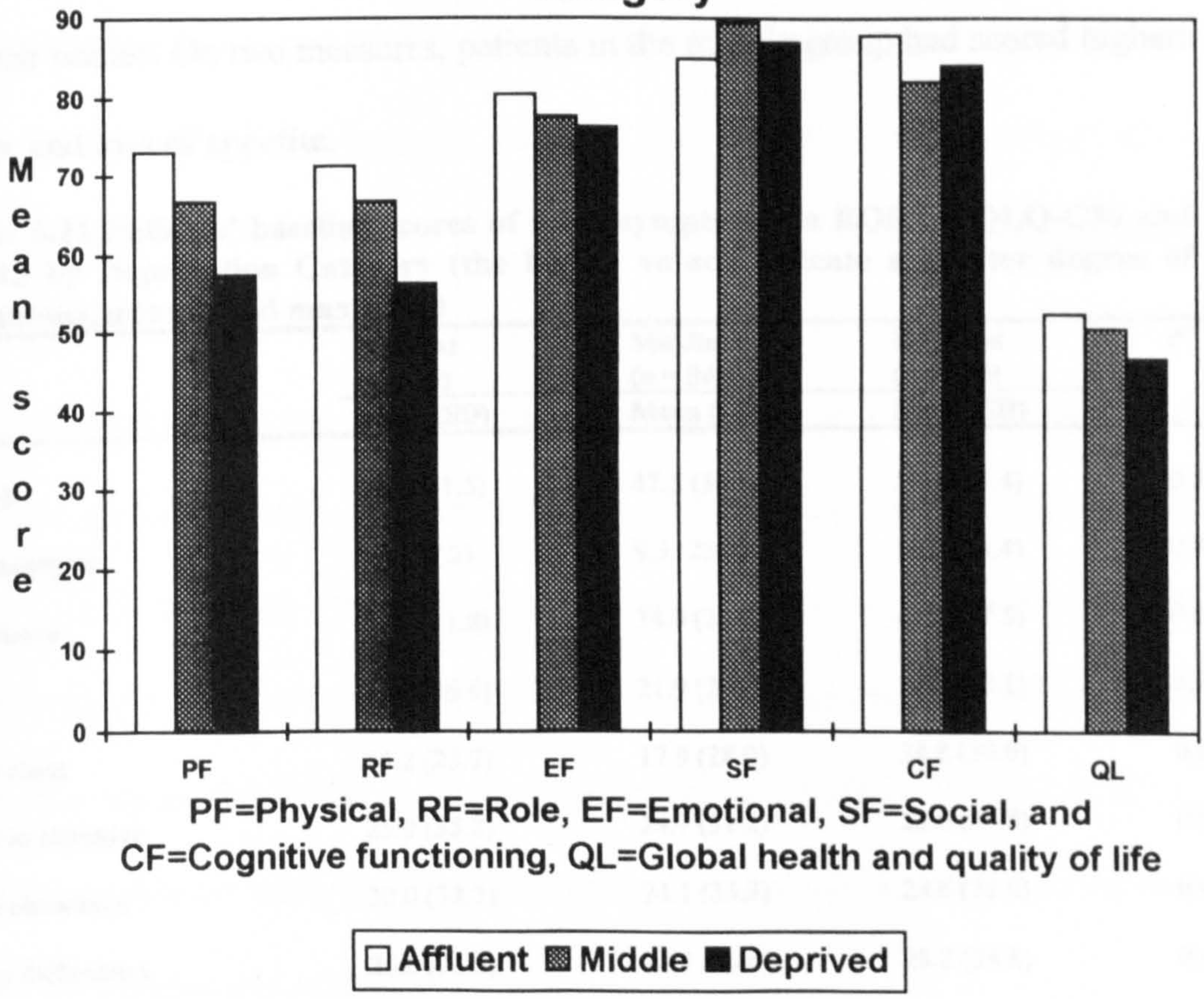
1. The mean scores of patients' functioning and global quality of life on the EORTC QLQ-C30 by Deprivation Category are shown in Table 6.10. Performing the ANOVA, there were significant differences among affluent, middle, and deprived groups in physical functioning ($p = 0.002$), and role functioning ($p = 0.02$) indicating that the patients of lower socio-economic status had a lower level of functioning. In other measures the differences were not statistically significant.

There was a clear trend of differences among these groups indicating that the patients in the deprived group had lower scores than the other groups. Only in one measure (social functioning), did patients in the middle group have a better mean score than affluent and deprived groups. The results are presented graphically in Figure 6.5.

Table 6.10 Patients' baseline functioning and global quality of life scores on EORTC QLQ-C30 by Deprivation Category (the higher values indicate a higher level of functioning and quality of life, min: 0 and max.: 100)

	Affluent (n = 40)	Middle (n = 54)	Deprived (n = 144)	P[+]
	Mean (SD)	Mean (SD)	Mean (SD)	
Physical functioning	73.0 (25.4)	66.7 (24.9)	57.5 (27.0)	0.002*
Role functioning	71.3 (33.8)	66.7 (37.6)	56.3 (34.9)	0.02*
Emotional functioning	80.4 (22.1)	77.6 (20.5)	76.3 (23.1)	0.5
Social functioning	84.9 (23.4)	89.5 (20.3)	87.0 (23.7)	0.5
Cognitive functioning	87.9 (20.7)	82.1 (23.8)	84.1 (22.4)	0.3
Global quality of life	52.7 (25.2)	50.8 (23.9)	47.0 (23.4)	0.2

Figure 6.5 EORTC QLQ-C30 by Deprivation Category



[+] Probability based on Kruskal-Wallis one way analysis of variance corrected for ties.
* Significant at 5% level.

2. Table 6.11 presents the mean scores of patients' symptoms on the EORTC QLQ-C30 and the QLQ-LC13 by Depcat. Performing the ANOVA, there were no significant differences among affluent, middle, and deprived groups, except for dyspnoea (p = 0.01) indicating that patients of lower socio-economic status had a significantly greater degree of dyspnoea as compared to the other groups.

However there were marked differences among these groups in the following symptoms: cough, haemoptysis, pain, pain in chest, and fatigue indicating that patients in the deprived group had more symptoms. In contrast, patients in the affluent group had more problems with: pain in shoulder, and pain in other parts of their bodies. On two measures, patients in the middle group had scored higher: sleep, and loss of appetite.

Table 6.11 Patients' baseline scores of main symptoms on EORTC QLQ-C30 and LC-13 by Deprivation Category (the higher values indicate a greater degree of symptoms, min: 0, and max.: 100)

	Affluent (n = 40) Mean (SD)	Middle (n = 54) Mean (SD)	Deprived (n = 144) Mean (SD)	P+
Cough	44.2 (31.5)	47.5 (34.6)	50.9 (33.4)	0.5
Haemoptysis	6.7 (17.2)	9.3 (22.8)	10.2 (24.4)	0.8
Dyspnoea	32.9 (31.8)	34.0 (26.0)	44.4 (27.5)	0.01*
Pain	23.3 (26.6)	21.9 (26.5)	24.5 (28.1)	0.8
Pain chest	14.2 (23.7)	17.9 (28.0)	24.8 (30.0)	0.06
Pain in shoulder	25.0 (35.2)	24.7 (31.2)	23.6 (31.8)	0.9
Pain elsewhere	30.0 (32.7)	24.1 (33.3)	23.6 (32.0)	0.4
Sleep difficulties	25.0 (33.5)	34.5 (36.6)	28.2 (36.8)	0.4
Fatigue	34.4 (32.6)	32.1 (27.4)	38.0 (28.9)	0.4
Appetite loss	27.5 (29.1)	29.6 (33.4)	28.0 (34.7)	0.8

+ Probability based on Kruskal-Wallis one way analysis of variance corrected for ties.
* Significant at 5% level.

2.4. Pain medication

When, based on the EORTC QLQ-C30, patients were asked "Did you take any medicine for pain", 124 patients (52%) responded "yes". There was no significant difference between cases and controls ($p = 0.08$). Of these, 17 patients (14%) stated that pain medication did not help them at all, 53 (42%) reported that it did help a little, 48 (39%) indicated that it did help quite a bit, and 6 patients (5%) said that it did help very much. Again, there was no significant difference between cases and controls ($p = 0.09$).

2.5. Prediction of baseline quality of life

It was hypothesised that patients' baseline quality of life as measured by the standard instruments (the NHP, and the EORTC questionnaires) may be the result of patients' socio-economic status or their social support systems rather than the effect of their diseases or health status alone. Thus, to examine such an hypothesis, some relevant subscales of the NHP Part-I and the EORTC QLQ-C30 were selected as outcome measures, and the socio-economic and support variables (such as family support) and some other psycho-social indicators as predictor variables. The selection of these subscales was due to the fact that it was thought these variables might explain how patients' socio-economic status and social support system contribute to their quality of life. A logistic regression analysis, as described in the methods section, was carried out to investigate this relationship.

2.5.1. *Emotional problems*

Based on patients' scores for emotional reactions on the NHP, they were divided into two groups, those with no emotional problems and those with emotional problems. It was found that several variables had significant value in predicting emotional problems. These were: marital status (being single, p = 0.002), family support (those who did not receiving any support, p = 0.03). In addition, the analysis indicated that energy (p = 0.002), sleep (p = 0.003), social isolation (p = 0.0003) and global quality of life (p = 0.01) were all predictors of emotional problems. Figure 6.6 shows a simplified print out of the logistic regression analysis.

Figure 6.6 Logistic regression analysis-Baseline emotional reactions

Number of cases included in the analysis: 238
Parameter coding (categorical data)

	Value	Freq	Coding (1)	(2)
NEIGHBOUR SUPPORT				
never/almost never	1	172	1.000	.000
sometimes	2	25	.000	1.000
almost always/always	3	41	.000	.000
FAMILY SUPPORT				
never/almost never	1	187	1.000	.000
sometimes	2	20	.000	1.000
almost always/always	3	31	.000	.000
CHILDREN SUPPORT				
never/almost never	1	122	1.000	.000
sometimes	2	20	.000	1.000
almost always/always	3	96	.000	.000
MARITAL STATUS				
married	1	133	.000	.000
single	2	17	1.000	.000
widowed/separated/divorced	3	88	.000	1.000
DEPRIVATION CATEGORY				
affluent	1	40	.000	.000
middle	2	54	1.000	.000
deprived	3	144	.000	1.000
CASE				
case	1	129	1.000	
control	2	109	.000	
SEX				
male	1	134	.000	
female	2	104	1.000	

Dependent Variable.. Baseline Emotional Reactions

* Constant is included in the model.

Beginning Block Number 1. Method: Enter

Variable(s) Entered on Step Number

1.. AGE Age
SEX sex
MARITAL Marital status
DEPCAT Deprivation Category
CASE Case or control
CHILHEL Support receiving from children
FAMILYH Support receiving from family
NEIGHBH Support receiving from neighbours
TEN1 Total energy-baseline
TP1 Total pain-baseline
TPM1 Total physical mobility-baseline
TSL1 Total sleep-baseline
TSO1 Total social isolation-baseline
XQL1 Global quality of life-baseline

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
AGE	.0133	.0245	.2959	1	.5865	.0000	1.0134
SEX(1)	-.2387	.5149	.2149	1	.6429	.0000	.7876
MARITAL			10.0246	2	.0067	.1537	
MARITAL(1)	-3.4208	1.1153	9.4065	1	.0022	-.1705	.0327
MARITAL(2)	-1.1271	.6247	3.2552	1	.0712	-.0702	.3240
DEPCAT			.5901	2	.7445	.0000	
DEPCAT(1)	-.0875	.6922	.0160	1	.8995	.0000	.9163
DEPCAT(2)	.3209	.5967	.2893	1	.5907	.0000	1.3784
CASE(1)	.2687	.4851	.3068	1	.5797	.0000	1.3082
CHILHEL			2.2999	2	.3167	.0000	
CHILHEL(1)	-.5651	.5098	1.2287	1	.2677	.0000	.5683
CHILHEL(2)	.6410	.9372	.4678	1	.4940	.0000	1.8983
FAMILYH			5.9877	2	.0501	.0883	
FAMILYH(1)	-1.7498	.8075	4.6959	1	.0302	-.1028	.1738
FAMILYH(2)	-.1685	1.1680	.0208	1	.8853	.0000	.8450
NEIGHBH			3.4896	2	.1747	.0000	
NEIGHBH(1)	1.3212	.7733	2.9187	1	.0876	.0600	3.7479
NEIGHBH(2)	.3327	1.0416	.1020	1	.7494	.0000	1.3947
TEN1	.0392	.0129	9.2192	1	.0024	.1683	1.0400
TP1	-.0034	.0182	.0348	1	.8519	.0000	.9966
TPM1	-.0048	.0162	.0886	1	.7659	.0000	.9952
TSL1	.0301	.0101	8.8731	1	.0029	.1642	1.0306
TSO1	.1807	.0500	13.0677	1	.0003	.2084	1.1981
XQL1	-.0352	.0145	5.9274	1	.0149	-.1241	.9654
Constant	1.2048	2.0516	.3449	1	.5570		

2.5.2 *Social isolation*

The same analysis was carried out to find out which variables best predicted social isolation. It was found that gender (being female, p = 0.01), marital status (being single, p = 0.02; being widowed/separated/divorced, p = 0.004), family visit (those who were not visiting their relatives, p = 0.02), emotional problems (p = 0.0000), energy (p = 0.008), pain (p = 0.004), physical mobility (p = 0.01) all were predictors of social isolation. The other variables such as children's visits, contact with neighbours, and Deprivation Category were not significant predictors. A simplified print out of the logistic regression analysis is shown in Figure 6.7.

2.5.3. *Global quality of life*

Global quality of life as measured by the EORTC QLQ-C30 was best predicted by the following variables: age (p = 0.02), Depcat (deprived group, p = 0.04), employment status (being unemployed, p = 0.04; being retired, p = 0.02), The other socio-economic variables were not significant predictors. Figure 6.8 presents a simplified print out of the logistic regression analysis.

Figure 6.7 Logistic regression analysis-Baseline social isolation

Number of cases included in the analysis: 238
Parameter coding (categorical data)

	Value	Freq	Coding (1)	(2)
NEIGHBOUR CONTACT				
never/almost never	1	123	1.000	.000
sometimes	2	35	.000	1.000
almost always/always	3	80	.000	.000
FAMILY VISIT				
never/almost never	1	102	1.000	.000
sometimes	2	49	.000	1.000
almost always/always	3	87	.000	.000
CHILDREN VISIT				
never/almost never	1.00	68	1.000	.000
sometimes	2.00	42	.000	1.000
almost always/always	3.00	128	.000	.000
MARITAL STATUS				
married	1	133	.000	.000
single	2	17	1.000	.000
widowed/separated/divorced	3	88	.000	1.000
DEPRIVATION CATEGORY				
affluent	1	40	.000	.000
middle	2	54	1.000	.000
deprived	3	144	.000	1.000
CASE				
case	1	129	1.000	
control	2	109	.000	
SEX				
male	1	134	.000	
female	2	104	1.000	

Dependent Variable.. Baseline Social Isolation
* Constant is included in the model.
Beginning Block Number 1. Method: Enter
Variable(s) Entered on Step Number

1..	AGE	Age
	SEX	sex
	MARITAL	Marital status
	DEPCAT	Deprivation Category
	CASE	Case or control
	CHILVI	Children visit
	FAMILYV	Family visit
	NEIGHBV	Neighbour contact
	TEM1	Total emotional reactions-baseline
	TEN1	Total energy-baseline
	TP1	Total pain-baseline
	TPM1	Total physical mobility-baseline
	TSL1	Total sleep-baseline
	XQL1	Global quality of life scale-baseline

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
AGE	-.0015	.0212	.0049	1	.9443	.0000	.9985
SEX(1)	-1.0482	.4186	6.2700	1	.0123	-.1163	.3506
MARITAL			10.4696	2	.0053	.1432	
MARITAL(1)	2.1028	.8884	5.6028	1	.0179	.1068	8.1891
MARITAL(2)	1.3432	.4653	8.3317	1	.0039	.1416	3.8312
DEPCAT			.5065	2	.7763	.0000	
DEPCAT(1)	.4735	.6920	.4682	1	.4938	.0000	1.6056
DEPCAT(2)	.2164	.6077	.1269	1	.7217	.0000	1.2417
CASE(1)	-.7410	.3997	3.4370	1	.0638	-.0675	.4766
CHILVI			1.8167	2	.4032	.0000	
CHILVI(1)	.1584	.5232	.0917	1	.7621	.0000	1.1716
CHILVI(2)	-.6891	.5715	1.4539	1	.2279	.0000	.5020
FAMILYV			5.5996	2	.0608	.0712	
FAMILYV(1)	1.0653	.4506	5.5881	1	.0181	.1066	2.9017
FAMILYV(2)	.5914	.5703	1.0752	1	.2998	.0000	1.8065
NEIGHBV			.5552	2	.7576	.0000	
NEIGHBV(1)	-.0044	.4565	.0001	1	.9923	.0000	.9956
NEIGHBV(2)	.4154	.6206	.4482	1	.5032	.0000	1.5150
TEM1	.0779	.0130	35.9003	1	.0000	.3277	1.0810
TEN1	-.0213	.0081	6.9888	1	.0082	-.1257	.9789
TP1	.0255	.0088	8.3125	1	.0039	.1414	1.0258
TPM1	.0279	.0111	6.3401	1	.0118	.1173	1.0283
TSL1	-.0107	.0072	2.1925	1	.1387	-.0247	.9894
XQL1	-.0228	.0120	3.6053	1	.0576	-.0713	.9775
Constant	-2.2027	1.7471	1.5895	1	.2074		

Figure 6.8 Logistic regression analysis-Baseline Global quality of Life

Number of cases included in the analysis: 238

Parameter coding (categorical data)

	Value	Freq	Coding (1)	(2)	(3)
EMPLOYMENT STATUS					
employed	1	34	.000	.000	.000
unemployed	2	22	1.000	.000	.000
housewife	3	50	.000	1.000	.000
retired	4	132	.000	.000	1.000
DEPRIVATION CATEGORY					
affluent	1	40	.000	.000	
middle	2	54	1.000	.000	
deprived	3	144	.000	1.000	
MARITAL STATUS					
married	1	133	.000	.000	
single	2	17	1.000	.000	
widowed/separated/divorced	3	88	.000	1.000	
CASE					
case	1	129	1.000		
control	2	109	.000		
SEX					
male	1	134	.000		
female	2	104	1.000		

Dependent Variable.. Baseline Global Quality of Life

* Constant is included in the model.

Beginning Block Number 1. Method: Enter

Variable(s) Entered on Step Number
1.. AGE Age
SEX sex
MARITAL Marital status
DEPCAT Deprivation Category
EMPLOY Employment status
CASE Case or control

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
AGE	-.0457	.0189	5.8116	1	.0159	-.1087	.9553
SEX(1)	-.0527	.3601	.0214	1	.8836	.0000	.9487
MARITAL			1.6614	2	.4358	.0000	
MARITAL(1)	-.6919	.5814	1.4163	1	.2340	.0000	.5006
MARITAL(2)	.0714	.3230	.0489	1	.8250	.0000	1.0740
DEPCAT			5.8225	2	.0544	.0752	
DEPCAT(1)	.2842	.4787	.3523	1	.5528	.0000	1.3286
DEPCAT(2)	.8712	.4210	4.2828	1	.0385	.0841	2.3898
EMPLOY			6.6020	3	.0857	.0432	
EMPLOY(1)	1.2862	.6217	4.2800	1	.0386	.0841	3.6190
EMPLOY(2)	.8495	.5741	2.1894	1	.1390	.0242	2.3385
EMPLOY(3)	1.1978	.5090	5.5370	1	.0186	.1047	3.3129
CASE(1)	.1245	.2845	.1915	1	.6616	.0000	1.1326
Constant	1.0522	1.1762	.8003	1	.3710		

2.6. Does the interview setting matter?

Out of 238 baseline interviews with patients, 60 interviews (25%) took place at patients' homes and 178 (75%) in the clinic. To examine whether this had any effects on outcomes, a comparison was made between baseline scores obtained at home and in the clinic.

Although there were some differences between scores obtained at home and in the clinic, these were not significant except for emotional reactions ($p = 0.04$) indicating that those who were interviewed at home reported more emotional problems.

Both on the NHP, and the EORTC questionnaires the patients at home reported more problems than those interviewed in the clinic. In some areas either there were no differences (pain from the NHP), or the differences were in opposite directions (pain, and pain in shoulder from the EORTC questionnaire were reported more in the clinic as compared to the home interview).

Tables 6.12, 6.13, and 6.14 present the data obtained from the whole study samples, both cancer patients and the chronic respiratory disease controls. As described the results suggest that patients in the clinic perceived themselves to be healthier than those who were interviewed at home. When the analysis was

restricted only to cancer patients in the study, the results were the same (to avoid repetition, the data are not shown).

Table 6.12 Patients' baseline scores on NHP-Part I by interview settings (the higher values indicate more perceived health problems, min: 0, max.: 100)

	Home (n = 60) Mean (SD)	Clinic (n = 178) Mean (SD)	P+
Energy	52.8 (40.3)	40.7 (40.7)	0.05
Pain	22.3 (25.7)	22.2 (29.1)	0.6
Emotional reactions	31.1 (26.1)	23.8 (23.0)	0.04*
Sleep	37.7 (35.3)	38.9 (30.9)	0.5
Social isolation	16.6 (23.2)	13.1 (21.7)	0.2
Physical mobility	33.0 (27.7)	28.6 (27.6)	0.3

Table 6.13 Patients' baseline functioning and global quality of life scores on EORTC QLQ-C30 by interview settings (the higher values indicate a higher level of functioning and quality of life, min.: 0 and max.: 100)

	Home (n = 60) Mean (SD)	Clinic (n = 178) Mean. (SD)	P+
Physical functioning	60.3 (25.9)	62.8 (27.2)	0.4
Role functioning	58.3 (34.6)	62.1 (36.2)	0.4
Emotional functioning	73.9 (25.0)	78.4 (21.3)	0.4
Social functioning	86.4 (24.8)	87.5 (22.2)	0.8
Cognitive functioning	80.3 (24.5)	85.7 (21.6)	0.1
Global quality of life	45.3 (25.0)	50.0 (23.3)	0.2

+ 2-tailed probability based on Mann-Whitney U test.
* Significant at 5% level.

Table 6.14 Patients' baseline scores of main symptoms on EORTC QLQ-C30 and QLQ-LC13 by interview settings (the higher values indicate a greater degree of symptoms, min: 0 and max.: 100)

	Home (n = 60) Mean (SD)	Clinic (n = 178) Mean. (SD)	P+
Cough	52.8 (35.9)	47.8 (32.4)	0.3
Haemoptysis	12.2 (28.8)	8.4 (20.6)	0.7
Dyspnoea	45.7 (29.8)	38.2 (27.7)	0.09
Pain	21.7 (25.5)	24.4 (28.0)	0.7
Pain in chest	25.0 (27.2)	20.2 (29.3)	0.1
Pain in shoulder	20.6 (28.2)	25.3 (33.3)	0.5
Pain elsewhere	26.7 (32.9)	24.2 (32.2)	0.6
Sleep difficulties	28.9 (37.6)	29.2 (35.9)	0.8
Fatigue	37.6 (29.8)	35.5 (29.1)	0.6
Appetite loss	29.4 (30.7)	27.9 (34.4)	0.5

2.7. Does knowing diagnosis matter?

At baseline interviews most lung cancer patients and the researcher were blind to the final diagnosis. However, in some instances the assessments (30 interviews) were made after the diagnosis and before the start of the treatment. Thus, this group of patients were interviewed while they knew their diagnosis. To investigate whether this would affect the patients' perception of their own quality of life, a comparison was made between scores of the patients who did not know their diagnosis (n = 99, 77%) and those who knew their cancer diagnosis (n = 30, 23%). There was no significant sex difference between these two groups, while the age difference between them was significant

+ 2-tailed probability based on Mann-Whitney U test.

indicating that those who knew their diagnosis were younger than those who did not ($p = 0.04$). The mean age of those who knew their diagnosis was 64.5 years ($SD = 8.7$), whereas the mean age of those who did not was 68.4 years ($SD = 9.0$).

Tables 6.15, 6.16, and 6.17 present mean scores of the cancer patients who knew their diagnosis and those did not know. Although there were some differences between those who knew their diagnosis and those who did not, there were no significant differences between these two groups of patients nor did any consistent pattern emerge.

Patients who did not know their cancer diagnosis reported more problems for some measures, while in some others the patients who knew their diagnosis had more problems. For example, on the NHP, patients who knew their diagnosis reported more problems with regard to energy, and physical mobility, whereas patients who did not know their diagnosis reported more problems with pain, sleep, and social isolation. The emotional reaction for both groups were the same. On the other hand, on the EORTC QLQ-C30, patients who knew their diagnosis reported a better global quality of life as compared to those who did not know their cancer diagnosis.

Table 6.15 Baseline scores on NHP-Part I by patients who knew their cancer diagnosis and those who did not know (the higher values indicate more perceived health problems, min: 0, max.: 100)

	Knew (n = 30) Mean (SD)	Did not know (n = 99) Mean (SD)	P+
Energy	49.1 (40.3)	40.8 (42.0)	0.3
Pain	18.6 (25.4)	26.3 930.2)	0.2
Emotional reactions	26.2 (23.0)	25.6 (24.6)	0.8
Sleep	33.7 (31.0)	39.7 (32.9)	0.5
Social isolation	11.9 (19.5)	12.9 (22.8)	1.0
Physical mobility	38.5 (29.5)	27.7 (27.2)	0.07

Table 6.16 Baseline functioning and global quality of life scores on EORTC QLQ-C30 by patients who knew their cancer diagnosis and those who did not (the higher values indicate a higher level of functioning and quality of life, min.: 0 and max.: 100)

	Knew (n = 30) Mean (SD)	Did not know (n = 99) Mean. (SD)	P+
Physical functioning	54.0 (28.8)	64.2 (26.8)	0.1
Role functioning	48.3 (38.2)	62.1 (36.5)	0.08
Emotional functioning	79.4 (21.0)	78.1 (21.8)	0.7
Social functioning	85.0 (27.5)	87.5 (22.0)	1.0
Cognitive functioning	87.2 (20.8)	85.0 (21.0)	0.4
Global quality of life	51.7 (25.2)	49.2 (22.5)	0.9

+ 2-tailed probability based on Mann-Whitney U test.

Table 6.17 Baseline scores of main symptoms on EORTC QLQ-C30 and QLQ-LC13 by patients who knew their cancer diagnosis and those who did not know (the higher values indicate a greater degree of symptoms, min: 0 and max.: 100)

	Knew (n = 30) Mean (SD)	Did not know (n = 99) Mean. (SD)	P+
Cough	46.7 (32.3)	46.8 (33.0)	1
Haemoptysis	10.0 (23.4)	10.1 (23.5)	1
Dyspnoea	39.7 (28.8)	37.0 (27.1)	0.7
Pain	20.6 (26.5)	29.1 (29.2)	0.2
Pain in chest	20.0 (27.1)	22.2 (29.4)	0.8
Pain in shoulder	18.9 (32.4)	30.0 (35.2)	0.1
Pain elsewhere	31.1 (37.1)	22.9 (32.2)	0.2
Sleep difficulties	17.8 (32.4)	34.7 (37.8)	0.02•
Fatigue	37.0 (25.2)	37.4 (30.5)	0.8
Appetite loss	41.1 (32.4)	32.3 (34.8)	0.1

+ 2-tailed probability based on Mann-Whitney U test.
• Significant at 5% level.

3. Follow-up assessments

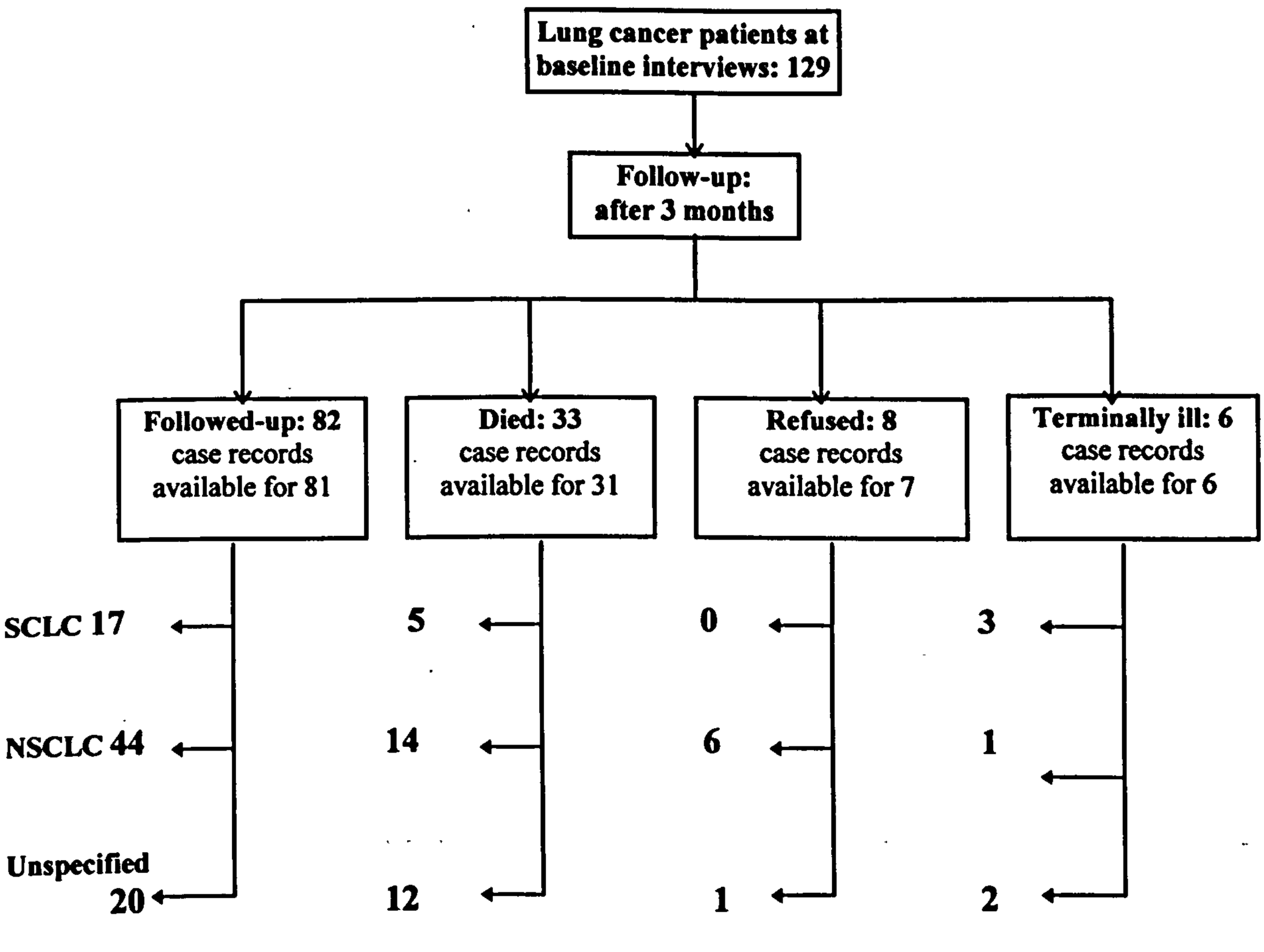
All lung cancer patients were followed-up after the completion of their initial management. The follow-up assessments were scheduled for three months after the baseline interviews. At the time of follow-up, out of 129 lung cancer patients, 33 (25%) were dead, 8 (6%) refused to take part in the study for the second time, 6 (5%) were terminally ill and it was not appropriate to interview these patients, and 82 (64%) were interviewed. Considering that at follow-up stage 90 patients were alive and suitable for interview, the response rate was 91%. The mean follow-up time was 98 days (SD = 11.1). In the following sections the analysis will be restricted to the 82 patients who were alive and where it was possible to compare their present situations with their previous status.

Furthermore, 4 hospital case records were missing at the time of analysis and therefore, when the analysis depended on the clinical characteristics of the patients the number of patients in the follow-up group was 81, those who had died 31, the refusal group 7, and the terminally ill patients 6. Figure 6.9 is a schematic view of the study population at the follow-up stage.

The characteristics of patients are given in Table 6.18. Due to the small sample sizes it was not appropriate to carry out tests of significance.

Finally, it is worth noting that from 82 follow-up interviews 50 interviews (63%) took place at patients' home and the remaining 30 interviews (37%) conducted in the clinic. In this respect, comparing these figures with the baseline, it is clear that at follow-up there were more home interviews (63% vs. 25%).

Figure 6.9 A schematic view of the study population at follow-up stage



Key: SCLC = small cell lung cancer; NSCLC= non-small cell lung cancer; Unspecified = clinically diagnosed lung cancer patients

Table 6.18 Lung cancer patients' demographic and clinical characteristics

	Baseline (n = 129)	Followed-up (n = 82)	Died (n = 33)	Refused (n = 8)	Terminally ill (n = 6)
	N0. (%)	No. (%)	No. (%)	No. (%)	N0. (%)
Sex					
male	77 (60)	48 (58)	22 (67)	4 (50)	3 (50)
female	52 (40)	34 (42)	11 (33)	4 (50)	3 (50)
Age					
mean (sd)	67.5 (9.1)	66.2 (8.6)	70.0 (9.9)	73.1 (7.1)	63.5 (7.5)
Deprivation category					
affluent	23 (18)	16 (20)	5 (15)	2 (25)	00 (00)
middle	32 (25)	19 (23)	9 (27)	2 (25)	2 (33)
deprived	74 (57)	47 (57)	19 (58)	4 (50)	4 (67)
Diagnosis					
non-small cell	67 (52)	44 (54)	14 (43)	6 (75)	3 (50)
small cell	23 (18)	17 (21)	5 (15)	00 (00)	1 (17)
unspecified*	35 (27)	20 (24)	12 (36)	1 (13)	2 (33)
not available**	4 (3)	1 (1)	2 (6)	1 (13)	00 (00)
Extent of disease					
limited	101 (78)	70 (85)	20 (61)	7 (88)	4 (67)
extensive	24 (19)	11 (14)	11 (33)	00 (00)	2 (33)
not available**	4 (3)	1 (1)	2 (7)	1 (12)	00 (00)
Initial treatment					
chemotherapy	32 (25)	25 (31)	6 (18)	00 (00)	1 (17)
radiotherapy	39 (30)	29 (35)	6 (18)	2 (25)	2 (33)
surgery	6 (5)	6 (7)	00 (00)	00 (00)	00 (00)
supportive care	48 (37)	21 (26)	19 (58)	5 (63)	3 (50)
not available**	4 (3)	1 (1)	2 (6)	1 (13)	00 (00)
Baseline performance status (ECOG Scale)					
0 (normal activity)	29 (23)	21 (26)	4 (12)	2 (25)	2 (33)
1 (symptoms)	60 (47)	42 (51)	12 (36)	4 (50)	2 (33)
2 (sometimes in bed)	25 (19)	13 (16)	10 (30)	1 (13)	1 (17)
3 (need to be in bed)	15 (11)	6 (7)	7 (21)	1 (13)	1 (17)
4 (confined to bed)	00	00	00	00	00
Weight loss					
significant weight loss	51 (40)	33 (40)	15 (45)	00 (00)	3 (50)
weight steady	40 (31)	26 (32)	7 (21)	5 (62)	2 (33)
possible weight loss	12 (9)	7 (9)	4 (12)	1 (13)	00 (00)
no comment	22 (17)	15 (18)	5 (15)	1 (13)	1 (17)
not available**	4 (3)	1 (1)	2 (6)	1 (13)	00 (00)

* Unspecified cases were those for whom diagnosis was not based on pathology reports and they were clinically diagnosed lung cancer patients.
** Not available refers to those for whom case notes were not available.

3.1. Baseline quality of life as indicator of length of survival

3.1.1. *Descriptive analysis*

There were 4 groups of lung cancer patients: those who were alive and participated in the study for the second time, those who were alive and refused to participate in the study, those who were terminally ill,* and those who were dead. Examining these 4 groups of patients' baseline quality of life, it was found that baseline quality of life was a good indicator of patients' length of survival. In other words, when at follow-up stage, lung cancer patients' baseline scores were reviewed, it was found that their scores at baseline were good pointers in indicating that what might happen to the patients in the future

Table 6.19 presents lung cancer patients' baseline perceived health status (NHP) in the four groups. Except for social isolation, all other measures were significantly different indicating that those who were dead or were in terminal stage had lower quality of life at baseline assessments.

Patients' baseline functioning and global quality of life scores on the EORTC QLQ-C30 are shown in Table 6.20. On three measures (physical, role and cognitive functioning) there were significant differences among these 4 groups of patients indicating that those who had died or were terminally ill by the follow-up stage had lower levels of functioning at their baseline as compared to those who were alive. On the remaining measures (emotional and

* Patients who were confined to bed and in fact, they were in the last stages of their lives. It was impossible to interview these patients at the time of follow-up as they died soon after.

social functioning and global quality of life), although not significant, the differences were in the same directions.

Table 6.19 Lung cancer patients' baseline scores on NHP-Part I (higher values indicate more perceived health problems, min.: 0, max.: 100)

	Refused (n = 8)	Followed-up (n = 82)	Died (n = 33)	Terminally ill (n = 6)	P+
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Energy	32.9 (38.9)	33.6 (37.5)	63.4 (44.5)	66.7 (41.4)	0.007*
Pain	7.3 (17.3)	21.1 (27.7)	30.9 (29.0)	59.3 (35.5)	0.005*
Emotional reactions	20. 6 (16.8)	22.6 (23.9)	30.4 (22.3)	51.0 (32.0)	0.04*
Sleep	32.6 (24.6)	35.8 (32.0)	37.7 (30.7)	83.3 (31.2)	0.02*
Social isolation	2.5 (7.1)	12.1 (22.8)	13.5 (19.3)	28.9 (31.8)	0.1
Physical mobility	22.4 (26.9)	23.8 (25.2)	46.2 (26.9)	40.9 (40.1)	0.001*

Table 6.20 Lung cancer patients' baseline functioning and global quality of life scores on EORTC QLQ-C30 (higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100)

	Refused (n = 8)	Followed-up (n = 82)	Died (n = 33)	Terminally ill (n = 6)	P+
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Physical functioning	67.5 (26.0)	67.1 (25.0)	47.9 (28.7)	60.0 (35.8)	0.01*
Role functioning	62.5 (44.3)	64.6 (34.7)	42.4 (35.6)	66.7 (51.6)	0.03*
Emotional functioning	75.0 (25.2)	79.0 (22.3)	80.1 (17.8)	66.6 (26.9)	0.6
Social functioning	95.8 (11.8)	86.2 (24.5)	85.4 (23.5)	94.4 (13.6)	0.5
Cognitive functioning	91.7 (17.8)	86.2 (20.8)	87.9 (15.7)	55.6 (31.0)	0.04*
Global quality of life	51.0 (15.1)	53.8 (22.3)	41.2 (24.7)	41.7 (21.7)	0.08

+ Probability based on Kruskal-Wallis one way analysis of variance corrected for ties.
* Significant at 5% level.

3.1.2. *Cox regression analysis*

To confirm the above mentioned results, the Cox's regression analysis was carried out. This analysis allowed the investigation of relationship between patients' baseline quality of life and survival. The survival time for each patient was calculated from the baseline interview to the follow-up interview. If a patient was dead at follow-up stage, his or her survival time was calculated from the baseline interview to death. The dates of death were worked out from medical records and death certificates (from the West of Scotland Cancer Surveillance Unit). As described in the methodology, in the Cox's regression analysis survival was the dependent variable and quality of life scores as measured by the NHP and the EORTC QLQ-C30 were independent variables (predictors).

The mean survival time (from the baseline to the follow-up interview) for survivors was 98 days (SD = 11.1), while for patients who died (from the baseline interview to death) was 47 days (SD = 18.7).

Figure 6.10 presents a summary of the analysis based on the aggregate scores of each patients on the NHP as a general health measure. The plot represents survival function showing the probability of surviving. Patients based on their aggregate scores on the NHP were categorised into two groups: those with scores below the mean (good general health) and those above (poor general health). Based on the analysis, patients' baseline scores on the NHP was a

significant predictor of survival (p = 0.003) and the probability of dying for those with poor general health was 3 times higher as compared to those with a good general heath status [Exp (B)/Expected regression coefficient = 3.0].*

The same analysis with the same procedure was carried out for the relationship between patients' baseline functioning scores (physical, role, emotional, social and cognitive as measured by the EORTC QLQ-C30) and survival. The analysis is shown in Figure 6.11. It was found that the baseline functioning was a significant predictor of survival (p = 0.03). The plot presents survival function as described earlier. The probability of dying for those with low level of functioning was 2 times higher as compared to those with high level of functioning at baseline assessment [Exp (B) = 2.2].

Again, the relationship between baseline global quality of life as measured by the EORTC QLQ-C30 and the survival was investigated. The result is shown in Figure 6.12. It was found that baseline global quality of life was a significant predictor of survival (p = 0.03). The hazard function as indicated by the Expected (B) was 2.2, indicating that those with lower global quality of

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* Exp (B) is the hazard function, or death rate at time *t*. It indicates how likely it is for a case to experience an event, given that it has survived to that time. The hazard function is not a probability but a death rate per unit of time, so it needs not to be less than 1. Thus, Exp (B) for continous variables shows the percentage change in the hazard rate for a unit increase in the covariate. For a dichotomous variable, such as sex or extent of disease, when two sequential numbers are used for coding and the larger of the two indicates presence of the characteristics, the Exp (B) is the ratio of the estimated hazard for a case with the characteristic to that for a case without the characteristics. This is often called the relative risk associated with the variable (Norusis, 1994).

life 2 times were more likely to die as compared to those who had a better global quality of life.

3.1.3. *Split between Survivors and non-survivors at follow-up*

When the above analysis was restricted only to survivors at follow-up (n = 82), there was no significant difference between those initially with high level of functioning, global quality of life, and a better general health status and those with low level on these three measures. This was observed with non-survivors as well when the analysis was restricted to those who were dead at follow-up (n = 33).

However these findings also indicated that at the time of second interview there was no evidence of selection bias in interviewing patients with a better quality of life later than patients with a lower quality of life.

3.1.4. *Cox regression analysis-forward selection of variables*

In order to allow for adjustment of known prognostic factors, that is age, sex, performance status, weight loss, and extent of disease, and also baseline general health status, and functioning, the Cox's regression analysis was repeated by selecting the 'forward conditional' model. Based on this selection, variables are considered one at time for entry in the model. The results indicated that the baseline global quality of life subscale as measured by the EORTC QLQ-C30 was the strongest significant predictor of length of survival

(age p = 0.0035, extent of disease p = 0.0034, global quality of life p = 0.0029), while sex, weight loss, performance status, the NHP and functioning (as measured by the EORTC QLQ-C30) were not. The following table shows the significant levels for each variable at the start and the final stage of the analysis. The table clearly suggests that there were strong interactions between extent of disease, performance status, baseline functioning and general health status. It also indicates that although performance status was significant at start, age and extent of disease strongly interacted with it to make it non-significant at the end. Unlike performance status, due to the interactions between age and extent of disease and baseline global quality of life, global quality of life by its own became the most significant predictor of survival.

Variables	Significant level at start p	Significant level at final stage p
Age	0.03*	0.0035*
Sex	0.54	0.55
ECOG Performance status	0.006*	0.16
Extent of disease	0.003*	0.0034*
Weight loss	0.56	0.68
Baseline general health status (NHP)	0.006*	0.16
Baseline functioning (EORTC QLQ-C30)	0.025*	0.56
Global quality of life (EORTC QLQ-C30)	0.009*	0.0029*

However, it is interesting to know that the extent of disease had an adjusted relative risk of 3.1, and global quality of life an adjusted relative risk of 3.2 (even higher than its unadjusted relative risk of 2.2, see above section 3.1.2). For the continuous variable (age), the hazard ratio showed increase of 8% for each year. This means that with an increase of 1 year in the patients' age, the rate of death will increase by 8%.

* Significant at 5% level.

Figure 6.10 Cox regression analysis-Survival by baseline general health status as measured by the NHP

Indicator Parameter Coding

	Value	Freq	(1)
NHP	General health		
	good	73	.000
	poor	56	1.000

129 Cases available for the analysis

Dependent Variable: SURVIVAL Survival time since baseline interview (days)

Died	Alive
33	96 (74.4%)

Beginning Block Number 1. Method: Enter
Variable(s) Entered at Step Number 1..
NHP Baseline General health

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
NHP	1.1037	.3696	8.9181	1	.0028	.1490	3.0152

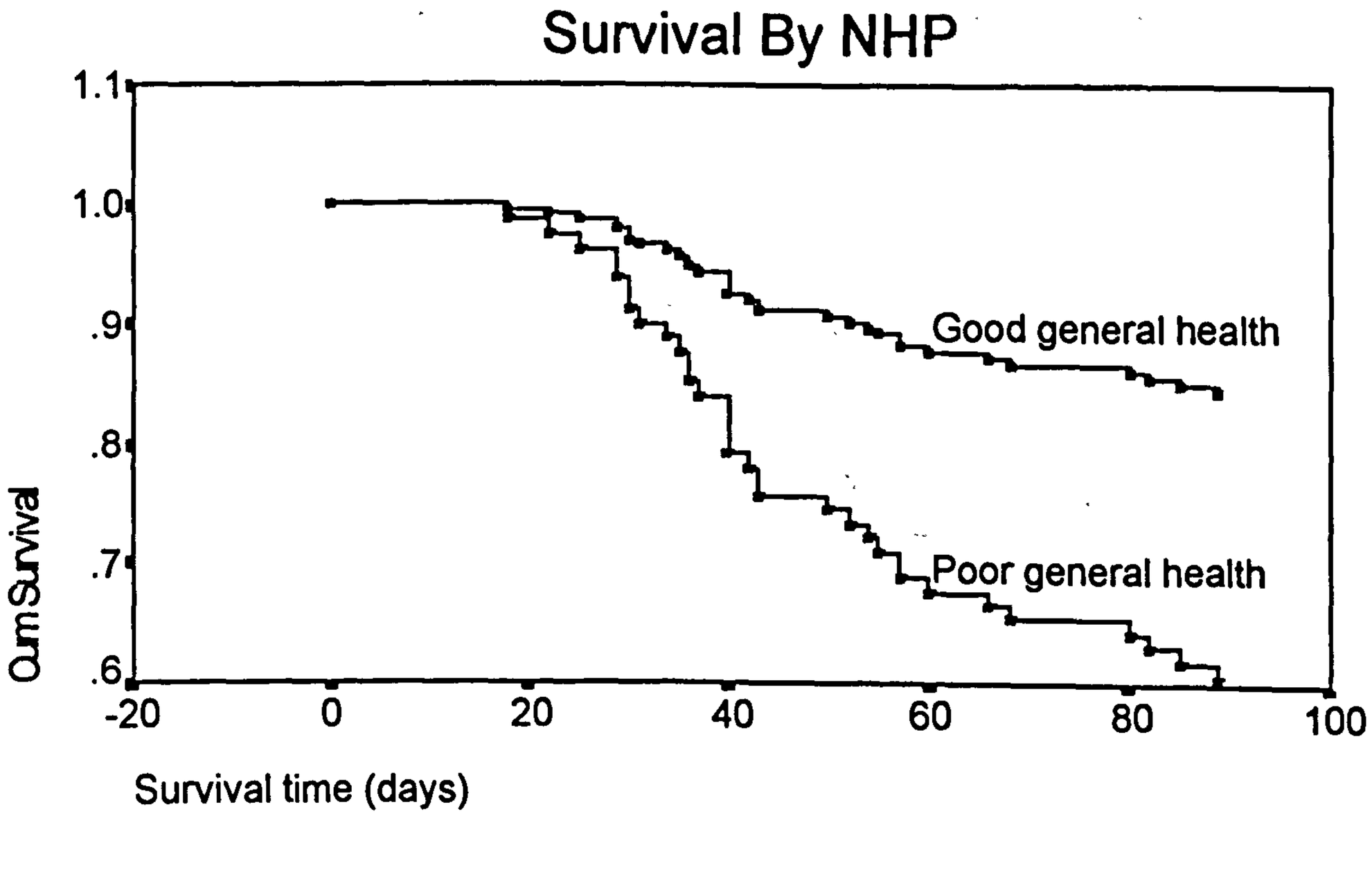


Figure 6.11 Cox regression analysis-Survival function by baseline functioning as measured by the EORTC QLQ-C30

Indicator Parameter Coding

	Value	Freq	(1)
FUNCT	Functioning		
	high level	72	.000
	low level	57	1.000

129 Cases available for the analysis

Dependent Variable: SURVIVAL Survival time since baseline interview (days)

Died	Alive
33	96 (74.4%)

Beginning Block Number 1. Method: Enter
Variable(s) Entered at Step Number 1..
FUNCT Baseline Functioning

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
FUNCT	.7666	.3564	4.6249	1	.0315	.0918	2.1524

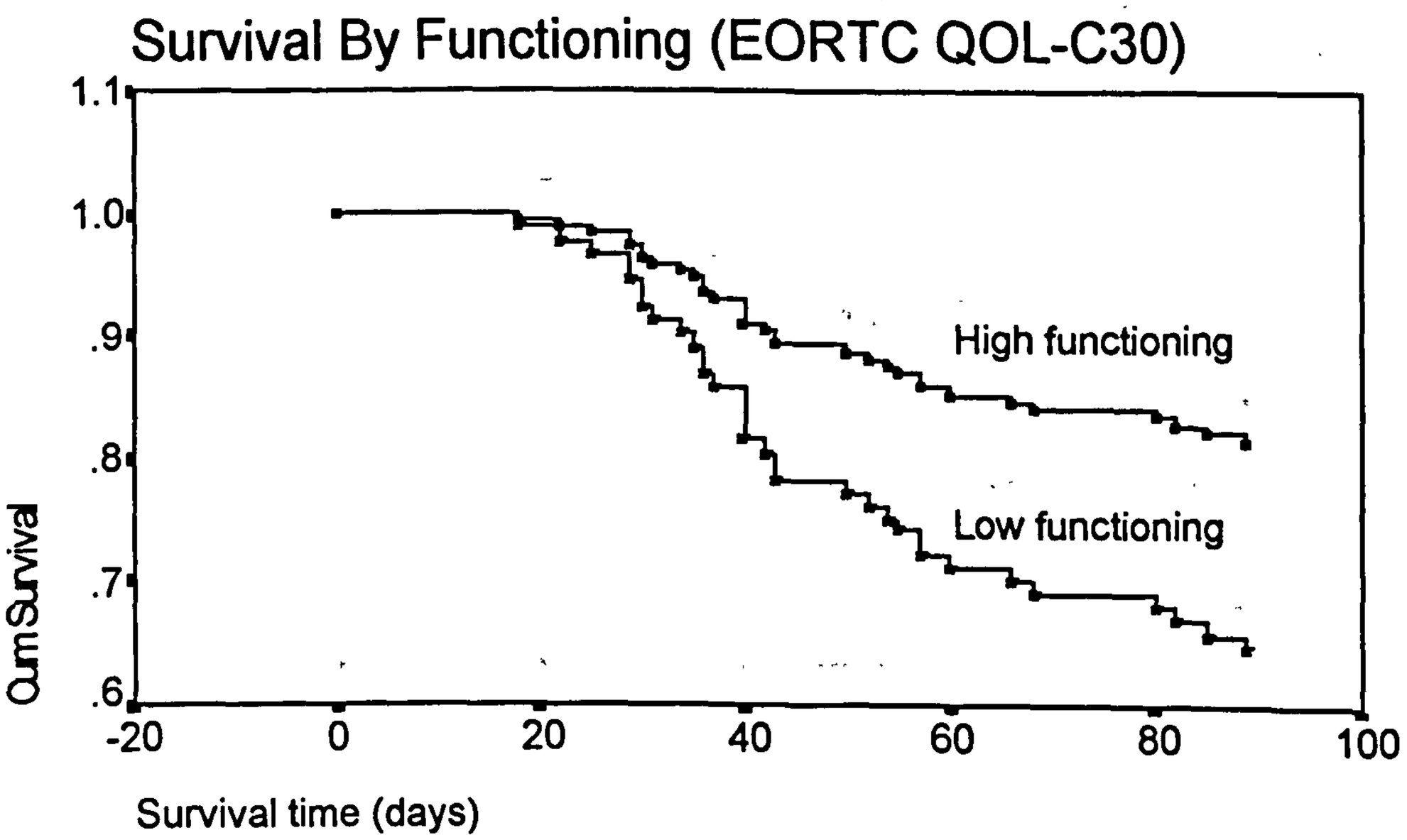


Figure 6.12 Cox regression analysis-Survival function by baseline global quality of life as measured by the EORTC QOL-C30

Indicator Parameter Coding

	Value	Freq	(1)
QOL	Global quality of life		
	high level	76	.000
	low level	53	1.000

129 Cases available for the analysis

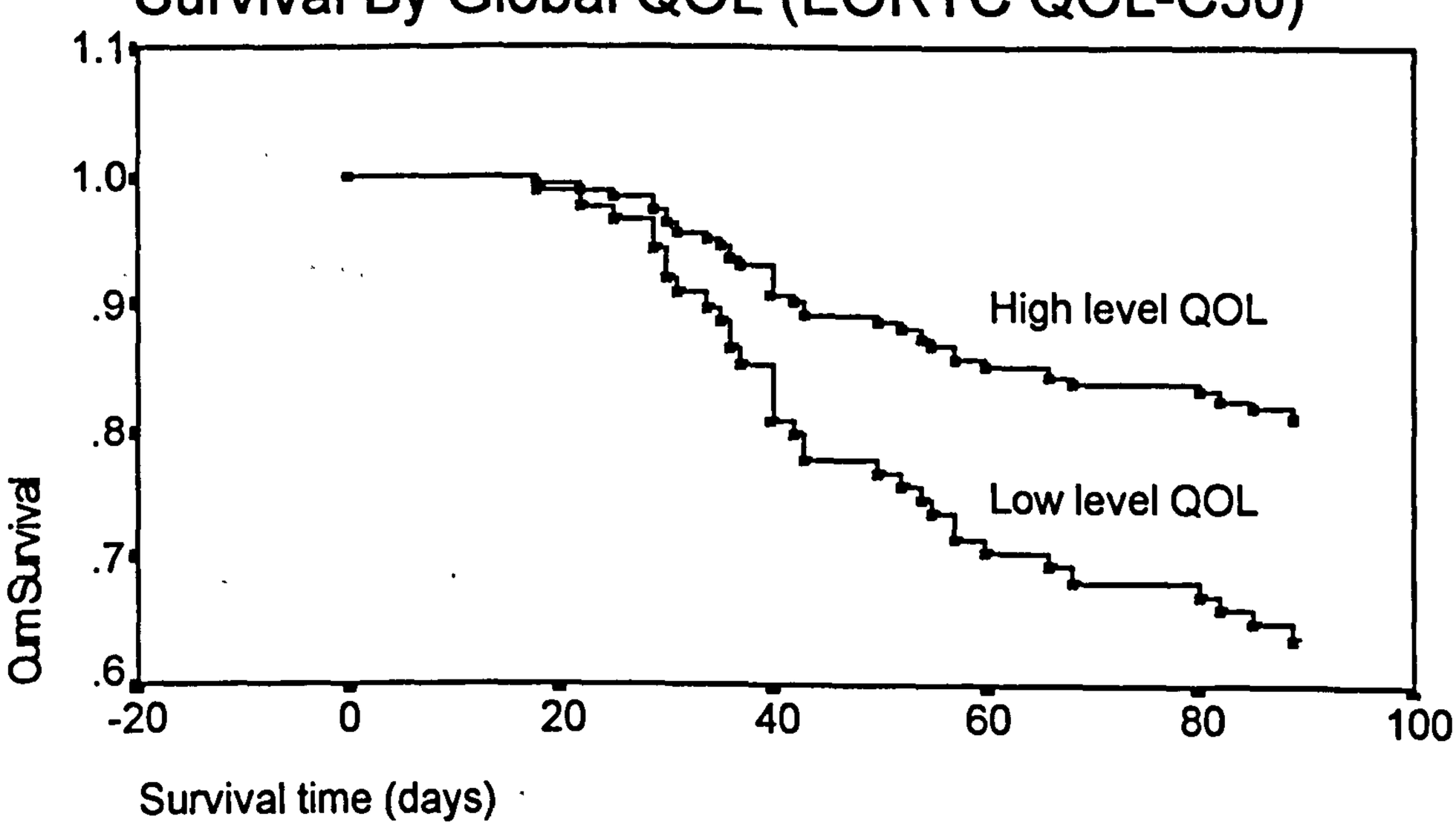
Dependent Variable: SURVIVAL Survival time since baseline interview (days)

Died	Alive
33	96 (74.4%)

Beginning Block Number 1. Method: Enter
Variable(s) Entered at Step Number 1..
QOL Baseline Global quality of life

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
QOL	.7813	.3524	4.9156	1	.0266	.0967	2.1843



3.2 Comparing baseline with follow-up assessments

Data obtained from the 82 patients at baseline and follow-up stage were compared to examine what happened to the patients after diagnosis and completion of the initial treatment. The Wilcoxon Matched-Pairs Signed Ranks Test were carried out to achieve this. In the following sections these are presented.

3.2.1 *General health*

Table 6.21 presents patients' baseline and follow-up scores on the NHP. Except for slight improvement with sleep difficulties (35.8 at baseline *vs.* 34 at follow-up), on all other measures patients reported that their perceived health problems increased. Notably deterioration in energy, social isolation and physical mobility at follow-up as compared to baseline assessments were highly significant (energy $p = 0.0004$, social isolation $p = 0.02$, and physical mobility $p = 0.0008$).

3.2.2 *Functioning and global quality of life*

Baseline and follow-up assessments of the patients' functioning and global quality of life as measured by the EORTC QLQ-C30 are shown in Table 6.22. In all areas the patients' functioning and global quality of life decreased. These reductions in patients' physical, role and cognitive functioning were highly significant ($p = 0.0003$, 0.0004, and 0.04 respectively), while on other

measures (including emotional and social functioning and global quality of life), they were not.

3.2.3 *Symptoms*

The only significant improvement after treatment was seen in patients' coughing ($p = 0.006$). Although not significant, there were also some improvement in haemoptysis, pain in shoulder, sleep difficulties, and diarrhoea. Three measures did not change: dyspnoea, pain, and pain in other sites of the bodies. In all other symptoms, patients' scores increased, indicating that their quality of life had deteriorated. Of these, 4 measures had significant increases as compared to baseline assessments: fatigue ($p = 0.02$), hair loss ($p = 0.0000$), constipation ($p = 0.007$), and sore mouth ($p = 0.0004$) indicating side-effects of the treatment on patients' quality of life. These are shown in Table 6.23.

Table 6. 21 Lung cancer patients' baseline and follow-up scores on NHP-Part I (the higher values indicate more perceived health problems, min.: 0, max.: 100)

	Baseline (n = 82) Mean (SD)	Follow-up (n = 82) Mean (SD)	P+
Energy	33.9 (37.5)	51.1 (38.6)	0.0004*
Pain	21.1 (27.7)	25.4 (27.2)	0.2
Emotional reactions	22.6 (23.9)	28.9 (29.2)	0.06
Sleep	35.8 (32.0)	34.0 (31.2)	0.7
Social isolation	12.1 (22.8)	18.9 (26.3)	0.02*
Physical mobility	23.8 (25.2)	34.7 (27.2)	0.0008*

Table 6.22 Lung cancer patients' baseline and follow-up functioning and global quality of life scores on EORTC QLQ-C30 (the higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100)

	Baseline (n = 82) Mean (SD)	Follow-up (n = 82) Mean (SD)	P+
Physical functioning	67.1 (25.0)	55.9 (24.9)	0.0003*
Role functioning	64.3 (34.9)	46.3 (30.2)	0.0004*
Emotional functioning	79.0 (22.2)	75.8 (22.1)	0.3
Social functioning	86.2 (24.5)	82.1 (22.9)	0.06
Cognitive functioning	86.2 (20.8)	80.7 (24.1)	0.04*
Global quality of life	53.8 (22.3)	51.8 (25.6)	0.6

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

Table 6.23 Lung cancer patients' baseline and follow-up symptoms scores on EORTC QLQ-C30 and QLQ-LC13 (the higher values indicate a greater degree of symptoms, min.: 0, max.: 100)

	Baseline (n = 82) Mean (SD)	Follow-up (n = 82) Mean (SD)	P+
Cough	50.0 (31.5)	37.8 (30.0)	0.006*
Haemoptysis	10.6 (23.4)	4.1 (15.2)	0.05
Dyspnoea	35.8 (26.9)	35.8 (27.5)	0.9
Pain	24.2 (24.9)	24.4 (28.5)	0.8
Pain in chest	22.0 (28.3)	24.4 (31.9)	0.7
Pain in shoulder	26.0 (33.5)	18.7 (27.8)	0.05
Pain elsewhere	19.9 (29.1)	20.3 (29.5)	1
Sleep difficulties	29.7 (36.3)	24.8 (32.6)	0.3
Fatigue	33.1 (28.2)	40.0 (27.0)	0.02*
Appetite loss	30.9 (33.4)	32.1 (33.3)	0.7
Hair loss	0.8 (5.2)	23.2 (38.4)	0.0000*
Nausea and vomiting	7.7 (16.0)	12.2 (20.5)	0.08
Constipation	15.9 (28.8)	28.9 (36.2)	0.007*
Diarrhoea	7.3 (18.9)	4.1 (13.2)	0.2
Peripheral neuropathy	12.2 (28.0)	17.5 (26.3)	0.1
Sore mouth	0.8 (5.2)	13.0 (27.6)	0.0004*
Trouble swallowing	7.3 (19.6)	12.6 (24.4)	0.1
Financial difficulties	7.7 (19.8)	8.9 (24.0)	0.6

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

3.3 Quality of life and different types of treatments

At follow-up stage 82 patients were interviewed. Of these, one patient's case record was not available. Thus, data obtained from 81 patients at baseline and follow-up assessments were analysed to investigate the outcomes based on the different types of initial treatments that patients received. These are: chemotherapy, radiotherapy, surgery, and best supportive care. Twenty five patients were initially treated with chemotherapy, 29 radiotherapy, 6 surgery, and 21 supportive care. It is worth noting that some patients also received other adjuvant treatments in addition to their initial management, but the following analyses are based on patients' initial management.

3.3.1 *General health*

Table 6.24 shows patients' scores on the NHP by treatment types. Not only were there no improvements, but almost on all measures, patients reported more perceived problems after their treatments. Chemotherapy caused significant problems relating to social isolation ($p = 0.02$), radiotherapy in energy ($p = 0.02$) and emotional reactions ($p = 0.04$), surgery in physical mobility ($p = 0.03$), and supportive care in energy ($p = 0.02$). Only slight improvement can be seen in patients sleep scores where they had received radiotherapy and surgery.

3.3.2 *Functioning and global quality of life*

Except emotional functioning which improved slightly in those who received chemotherapy, surgery and best supportive care, almost all other scores have decreased indicating that patients' functioning and global quality of life had deteriorated. Those who received chemotherapy and radiotherapy reported significant deterioration in physical functioning ($p = 0.01$ and $p = 0.007$ respectively). The patients' functioning and global quality of life scores as measured by the EORTC QLQ-C30 are shown in Table 6.25.

3.3.3 *Symptoms*

Table 6.26 presents patients' scores on the EORTC QLQ-C30 and QLQ-LC13 before and after treatment. It shows that patients' scores on cough and haemoptysis reduced after they had received treatment indicating that patients had some symptom relief. This is true for other symptoms such as dyspnoea, pain, pain in chest, pain in shoulder, and sleep difficulties, although there were some variations between different treatment regimens especially in those who had received supportive care or radiotherapy where some of these symptoms not only did not reduce, but increased.

In contrast to symptom relief, there were increases in side-effects of treatment including nausea and vomiting, hair loss, constipation, peripheral neuropathy, sore mouth, and trouble swallowing depending on the treatment types. For example, those who received chemotherapy reported significant increase in

hair loss (p = 0.0001) and sore mouth (p = 0.003), while those who received radiotherapy reported increase in trouble swallowing (p = 0.01).

Table 6.24 The changes in lung cancer patients' general health status as measured by NHP-Part I before and after treatment [the higher values indicate more perceived health problems, min.: 0, max.: 100, all figures are mean scores (sd)]

	Chemotherapy (n = 25)		P+	Radiotherapy (n = 29)		P+	Surgery (n = 6)		P+	Supportive care (n = 21)		P+
	Before	After		Before	After		Before	After		Before	After	
Energy	33.5 (36.3)	42.9 (35.8)	0.2	32.2 (38.5)	51.5 (39.9)	0.02*	00.0 (00.0)	43.5 (39.2)	0.07	44.8 (39.7)	65.0 (38.2)	0.02*
Pain	17.4 (21.8)	20.2 (22.6)	0.6	27.4 (32.1)	29.4 (29.8)	0.7	8.6 (21.0)	13.2 (17.2)	0.5	21.3 (29.1)	30.7 (30.0)	0.1
Emotional reactions	21.1 (20.6)	20.8 (27.0)	0.7	23.5 (27.6)	33.3 (28.0)	0.04*	10.9 (16.4)	22.8 (38.5)	0.6	25.8 (24.5)	33.5 (31.3)	0.2
Sleep	30.5 (26.0)	30.4 (30.3)	0.8	35.1 (30.8)	31.1 (31.0)	0.5	21.4 (30.3)	19.0 (23.5)	0.9	45.2 (38.7)	47.7 (34.2)	0.8
Social isolation	7.3 (11.5)	18.2 (25.2)	0.02*	19.2 (30.0)	24.2 (27.5)	0.2	00.0 (00.0)	16.7 (40.8)	0.3	12.0 (23.2)	13.1 (22.2)	0.9
Physical mobility	22.4 (24.7)	34.4 (29.9)	0.05	19.9 (21.6)	29.1 (25.0)	0.07	7.2 (13.1)	39.5 (24.3)	0.03*	36.7 (28.9)	42.9 (27.0)	0.4

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

Table 6.25 The changes in lung cancer patients' functioning and global quality of life scores as measured by EORTC QLQ-C30 before and after treatment [the higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100, all figures are mean scores (sd)]

	Chemotherapy (n = 25)		P+	Radiotherapy (n = 29)		P+	Surgery (n = 6)		P+	Supportive care (n = 21)		P+
	Before	After		Before	After		Before	After		Before	After	
Physical functioning	67.2 (25.7)	52.0 929.4)	0.01*	70.3 (22.4)	57.9 921.6)	0.007*	86.7 (16.3)	73.3 (20.7)	0.2	55.2 (25.2)	51.4 (23.3)	0.6
Role functioning	60.0 (38.2)	42.0 (34.4)	0.05	67.2 (33.5)	44.8 (27.9)	0.01*	91.7 (20.4)	50.0 (31.6)	0.07	57.1 (32.7)	52.4 (29.5)	0.6
Emotional functioning	84.0 (18.6)	75.3 (27.9)	0.2	77.9 (21.3)	73.6 918.2)	0.2	77.8 (26.7)	80.6 (25.1)	0.9	74.6 (26.8)	77.8 (20.0)	0.4
Social functioning	79.3 (29.8)	79.3 (25.1)	0.8	88.5 (25.2)	86.2 (18.9)	0.4	86.1 (22.2)	75.0 (29.3)	0.2	90.5 (16.3)	81.0 (24.3)	0.05
Cognitive functioning	87.3 (22.2)	77.3 (28.8)	0.07	84.5 (21.3)	79.9 (21.5)	0.3	91.7 (13.9)	88.9 (27.2)	1.0	84.9 (21.0)	83.3 (21.7)	0.6
Global quality of life	52.0 (23.5)	48.7 (28.0)	0.8	50.3 (25.7)	53.2 (23.8)	0.7	56.9 (18.6)	52.8 (36.0)	0.9	59.5 (16.9)	52.8 (23.9)	0.2

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

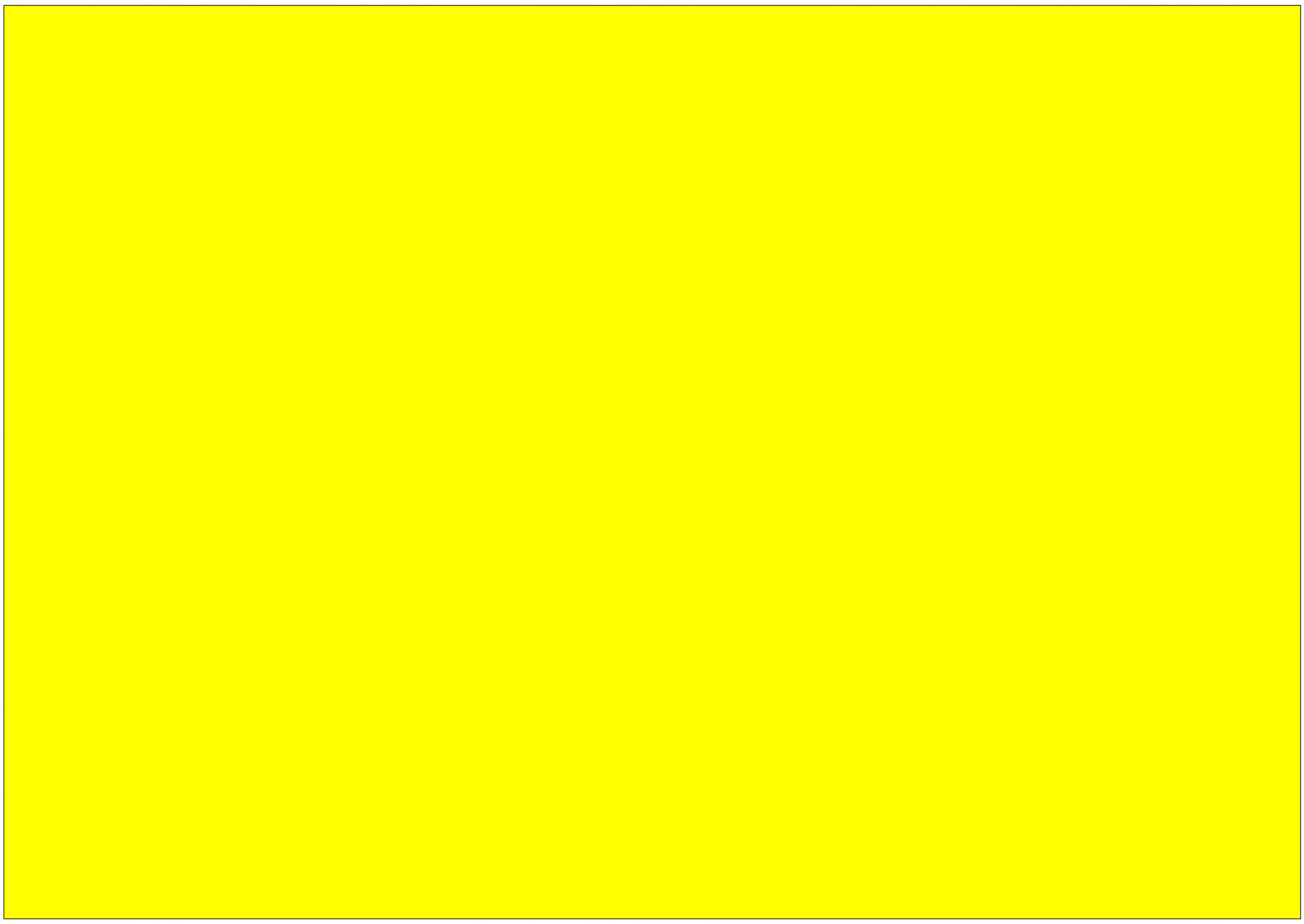
Table 6.26 The changes in lung cancer patients' symptoms scores as measured by EORTC QLQ-C30 and QLQ-LC13 before and after treatment (the higher values indicate a greater degree of symptoms, min.: 0, max.: 100, all figures are mean scores (sd) and probabilities calculated as same as previous tables, and those with * are significant at 5% level)

	Chemotherapy (n = 25)		P+	Radiotherapy (n = 29)		P+	Surgery (n = 6)		P+	Supportive care (n = 21)		P+
	Before	After		Before	After		Before	After		Before	After	
Cough	60.0 (31.9)	32.0 (31.2)	0.005*	41.4 (30.4)	39.1 (23.7)	0.7	38.9 (25.1)	22.2 (27.2)	0.3	50.8 (30.9)	46.0 (35.7)	0.6
Haemoptysis	12.0 (23.3)	5.3 (15.8)	0.3	11.5 (24.0)	2.3 (8.6)	0.09	00.0 (00.0)	00.0 (00.0)	1.0	11.1 (26.5)	6.3 (22.7)	0.5
Dyspnoea	38.0 (26.9)	31.3 (28.0)	0.2	31.6 (29.1)	33.6 (27.0)	0.5	26.4 (29.1)	25.0 (22.4)	0.9	43.3 (22.1)	48.4 (26.4)	0.4
Pain	25.3 (22.6)	18.0 (30.8)	0.2	28.2 (27.1)	29.3 (27.3)	0.6	33.3 (27.9)	16.7 (25.8)	0.3	15.9 (22.7)	28.6 (28.0)	0.03*
Pain in chest	20.0 (25.5)	20.0 (33.3)	0.8	23.0 (31.0)	20.7 (24.3)	0.7	33.3 (36.5)	27.8 (32.8)	0.8	20.6 (26.8)	34.9 (38.7)	0.2
Pain in shoulder	24.0 (32.7)	20.0 (28.9)	0.5	31.0 (37.7)	14.9 (22.9)	0.009*	22.2 (27.2)	16.7 (27.9)	0.7	23.8 (31.9)	23.8 (33.6)	1.0
Pain elsewhere	24.0 (28.1)	22.7 (31.5)	0.7	14.9 (27.6)	21.8 (31.2)	0.3	27.8 (32.8)	11.1 (17.2)	0.3	20.6 (32.4)	19.0 (29.0)	0.8
Sleep difficulties	30.7 (40.7)	26.7 (33.3)	0.8	31.0 (37.7)	21.8 (31.2)	0.2	22.2 (27.2)	22.2 (27.2)	1.0	27.0 (32.7)	28.6 (36.9)	0.9
Fatigue	32.0 (26.1)	38.2 926.1)	0.3	32.2 (31.3)	41.4 (26.2)	0.08	35.2 (32.5)	29.6 (26.9)	0.7	34.4 (27.4)	44.4 (29.8)	0.2
Appetite loss	36.0 (34.6)	36.0 (35.9)	1.0	23.0 (28.3)	24.2 (27.5)	0.4	50.0 (45.9)	44.4 (40.4)	0.9	31.7 (34.1)	31.7 (34.1)	1.0
Hair loss	00.0 (00.0)	62.7 (40.0)	0.0001*	1.1 (6.2)	6.9 (22.5)	0.2	00.0 (00.0)	00.0 (00.0)	1.0	1.6 (7.3)	4.8 (21.8)	0.3
Nausea and vomiting	8.7 (12.8)	12.7 (20.0)	0.4	11.0 (21.9)	16.1 (23.4)	0.3	8.3 (13.9)	8.3 (13.9)	1.0	2.4 (8.0)	7.9 (18.7)	0.2
Constipation	20.0 (28.9)	20.0 (28.9)	1.0	14.9 (30.3)	33.3 (36.7)	0.02*	16.7 (40.8)	27.8 (44.3)	0.8	12.7 (24.7)	34.9 (41.5)	0.04*
Diarrhoea	9.3 (20.5)	8.0 (17.4)	0.8	6.9 (18.6)	2.3 (12.4)	0.3	11.1 (27.2)	5.6 (13.6)	0.7	3.1 (14.5)	1.6 (7.2)	0.7
Peripheral neuropathy	5.3 (15.8)	16.0 (27.4)	0.07	13.8 (31.5)	20.7 (27.3)	0.2	00.0 (00.0)	5.6 (13.6)	0.3	22.2 (35.5)	19.0 (27.0)	0.8
Sore mouth	00.0 (00.0)	25.3 (32.3)	0.003*	1.1 (6.2)	5.7 (18.0)	0.2	00.0 (00.0)	11.1 (27.2)	0.3	1.6 (7.2)	9.5 (30.1)	0.2
Trouble swallowing	12.0 (28.7)	8.0 (17.4)	0.5	3.4 (10.3)	18.4 (30.3)	0.01*	00.0 (00.0)	22.2 (34.4)	0.2	9.5 (18.7)	7.9 (18.0)	0.8
Financial difficulties	10 7 (23 0)	18.7 (32.0)	0.1	4 6 (17.1)	8.0 (19.2)	0.3	00.0 (00 0)	00.0 (00.0)	1.0	6.3 (20.1)	6.3 (22.7)	1.0

Respiratory Medicine Day Unit

Stobhill Hospital

A female patient with lung cancer at follow-up assessment of quality of life. She received chemotherapy, but died a few months later



3.4 Small and non-small cell lung cancer and quality of life

In this section analysis is restricted to small and non-small cell lung cancer patients. Two methods of analyses were performed. First, comparison was made between small and non-small cell lung cancer patients' baseline and follow-up scores. This provided opportunity to examine whether patients with different cell types were scored differently or not. Secondly, small and non-small cell lung cancer patients' baseline scores (before treatment) were compared to their follow-up scores (after treatment). This facilitated the investigation of the treatment effects on these two groups of patients.

3.4.1 *Comparing quality of life in small and non-small cell lung cancer*

The results are shown in Tables 6.27, 6.28., and 6.29. Although there were some differences between small and non-small cell lung cancer patients' scores on the NHP, both at baseline and follow-up assessments, these differences were not significant. Non-small cell lung cancer patients tended to score higher than small cell lung cancer patients indicating that they had more perceived health problems (Table 6.27).

The same pattern of scoring was apparent on the EORTC QLQ-C30 indicating that patients with non-small cell lung cancer had a lower level of functioning and quality of life. Only on one measure (emotional functioning) was the difference significant ($p = 0.01$) (Table 6.28).

At baseline assessments there were no significant differences between small and non-small cell lung cancer patients' scores on symptom subscales on the EORTC QLQ-C30 and QLQ-LC13, although on some of the measures (for example, haemoptysis, dyspnoea, pain, pain in chest, fatigue and appetite loss) non-small cell lung cancer patients scored higher indicating that they had a greater degree of symptoms. However, on some of the measures small cell lung cancer patients had higher scores such as scores on cough, and pain in shoulder (Table 6.29).

At follow-up assessments except for scores on pain ($p = 0.005$), hair loss ($p = 0.000$), and sore mouth ($p = 0.006$), there were no significant differences between small cell and non-small cell lung cancer patients. However, there was a clear pattern of scoring indicating that non-small cell lung cancer patients had higher scores on disease-related symptoms, while small cell lung cancer patients had higher scores on treatment-related symptoms (Table 6.29).

Finally, it is important to note that the difference between small and non-small cell lung cancer patients' scores may be due to the different treatments they received rather than the difference in cell type (see the following table).

Treatment	Small cell Baseline (n = 23)	Non-small cell Baseline (n = 67)	Small cell Follow-up+ (n = 17)	Non-small cell Follow-up* (n = 44)
Chemotherapy	23	7	17	7
Radiotherapy	0	24	0	18
Surgery	0	6	0	6
Supportive care	0	30	0	13

+ At follow-up 18 SCLC patients were alive. Of these, 17 took part in the study and 1 was terminally ill.

* At follow-up 53 NSCLC patients were alive. Of these, 44 took part in the study, 6 refused and 3 were terminally ill.

Table 6.27 Comparison of small and non-small cell lung cancer patients' scores at baseline and follow-up assessments on NHP-Part I [the higher values indicate more perceived health problems, min.: 0, max.: 100, all figures are mean scores (sd)]

	Baseline		P+	Follow-up		P+
	small cell (n = 23)	non-small cell (n = 67)		small cell (n = 17)	non-small cell (n = 44)	
Energy	35.4 (36.0)	41.1 (42.4)	0.9	44.9 (33.2)	57.9 (40.2)	0.2
Pain	17.7 (20.8)	24.4 (30.8)	0.7	17.3 (18.2)	29.8 (28.0)	0.1
Emotional reactions	17.5 (14.6)	27.7 (26.3)	0.2	14.1 (16.5)	33.2 (31.3)	0.05
Sleep	33.3 (27.4)	39.3 (32.3)	0.6	25.3 (21.6)	35.4 (33.6)	0.5
Social isolation	5.2 (10.8)	11.5 (19.7)	0.2	15.7 (23.5)	17.9 (28.0)	0.9
Physical mobility	27.9 (26.1)	28.1 (28.1)	0.9	39.4 (29.5)	36.4 (27.3)	0.8

Table 6.28 Comparison of small and non-small cell lung cancer patients' functioning and global quality of life scores at baseline and follow-up assessments on EORTC QLQ-C30 [the higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100, all figures are mean scores (sd)]

	Baseline		P+	Follow-up		P+
	small cell (n = 23)	non-small cell (n = 67)		small cell (n = 17)	non-small cell (n = 44)	
Physical functioning	63.5 (26.7)	64.5 (27.8)	0.9	48.2 (31.7)	57.7 (21.2)	0.3
Role functioning	56.5 (37.9)	62.7 (38.3)	0.5	35.3 (34.3)	48.9 (24.2)	0.1
Emotional functioning	88.0 (14.0)	76.4 (20.0)	0.01*	81.3 (18.3)	72.2 (23.9)	0.2
Social functioning	83.3 (29.7)	90.0 (17.9)	0.5	81.4 (26.9)	80.3 (24.5)	0.7
Cognitive functioning	90.6 (19.3)	84.1 (19.1)	0.06	75.5 (32.9)	82.6 (22.7)	0.7
Global quality of life	54.3 (24.3)	47.5 (23.6)	0.3	51.5 (29.0)	48.3 (24.2)	0.6

+ 2-tailed probability based on Mann-Whitney U test (mean rank).
* Significant at 5% level.

Table 6.29 Comparison of small and non-small cell lung cancer patients' symptoms scores on EORTC QLQ-C30 and QLQ-LC13 at baseline and follow-up assessments [the higher values indicate a greater degree of symptoms, min.: 0, max.: 100, all figures are mean scores (sd)]

	Baseline		P+	Follow-up		P+
	small cell (n = 23)	non-small cell (n = 67)		small cell (n = 17)	non-small cell (n = 44)	
Cough	53.6 (31.4)	48.8 (32.5)	0.6	31.4 (34.3)	39.4 (29.9)	0.3
Haemoptysis	8.7 (23.0)	13.9 (27.3)	0.4	2.0 (8.1)	2.3 (8.5)	0.9
Dyspnoea	34.4 (24.4)	38.9 (27.5)	0.5	30.4 (27.5)	39.2 (26.4)	0.2
Pain	21.7 (22.2)	26.4 (27.9)	0.7	14.7 (30.6)	31.4 (27.7)	0.005*
Pain in chest	20.3 (28.0)	22.4 (29.2)	0.8	21.6 (35.2)	25.7 (30.4)	0.4
Pain in shoulder	26.1 (31.7)	23.9 (33.2)	0.6	11.8 (20.2)	18.2 (27.3)	0.5
Pain elsewhere	27.5 (27.8)	26.4 (33.6)	0.6	21.6 (28.7)	23.5 (30.1)	0.9
Sleep difficulties	26.1 (37.5)	30.3 (35.2)	0.5	23.5 (30.7)	25.8 (32.8)	0.8
Fatigue	32.9 (25.6)	37.5 (29.8)	0.6	37.9 (25.8)	43.9 (26.4)	0.4
Appetite loss	34.8 (34.1)	38.3 (33.5)	0.6	37.3 (37.0)	37.1 (33.1)	1.0
Hair loss	00.0 (00.0)	1 (5.7)	0.4	84.3 (26.7)	6.8 (19.8)	0.000*
Nausea and vomiting	11.6 (13.7)	8.5 (18.0)	0.07	11.8 (18.4)	14.4 (22.9)	0.8
Constipation	17.4 (28.2)	22.9 (33.9)	0.6	23.5 (30.7)	35.6 (40.3)	0.3
Diarrhoea	10.1 (21.2)	4.5 (16.3)	0.07	7.8 (18.7)	3.8 (12.9)	0.3
Peripheral neuropathy	4.3 (15.3)	9.5 (23.1)	0.3	21.6 (31.0)	15.9 (25.4)	0.5
Sore mouth	1.4 (7.0)	4.0 (15.9)	0.6	29.4 (35.1)	8.3 (22.9)	0.006*
Trouble swallowing	14.5 (29.9)	8.0 (22.5)	0.2	7.8 (14.6)	15.2 (27.3)	0.6
Financial difficulties	5.8 (16.4)	10.4 (24.8)	0.5	19.6 (33.5)	9.1 (24.2)	0.2

+ 2-tailed probability based on Mann-Whitney U test (mean rank).
* Significant at 5% level.

3.4.2 *Effect of treatment on small cell and non-small cell lung cancer patients*

Small and non-small cell lung cancer patients' scores were compared to their own follow-up scores. This was a paired-matched comparison, that is, comparing baseline and follow-up scores where data were available for the same patients.

Table 6.30 presents both small and non-small lung cancer patients' general health status as measured by the NHP. Not only had patients' general health status not improved, but there were also significant deterioration on measures such as social isolation ($p = 0.04$), and physical mobility ($p = 0.03$)- for small cell lung cancer patients; and on energy ($p = 0.0004$), pain ($p = 0.03$), and physical mobility ($p = 0.007$)- for non-small cell lung cancer patients. However, after treatment there were slight improvements for small cell lung cancer patients with lower scores on emotional reactions and sleep difficulties.

Similar results were found when patients' functioning and global quality of life scores were measured by the EORTC QLQ-C30. There was a significant deterioration in patients physical and role functioning, both in small and non-small cell lung cancer patients. In addition, there was a significant reduction in non-small cell lung cancer patients' social functioning, while small cell lung cancer showed slight improvement in this measure (Table 6.31).

Table 6.32 shows the patients' disease- and treatment-related symptoms as measured by the EORTC QLQ-C30 and QLQ-LC13. Except on two measures (cough in small cell lung cancer patients and haemoptysis in non-small cell lung cancer patients), there was no significant symptom relief. However, after treatment small cell lung cancer patients reported a lesser degree of disease-related symptoms. Both small and non-small cell lung cancer patients scored higher on measures related to side-effects of treatment as compared to their baseline scores. For example, non-small cell lung cancer patients reported significant increase on fatigue ($p = 0.007$), constipation ($p = 0.02$), peripheral neuropathy ($p = 0.03$), sore mouth ($p = 0.04$), and trouble swallowing ($p = 0.01$).

Table 6.30 Small and non-small cell lung cancer patients' mean scores (sd) on NHP-Part I before and after treatment (the higher values indicate more perceived health problems, min.: 0, max.: 100)

	Small cell (n = 17)		P+	Non-small cell (n = 44)		P+
	Before	After		Before	After	
Energy	34.7 (36.2)	44.9 (33.2)	0.2	31.9 (37.9)	57.9 (40.2)	0.0004*
Pain	16.4 (22.1)	17.3 (18.2)	0.9	19.8 (27.6)	29.8 (28.0)	0.03*
Emotional reactions	16.1 (12.2)	14.1 (16.5)	0.5	24.6 (26.0)	33.2 (31.3)	0.07
Sleep	29.5 (23.5)	25.3 (21.6)	0.6	34.8 (31.8)	35.4 (33.6)	0.8
Social isolation	7.1 (12.2)	15.7 (23.5)	0.04*	11.4 (21.4)	17.9 (28.0)	0.1
Physical mobility	23.3 (23.7)	39.4 (29.5)	0.03*	23.5 (25.2)	36.4 (27.3)	0.007*

Table 6.31 Small and non-small cell lung cancer patients' functioning and global quality of life mean scores (sd) on EORTC QLQ-C30 before and after treatment (the higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100)

	Small cell (n = 17)		P+	Non-small cell (n = 44)		P+
	Before	After		Before	After	
Physical functioning	63.5 (23.7)	48.2 (31.7)	0.03*	70.0 (25.0)	57.7 (21.2)	0.004*
Role functioning	55.9 (34.8)	35.3 (34.3)	0.04*	69.3 (36.1)	48.9 (24.2)	0.008*
Emotional functioning	88.7 (13.2)	81.3 (18.3)	0.2	78.6 (19.3)	72.2 (23.9)	0.2
Social functioning	77.5 (32.8)	81.4 (26.9)	0.5	90.9 (17.8)	80.3 (24.5)	0.004*
Cognitive functioning	89.2 (22.0)	75.5 (32.9)	0.05	85.6 (17.8)	82.6 (22.7)	0.4
Global quality of life	52.0 (26.3)	51.5 (29.0)	0.8	54.5 (19.3)	48.3 (24.2)	0.1

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

Table 6.32 Small and non-small cell lung cancer patients' symptoms mean scores (sd) on EORTC QLQ-C30 and QLQ-LC13 before and after treatment (the higher values indicate a greater degree of symptoms, min.: 0, max.: 100)

	Small cell (n = 17)		P+	Non-small cell (n = 44)		P+
	Before	After		Before	After	
Cough	56.9 (30.7)	31.4 (34.3)	0.03*	48.5 (32.5)	39.4 (29.9)	0.1
Haemoptysis	9.8 (25.7)	2.0 (8.1)	0.3	14.4 (26.3)	2.3 (8.5)	0.009*
Dyspnoea	40.2 (25.7)	30.4 (27.5)	0.08	34.5 (25.3)	39.2 (26.4)	0.2
Pain	22.5 (22.0)	14.7 (30.6)	0.3	23.9 (25.8)	31.4 (27.7)	0.07
Pain in chest	17.6 (26.7)	21.6 (35.2)	0.8	22.7 (27.6)	25.7 (30.4)	0.7
Pain in shoulder	25.5 (32.3)	11.8 (20.2)	0.06	23.5 (31.0)	18.2 (27.3)	0.2
Pain elsewhere	25.5 (27.7)	21.6 (28.7)	0.6	21.2 (28.8)	23.5 (30.1)	0.7
Sleep difficulties	27.5 (39.5)	23.5 (30.7)	0.8	27.3 (33.9)	25.8 (32.8)	0.8
Fatigue	34.0 (28.2)	37.9 (25.8)	0.7	31.3 (26.3)	43.9 (26.4)	0.007*
Appetite loss	39.2 (37.7)	37.3 (37.0)	0.9	32.6 (31.7)	37.1 (33.1)	0.4
Hair loss	00.0 (00.0)	84.3 (26.7)	0.0004*	00.8 (5.0)	6.8 (19.8)	0.06
Nausea and vomiting	11.8 (14.1)	11.8 (18.4)	0.9	7.6 (17.0)	14.4 (22.9)	0.08
Constipation	23.5 (30.7)	23.5 (30.7)	1.0	17.4 (30.1)	35.6 (40.3)	0.02*
Diarrhoea	13.7 (23.7)	7.8 (18.7)	0.4	5.3 (17.5)	3.8 (12.9)	0.6
Peripheral neuropathy	5.9 (17.6)	21.6 (31.0)	0.07	7.6 (21.4)	15.9 (25.4)	0.03*
Sore mouth	00.0 (00.0)	29.4 (35.1)	0.01*	1.5 (7.0)	8.3 (22.9)	0.04*
Trouble swallowing	17.6 (33.6)	7.8 (14.6)	0.1	3.8 (10.7)	15.2 (27.3)	0.01*
Financial difficulties	7.8 (18.7)	19.6 (33.5)	0.1	8.3 (20.5)	9.1 (24.2)	0.7

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

3.5 Limited and extensive diseases and quality of life

Two approaches were chosen to examine quality of life in patients with limited and extensive disease. First, analysis was performed to compare limited and extensive disease at baseline and follow-up assessments to look at the differences. Secondly, data were obtained from the same patients, at baseline (before treatment) and follow-up (after treatment) to compare the effects of treatment.

3.5.1 *Comparison between limited and extensive disease*

At baseline and follow-up assessments patients with extensive disease had a lower quality of life as compared to patients with limited disease. These differences were more profound at baseline. Table 6.33 presents patients' general health status as measured by the NHP. At baseline, patients with extensive disease scored significantly higher on energy ($p = 0.01$), pain ($p = 0.0004$), and physical mobility ($p = 0.04$), indicating that they had more perceived health problems. Again, at follow-up while patients with extensive disease scored higher, none of the scores were significantly different.

Table 6.34 presents patients' functioning and global quality of life scores. While both at baseline and follow-up patients with extensive disease had lower functioning and quality of life, on most measures the differences were not significant. Only at baseline assessments, patients with extensive disease

scored lower significantly on two measures, physical functioning ($p = 0.04$) and global quality of life ($p = 0.01$).

A similar pattern of scoring was found in patients' evaluation of their own disease- and treatment-related symptoms and side-effects as measured by the EORTC QLQ-C30 and QLQ-LC13. There were either no differences at all (cough) or the directions were against patients with extensive disease indicating that they had more symptoms and treatment-related side-effects as compared to the patients with limited disease. However, on some of the measures patients with limited disease scored higher; for example, diarrhoea (at baseline) and haemoptysis and sore mouth (at follow-up). These are shown in Table 6.35.

Table 6.33 Comparison of scores of patients with limited and extensive disease on NHP-Par I at baseline and follow-up [the higher values indicate more perceived health problems, min.: 0, max.: 100, all figures are mean scores (sd)]

	Baseline		P+	Follow-up		P+
	Limited (n = 101)	Extensive (n = 24)		Limited (n = 70)	Extensive (n = 11)	
Energy	37.4 (40.7)	62.2 (41.9)	0.01*	49.6 (39.7)	65.2 (26.7)	0.2
Pain	20.2 (26.8)	44.2 (33.0)	0.0004*	22.5 (23.6)	46.2 (39.0)	0.1
Emotional reactions	23.9 (22.9)	32.4 (29.1)	0.2	27.3 (29.3)	37.6 (30.2)	0.2
Sleep	35.3 (31.7)	49.9 (33.9)	0.04*	32.7 (31.9)	44.4 (30.4)	0.2
Social isolation	11.9 (22.3)	15.0 (20.3)	0.2	18.8 (27.5)	19.3 (20.2)	0.5
Physical mobility	27.1 (26.6)	41.8 (31.6)	0.04*	33.7 (26.8)	43.9 (28.9)	0.2

Table 6.34 Comparison of functioning and global quality of life scores of patients with limited and extensive disease on EORTC QLQ-C30 at baseline and follow-up [the higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100, all figures are mean scores(sd)]

	Baseline		P+	Follow-up		P+
	Limited (n = 101)	Extensive (n = 24)		Limited (n = 70)	Extensive (n = 11)	
Physical functioning	64.0 (28.1)	51.7 (24.3)	0.04*	56.6 (25.9)	49.1 (16.4)	0.3
Role functioning	61.9 (35.5)	47.9 (42.9)	0.1	47.9 (31.2)	36.4 (23.4)	0.3
Emotional functioning	79.3 (22.0)	73.3 (20.3)	0.1	76.1 (22.1)	73.5 (23.8)	0.7
Social functioning	88.0 (23.6)	84.0 (18.7)	0.07	82.6 (23.6)	77.3 (18.7)	0.2
Cognitive functioning	86.1 (20.3)	80.6 (23.9)	0.3	82.1 (23.6)	71.2 (27.0)	0.2
Global quality of life	52.5 (21.3)	37.8 (28.2)	0.01*	51.9 (25.9)	50.0 (25.8)	0.8

+ 2-tailed probability based on Mann-Whitney U test (mean rank)
* Significant at 5% level.

Table 6.35 Comparison of symptoms scores of patients with limited and extensive disease on EORTC QLQ-C30 and QLQ-LC13 at baseline and follow-up [the higher valued indicate a greater degree of symptoms, min.: 0, max.: 100, all figures are mean scores (sd)]

	Baseline		P+	Follow-up		P+
	Limited (n = 101)	Extensive (n = 24)		Limited (n = 70)	Extensive (n = 11)	
Cough	46.5 (32.7)	45.8 (33.8)	0.9	35.7 (29.1)	48.5 (34.5)	0.2
Haemoptysis	8.6 (20.9)	15.3 (31.1)	0.4	4.8 (16.3)	00.0 (00.0)	0.3
Dyspnoea	36.8 (28.5)	40.6 (22.4)	0.4	35.8 (27.5)	37.9 (28.2)	0.8
Pain	22.6 (25.0)	45.1 (33.9)	0.003*	22.1 (26.1)	40.9 (38.3)	0.2
Pain in chest	20.1 (27.5)	27.8 (33.6)	0.4	23.8 (31.2)	30.3 (37.9)	0.7
Pain in shoulder	24.1 (33.0)	37.5 (38.5)	0.1	17.6 (26.4)	27.3 (36.0)	0.4
Pain elsewhere	22.1 (31.7)	36.1 (36.7)	0.08	20.5 (28.5)	21.2 (37.3)	0.8
Sleep difficulties	27.4 (35.7)	44.4 (41.3)	0.07	24.3 (32.1)	30.3 (37.9)	0.7
Fatigue	33.2 (28.1)	53.2 (30.0)	0.004*	38.3 (27.2)	53.5 (22.1)	0.07
Appetite loss	30.4 (32.7)	50.0 (35.4)	0.01*	29.0 (33.5)	54.5 (22.5)	0.008*
Hair loss	00.7 (4.7)	1.4 (6.8)	0.5	21.9 (38.0)	30.3 (43.3)	0.6
Nausea and vomiting	7.6 (16.6)	16.7 (21.4)	0.004*	11.2 (18.5)	19.7 (30.6)	0.5
Constipation	16.5 (30.8)	31.9 (36.0)	0.02*	27.1 (36.0)	42.4 (36.8)	0.2
Diarrhoea	7.3 (20.9)	2.8 (9.4)	0.6	4.8 (14.2)	00.0 (00.0)	0.2
Peripheral neuropathy	12.2 (27.4)	9.7 (25.0)	0.7	15.7 (23.9)	30.3 (37.9)	0.2
Sore mouth	2.0 (11.4)	4.2 (14.9)	0.4	14.3 (28.7)	6.1 (20.1)	0.3
Trouble swallowing	7.6 (20.5)	9.7 (28.6)	0.8	11.9 (22.7)	18.2 (34.5)	0.7
Financial difficulties	8.3 (21.8)	8.3 (20.3)	0.8	9.5 (24.8)	6.1 (20.1)	0.6

+ 2-tailed probability based on Mann-Whitney U test (mean rank).
* Significant at 5% level.

3.5.2 *Effect of treatment on patients with limited and extensive disease*

Eighty-two patients were followed-up. Of these, case records for 81 patients were available indicating that there were 70 patients with limited and 11 with extensive diseases. Thus, the baseline and follow-up assessments for each group were matched and compared.

Tables 6.36 and 6.37 presents patients' general health status and functioning scores as measured by the NHP and the EORTC QLQ-C30. Both patients with limited and extensive disease reported deterioration in their quality of life after they had received treatment. However, patients with limited disease reported slight improvement in sleep, and patients with extensive disease in emotional functioning.

Table 6.38 presents patients' evaluation of their own disease symptoms and treatment side-effects as measured by the EORTC QLQ-C30 and QLQ-LC13. For patients with limited disease the only significant improvement was on cough ($p = 0.005$), while this was not the case for patients with extensive disease. On the other hand, patients developed significant treatment-related side-effects such as hair loss ($p = 0.0001$ in limited disease and $p = 0.04$ in extensive disease), sore mouth ($p = 0.0005$ in limited disease). Overall, as indicated in Table 6.38 the treatment not only did not improve patients' quality of life significantly, but also caused them several new problems related to the treatment they had received.

Table 6.36 Patients' mean scores (sd) on the NHP-Part I before and after treatment by those who had limited disease and those with extensive disease (the higher values indicate more perceived health problems, min.: 0, max.: 100)

	Limited disease (n = 70)		P+	Extensive disease (n = 11)		P+
	Before	After		Before	After	
Energy	32.0 (37.6)	49.6 (39.7)	**0.0007***	42.9 (39.6)	65.2 (26.7)	**0.1**
Pain	19.2 (26.3)	22.5 (23.6)	**0.2**	34.9 (34.2)	46.2 (39.0)	**0.4**
Emotional reactions	21.1 (22.2)	27.3 (29.3)	**0.08**	31.2 (33.1)	37.6 (30.2)	**0.6**
Sleep	34.3 (31.6)	32.7 (31.9)	**0.7**	41.6 (34.1)	44.4 (30.4)	**0.3**
Social isolation	11.1 (22.8)	18.8 (27.5)	**0.02***	19.2 (23.9)	19.3 (20.2)	**1.0**
Physical mobility	23.0 (24.5)	33.7 (26.8)	**0.001***	30.9 (29.5)	43.9 (28.9)	**0.3**

Table 6.37 Patients' functioning and global quality of life mean scores (sd) on EORTC QLQ-C30 before and after treatment by those who had limited disease and those with extensive disease (the higher values indicate a higher level of functioning and quality of life, min.: 0, max.: 100)

	Limited disease (n = 70)		P+	Extensive disease (n = 11)		P+
	Before	After		Before	After	
Physical functioning	67.4 (26.0)	56.6 (25.9)	**0.001***	61.8 (16.6)	49.1 (16.4)	**0.08**
Role functioning	65.0 (33.4)	47.9 (31.2)	**0.001***	59.1 (43.7)	36.4 (23.4)	**0.2**
Emotional functioning	80.6 (22.8)	76.1 (22.1)	**0.2**	68.2 (16.2)	73.5 (23.8)	**0.3**
Social functioning	86.4 (25.3)	82.6 (23.6)	**0.09**	83.3 (21.1)	77.3 (18.7)	**0.4**
Cognitive functioning	87.1 (20.1)	82.1 (23.6)	**0.1**	78.8 (24.8)	71.2 (27.0)	**0.3**
Global quality of life	54.2 (21.3)	51.9 (25.9)	**0.6**	50.8 (30.2)	50.0 (25.8)	**0.9**

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant at 5% level.

Table 6.38 Patients' symptoms mean scores (sd) on EORTC QLQ-C30 and QLQ-LC13 before and after treatment by those who had limited disease and those with extensive disease (the higher values indicate a greater degree of symptoms, min.: 0, max.: 100)

	Limited disease (n = 70)		P+	Extensive disease (n = 11)		P+
	Before	After		Before	After	
Cough	48.6 (30.4)	35.7 (29.1)	0.005*	54.5 (37.3)	48.5 (34.5)	.7
Haemoptysis	9.5 (21.3)	4.8 (16.3)	0.2	18.1 (34.5)	00.0 (00.0)	0.1
Dyspnoea	35.2 (27.2)	35.8 (27.5)	1.0	42.4 (24.0)	37.9 (28.2)	0.8
Pain	22.4 (23.6)	22.1 (26.1)	0.9	37.9 (30.0)	40.9 (38.3)	0.7
Pain in chest	21.4 (27.2)	23.8 (31.2)	0.7	27.3 (36.0)	30.3 (37.9)	0.8
Pain in shoulder	23.8 (31.2)	17.6 (26.4)	0.1	42.4 (45.0)	27.3 (36.0)	0.1
Pain elsewhere	18.6 (27.6)	20.5 (28.5)	0.7	30.3 (37.9)	21.2 (37.3)	0.6
Sleep difficulties	27.1 (34.7)	24.3 (32.1)	0.6	42.4 (44.9)	30.3 (37.9)	0.5
Fatigue	31.7 (27.8)	38.3 (27.2)	0.03*	40.4 (31.9)	53.5 (22.1)	0.2
Appetite loss	29.5 (32.9)	29.0 (33.5)	1.0	42.4 (36.8)	54.5 (22.5)	0.4
Hair loss	1.0 (5.6)	21.9 (38.0)	0.0001*	00.0 (00.0)	30.3 (43.3)	0.04*
Nausea and vomiting	5.7 (13.0)	11.2 (18.5)	0.04*	21.2 (26.0)	19.7 (30.6)	0.9
Constipation	15.7 (29.3)	27.1 (36.0)	0.03*	18.2 (27.3)	42.4 (36.8)	0.09
Diarrhoea	7.1 (19.6)	4.8 (14.2)	0.4	6.1 (13.5)	00.0 (00.0)	0.2
Peripheral neuropathy	12.9 (28.0)	15.7 (23.9)	0.3	9.1 (30.2)	30.3 (37.9)	0.1
Sore mouth	1.0 (5.6)	14.3 (28.7)	0.0005*	00.0 (00.0)	6.1 (20.1)	0.3
Trouble swallowing	6.7 (17.6)	11.9 (22.7)	0.1	12.1 (30.8)	18.2 (34.5)	0.6
Financial difficulties	8.1 (20.0)	9.5 (24.8)	0.6	6.1 (20.1)	6.1 (20.1)	1.0

+ Probability based on Wilcoxon matched-pairs signed-ranks test.
* Significant a 5% level.

3.6. Pain medication at follow-up

Out of 82 patients who were followed-up, 33 lung cancer patients (40%) indicated that they did not take any pain medications during the last week prior to the interview, and the remaining 49 (60%) said that they received pain killers. The analysis showed that the pattern of pain medication in these patients as compared to their baseline conditions did not change significantly ($p = 0.9$).

Of those who received pain killers, 5 patients (10%) stated that it did not help them at all, 29 (60%) said that it did help a little, 10 (20%) reported that it did help quite a bit, and finally 5 patients (10%) indicated that it did help them very much. When this pattern was examined against the baseline pattern in the same patients, there was no significant difference between the baseline and the follow-up patterns ($p = 0.4$).

3.7. Prediction of global quality of life at follow-up assessments

The only index of global quality of life was that of the EORTC QLQ-C30 which consisted of two 7-point scales of patients' general health status and quality of life. Thus, in a follow-up stage to investigate which variables predicted global quality of life, a similar analysis to the baseline assessments (logistic regression) was performed. The global quality of life at follow-up assessment was chosen as an outcome (dependent variable), and in 5 separate equations 6 groups of variables were chosen as predictors (independent

variables). In the first model the functioning scales (from the EORTC QLQ-C30); in the second the disease- and treatment related symptoms (from the EORTC QLQ-C30 and QLQ-LC13); in the third the prognostic factors, these were (age, sex, extent of disease, weight loss, and performance status); in the fourth the NHP scales, in the fifth some related socio-demographic, clinical and support variables and finnaly, all above variavles were chosen. In the following sections the results of the analysis are presented.

(I) Of functioning scores the social and physical functioning were significant predictors of global quality of life at follow-up (Figure 6.13).

(II) Of patients' symptoms two were significant predictors of global quality of life at follow-up: firstly nausea and vomiting and secondly, pain in other sites in the body (Figure 6.14)

(III) Of prognostic factors at baseline, only the performance status was a significant predictor of global quality of life at follow-up (Figure 6.15).

(IV) None of the patients' scores on the NHP were significant predictors of global quality of life at follow-up (Figure 6.16).

(V) When analysis was performed based on socio-economic, clinical and support variables, Deprivation Category and marital status were significant predictors of patients' global quality of life at follow-up predicting that those who lived in deprived areas and were widowed, separated, and divorced had a lower global quality of life ($p = 0.03$, and 0.01 respectively). Surprisingly, none of the medical factors (diagnosis and treatment modalities) was

significant in predicting what might happen to the patients' global quality of life at follow-up (Figure 6.17).

(VI) Finally all the above variables were chosen and the regression analysis was performed by selecting the 'forward conditional' model. Only two variables (fatigue, nausea and vomiting) were found to be significant predictors of global quality of life at follow-up ($p = 0.0002$, and 0.009 respectively).

The analysis also indicated that fatigue accounted for the apparent influence on many perceived health problems (e.g. pain, energy, sleep difficulties), performance status, functioning (e.g. role, and social functioning), and symptoms (e.g. loss of appetite, dyspnoea, cough). Nausea and vomiting, in turn, accounted for the apparent effect of the residual variables including physical mobility, emotional functioning, and pain in other sites of the body.

Figure 6.13 Logistic regression analysis-Global quality of life and functioning

```
Number of cases included in the analysis: 82
Dependent Variable..   Follow-up Global quality of life
* Constant is included in the model.
Beginning Block Number  1.  Method: Enter
Variable(s) Entered on Step Number
1..        XPF2       Physical functioning-follow up
           XRF2       Role functioning-follow up
           XEF2       Emotional functioning-follow up
           XSF2       Social functioning-follow up
           XCF2       Cognitive functioning-follow up
---------------------- Variables in the Equation -----------------------
Variable            B        S.E.     Wald     df      Sig        R    Exp(B)

XPF2             -.0349      .0172   4.1233     1     .0423   -.1371     .9657
XRF2             -.0008      .0133     .0039    1     .9500    .0000     .9992
XEF2             -.0115      .0153     .5683    1     .4509    .0000     .9885
XSF2             -.0441      .0194   5.1933     1     .0227   -.1682     .9568
XCF2             -.0066      .0156     .1820    1     .6697    .0000     .9934
Constant         7.4525     1.9910  14.0110     1     .0002
```

Figure 6.14 Logistic regression analysis-Global quality of life and symptoms

```
Number of cases included in the analysis: 82
Dependent Variable..   Follow-up Global quality of life
* Constant is included in the model.
Beginning Block Number  1.  Method: Enter
Variable(s) Entered on Step Number
1..        XAP2       Appetite loss-follow up
           XBR2       Dyspnoea-follow up
           XCO2       Constipation-follow up
           XCOU2      Cough-follow up
           XDI2       Diarrhoea-follow up
           XFA2       Fatigue-follow up
           XFI2       Financial difficulties-follow up
           XHL2       Hair loss-follow up
           XHP2       Haemoptysis-follow up
           XNV2       Nausea and vomiting-follow up
           XPA2       Pain-follow up
           XPC2       Chest pain-follow up
           XPS2       Pain in arm & shoulder-follow up
           XPE2       Pain elsewhere-follow up
           XPN2       Peripheral neuropathy-follow up
           XSL2       Sleep-follow up
           XSM2       Sore mouth-follow up
           XSW2       Trouble swallowing-follow up
---------------------- Variables in the Equation -----------------------
Variable            B        S.E.     Wald     df      Sig        R    Exp(B)
XAP2             .0364      .0204   3.1854     1     .0743    .1025    1.0371
XBR2             .0107      .0295     .1310    1     .7174    .0000    1.0107
XCO2            -.0194      .0147   1.7393     1     .1872    .0000     .9807
XCOU2            .0308      .0176   3.0587     1     .0803    .0968    1.0313
XDI2            -.0903      .0557   2.6265     1     .1051   -.0745     .9137
XFA2             .0182      .0343     .2811    1     .5960    .0000    1.0183
XFI2             .1373      .7911     .0301    1     .8622    .0000    1.1472
XHL2            -.0089      .0126     .4899    1     .4840    .0000     .9912
XHP2             .0343      .0424     .6539    1     .4187    .0000    1.0349
XNV2             .1059      .0407   6.7552     1     .0093    .2052    1.1117
XPA2            -.0135      .0283     .2285    1     .6327    .0000     .9866
XPC2            -.0108      .0173     .3862    1     .5343    .0000     .9893
XPS2             .0082      .0159     .2649    1     .6068    .0000    1.0082
XPE2             .0389      .0181   4.6130     1     .0317    .1521    1.0397
XPN2            -.0231      .0207   1.2455     1     .2644    .0000     .9772
XSL2            -.0092      .0150     .3767    1     .5394    .0000     .9908
XSM2             .0103      .0169     .3697    1     .5432    .0000    1.0103
XSW2             .0266      .0226   1.3847     1     .2393    .0000    1.0270
Constant        -3.2682     .9628  11.5226     1     .0007
```

Figure 6.15 Logistic regression analysis-Global quality of life and prognostic factors

Number of cases included in the analysis: 81
Parameter coding (categorical data)

	Value	Freq	Coding (1)	(2)	(3)
WEIGHT LOSS					
significant weight loss	1.00	33	1.000	.000	.000
weight steady	2.00	26	.000	1.000	.000
possible weight loss	3.00	7	.000	.000	1.000
no comment	4.00	15	.000	.000	.000
EXTENT OF DISEASE					
limited	1.00	70	.000		
extensive	2.00	11	1.000		
SEX					
male	1	48	.000		
female	2	33	1.000		

Dependent Variable.. Follow-up Global quality of life
* Constant is included in the model.
Beginning Block Number 1. Method: Enter
Variable(s) Entered on Step Number
1.. AGE Age
SEX sex
EXTENT Extent of disease
WEIGHLOS Weight loss
ECOG2 Performance status/ECOG2- follow up

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
AGE	.0077	.0310	.0614	1	.8043	.0000	1.0077
SEX(1)	-.8580	.5784	2.2004	1	.1380	-.0424	.4240
EXTENT(1)	.0338	.8257	.0017	1	.9674	.0000	1.0344
WEIGHLOS			4.4933	3	.2129	.0000	
WEIGHLOS(1)	-1.2614	.7809	2.6096	1	.1062	-.0740	.2832
WEIGHLOS(2)	-.2292	.8081	.0805	1	.7767	.0000	.7952
WEIGHLOS(3)	-1.4101	1.1923	1.3987	1	.2369	.0000	.2441
ECOG2	1.5089	.4136	13.3089	1	.0003	.3188	4.5220
Constant	-1.2118	2.2862	.2809	1	.5961		

Figure 6.16 Logistic regression analysis-Global quality of life and NHP

Number of cases included in the analysis: 82
Dependent Variable.. Follow-up Global quality of life
* Constant is included in the model.
Beginning Block Number 1. Method: Enter
Variable(s) Entered on Step Number
1.. TEM2 Emotional reactions-follow up
TEN2 Energy-follow up
TP2 Pain-follow up
TPM2 Physical mobility-follow up
TSL2 Sleep- follow up
TSO2 Social isolation-follow up

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
TEM2	.0264	.0155	2.9038	1	.0884	.0895	1.0267
TEN2	.0145	.0099	2.1260	1	.1448	.0334	1.0146
TP2	.0039	.0151	.0654	1	.7981	.0000	1.0039
TPM2	.0261	.0141	3.4013	1	.0651	.1114	1.0264
TSL2	-.0031	.0102	.0936	1	.7597	.0000	.9969
TSO2	-.0265	.0157	2.8388	1	.0920	-.0862	.9738
Constant	-1.5738	.5036	9.7671	1	.0018		

Figure 6.17 Logistic regression analysis-Global quality of life and socio-demographic, clinical and social support variables

Number of cases included in the analysis: 81
Parameter coding (categorical data)

	Value	Freq	Coding (1)	(2)	(3)
EMPLOYMENT STATUS					
employed	1	12	.000	.000	.000
unemployed	2	7	1.000	.000	.000
housewife	3	15	.000	1.000	.000
retired	4	47	.000	.000	1.000
TYPE OF ACCOMMODATION					
flat	1	30	1.000	.000	.000
semi-detached	2	23	.000	1.000	.000
4 in Block	3	10	.000	.000	1.000
terrace house/house/others	4	18	.000	.000	.000
TREATMENT					
chemotherapy	1	25	1.000	.000	.000
radiotherapy	2	29	.000	1.000	.000
surgery	3	6	.000	.000	1.000
supportive care	4	21	.000	.000	.000
NEIGHBOUR SUPPORT					
never/almost never	1	61	1.000	.000	
sometimes	2	9	.000	1.000	
almost always/always	3	11	.000	.000	
MARITAL STATUS					
married	1	49	.000	.000	
single	2	4	1.000	.000	
widowed/separated/divorced	3	28	.000	1.000	
DIAGNOSIS					
non-small cell	1	44	1.000	.000	
small cell	2	17	.000	1.000	
unspecified	3	20	.000	.000	
FAMILY SUPPORT					
never/almost never	1	67	1.000	.000	
sometimes	2	5	.000	1.000	
almost always/always	3	9	.000	.000	
CHILDREN SUPPORT					
never/almost never	1	42	1.000	.000	
sometimes	2	4	.000	1.000	
almost always/always	3	35	.000	.000	
DEPRIVATION CATEGORY					
affluent	1	16	.000	.000	
middle	2	19	1.000	.000	
deprived	3	46	.000	1.000	

Dependent Variable.. Follow-up Global quality of life

* Constant is included in the model.

Beginning Block Number 1. Method: Enter

Variable(s) Entered on Step Number

1.. DEPCAT Deprivation Category
EMPLOY Employment status
TYPEHOM Type of accommodation
MARITAL Marital status
DIAGNOS Diagnosis
TREATMEN Types of treatment
CHILHEL Help receiving from children
FAMILYH Help receiving from family
NEIGHBH Help receiving from neighbour

---------- Variables in the Equation ----------

Variable	B	S.E.	Wald	df	Sig	R	Exp(B)
DEPCAT			4.6858	2	.0960	.0785	
DEPCAT(1)	1.5043	.9720	2.3953	1	.1217	.0596	4.5009
DEPCAT(2)	2.0421	.9434	4.6857	1	.0304	.1553	7.7065
EMPLOY			2.3626	3	.5006	.0000	
EMPLOY(1)	-1.7355	1.3651	1.6162	1	.2036	.0000	.1763
EMPLOY(2)	-.4672	1.1473	.1658	1	.6839	.0000	.6268
EMPLOY(3)	-.0741	.9922	.0056	1	.9404	.0000	.9285
TYPEHOM			4.5426	3	.2085	.0000	
TYPEHOM(1)	.4038	.8444	.2287	1	.6325	.0000	1.4975
TYPEHOM(2)	.3350	.8495	.1555	1	.6933	.0000	1.3979
TYPEHOM(3)	-1.8170	1.2067	2.2674	1	.1321	-.0490	.1625
MARITAL			5.5565	2	.0621	.1183	
MARITAL(1)	-.9890	1.4685	.4535	1	.5007	.0000	.3720
MARITAL(2)	-1.6854	.7152	5.5528	1	.0185	-.1787	.1854
DIAGNOS			3.1604	2	.2059	.0000	
DIAGNOS(1)	.6851	.7356	.8673	1	.3517	.0000	1.9840
DIAGNOS(2)	-1.5191	1.4528	1.0933	1	.2957	.0000	.2189
TREATMEN			4.6111	3	.2026	.0000	
TREATMEN(1)	1.6233	1.3278	1.4947	1	.2215	.0000	5.0698
TREATMEN(2)	-.2304	.7750	.0883	1	.7663	.0000	.7942
TREATMEN(3)	-1.9733	1.3093	2.2716	1	.1318	-.0494	.1390
CHILHEL			.0846	2	.9586	.0000	
CHILHEL(1)	.1024	.6472	.0250	1	.8743	.0000	1.1078
CHILHEL(2)	-.2858	1.4285	.0400	1	.8414	.0000	.7514
FAMILYH			4.3292	2	.1148	.0544	
FAMILYH(1)	1.4483	1.0217	2.0093	1	.1563	.0091	4.2558
FAMILYH(2)	3.5853	1.7763	4.0741	1	.0535	.1365	36.0650
NEIGHBH			.7859	2	.6750	.0000	
NEIGHBH(1)	.6692	.8789	.5798	1	.4464	.0000	1.9527
NEIGHBH(2)	.1145	1.3173	.0076	1	.9307	.0000	1.1213

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The remaining 9 patients (4%) who found being interviewed "not very or not at all" acceptable, stated that this was due the following reasons: "It was too long" (2 Patients), "Because of my health" (3 patients), "I could not see the relevance of the questions to myself" (2 patients), "It disturbed me" (1 patient), and "I just did not like it" (1 patient).

The association between gender, age, deprivation category, diagnosis, general health status, global quality of life status, and interview setting, and the patients' preferences and the reasons they stated for acceptability were investigated. These are shown in Tables 6.40 and 6.41. There were no significant associations between these variables except for age where there were significant differences between older and relatively younger patients in the reasons they gave for being interviewed acceptable.

However, the evaluation results indicated that: patients preferred to be interviewed rather than to fill in a questionnaire, and that interview was acceptable to them regardless of their characteristics including socio-economic status, clinical characteristics, their general health status and global quality of life, and the interview setting. Finally, they expressed four main reasons for the acceptability of the interviews. All these are considered to be components of an effective communication indicating that understanding patients' feelings is essential. How to achieve this remains the major question.

Table 6.39 Patients' reactions toward the study (acceptability questionnaire)

	No.	%
Were the questions easy to understand?		
very easy	184	77
moderately easy	51	22
not very easy	3	1
not at all	000	00
Did you find the questions relevant?		
very relevant	125	52
moderately relevant	92	39
not very relevant	18	8
not at all	3	1
Do you prefer to fill in a questionnaire or to be interviewed?		
fill in a questionnaire	23	10
to be interviewed	168	70
either	43	18
don't know	4	2
Do you think if you wanted to fill in questionnaires, you might had difficulties?		
very difficult	11	5
quite difficult	27	11
not very difficult	37	16
not at all	163	69
Do you find being interviewed acceptable?		
very acceptable	191	80
quite acceptable	38	16
not very acceptable	7	3
not at all	2	1
Can you give reasons?		
it did not bother me	56	24
felt at ease and relaxed	62	26
it was nice to talk	44	18
it was conversational/the way of interview	67	28
other reasons (unacceptable)	9	4
Do you prefer to be interviewed at home or in the clinic?		
clinic	55	23
home	108	45
either	71	28
don't know	4	2

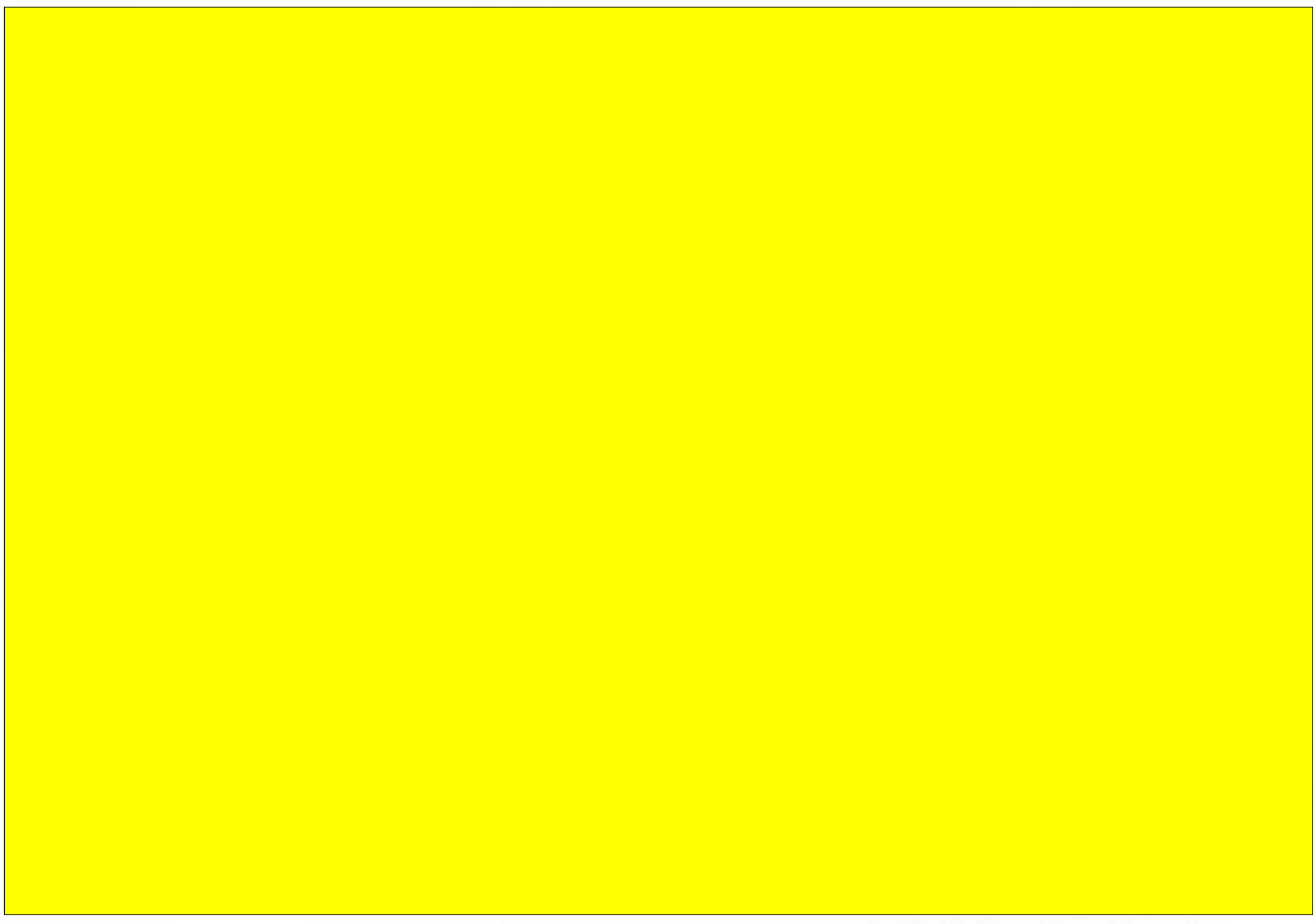
Table 6.40 Patients' preferences by their demographic characteristics, general health status, global quality of life, and interview setting

	Fill in questionnaire (n =23) No. (%)	To be interviewed (n = 168) No. (%)	Either (n = 43) No. (%)	P
Sex				
male	15 (65)	89 (53)	28 (65)	
female	8 (35)	79 (47)	15 (35)	
				0.2
Age				
65<	11 (48)	72 (43)	19 (44)	
65>	12 (52)	96 (57)	24 (56)	
				0.9
Deprivation category				
affluent	7 (30)	40 (24)	15 (35)	
deprived	16 (70)	128 (76)	28 (65)	
				0.3
Diagnosis				
lung cancer cases	10 (44)	93 (55)	22 (51)	
respiratory disease controls	13 (56)	75 (45)	21 (49)	
				0.5
General health status				
very poor/poor	7 (30)	66 (39)	16 (37)	
good	8 (35)	53 (32)	17 (40)	
very good/excellent	8 (35)	49 (29)	10 (23)	
				0.8
Global quality of life				
very poor/poor	4 (17)	55 (33)	11 (26)	
good	10 (44)	57 (34)	9 (21)	
very good/excellent	9 (39)	56 (33)	23 (53)	
				0.08
Interview setting				
home	8 (35)	38 (23)	14 (33)	
clinic	15 (65)	130 (77)	29 (67)	
				0.2

It is nice to talk

Effective communication
A key in interviewing cancer patients

Interview approach was found to be very acceptable



5. Patients' perceptions of quality of life

Patients' perceptions of quality of life were investigated. Due to practical considerations (patients' time, crowded clinics, etc.), only 200 patients were asked to define quality of life, to identify what a good quality of life is for themselves, and to indicate the importance attached to the components parts of their quality of life. Of these, 108 were cases and 92 controls. Fifty-six percent (112) of the patients were males and 44% (88) females. There were no significant differences between cases and controls in socio-demographic characteristics nor with the original sample who participated in the study.

5.1. Definition of quality of life by patients

When patients were asked to define quality of life, contradictory to expectation they identified a limited number of areas of life. In total 8 areas of life were extracted from patients' responses. All patients identified at least one aspect of life, 87% two dimensions of life, 59% mentioned three areas, while only 21% nominated four dimensions of life as definition of the quality of life. The highest proportion of respondents (42%) mentioned "health" as a definition of quality of life while only 5% of patients indicated that "living longer" mean quality of life. There was no significant difference between cases and controls in most dimensions except in financial security. The controls tend significantly to consider financial security as one of the components of quality of life more than cases. In contrast, although not significant, the cases tended to nominate health, happiness, and survival more and family life less than controls (Table 6.42).

5.2. A good quality of life as perceived by patients

Respondents were asked to identify what a good quality of life is for themselves. "Family life" was mentioned by 58% of the respondents as an area that makes life better for them. In second place their "own health" was

nominated (51%), and "social life" by 43%. Although there was no significant difference between cases and controls, cases mentioned health more than controls as an area that make their quality of life better. It is worth noting that when cases were asked to define quality of life in general they did mention family life less than controls, but when they described their own quality of life they considered family life as important as their own health (Table 6.43).

5.3. Order of importance

Finally, patients were asked to rank nominated items in order of importance. The overall results are shown in Table 6.44. The highest proportion of patients nominated family life as the most important factor (27%), followed by their own health (25%). Health was mentioned as the second most important factor (21%), followed by family life (18%), and financial security (18%). This, however, clearly suggests that family life and health were the most or second most important factors. As described earlier, most patients considered that a good quality of life depends on only two factors. In contrast, only half the patients or less identified third and fourth factors. For example, in relation to the fourth important factor for a good quality of life the highest proportion of patients nominated social life (27%), followed by happiness (17%), and enjoyment of life (15%).

The stratified analysis indicated that in almost all nominated areas there were no significant differences between cases and controls. Twenty eight cases and 26 controls nominated "family life" as the most important factor of a good quality of life, followed by their own health (32 cases and 18 controls). Health

is placed second by 22 cases and 14 controls, followed by family life (20 cases and 12 controls, and financial security (15 cases and 17 controls). The results are shown in Table 6.45.

Table 6.42 Definition of quality of life by lung cancer cases and respiratory disease controls

Nominated areas	Cases (n = 108)	Controls (n = 92)	Total* (n = 200)	OR (95% CI)
	No. (%)	No. (%)	No. (%)	
Ability to do what one wants to do/work	15 (14)	16 (17)	31 (16)	0.77 (0.33 to 1.76)
Enjoyment of life	24 (22)	25 (27)	49 (25)	0.77 (0.38 to 1.53)
Family life	20 (19)	27 (29)	47 (24)	0.55 (0.27 to 1.11)
Financial security	12 (11)	20 (22)	32 (16)	0.45 (0.19 to 1.04)**
Happiness	24 (22)	17 (18)	41 (21)	1.26 (0.60 to 2.68)
Health	49 (45)	35 (38)	84 (42)	1.35 (0.74 to 2.48)
Living longer	7 (6)	2 (2)	9 (5)	3.12 (0.75 to 31.4)
Social life/ leisure activities	12 (11)	14 (15)	26 (13)	0.70 (0.28 to 1.71)

* Since some respondents nominated more than one area, the total exceeds 100% and total sample size.
** $P < 0.05$

Table 6.43 A good quality of life as perceived by lung cancer cases and respiratory disease controls

Items	Cases (n = 108)	Controls (n = 92)	Total* (n = 200)	OR (95% CI)
	No. (%)	No. (%)	No. (%)	
Ability to do what one wants to do/work	17 (16)	16 (17)	33 (16)	0.89 (0.39 to 2.00)
Enjoyment of life	37 (34)	31 (34)	68 (34)	1.03 (0.55 to 1.92)
Family life	59 (55)	56 (61)	115 (58)	0.77 (0.42 to 1.42)
Financial security	28 (26)	29 (32)	57 (28)	0.76 (0.39 to 1.47)
Happiness	28 (26)	28 (30)	56 (28)	0.80 (0.41 to 1.55)
Health (own health)	60 (56)	41 (45)	101 (51)	1.55 (0.86 to 2.83)
Living longer	10 (9)	6 (7)	16 (8)	1.46 (0.46 to 5.10)
Social life/ leisure activities	45 (42)	40 (43)	86 (43)	0.93 (0.51 to 1.69)

* Since some respondents nominated more than one area, the total exceeds 100% and total sample size.

Table 6.44 Dimensions of life mentioned as a good quality of life in order of importance (overall results)

Items	1st important (n = 200)	2nd important (n = 174)	3rd important (n = 118)	4th important (n = 41)
	No. (%)	No. (%)	No. (%)	No.(%)
Ability to do what one wants to do/work	11 (6)	8 (5)	9 (8)	5 (12)
Enjoyment of life	28 (14)	19 (11)	15 (13)	6 (15)
Family life	54 (27)	32 (18)	26 (22)	3 (7)
Financial security	6 (3)	32 (18)	16 (14)	3 (7)
Happiness	20 (10)	15 (9)	14 (12)	7 (17)
Health (own health)	50 (25)	36 (21)	13 (11)	4 (10)
Living longer	4 (4)	5 (3)	5 (4)	2 (5)
Social life/ leisure activities	27 (14)	27 (16)	20 (17)	11 (27)

Table 6.45 Dimensions of life mentioned as a good quality of life in order of importance by cases and controls

Items[+]	1st important (n = 200)		2nd important (n = 174)		3rd important (n = 118)		4th important (n = 41)	
	Cases	Controls	Cases	Controls	Cases	Controls	cases	controls
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No.(%)	No. (%)
Ability to do what one wants to do/work	6 (6)	5 (4)	5 (5)	3 (4)	3 (5)	6 (11)	3 (14)	2 (11)
Enjoyment of life	12 (11)	16 (17)	10 (11)	9 (11)	12 (20)	3 (5)	3 (14)	3 (16)
Family life	28 (26)	26 (28)	20 (22)	12 (15)	9 (15)	17 (30)	2 (9)	1 (5)
Financial security	1 (1)	5 (5)	15 (16)	17 (21)	11 (18)	5 (9)	1 (5)	2 (11)
Happiness	12 (11)	8 (9)	6 (7)	9 (11)	4 (7)	10 (18)	6 (27)	1 (5)
Health (own health)	32 (30)	18 (20)	22 (24)	14 (17)	6 (10)	7 (12)	0 (0)	4 (21)
Living longer	3 (3)	1 (1)	2 (2)	3 (4)	4 (7)	1 (2)	1 (5)	1 (5)
Social life/ leisure activities	14 (13)	13 (14)	13 (14)	14 (17)	12 (20)	8 (14)	6 (27)	5 (26)
Total	108 (100)	92 (100)	93 (100)	81 (100)	61 (100)	57 (100)	22 (100)	19 (100)

[+] There were no significant differences between cases and controls except those are indicated in the Table.

CHAPTER SEVEN

7

DISCUSSION

Contents

- Introduction

1. General discussion

2. Study population

3. Baseline assessment

4. Follow-up assessment

5. Patients' reactions to the study

Introduction

This chapter discusses the study findings and provides explanations relevant to quality of life in patients with lung cancer. First, a general discussion is provided and then based on the study findings, several topics are covered and presented in the following sections.

1. General discussion

1.1 The study findings

There were several major findings in this study, including the following:-

- Global quality of life prior to diagnosis was a predictor of length of survival in lung cancer patients.
- There was a difference between patients' and health professionals' perception of quality of life
- There was no significant difference between the socio-demographic characteristics of lung cancer cases and chronic respiratory disease controls.
- There were no significant differences between quality of life in cases and controls except for pain and loss of appetite.
- There was no significant difference in quality of life of lung cancer patients before and after treatment.
- Social support, social networks, and patients' socio-economic background were found to be important determinants of their baseline quality of life.

- Non-medical factors (Deprivation Category and marital status) were found to be significant predictors of patients' global quality of life at follow-up, whereas medical factors (cell type and treatment modalities) were not.
- Patients' reactions to the study indicated that they did not find the study intrusive. However, they preferred to be interviewed at home rather than to fill in a questionnaire in the clinic.

The implications of the above findings in research, and management of lung cancer are explored in the following sections.

1.2. Quality of life

Quality of life is difficult to define and varies among individuals. The findings of this study are advances in the debate. For example, most recent quality of life measures are developed within the framework proposed by the European Organisation for Research and Treatment of Cancer (EORTC) which has its own merit, especially since it is necessary to provide a "common language" and prevent haphazard developments. Yet, these instruments carry health professionals' value systems rather than the values and preferences of the public including healthy individuals and patients.

The most interesting results in this study relate to the role of family, and importance of social life, leisure activities and financial security in patients' quality of life. These are vital issues and are often neglected in most of the

well-known measures of quality of life or have, at best, received little attention. Most instruments focus on health, concentrate on feelings, functions and problems associated with the ill health, disability or disease. This study and several recent studies clearly suggest that these instruments should either be reviewed or supplemented with additional items covering family, social life, leisure activities and other areas identified in this study and other studies.

The other interesting finding in this study was that patients defined quality of life in one way, and perceived a good quality of life for themselves in another (Tables 6.42 and 6.43). In addition, their values were very different from those of health professionals as found from the literature, and most existing quality of life instruments. The number of available quality of life instruments is a reflection of such differences, where expert-developed tools still mainly focus on disease or treatment-related symptoms. In terms of understanding the complexity of the individual value system and preferences, these differences are noteworthy. The recent studies on development of a new instrument, the Subjective Quality of Life Profile (SQLP), confirms that these differences are real and should be understood on the basis of difference in individuals' values, that is, the importance they attribute to each area of their lives (Dazord, 1995).

Delivery of effective care requires a much better understanding of patients' views (Montazeri et al., 1996c). The majority of patients in this study were from deprived areas, with low levels of education and yet it seemed that they

had wider and different views about life and its quality as compared to the clinicians who mainly relate quality of life to medical dimensions of patients' daily activities, neglecting the other important aspects of their lives.

However, there are two major problems associated with this and other studies on the subject. First, the problem of change over time and the course of disease, since the perception of patients may change over time. For example, the wish for survival (which was low in this study, 9 out of 200 patients, also see Table 6.42) may become more important than other items near the end of life (which was not studied because the study was not designed for this purpose, and usually at this stage patients are very ill and it is very difficult to ask them their views). Second, the problem related to the flexibility of the individual judgement due to fluctuating defence mechanisms (Jenkinson, 1994a). For example, one may argue that the relatively low rating of "one's own health" as an important factor of quality of life (see Tables 6.43, and 6.44) may be an expression of denial of the threat that cancer and its treatment represents to the individual. Denial may fluctuate over the course of disease and a patient may learn to live with the threat. Then, "one's own health" may become a very important domain.

The main difference in this study from previous work rests on the fact that it was observed that a relatively small number of patients identified more than three areas of life as important components of quality of life or they perceived

to be important for their own quality of life. One explanation is that in this study patients did not receive any instructions such as showcards or a list of suggested dimensions of life which were often used in other studies (Ruta et al., 1994; Bowling, 1995b). This however, indicates that showcards may to some extent create biased results. This study included two general but simple principles: patients were allowed to identify the items that affect their quality of life, and were invited to rate the relative importance of these items to their quality of life.

As compared to controls, cases were more concerned about their own health. This is not surprising since the cases were newly diagnosed lung cancer patients. However, they were concerned about family as much as their own health. These findings are similar to previous and current studies (Bowling, 1995b; Belli et al., 1996) where family was the most important item rated by either general public, or patients with different types of diseases including cancer patients.

1.3. Methodological issues

This is the first epidemiological based study to measure health-related quality of life in patients with lung cancer. Eight criteria in this study were brought together that had not been previously. Although these have been listed in the introduction, it is worthwhile to remind readers once again of these criteria:

1. Quality of life was the main outcome measure.

2. It was a population-based study over a full year rather than a clinic-based study.

3. It was a prospective case-control study.

4. At the baseline assessment of quality of life both patients and interviewer were blind to the diagnosis.

5. There was a detailed investigation of the socio-economic status of patients.

6. The assessment was made using an interviewer-administered approach.

7. The data were obtained either at patients' home or in the clinic.

8. Patients' attitudes toward the study were examined.

This was a double blind study. At the time of baseline assessment of quality of life, the intention was to keep patients and the researcher blind to the diagnosis. At the start of the investigation it was thought this might not be practicable. The investigator was able to interview 208 patients (87%) blind, less than intended. From this, two major methodological issues became clear. Firstly, it was shown that it was possible to conduct a double-blind case-control assessment of quality of life. This was apparently the first time this has been carried out. The advantage of this method of data collection is that it reduces both interviewee and interviewer bias. The only study in the literature similar in design to this project was that of Hughes (1985a; 1985b). Although that was a prospective case-control study, neither patients nor the researcher were blind, and it was primarily a psychiatric assessment rather than a quality

of life study (see Table 3.2). Secondly, until now it was not clear whether knowledge of cancer diagnosis could affect the way in which patients respond to the quality of life questionnaires or not. This was examined and it was found that knowledge of cancer diagnosis does not significantly affect the results.

Another feature of this study was the addition of a study to find out reactions of patients to having their quality of life examined. Having searched the literature thoroughly, this appears to be the first systematic evaluation of patients' feelings about quality of life studies in cancer, since previous researchers have mainly reported on, for example, the proportion of patients who completed the scheduled questionnaires as an indicator of acceptability or feasibility in conducting quality of life assessments in clinical settings (Hurny et al., 1992).

Surprisingly there were no refusals at the time of baseline assessment. Missing cases resulted in a response rate of 89%. At follow-up assessments, out of 90 patients who were suitable for interview, only 8 patients refused to participate. Again, the response rate was high (91%).

More interestingly, there were no refusals from GPs both at baseline and follow-up assessments of patients' quality of life. This was due to several reasons such as prior discussion with their representatives, the contribution of

the study co-ordinator to seek their agreement for each interview, and the importance of the research topic which is one of the main public health problems in the area with a 50% higher incidence rate of lung cancer than the Glasgow average.

There are several reasons for the high response rates in this study, both at baseline and at follow-up. First, the General Practitioners (GPs) in the Stobhill catchment area were well informed about the study. Prior to the start of the study all agreed that their potential patients could be interviewed. The study had a high profile for GPs in Stobhill catchment area. Secondly, the chest physicians in the Stobhill Hospital were very interested in the project and they encouraged recruitment of patients into the study. For example, during the study period several times they forgot on several occasions to talk to the patients about the study during the medical examination in their clinics, but to include these missing patients in the study, physicians followed them through the out-patient department explaining about the study and asked if they wished to participate in the study. There was also a good relationship between researcher and nursing staff, both in the out-patient department and in the ward. This led the researcher to have much easier access to patients and the opportunity to talk them and ask for their consent. Finally, because the researcher was not a native investigator, patients may have wanted to co-operate more than usual. The influence of researchers' social and ethnic background and gender in outcome of interviewer-administered studies has

been acknowledged (Streiner and Norman, 1995). For example, it has been observed that female interviewers usually had fewer refusals and higher completion rates than males.

These high response rates are important in supporting the robust nature of the findings, since difficulties with data collection and low compliance with quality of life studies among patients appear to be the most significant barriers to the successful implementation of quality of life investigations in clinical research (Aaronson, 1991). For example, Ganz et al. (1989) described their experiences in a quality of life study of patients with lung cancer in a clinical trial and acknowledged that the quality of life data from the trial was not suitable for evaluation because of poor quality and low response. Similar problems were reported in an EORTC study of patients with prostate cancer, 29 centres randomised 171 patients and only 13 centres participated in the complementary quality of life study, randomising a total of 90 patients. Only 72 of these patients completed baseline questionnaire and only 43 patients had at least one post-treatment questionnaire (Fossa et al., 1990). As one might realise here, the number of patients in the trial is not the focus of discussion, but the emphasis is on a low response rate in the quality of life study.

It is argued that there are five possible obstacles in collection of quality of life data. These were identified by the US National Cancer Institute (Yancik et al., 1989); administration of questionnaires which were too long, variability

related to the severity of patients' illness, variability of co-operation with quality of life studies by clinical staff, variability of the place of the interview, and institutional variables (problems of the data collection). Another example of poor compliance with quality of life assessment was reported by the Swiss Group for Clinical Cancer Research (Hurny et al., 1992), who called it " a lesson from the real world". Their multicentre trial comparing two different chemotherapy regimens in patients with small-cell lung cancer recruited 188 patients. Their compliance rate varied between 21% and 68% among the seven participating centres. They found that patients' age, sex, education and biological prognostic factors were not predictors of compliance, while only institutional variables were significant factors predicting compliance.

In contrast, extremely high compliance rates (95%) have been reported by the Canadian Clinical Trials Group (Sadura et al., 1992) from three of their current trials on malignant melanoma, breast cancer and on the effects of two antiemetics. Their success have been attributed to a set of specific measures including implementation of a pre-trial workshop for the medical staff on the procedure of data collection.

Above all, the data in this study were collected by means of interviewer-administered approach. This even by itself explains why the response rates were high. There were no incomplete questionnaires at all, nor was there any missing information. Thus, no individual data were discarded.

The interview allowed the researcher to have a better understanding of patients' concerns and on the other hand, helped patients to understand the study and purposes of the investigation. It is clear that when one leaves a patient alone, especially an elderly patient with a low educational level, and asks him or her to complete a questionnaire, the quality of such data is questionable despite the fact that the interview approach may also carry other drawbacks. The emphasis here is to show why interview-administered method in studies such as quality of life in lung cancer patients in a population of elderly people usually of low social class is a better approach.

It is essential that interviewers are properly trained in order to reduce bias and that questions are structured in order to avoid ambiguity (Bowling, 1995a). Prior to the commencement of this study, practical skills in these areas were acquired through participation in the Tak Tent cancer support group (see Appendices I and II). In addition, the investigator applied himself diligently to the study, making use of interpersonal and communication skills which played a major role in this project to be conducted successfully.

1.4. What should be assessed?

Studying quality of life, especially in patients with life threatening diseases such as cancer is becoming increasingly important. It is argued that such understanding may help to deliver effective and efficient health care.

As many researchers seek to include quality of life measurements in their investigations, the initial question is: what should be assessed? The literature suggests that to have a comprehensive assessment of quality of life in cancer patients it is better to use one generic measure, one disease specific instrument and one study specific questionnaire (Jonsson, 1987). This, however has advantages and disadvantages. While including different instruments in a study may help to examine a broader concept of quality of life, administration of lengthy instruments could be burdensome both to patients and researchers. Such a problem could be solved by using simple and short questionnaires. Thus, in this project to provide a comprehensive assessment, three valid, simple and short instruments were chosen.

The use of the NHP alongside the EORTC questionnaires provided useful information to interpret the results. In fact, the NHP provided a very realistic picture of patients' general health status. For example, it showed a clear pattern of difference between health status of patients with different socio-economic backgrounds (Figure 6.4). The EORTC quality of life questionnaires were also appropriate for study, since according to the literature (e.g., Bowling, 1995a) they are among the best developed instruments for measuring quality of life in patients with cancer.

However, one may argue that since the response categories on NHP are restricted to "yes" and "no", this may result in losing some useful information.

For example, if a patient wants to respond he or she may become fatigued (one of the NHP questions), there is no option of saying "sometimes". However, an apparent danger of inclusion of an extra response category is the likelihood that patients would always lean towards "sometime". In this regard therefore, the two existing response categories (yes and no) would be an advantage. Yet the question remains, how could one possibly resolve this issue. Replacing the NHP with one of emerging generation of new general health measures such as the Medical Outcomes Study Short Form 36-item questionnaire (known as SF-36, a new general health measure) is definitely not the solution, because SF-36 also has its own limitations such as low internal reliability of the "general health" and "mental health" scales; has difficult questions to answer; and lacks sensitivity to change over time (Hill et al., 1996; Jenkinson et al., 1996).

In addition to loss of useful information, this problem equally makes the analysis of the data obtained difficult. The difficulty usually arises because such data are not normally distributed and many patients were at extremes (Appendix XIV). This was the reason why in this study non-parametric tests were used. The most interesting feature of the NHP was that patients found it very easy to understand and felt at ease with the questions.

The EORTC questionnaires in turn, were very specific and therefore at baseline (pre-diagnosis) interview some patients were surprised by the

questions, for example about hair loss or sore mouth. Furthermore, it was found that some questions do not make sense for patients in the UK setting, for example the question about financial difficulties. Most elderly people were more or less in the same financial positions. In other words, the EORTC questionnaire is limited in indicating patients' needs with regard to financial difficulties, or even issues relating to the patients' family and social life. The wording of the questions are inadequate and that they are unlikely to identify patients' needs in this way. In addition, it was found that the EORTC questionnaires were not very specific to cancer or lung cancer as intended, since they could not clearly differentiate between controls and lung cancer cases.

1.5. How to influence clinical practice

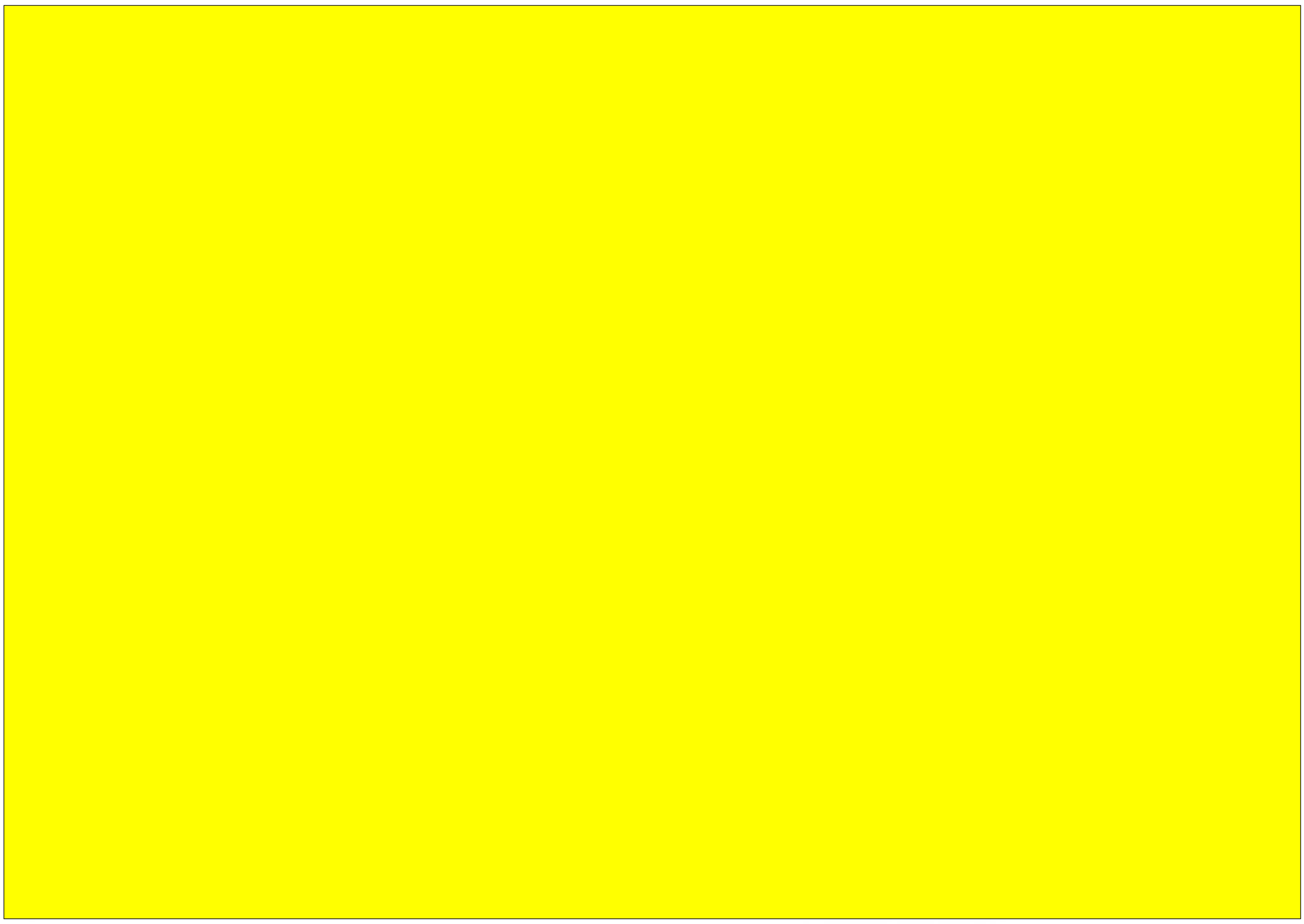
One of the challenging issues in measuring quality of life relate to such practical considerations as, whether it is possible to use these measures routinely in day-to-day practice, or how quality of life investigators may influence clinicians to use these measures in their practices. Some of the barriers have already been discussed in chapter 2, section 3.6.

To overcome these problems one might consider the following suggestions:

In-patient Respiratory Medicine

Stobhill Hospital-Ward 12A

A patient with lung cancer while responding to the quality of life questionnaires



1. Quality of life data should be collected based on robust methodological approaches to convince clinicians that the information provided by these studies is valid.

2. Findings from quality of life studies should be disseminated to clinicians and must be presented in simple and clear ways. Complicated presentations of data make clinicians ignore findings because they might think that these findings are just manipulating data rather than real patient-centred measures of health care and clinical outcomes.

3. There should be short and easy-to-use questionnaires to allow administration in busy clinics. Asking clinicians to assess quality of life comprehensively to meet all standard criteria is not realistic, since clinicians have limited time even for satisfactory management of their patients.

4. Quality of life issues should be recorded in case notes as part of good clinical practice. This may help clinicians find out valuable information and enhance their communication with their patients by obtaining such information.

2. Study population

2.1. Representativeness

The findings in the study give an insight to the characteristics of study population including lung cancer cases and patients with chronic respiratory disease. As it was demonstrated except for two variables (age, and children

support), in all other variables studied their characteristics were similar. In other words, the study findings indicate that not only lung cancer patients, but also patients with chronic respiratory disease are those who mostly live in deprived areas in rented high rise flats, about 40% living alone, suffering from a weak social network and social support system.

Since the study population were elderly patients, it could be well explained why some characteristics of patients differed from that of national norms, for example, car ownership, educational level, and employment status. However, compared with local figures (these are figures from the northern sector of Glasgow, see Table 6.2 and 6.5), it seems that patients' characteristics in this study were a true reflection of the community in which they lived.

Comparing the characteristics of the 1995 lung cancer patients in this study with those registered from the Stobhill catchment area in 1994, again there was a reasonable similarity indicating that the sample was representative (see Tables 5.4 and 6.2).

2.2. Missing cases

There were 13 cases excluded from the study and 18 cases who were missing (overall, 31 lung cancer cases). In Table 5.1 it is clear that there were no significant differences between lung cancer patients in the study and those who were excluded or missed. For example, since 14 of these cases had

unspecified lung cancer, it is unlikely to expect any changes in the results where the analysis was based on patients' cell type. Thirteen cases were excluded because they had their treatment before any assessment was made. Thus, to adhere to the study protocol they were excluded. Excluding such a small number of patients would not make any difference in the results.

2.3. Characteristics of cases and controls

Two characteristics were significantly different between cases and controls. The controls tended to be relatively younger ($p = 0.02$, Table 6.2) and received less support from their children as compared to lung cancer patients ($p = 0.007$, Table 6.3).

Lung cancer patients were older and probably reflecting the fact that lung cancer is the disease of elderly people. Thus, in this respect, the study finding is not unexpected.

Receiving less support as mentioned by controls may possibly relate to being younger and able to manage their own affairs and not needing help, or that they had chronic disease and their children might have been tired of supporting and helping them. Finally, contradictory to the first explanation, it might be that the expectations of these patients were higher than lung cancer patients considering that lung cancer cases were newly diagnosed and did not have any previous experience of being seriously ill. Such an argument can be

supported by the data where it was found that lung cancer cases had significantly less comorbidity as compared to the controls (see Table 6.2). The hospital admission was used as a proxy of comorbidity, although the time frame was limited only to one year prior to the baseline interview and might not reflect a true picture of the lung cancer patients' comorbidity.

2.4. Social support

One of the most important findings in the study relates to the fact that most patients, both lung cancer cases and chronic respiratory disease controls, reported that they did not receive any support from their children, families and neighbours.

Social support not only has an effect on adaptation after life events, but can also lead to a reduction of health problems because of more skill in avoiding and coping with problems (Wortman, 1984; Cohen and Wills, 1985).

There are two explanations of social support and its relation to health: the direct effects and buffering hypothesis. The former identifies social support as being beneficial both during normal life and illness while the later argues it is beneficial only during stressful life events.

Direct or buffering processes are established in empirical research when different concepts and types of measurement of social support are used. Direct

effects tend to be found when support is measured by the degree to which a person is integrated within a social network, while buffering effects tend to be shown when support is indicated by the availability of resources that help one respond to stressful events (Northouse, 1989).

Surprisingly until now there is no investigation about social support and its relation to the quality of life, although the support needs of cancer patients have been studied extensively (e.g., Broadhead and Kaplan, 1991, Kobasa et al., 1991).

In this study the relationship between social support and quality of life as measured by the NHP and the EORTC QLQ-C30 was examined and it was found that social support variables are good predictors of patients' baseline quality of life. This will be discussed in more detail in the following sections.

3. Baseline quality of life

At baseline assessments (pre-diagnosis) there were three important findings: first, there were no significant differences between cases and controls, secondly less affluent patients had poorer quality of life, and finally the study of the relationship between quality of life and patients' socio-economic characteristics showed significant relationships between these variables and baseline quality of life.

3.1. Quality of life in cases and controls

Baseline quality of life as measured by the NHP and the EORTC questionnaires showed no significant differences between cases and controls. However, some differences were observed. These were in the expected directions. For example, cases had more pain since lung cancer is a painful disease, and had more physical mobility problems because they were older. In contrast, chronic respiratory disease controls had more problems with energy and social isolation because of dyspnoea (Table 6.6).

It became clear that the NHP, and the EORTC questionnaires (to a large extent), could not differentiate between these two groups of patients with sufficient clarity, although they highlighted some small differences between the two groups (e.g. pain, energy, loss of appetite, etc.). There are several other instruments to measure quality of life in patients with chronic respiratory disease (see for example, Curtis et al., 1994). The fact that the chronic respiratory disease controls received the EORTC questionnaires which may not have been specific to their conditions, may explains the failure to demonstrate statistically significant differences between these two groups. However, if different instruments were used for the two groups, then comparison between them would have been fundamentally flawed.

Other explanations may relate to the selection of control group. The question is, could the selection of the control group have biased the outcome?

In principle, there were three possibilities for the selection of controls: general population, other cancer patients, patients with respiratory disease.

Firstly, selection of a sample of the general population has some inherent limitations, especially, since the administration of the EORTC questionnaires to such a sample would be problematic on methodological grounds. Secondly, selection of a sample of patients with other types of cancers also has limitations, in the sense that it would be largely impracticable, and would result in conflicting findings since most of their symptoms and difficulties would be different. Thirdly, selection of a sample of patients with similar symptoms to lung cancer at presentation, and attending the same department while at the same time, keeping the researcher blind. This had advantages over the above mentioned possibilities, and was therefore, chosen for this study. Thus, the issue of selection of inappropriate controls could be rejected.

On the other hand, the lack of significant differences between these groups, does not necessarily reflect inadequacy of the questionnaires, but indicates that quality of life at baseline assessment in the two groups was very similar. Both suffered from low levels of quality of life, and this indeed, shows that assessment of quality of life is not only important for lung cancer patients, but also for patients with chronic respiratory disease, and indeed for all patients with all diseases!

Finally, comparing symptoms in lung cancer patients with chronic respiratory disease controls as measured by the EORTC QLQ-C30, and QLQ-LC13, it was found that lung cancer patients had significantly more pain and loss of appetite. These findings are not unexpected, since most studies of symptoms in cancer patients have reported that pain was the commonest symptom in advanced cancer (Curtis et al., 1991). Furthermore, the nature of pain in lung cancer patients and patients with chronic respiratory disease is totally different. The most frequent aetiology of pain in lung cancer patients is bone-related pain, while in chronic respiratory disease it relates to muscular pain (Cleeland and Syrjala, 1992).

Suffering from pain is one of the major concerns of lung cancer patients. In contrast to other types of cancer, patients with lung cancer may experience pain from the chest lesion or metastatic sites in the bone early in the disease. Chronic pain is frequently associated with symptoms such as sleep disorder, and loss of appetite and with clinical signs and symptoms that may elaborate a depressive disorder (Foley, 1985). This may explain why lung cancer cases in this study even before commencement of treatment, reported significantly more loss of appetite as compared to controls.

However, patients' pain scores, especially lung cancer patients on the NHP and the EORTC questionnaires were lower than anticipated. The possible

explanations for such an observation could be related to the fact that a majority of patients (52%) indicated that they took pain medication (e.g., Paracetamol) prior to the baseline assessment. Similar results have been observed by Bergman et al. (1994) where they reported that lung cancer patients' pre-treatment mean pain score was 29.9 (SD = 31.3). This was 27.1 (SD = 28.7) in this study. Also it has been observed that the EORTC lung cancer questionnaire needs some refinement of its pain subscale and further testing of its reliability (Hollen and Gralla, 1996).

The NHP has been applied in the assessment of health status in patients with chronic respiratory disease, and found to be valid (Alonso et al., 1992). Their findings in a study of 67 patients (mean age 62.2, SD = 7.1), are relatively similar to those of this study since, for example, the mean pain score (27; SD not included) was reported. In this study it was 19.5 (SD = 26.7).

Again, in an unpublished study of 63 new cancer patients including lung cancer patients (the numbers of patients with different cancer sites and age are not identified), Hunt et al. (1986) reported findings similar to those of this study. For example, the mean pain score for lung cancer patients in their study was about 32 (SD not included), while it was 24.5 (SD = 29.2) in this study.

Comparing patients' scores on the NHP with that of the UK norms for general population age over 65 years old (Hunt et al., 1993; McEwen, 1993), it was

found that both cases and controls had about 3 times higher mean scores on energy, pain, and emotional reactions, and about 2 times higher mean scores on sleep, social isolation and physical mobility. These could not be substantiated from raw data from these investigations.

3.2. Quality of life and deprivation

There was a clear pattern of difference in quality of life of the patients with different socio-economic deprivation backgrounds. It was found that in most areas as measured by the NHP and the EORTC questionnaires the patients in deprived groups had more health problems, less functioning, and more symptoms as compared to patients in the affluent groups. This clearly indicates how important it is to consider patient's socio-economic status when measuring quality of life. In other words, the findings of this study suggest that quality of life is not only the outcome of the disease, but also highly dependent on each patient's socio-economic characteristics.

In studies of quality of life in lung cancer patients the only investigation which acknowledges the issue of patients' socio-economic status is that of Sarna (1993a; 1993b; 1994). In a study of 69 females with lung cancer, she reported that there were a greater disruption in quality of life in women with low income. In her study she showed that income was a statistically significant predictor of baseline quality of life.

Several factors may explain why patients in lower social class had lower quality of life as compared to the affluent. First, these patients lived in deprived areas, and therefore their social environment and living conditions were not as good as their more affluent counterparts. The relationship between housing and quality of life may be explained by the hypothesis that housing environment has an impact on social relationships and therefore, affects health status and quality of life (Martin et al., 1987; Hunt, 1990). Secondly, they might had been referred late (though not cross-checked because of time constraint) and this had a significant effect on their baseline quality of life where their disease was at an advanced stage. Since there was no evidence of such delay, this might not be the case. In fact, if there were considerable delays, there would not be missing cases in the study. Some patients in this study were missed because they had been referred by a short notice and they had received a quick hospital appointment. Basically in the UK setting, access to hospital medical care for lung cancer, is equitable irrespective of social class (Angus et al., 1995). Finally, the lifestyle and health behaviour in this group of patients (deprived) might be associated with a lower quality of life. For example, Macintyre (1994) in her review of socio-economic variations in Scotland's health observes a clear gradient by socio-economic status for the major killers in Scotland, heart disease and cancer, with those in lower social class, living in more deprived areas, with less education, lower income, and rented accommodation, having higher rates of morbidity and mortality than the affluent.

From the researcher's personal observation and impression, it was obvious that the poor tended to be more emotionally adjusted to their condition than the affluent. In a typical example, a poor patient remarked, 'I have no money, I have no home, and now that I have lung cancer, I see it as yet another problem of life; but life is for living'. On the other hand, the affluent tended to be rather more anxious, yet this was not reflected in their responses to the standard questionnaires! The fact that these observations could not be supported by data from this study, again underscores the limitations of quality of life instruments in capturing certain complex issues related to human life.

3.3. What predicts the baseline quality of life?

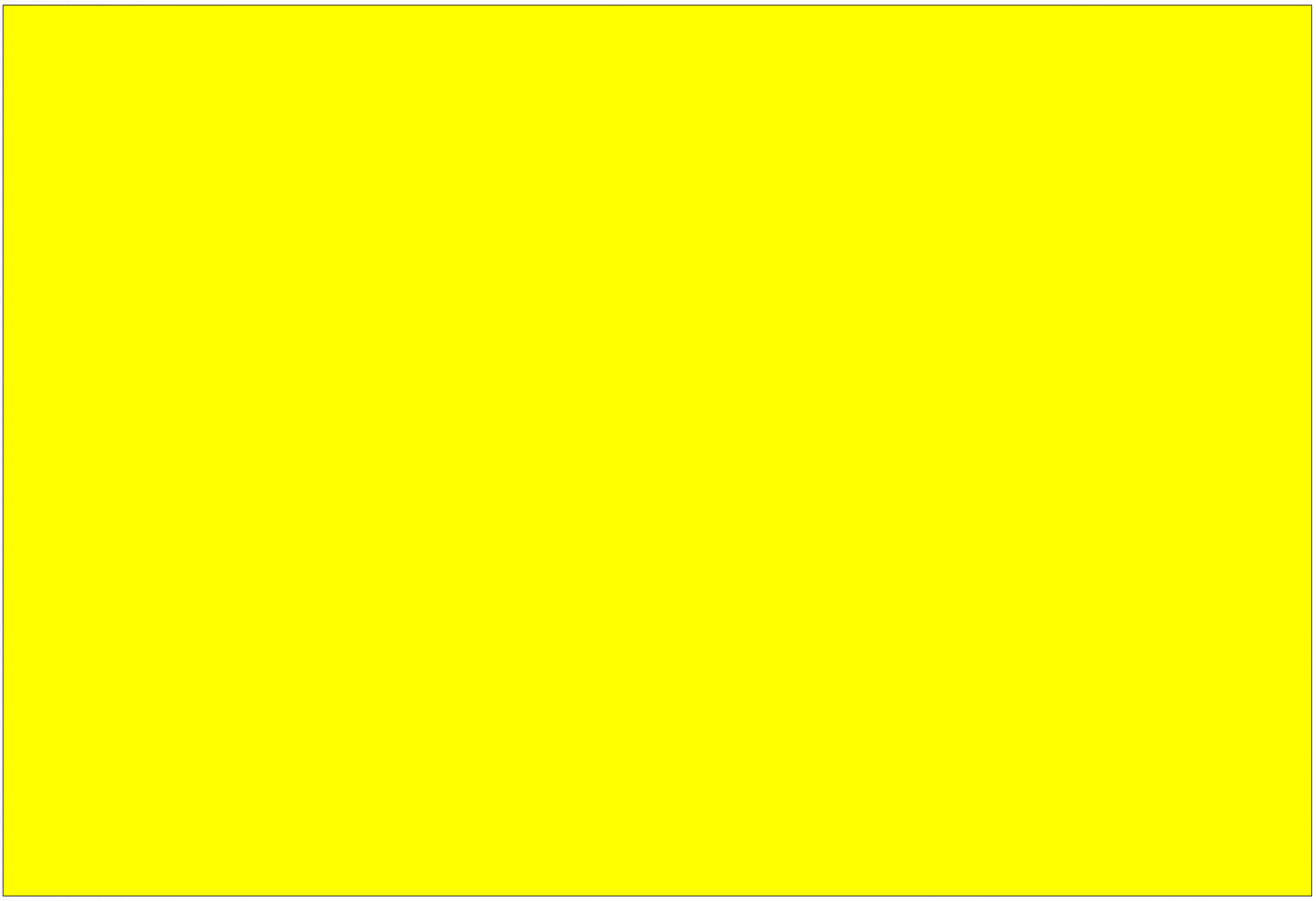
Three outcome measures were used to investigate the relationship between the baseline quality of life and the patients' socio-economic status and support systems. It was hypothesised that the disease may cause emotional reactions, social isolation, and affect the patients' global quality of life. When these were investigated, it was found that marital status, and family support, social isolation, energy, sleep difficulties, and global quality of life were all significant predictors of the patients' baseline emotional reactions as measured by the NHP at first assessment of their perceived health status (Figure 6.6).

Emotional reactions, to some extent, relate to psychological well-being. The study findings suggest that emotional reactions are not only health-related, but

Happy Man!

A male patient with lung cancer at follow-up assessment of quality of life

After completion of the initial treatment



strongly relate to the patients' social support and social network. As described earlier, the buffering hypothesis may well explain why patients who were single, and never received support from their family, had more emotional reactions. According to this hypothesis, in fact, these group of patients when in this situation need support to handle crisis and cope with their problems, but do not have any support resources (Tijhuis et al., 1995).

Social isolation which refers to one's social activities, again was best predicted by the social network variables. It was found that marital status (being single or widowed), visiting family, being female, emotional reactions, pain, energy, and physical mobility were significant predictors of the patients' social isolation. Unfortunately most studies of quality of life in patients with cancer do not include such key variables in their analyses.

There are several explanations for the contribution of these variables to the patients' quality of life. It has been observed that men and women with the fewest social connections were more often smokers and physically inactive than those with the greatest number of connections as estimated by a score based on marital status, contact with friends and relatives and membership of groups (Berkman and Syme, 1979). In a recent study of an elderly Swedish population, aspects of social isolation were associated with smoking, physical inactivity, and unhealthy diet (Hanson and Isacsson, 1992). These could

contribute to patients' health status and consequently to their quality of life (Osler, 1995).

The baseline global quality of life was best predicted by the patients' age, Deprivation Category, and employment status. Such phenomena, again, indicate the extent to which patients' socio-economic status contributes to their global quality of life. However, as "life" in general cannot be evaluated, the best approach is to evaluate a number of aspects of a patient's quality of life including patient's socio-economic status. In addition, 'life' has spiritual and material components, its quality therefore, depends on a balance between these important dimensions.

3.4. Interview setting

Most hospitals and clinics are not particularly suitable places for patients to reflect adequately on their quality of life. For example, it is argued that observation of social activities in particular is likely to be influenced by the hospital environment. It is to be expected, therefore, that the interview at home is to be preferred for quality of life assessments (Bakker, 1986).

The difference in assessing quality of life in different settings, that is, interviewing patients at home or in the clinic was investigated. Except for emotional reactions (NHP), there was no statistically significant difference between home or clinic settings. Patients at home reported significantly more

emotional problems. The reason for such a difference may be due to the fact that the home interviews only took place before patients' visits to hospital. This may be a reflection of their anxiety, especially if they suspected they had a serious illness, although the diagnosis was unknown to them at the time. However, although not significant, it was observed that in most of the measures studied patients reported more problems at home.

Two explanations may be put forward. Patients at home may have over-reacted to their problems or patients in the clinic may have under-estimated their problems. It was found that only with regard to pain patients in the clinic reported more problems. This is exactly what one may expect from a patient in the hospital environment. Others (Ziebland and Fitzpatrick, 1992) observed that the hospital setting itself may contaminate the results, for example with questions about sleep on the NHP, which because this refers to in-patient assessment of quality of life rather than out-patient assessment, may be irrelevant.

van Dam and Aaronson (1987) argue that the place where the data collection takes place (at home or in the clinic) can exert a strong influence on the way patients respond to questions. Thus, they recommend that one should try to avoid collecting data in different settings within a single study. For example, if at baseline data were collected in the clinic, at the follow-up also data should be collected in the clinic not for example at home. Such a statement

was made with regard to self-reported data collection, whereas in this study data were collected via the interviewer-administered approach.

3.5. Knowing the diagnosis of cancer and its relation to the outcomes

In almost all studies of quality of life, patients' quality of life was first assessed after the diagnosis and after or during each course of the treatment. Therefore, the question is to what extent does knowing the diagnosis affect the results. If a patient has recently received "bad news" indicating that he or she has developed lung cancer, any assessment, especially on psychological aspects such as emotional functioning, may be biased. No previous research on this topic has been identified.

A comparison was made between results obtained from quality of life assessment in two groups of lung cancer patients: those who did not know their cancer diagnosis and those who did, to find out how this may contribute to the outcome. For example, one may expect a significant differences in emotional reactions between those who knew their diagnosis and those who did not. The study results indicated that there was no evidence to suggest that knowing diagnosis may dramatically affect the result, because there were no differences between these two groups' emotional reactions or social isolation scores at all, while it was found that those who knew their diagnosis reported more physical problems (Tables 6.15, and 6.16). Certainly this was not due to

their age differences, since those who knew their diagnosis were relatively younger than those who did not know their cancer diagnosis.

Looking at patients' symptoms, again there was no significant difference between these two groups except for sleep difficulties indicating that those who did not know their diagnosis reported significantly more problems with sleep ($p = 0.02$). Although it is not clear why a significant difference emerged, it is possible to say that because those who did not know their diagnosis were older, and therefore they perceived more sleep difficulties.

4. Follow-up assessments

4.1. Baseline quality of life as a predictor of survival

The study findings suggest that the baseline quality of life is an important prognostic factor. Two types of analyses were carried out: simple and Cox's regression analysis. In the first analysis it was shown that most measures were significant indicators of the duration of patients' survival. For example, those who were dead at follow-up had significantly more problems with energy ($p = 0.007$) and pain ($p = 0.005$) at baseline as measured by the NHP (Tables 6.19 and 6.20). In the second analysis (Cox regression analysis) it was found that patients' aggregate scores on the NHP and EORTC QLQ-C30 (functioning, and global quality of life scores) were significant predictors of survival ($p = 0.003$, 0.03, and 0.03 respectively).

There have been similar findings in four previous quality of life studies of lung cancer patients. Kassa et al. (1989) studied quality of life in 102 non-small cell lung cancer patients and found that psycho-social well-being was the best predictive factor of survival. Ruchdeschel et al. (1989; 1991; 1994) in a series of quality of life studies using the Functional Living Index-Cancer (FLI-C) reported that the total baseline quality of life score (aggregate score on the FLI-C) alongside performance status, weight loss, and stage of disease were significant predictors of survival in 438 lung cancer patients. Ganz et al. (1991) also used the FLI-C to study quality of life in 40 lung cancer patients. Using Cox regression analysis and dividing the patients into two groups (low and high quality of life), they found that baseline quality of life was a significant predictor of subsequent survival. Finally, Gralla et al. (1995) in a study of 673 non-small cell lung cancer patients using the Lung Cancer Symptom Scale (LCSS) observed that the baseline quality of life not only predicts the survival, but also has greater impact than most known prognostic factors.

Similar findings have been reported both for other cancers for example, breast cancer where patients' physical well-being scores was found to be directly associated with survival (Coates et al., 1992), and for other diseases such as rheumatoid arthritis. Fitzpatrick et al. (1992) argue that quality of life instruments have been shown to be better than conventional rheumatological

measures as a predictors of long term outcomes in terms of both morbidity and mortality.

In contrast, a study of patients with malignant melanoma (Osoba et al., 1993) found that pre-treatment global quality of life scores as measured by the EORTC QLQ-C30, were not predictive of survival. It is argued that because these patients did not have advanced disease, as did the lung and breast cancer patients, it is possible to suggest that pre-treatment quality of life may not have predictive value in all patients with all cancers (Osoba, 1994).

This study by using a prospective design and performing Cox's regression analysis, suggests that even for patients in the early stage of disease initial quality of life is prognostic. In fact, the major difference between the present study and the above mentioned studies is due to the fact that they measured quality of life after diagnosis, but in this study quality of life was measured before the diagnosis. Therefore, the concept of baseline quality of life in this study is more precise than others. When others measured quality of life the disease and its diagnosis may already have had an effect on it.

These however, are major findings and have important implications.

1. Baseline quality of life is a significant prognostic factor for survival outcome like other known prognostic factors i.e. age, gender, disease stage, weight loss and performance status.

2. Baseline assessment of quality of life could help physicians in their clinical decisions as it directly relates to the patients' survival time. Thus, it should be integrated into clinical practice and evaluated prospectively.

However, one should be aware of Cox's regression limitations. One of the assumptions of the Cox regression model is that for any two cases or any two comparison groups (for example, in this study those with high and low level of global quality of life), the ratio of the estimated hazard across time is a constant (Norusis, 1994). For example, based on such an assumption for two patients with the same age and histology but different levels of global quality of life, the ratio of their estimated hazard rates across all time is considered to be constant. This is a strong assumption which may not always apply. It is quite possible that the hazard functions of patients with low and high level of global quality of life are not related by a constant and rather depend on time. It is, however, possible to modify the Cox regression model to overcome the problem, but this was not feasible in this study and discussion about the issue is beyond the scope of this section.

4.2. Baseline versus follow-up quality of life

At follow-up stage 82 patients were interviewed and their quality of life scores were compared with their baseline scores. In general, the comparison indicates that patients' quality of life had deteriorated. The only improvement

was seen for some symptoms such as coughing, haemoptysis, pain in the shoulder and sleep difficulties. These improvements, however, were not significant except for coughing which was possibly controlled by medication. The study findings indicate that in addition to the decrease in patients' general health status (physical health, and functioning), they developed treatment-related symptoms such as fatigue, hair loss, constipation, and sore mouth.

These findings are similar to those of studies conducted by Aaronson et al. (1993) and Bergman et al. (1994). They used the EORTC QLQ-C30 and the EORTC QLQ-LC13 to investigate the reliability and validity of the EORTC questionnaires. The mean scores reported in their studies and this study are very similar. For example, Aaronson et al. (1993) reported the mean scores of 65.8 (SD = 27.1) and 62.3 (SD = 28.3) for physical functioning before and during treatment. In this study these were 67.1 (SD = 25) and 55.9 (24.9) respectively. The slight difference observed could have resulted from the fact that while they administered the questionnaires during treatment, in this study questionnaires were administered after initial treatment.

The physical symptoms of lung cancer have a serious impact on the individual's functional or performance status as defined by the ability to do certain physical activities. At present, the systematic assessment of this key concept (performance status) continues to be measured in patients with lung cancer using either the Karnofsky Performance Scale (KPS), or Eastern

Cooperative Oncology Group Performance Status (also see chapter three, section 1.2.1).

Performance status is a global assessment of the patients' functioning and ability for self-care, and should not therefore, be considered to be equal to assessment of quality of life which refers to a broader concept. As the study results suggest, quality of life in lung cancer patients is not limited to physical functioning, but also other symptoms which result from either the progression of disease or side-effects of treatment. In addition, these types of instruments have been criticised for being crude measures with only modest reliability (e.g. Mor, 1984). Thus, comprehensive assessment of physical symptoms as well as physical functioning are important in evaluating lung cancer patients' quality of life both before and after treatment.

4.3. Effects of different treatment policies

Treatments for lung cancer often burden the patient with additional physical symptoms. Most investigations have focused on the side-effects of chemotherapy. Limited information is available about radiotherapy, surgery, and supportive care.

To show the effects of different treatment policies, based on initial management, patients were divided to four groups: patients who received chemotherapy (n = 25), those who received radiotherapy (n = 29), those who

underwent surgery (n = 6) and those who were treated with a supportive care policy (n = 21). In each group, patients' baseline scores were compared to their follow-up assessments.

In general not only were there no improvements, but there was a deterioration in patients' quality of life. Chemotherapy patients reported significant improvement in coughing and radiotherapy patients reported significant improvement for pain in the shoulder. Apart from these, there was no significant disease-related symptom relief, while there was an increase in treatment-related symptoms such as hair loss in chemotherapy patients, and constipation in radiotherapy patients. Although the sample size in each group was rather small, the findings clearly suggest that the effects of different treatment regimens were not entirely satisfactory, but without treatment their problems could have been worse. For example, patients who received chemotherapy reported significant problems with social isolation. In clinical experience and empirical research, lung cancer patients show a tendency toward social withdrawal. Symptoms of the disease, especially impaired functional status, dyspnoea, pain, and hair loss impose limitations on the patients' social life. Furthermore, many patients seem to dislike being dependent on others. Thus, they prefer, for example, to stay at home rather than to rely on the help of others to help them be socially active (McGeough et al., 1980).

However, it seems that patients who received surgery had a better quality of life as compared to the other groups, while patients in the supportive care group reported more problems. Comparing radiotherapy with chemotherapy, radiotherapy patients reported less problems (Tables 6.24, 6.25, and 6.26).

Ideally, the goal of cancer treatment should not be only to prolong disease-free survival, but to enhance the patients' ability to return to a normal life. Particularly for patients with advanced-stage disease, one can question the ability of cancer therapy to improve patients' quality of life. Clinical trials thus, can not sufficiently document the continuing impact of the disease and the extent to which treatment, including its failure to manage symptoms adequately, diminishes the well-being of cancer patients.

4.4. Small cell versus non-small cell lung cancer

Overall, there were no significant differences between small cell and non-small cell lung cancer patients indicating that both groups showed a similar quality of life either at baseline assessments or at follow-up stage. However, in some measures such as haemoptysis and pain, non-small cell lung cancer patients scored higher indicating that they had a greater degree of symptoms.

The study findings are similar to these of Hopwood et al. (1995) who investigated symptoms on 232 small cell and 423 non-small cell lung cancer patients. They reported that the overall pattern of symptom prevalence was

very similar for the two disease groups, the only major differences being the higher level of chest pain and coughing up blood reported in patients with non-small cell lung cancer patients.

Considering the impact of treatment on patients' quality of life, the study results suggest that there were no benefits for patients with non-small cell lung cancer, while there were some palliative improvements for small cell lung cancer patients. This is clearly reflected in patients scores where small cell lung cancer patients reported more treatment-related symptoms, while non-small cell lung cancer patients reported more disease-related symptoms. For example, small cell lung cancer patients significantly reported more hair loss, and sore mouth which are side-effects of chemotherapy, whereas non-small cell lung cancer patients reported significant pain distress (Table 6.29).

5. Patients' reactions to the study

One of the most interesting experiences in this study relates to the evaluation of the study by the patients themselves. This was investigated via a simple questionnaire. First, they indicated that they preferred to be interviewed rather than to fill in questionnaires. Secondly they indicated that they preferred to be interviewed at home as opposed to the interview in the clinic. Thirdly they found being interviewed very acceptable.

Communication aspects of interviewing patients by non-medical qualified investigators on quality of life is not well documented. This becomes more evident when one considers interviewing a cancer patient. With regard to quality of life studies and interviewing cancer patients, much attention in the literature has instead been given to practical and methodological issues (Montazeri et al., 1996d).

It is argued that the advantages of face-to face interview as compared to self-administered instruments include the fact that the interviewer knows about the characteristics of who is answering. Difficult items can be explained to respondents, is more flexible, and may create an opportunity for researchers to obtain additional and vital information they need (Streiner and Norman, 1995). Thus, in many respects this study reinforce the view that interview is a more convenient way of data collection, although the drawbacks should not be forgotten including the costs involved and the risk of interviewer bias, as discussed earlier.

Usually, there is an impression among medical staff that interviews may disturb patients if they have been told that they have lung cancer, by putting them in a difficult situation; that they do not want to talk, and that interviews are not a useful way to communicate with patients, in particular with cancer patients. Data obtained in this study indicates that the majority of patients (96%) found being interviewed very or quite acceptable. Only 4% of patients

stated that they found being interviewed not very or not acceptable. They expressed four main reasons for their feelings with the majority of patients indicating that being interviewed did not bother them, they felt at ease and relaxed, they were happy to talk, the interview was understandable and that they were satisfied with the way the interview had been carried out.

There were patients who felt that the voice and behaviour of the interviewer were appealing to them (Table 6.41). Since this may make the patient feel relaxed and comfortable, the issue of selecting a skilled interviewer in quality of life studies becomes important. Part of the patients' impression of pleasant behaviour may be attributed to the fact that the traditional question-answer interview style was avoided. In traditional style, the interviewee usually does not find a chance to talk and it is argued that obtaining accurate and complete understanding of the patients' health status in this way is very unlikely (Marshall, 1988). Many of the patients in this study indicated that they found being interviewed acceptable because they had a chance to talk. This was apparent from the patients' statements where they stated that "it was nice to talk", or "it was nice to talk to somebody who is not superior", or "it was nice to talk to somebody who is listening". Since it is argued that clinical teams including researchers mostly talk about the "case" rather than the person, and that in clinical medicine the eye is quicker than the ear (Spiro, 1992), the need for more effective communication and consideration of patients' experiences and feelings becomes essential.

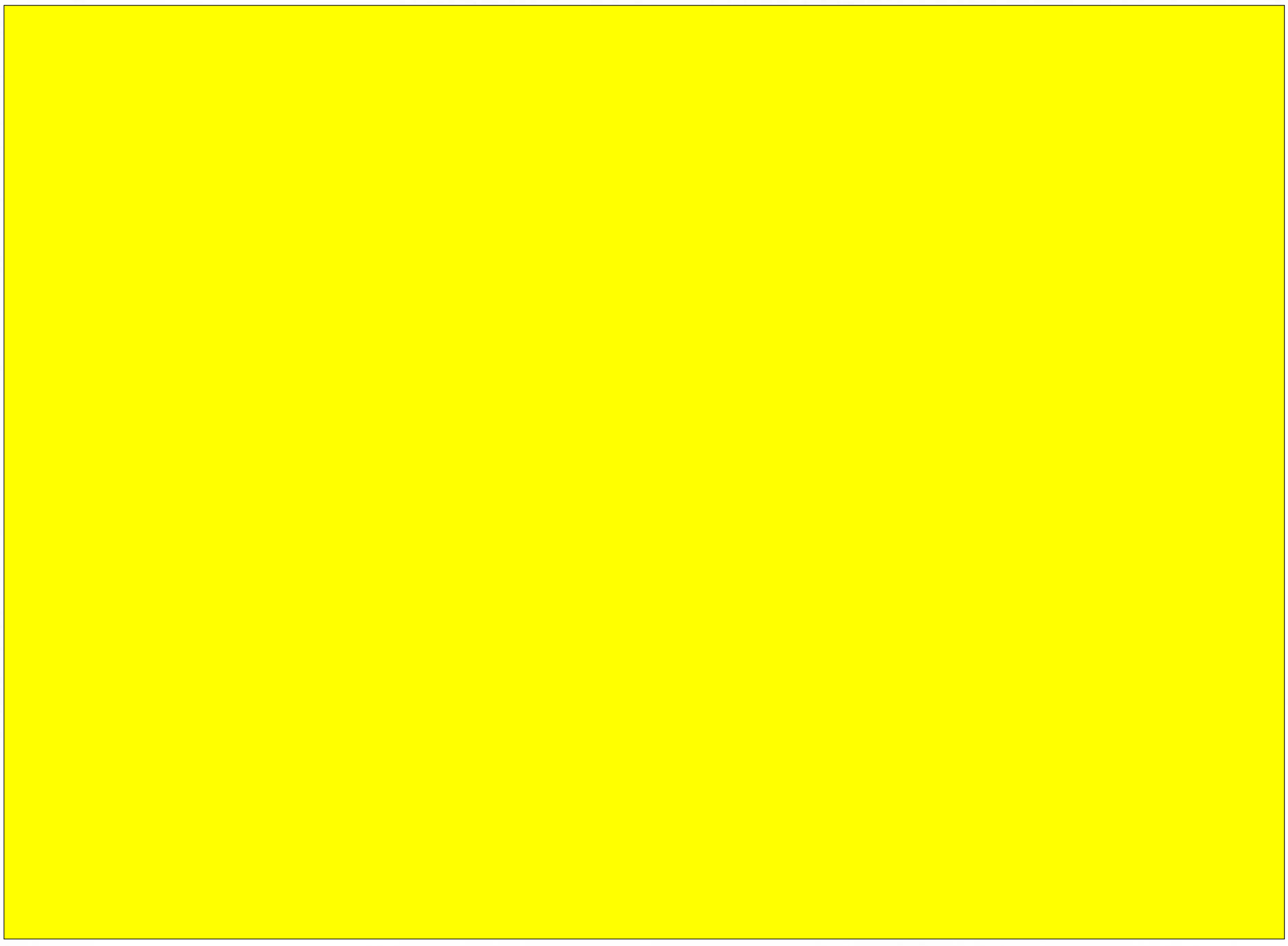
However, allowing patients to talk unrestrained has disadvantages. These include deviation from the main study questions, a lengthy interview, and too much involvement with patients' problems. A balanced approach may be the reasonable solution to the problem (May, 1991).

Finally, it has been shown that proper communication with patients plays an important role in collecting quality information. How to achieve this remains a major task for further investigation. Furthermore, researchers need to communicate effectively with medical and clinical staff. Without such links, there is no means of recruitment of patients.

Interviewing a patient at home

The majority of patients preferred to be interviewed at home rather than in the clinic

Follow-up assessment



CHAPTER EIGHT

8

CONCLUSIONS AND RECOMMENDATIONS

Contents

1. Conclusions

2. Recommendations

1. Conclusions

Several conclusions are made based on the study findings.

1. Lung cancer patients' quality of life prior to diagnosis was found to be a significant predictive factor of length of survival indicating the importance of quality of life as a prognostic factor, even after adjusting for known prognostic factors, these are, age, sex, extent of disease, weight loss, and performance status.

2. Patients' perception of quality of life was different from the perceptions of health professionals. This suggests that doctor-patient communication should be further developed. To achieve this, a better understanding of patients' concerns by knowing their values and preferences is needed.

3. There was surprisingly no significant difference between lung cancer cases and chronic respiratory disease controls with regard to their demographic and socio-economic status. This, may have implications for health care professionals. For example, both diseases are related to health behaviour and lifestyles. They are, to a large extent, some of the consequences of smoking, manifesting later in life. This underscores the need for appropriate targeting of health education and promotion programmes on adolescents, taking account of the socio-economic and demographic variables highlighted in this study. Such programmes must use an adequate constellation of methods (e.g., ban on

advertising, increased taxation on tobacco, different health education approaches, etc.) which seek to prevent youngsters from taking up smoking.

4. At baseline, there was no significant difference between quality of life in lung cancer cases and chronic respiratory disease controls. This observation highlights the extent to which patients with chronic respiratory disease suffer from their disease, and indicates the fact that health professionals might be under-estimating quality of life in patients with chronic respiratory disease.

5. Quality of life was found to be different in patients with different Deprivation Categories. This indicates the extent to which socio-economic status of patients contributes to their quality of life. The poor experience a lower level of quality of life as compared to their affluent counterparts. Although it was felt that the poor may have better quality of life by virtue of their supposedly stronger family ties (Atkinson, 1996), this was not supported by the data. Thus, the findings are in line with those previous studies on inequalities in health, which show markedly poorer health for those on the lower fringes of the socio-economic scale (e.g., Davey Smith and Egger, 1993).

6. Patients' social support and social networks were important determinants of patients' quality of life, as they were predictive factors for social isolation and emotional reactions, all of which are important components of psychological

health. This clearly suggests that not only disease and treatment-related factors contribute to the patients' health-related quality of life, but that other non-medical components also play an important role in shaping patients' quality of life. Available data did not highlight which of medical and non-medical components was a more important predictor of psychological health. This however, marks an important area for consideration in future studies on quality of life.

It is worth noting that the findings from this study indicated that non-medical factors such as Deprivation Category and marital status were significant predictors of global quality of life at follow-up, while medical factors such as cell type and treatment modalities were not.

7. Comparing patients' baseline quality of life with their follow-up assessments, the findings from this study showed that patients' quality of life had deteriorated indicating that overall, treatment is ineffective in improving lung cancer patients' quality of life regardless of cell type and stage of disease. Although one must realise the importance of treatment in palliation of symptoms, this finding detracts greatly from observations (see summary tables in chapter three) which suggest improvements in quality of life as a result of treatment.

8. There was no significant difference in quality of life between lung cancer patients who did not know their cancer diagnosis and those who knew their diagnosis. This suggests that knowing diagnosis did not significantly affect the way in which patients responded to the questionnaires. This is a crucial methodological finding which negates the current hypothesis that patients' awareness of their cancer diagnosis may influence the way in which they respond to quality of life questionnaires.

9. There was no significant difference in quality of life between patients who were interviewed at their homes and patients who were interviewed in the clinic. This indicates the place of interview does not significantly affect the results.

10. It was feasible to conduct quality of life studies based on robust epidemiological methods. This has allowed a more representative assessment to be made than clinical trials and clinical-based studies.

11. Reactions of patients to the study indicate that:

(i) A majority of the patients preferred to be interviewed rather than to fill in a questionnaire. There was no significant association between this preference and patients' age, gender, diagnosis, place of interview, patients' general health status and global quality of life.

(ii) A majority of the patients did not find the interview an intrusion.

(iii) The highest proportion of patients preferred to be interviewed at home rather than in the clinic.

12. Overall, the study findings indicate that considering patients' views when collecting quality of life data offers the advantage of improving the quality of data, reducing missing information and minimising refusals, thus ensuring efficient use of resources.

2. Recommendations

This study has provided useful information about quality of life in patients with lung cancer. Based on the findings and experiences gained through the study the following are recommended both for consideration in lung cancer care and for further research.

1. Since quality of life measures could have prognostic value, they should be included in clinical trials and epidemiological studies of outcomes in patients with lung cancer. However, such benefits from quality of life measures would be better enhanced if the limitations of current instruments as highlighted in the work are taken into account.

2. Doctor-patient communication needs to be further improved, since effective health care delivery requires a better understanding of patients' concerns. To achieve this it is recommended to provide resources available to make communication training part of post-graduate and continuing medical education.

3. Measuring quality of life in patients with lung cancer is essential and is recommended. This may provide additional psycho-social information likely to indicate individuals or sub-groups of patients who may benefit from particular treatment regimens. Purchasers of lung cancer care may rely on

such information to provide appropriate services which address specific psycho-social needs of patients.

4. Any assessment of quality of life needs to be considered in relation to patients' socio-economic status. Without such considerations it is difficult to provide a realistic picture of patients' quality of life.

5. The inclusion of general health measures such as the Nottingham Health Profile (NHP) in studies of quality of life is recommended since these instruments provide useful information on patients' perceived health status. However, there is a need for further development of the NHP in relation to its response category (yes and no) format. How to achieve this remains to be resolved. An ordinal response category, that is, a 4-point Likert scale format (not at all, a little, quite a bit, very much), may be the solution and is worth examining.

6. The EORTC questionnaires which are cancer specific were administered to both lung cancer cases and chronic respiratory disease controls. It was surprising that the instruments could not distinguish between these two populations. The fact that the instruments proved applicable to patients with chronic respiratory disease challenges the validity of the questionnaires, and underscores the need for their further developments. Specifically, there is need to improve their pain, family and social life subscales and to further

investigate their reliability and validity in the UK setting. Supplementation of a valid pain questionnaire may help to overcome the problem arising from the EORTC QLQ-LC13 pain subscale.

7. Clinical staff have an important role in quality of life studies. Thus, effective communication between researchers and clinical staff is essential and should be established if not present, since part of the high response rate in this study could be attributed to the rapport which existed between the researcher and clinical staff.

8. Assessment of quality of life should be acceptable to patients. Interview-administered approach is recommended to achieve this. This may improve the quality of data, reduce missing information and decrease the burden on patients. These may help to justify the cost associated with this method, although this study was not designed to answer such a question.

9. The study design in this project proved feasible and desirable. Thus, it is recommended that this experience be used in future research since it has the potential of ensuring a more representative result.

10. This study should be repeated with a larger sample in Glasgow and elsewhere. For such a research programme the following are recommended:

(i) The controls should also be included in the follow-up assessments.

(ii) A better way for enrolling all emergency admissions, and internal referrals is needed to enter all cases in the study.

(iii) There is need to use standard measures instead of ad hoc questionnaires when assessing social support and social networks. This would allow to provide valid and comparable data.

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QUALITY OF LIFE IN PATIENTS WITH LUNG CANCER

APPENDICES

Appendix I
The letter to Tak Tent

WEST OF SCOTLAND CANCER SURVEILLANCE UNIT

Director : Dr. C. R. GILLIS

GREATER GLASGOW HEALTH BOARD,
RUCHILL HOSPITAL,
GLASGOW, G20 9NB
Telephone : 041-946 7120 Ext. 270

17th March, 1994.

Mrs. Eileen Smith,
TAK TENT,
Western Infirmary,
GLASGOW,
G11 6NT.

Dear Mrs. Smith,

Re : Mr. Ali Montazeri, B.Sc. 1984 Teheran, MPH 1993 Glasgow

The above is presently an enrolled student at the University of Glasgow for the degree of PhD under my supervision and is a member of the University Department of Public Health.

The subject of his proposed thesis is 'Insights on the quality of life of cancer patients with particular reference to Ovarian Cancer in relation to optimal treatment'. Ultimately, he will carry out a study on ovarian cancer trying to determine instruments for measuring whether the optimal therapy we have found by research benefits quality of life.

However, I feel he should first learn to talk to patients with cancer and therefore thought of your Organisation as not only playing a guiding role in this project but offering him the possibility of talking to some of your members attending group meetings and gradually absorbing the use of Tak Tent.

I am sorry to trouble you with this request but feel sure you will be interested. Mr. Montazeri can be contacted at this address.

Yours sincerely,

[redacted]

Appendix II

Tak Tent: does cancer support work?
Studies of a cancer support group

Abstract

A descriptive study using two interviewer-administered questionnaires was conducted to know more about cancer support groups and the people who are using these services. All seventy one patients and relatives attending six cancer support groups at the time of investigation in the West of Scotland were interviewed. They were asked about their satisfaction with care and support, past and current concerns, global health and quality of life, and needs. The majority of participants were married females, middle class, aged 50 to 65 years old, and were long time survivors. Fifty-two per cent of cancer patients and 70% of their families stated that they were very satisfied with support were receiving. Nearly 90% of patients reported that they did not receive any counselling either during their treatment from their cancer specialists or at present from a professional counsellor. The "general perceived health", and "global quality of life" among patients and relatives were found to be moderately good or good. Concerns of patients and their families were studied. Patients reported optimistic changes while relatives were more negative. Needs assessment indicated that 52% of patients require symptom relief and family support, whereas 53% of relatives need counselling with a professional counsellor and informational support. One-third of patients reported that they had no problem at present and the rest identified difficulties with home duties, shopping and transportation, and financial problems. The study suggests that there is value in encouraging cancer patients and their relatives to take part in existing cancer support groups. This may help to reduce the burden of disease and care-burden imposed on families.

Key words Social support. Cancer support group. Concerns. Needs assessment. Quality of life.

Introduction

The stigma associated with cancer may explain why some patients evaluate their life as being negative and often conclude that "life is not worth living". Thus, it is argued that for many patients with cancer, treatment alone, is not enough and support from family and friends may help them to cope with stressful life events [17]. In addition, families of cancer patients also suffer. Studies in the past decade have revealed that outside help is necessary for such families [25]. A longitudinal study of the adjustment patterns to breast cancer reported that patients and their families experienced the same amount of psychological morbidity [27]. The association between psychological morbidity of cancer patients and their next-of-kin is well documented [6].

Supportive care is becoming recognised as critical in cancer medicine. It includes all rational forms of support ranging from basic cancer therapy to spiritual help [28]. In this respect, psychological interventions are being widely used to influence coping behaviour and improve both patients' and their relatives' perception of personal control during the course of the disease [35]. In doing so, individual or group therapy are considered to be a useful approach to reduce patients' distress, anxiety and depression [10,24]. Spiegel [31] argues that group experience enables patients to take control over their lives, it helps them to establish a social network and tolerate strong emotions, including negative affect, express their anger directly, and make use of available social supports.

Two types of group therapy in cancer medicine can be identified: professionally-run groups and self-help or lay-led support groups. It is argued that the group setting can provide a supportive atmosphere to share feelings and experiences with others who "are in the same boat". This means that the use of support groups can be viewed as an effective intervention to help cancer patients and their families [3,36]. People participate in support groups because of the benefits of seeing and talking with others experiencing the same problem [2]. Support groups are being formed increasingly and it is felt that these groups are a potential resource for individuals living with chronic illness - individuals with potential risk of developing psychological morbidity. Only a few studies have reported that support groups are of little value to patients and their families [15]. Fewer still, demonstrate that support group attenders may suffer from negative experiences [12].

To explore the issue, this paper reports the results of a descriptive study carried out in the West of Scotland. The main purpose of the study was to investigate the views of people who participated in a cancer support group known as "Tak Tent" which is the Old Scots for "Take Care". It sought to look at attenders characteristics to find out: who they are, their clinical background, their concerns, needs, and problems, and how they evaluate their own health status and quality of life.

Tak Tent began in the University Department of Clinical Oncology, Glasgow Gartnavel General Hospital in 1980, then spread to other parts of the West of

Scotland [4]. There are 14 Tak Tent groups and their membership is made up of patients, relatives and friends, and professionals. The mission statement of the group is: "to promote the care of cancer patients, their families, friends, and the staff involved professionally in cancer care by providing practical and emotional support". Usually, the size of the groups range from 10 to 20 members in each monthly meeting [32].

Tak Tent offers the following support programmes:

1. Informational support: Tak Tent provides up-to-date information for all those affected by cancer which can be used to help them cope with everyday problems which they might face.

2. Counselling support: this is a service for patients and their families both via telephone services and face-to-face individual counselling by trained counsellors. Counselling is based on conventional psychotherapy methods with regard to each individual's circumstances [21]. These include discussion of feelings, problems and solutions; teaching basic relaxation techniques; emphasising patients' ability to help self; giving suggestions on communication of feelings; etc.

3. Regular group meetings: usually in each meeting there is an invited speaker who discusses about different topics ranging from cancer-related topics to issues related to participants' daily life. Sometimes a group member may present a specific topic related to his or her experience. If patients or other group members choose to talk about their experience of cancer, the rest of the group will treat this in confidence [30].

4. Emotional support: recently, the Tak Tent Resource Centre has opened and the co-ordinator, formerly a MacMillan Nurse, sees patients and relatives in the centre, giving emotional support.

5. Social activities: this includes social evenings, excursions, and visiting other groups. The groups also act for practical help in the community.

However, of these, counselling and emotional support and group meetings are the most important components of the Tak Tent activities.

Methods

Data collection

A descriptive study was carried out by means of a structured interview with patients and relatives participating in Tak Tent meetings in the West of Scotland. To interview people, after permission by the Executive Committee, one of us (A. M) took part in all active groups on several occasions. The following groups were active at the time of investigation: Campbeltown, East Kilbride, Glasgow Southern General, Glasgow South Side, Hamilton, and Paisley. In each group the study was explained to participants, and those who wished to participate in the study were interviewed using study-specific questionnaires.

Subjects

Initially the study population was divided into two sub-groups: "patients" and "relatives". All present members in the six Tak Tent groups at the time of

investigation agreed to take part in the study and there were no refusals, giving a response rate of 100% - 31 patients and 40 relatives.

Measures

Although standardised measures are available to assess satisfaction with health care and service programmes, two questionnaires were constructed: one for patients, consisting of 22 questions and the other for relatives with 20 questions. The aim was to develop a study-specific questionnaire for using in a larger study on quality of life in patients with cancer (using standards measures). The questions was governed by a combination of previous research findings and the desire to take advantage from face-to face interviewing of study subjects.

Demographic status. Demographic variables included sex, age, marital status and Deprivation Category (Depcat) as an indicator of socio-economic status (Carstairs and Morris Depcat Index) [5]. The deprivation categories range from 1 (affluent) to 7 (deprived).

Clinical status. Clinical background was investigated by asking participants to identify cancer type, treatment modality, and time since the disease was diagnosed.

Psychological effects. To study the psychological effects of diagnosis and consequent outcomes on patients and relatives three measures were applied: the time it took to cope with diagnosis; their most important concern both at past and present. These were open-ended questions.

Satisfaction. The satisfaction with care and support were measured on a 4 point Likert scale ranging from 1 to 4 (very satisfied to not at all). In addition,

patients but not relatives were asked to indicate whether they received any counselling during the course of treatment and at present. Furthermore, patients were asked about support they were receiving from their family (either within the household or outside the home), and from friends or neighbours.

Global health and quality of life. There were two questions on health and global quality of life. The respondents were asked to rate their perceived health on a 5 point scale ranging from 0 to 4 (very poor to very good). They rated their quality of life on a 7 point scale ranging from 0 to 6 (extremely poor to excellent). Relatives were asked, in addition, to describe their associated patients' health and quality of life. The above scale was used with the additional category-dead.

Needs assessment. Finally, respondents were asked to identify their own important needs by ranking several topics including symptom relief, emotional support, social support, family support, informational support, counselling support, and better treatment. Questions on symptom relief and treatment issues were not asked of patients' relatives. Apart from these topics, patients (not relatives) were asked to indicate their problems with regard to home duties, shopping, transportation, finance, and other problems.

Analysis

The data were analysed in a descriptive fashion using Epi-info version 5, a multi-purpose computer programme for epidemiological researchers, produced jointly by the Centres for Disease Control, Atlanta, and the World Health Organisation, Geneva [26]. Based on the study objectives and due to the small

sample size, analysis was limited to a descriptive method containing numbers and percentages (mean scores and standard deviations where necessary) of responses for each response category of each variable.

Results

Demographic and clinical status

The demographic and clinical characteristics of patients (n = 31), and relatives (n = 40) are shown in Table 1. The majority of both were females-87% and 72% respectively. The mean age for patients was 55.5 years ranging from 25 to 77, and for relatives was 56.5 years ranging from 24 to 78. The study results suggest that the majority of people attending Tak Tent are from middle class background- 24 patients (77%) and 28 relatives (69%). Twelve patients (39%) survived more than five years. Sixteen relatives stated the same proportion of survival (40%) for their ill family members. Six patients (19%) were newly diagnosed (less than 1 year). This figure for those of relatives was very similar (20%). In eleven of the patients interviewed, breast cancer was the main diagnosis (36%), while seven of the relatives interviewed reported lung cancer (18%) as the main diagnosis of their patients.

Since twenty-six relatives (65%) reported that their patients had died, there is not a direct match between patients and relatives and this influences the findings that follow. Eleven patients (36%) stated that they were under treatment at present time, while relatives reported that five of their associated patients were under treatment (13%). Seventeen patients (55%) reported that

they received combined therapy. Relatives said that eleven of their associated patients received surgery (28%).

The relationship of relatives to their patients was studied. Nine of the relatives (23%) were wives and the same proportion were husbands (23%), three mothers (8%), four sisters (10%), four daughters (10%), and eleven fell in the category of others which included friends, nurses, sisters-in-law, brothers-in-law, etc. (26%).

Satisfaction with care and support

The respondents were asked to identify whether they were satisfied with the care and support they received. Eighteen patients (58%) stated that they were "very satisfied" with the care they received or, were receiving, whereas most relatives (60%) claimed that they were "fairly" satisfied with the care their relatives had received or were receiving. Sixteen patients (52%) and twenty-eight relatives (70%) stated that they were "very satisfied" with the support they were receiving from Tak Tent. Five patients (16%) and six relatives (15%) identified that apart from Tak Tent they receive support from other sources including GP, Church, and other support groups (Table 2).

Support from family and friends

When patients were asked whether they were receiving any support from their families, 21 patients (68%) responded "always/almost always", 5 (16%)

"sometimes", and 5 (16%) "almost never/never". Twelve patients (39%) stated that they received support from friends and neighbours "always/almost always", 13 (42%) "sometimes", and 6 (19%) "almost never/never". Only five patients (16%) indicated that they had received counselling support from their cancer specialists during their treatment, and three (10%) stated that they received counselling from a professional counsellor at present.

Coping with diagnosis

To find out how long it took to cope with the diagnosis, patients and relatives described different feelings. Nine patients (29%) stated that they coped "immediately" (less than one month), 14 (45%) said it took "several months/quite long time", 6 (19%) stated that it was "on-going process", and two patients (7%) reported that they "never" coped with their cancer diagnosis. On the other hand, 4 relatives (10%) claimed that they coped "immediately", 19 (47%) stated for "quite long time" they did not cope with the situation, 10 (25%) reported it was "on-going process", and 7 (18%) said "never/forever". As it is clear, the relatives showed a quite different pattern of coping style, and compared to the patients it took longer time for the relatives to cope with the cancer diagnosis.

Most important concern at past and present

The main concern of eleven patients at the time of diagnosis of disease was fear of dying (36%), while at present time ten patients (32%) claimed that their main concern was fear of recurrence. Ten patients (32%) stated that they wanted to

have a good life and live well. It was found that six patients (19%) at the time of diagnosis were worried about how to cope with the disease while at the time of interview, five patients (16%) hoped to be cured. Relatives reported different features for their most important concern. Ten relatives (25%) indicated that at present they feel depressed, while eleven relatives (27%) stated that they were worried at the time of the diagnosis. Seven relatives (18%) reported that they had some hopes that their patients would get better, whereas as time went on, this figure reduced to five-13% (Table 3).

Perceived health and global quality of life

The mean score of perceived health for patients was 2.5 (SD = 0.85) and 3.4 (SD = 1.05) for relatives, indicating that they perceived their own health as being good (patients) and very good (relatives). Since a low score indicates poor health, this means patients rated their health poorer as compared to the relatives. The mean scores of global quality of life for patients and relatives were the same- 4.5 (SD = 0.96) and 4.4 (SD = 1.2) respectively. This indicates both patients and relatives rated their own quality of life between moderately good and good.

When relatives were asked to describe the health and quality of life of their patients, the mean scores became 3.6 and 4.8, indicating that the survivors have good health and moderately good quality of life as perceived by their relatives (relatives who reported that their patients had died were excluded from analysis).

Needs assessment

Sixteen patients (52%) indicated that symptom relief and family support were their important needs, while twenty-one relatives (53%) stated that they needed counselling (with a professional counsellor) and informational support. The remaining 15 patients stated that they need emotional support (13%), informational support (13%), better treatment (13%) and counselling support (10%), whereas the remaining 19 relatives reported that they need family support (18%), emotional support (15%), and 15% told that they have no special needs.

In addition patients were asked to identify their main problems at the present time. Ten patients (32%) reported that they have no problem, five (16%) responded difficulties in doing home duties, four (13%) financial, three (10%) shopping and transportation, and six (29%) claimed that they had other problems including pain, lack of support from GP, other physical disability, psychological distress and adjustment problems.

Discussion

This paper presents data collected from patients and relatives who take part every month in a cancer support group. The results show that married females, middle class people, aged 50 to 69 years old mostly attend Tak Tent cancer support group. This result is in line with that of Chesler et al.[7] and Slevin et al. [29] which indicated that women are more likely than men to use cancer

support groups. Most notably there were marked differences in clinical characteristics between patients who attend cancer support group and relatives' patients (see Table 1). Studies have shown that female survivors will come primarily from patients with breast cancer while among men the largest numbers of survivors would be patients with prostate, colorectal, and bladder cancers. Lung cancer survivors for both males and females are few [1]. Thus, since in this study most participants were female, both as patients and relatives, it is possible to say that within the patient group the prevalence of breast cancer was high whereas most relatives reported their patients had lung cancer-who already have died of their disease. Obviously, this also explains why there were differences in the pattern of treatment.

The findings of this study suggest that for relatives a longer process of coping was apparent. However, some patients and relatives stated that coping with the diagnosis is a continuing process. This means that as time passes, they being to come to terms with the idea of having cancer. A patient reported that "the initial shock could take up to 6 months, then eases, but never really goes away". Another patient stated that "I guess it would always be at the back of my mind, but life is for living".

The most important concern of patients at the time of diagnosis and at the present time may explain why coping is a continuing process. For example, it was found that some patients were, at the time of diagnosis, worried how to cope with the disease while now hoped to be cured. It appears that "hope" and

"coping" to some extent are related. Coping can be seen as strategies used to deal with threat and it is argued that variables that affect coping include: interpersonal, environmental, and illness-related factors [22]. On the other hand, hope is multi-dimensional, process oriented, and a complex of many thoughts, feelings, and actions that change with time [8]. Relatives showed different responses to hope and coping. Some relatives reported that they had initial hopes that their patients would be cured, but with time, their hopes diminished and instead, they began to experience depression, and only a few stated that they were managing to cope with the situation (see Table 3). Recent studies have shown that relatives of newly diagnosed cancer patients report high levels of concerns and psychological distress and deserve greater attention than they currently receive [14].

It was found that fear of dying changed to fear of recurrence. Cancer is feared perhaps because in many cases after all it is a fatal disease [18] and concern about fear of recurrence at present time can be easily understood. Recurrence may cause the past experiences to be remembered for example the difficult time of being in hospital or treatment period [20]. Others observed that many cancer survivors worry about suffering a recurrence and about developing a secondary cancer [16]. According to one patient "hoping I never need be in hospital. Being at hospital scares me". In a study on attitudes of cancer patients a similar finding was reported. The study described that a continuous remembering of the treatment experience was evident among cancer patients; sometimes called flash-back phenomena [34].

Using relatively simple measures general perceived health and global quality of life were found to be good for both patients and their relatives. One might argue that global measurement does not reflect the problems patients and their families are facing. However, several studies indicate that quality of life improved with a cancer diagnosis [11,13]. This was attributed to the fact that cancer patients might experience increased empathy and understanding from others as well as a positive image of life after their cancer diagnosis. In a study in the Netherlands [33] it was found that cancer patients had more positive social experiences than the normal population. It is argued that cancer experience often brings with it benefits including strengthened relationships, appreciation of life, and enhancement of self-concept [19,34].

Compared to other studies, patients in our study showed fewer problems. For example, in the Home Care study [23] the authors reported that 14% of patients needed help with personal care, 51% needed help with household tasks, and 58% reported needing help with transportation while in this study the most common response (32%) indicated that the patients had no problem.

Finally, as patients and their relatives indicated, one might conclude that cancer support groups could be seen as a useful means of allowing cancer survivors to share their experiences and at least overcome some of their own problems and develop their own social networks. It is also interesting to note the continued attendance of relatives of deceased cancer patients who presumably are still

obtaining benefit from attending and contributing to the groups. It has been suggested that with the increasing care-burden imposed on families, the level of distress they experience and their importance for patients' well-being, non-provision of support services for relatives may be short-sighted [9].

It is difficult to come to a general conclusion from such a small study. However, since the majority of participants indicated that they were very or fairly satisfied with the support they received, it seems that there is need to encourage cancer patients and their families to take part in one of the existing cancer support groups and they should be informed about the existence of cancer support groups. This may help to reduce the burden of disease and enhance quality of life in individuals who are suffering. In contrast, a rather sizeable percentage of the respondents appeared not to be entirely satisfied with the support they were received (Table 2). This, however, need to be taken as a signal that programmes are not working optimally. It would seem essential that Tak Tent co-ordinators devote more attention to identifying aspects of their programmes where participants were relatively dissatisfied.

Those who are attending Tak Tent groups are not representative of the larger population of patients and their relatives. Thus, it is not clear whether those who chose not to take part in support groups would benefit from doing so. It would be interesting to carry out a study on non-member or non-attendance for these support groups. It may be that the majority of patients and relatives feel no need for such support groups or that they prefer other approaches based on individual

counselling or telephone contact with a professional counsellor. As mentioned earlier, Tak Tent provides telephone services and individual counselling and many of patients and relatives use these services and do not attend group meetings. The study of the characteristics of these people could be a potential area for further investigation. This may also explain why relatively a few numbers of people attend group meetings. It would be stimulating to investigate why so few patients take advantage of the availability of support groups. Is it a problem of accessibility, lack of awareness of their availability, lack of interest in this approach to providing support, or a combination of such factors? These, however, remain to be answered.

On the other hand, cancer support groups require to develop their communication network to inform patients and their families more effectively and efficiently. Also in order to offer appropriate support and information to patients and their families it is important that at least some members of support groups have received training in group dynamics and listening and communication skills.

It seems that symptom relief and family support for patients, and counselling and informational support for relatives are the most important needs which should be considered. For those who do not have a support system, more psychosocial care may be necessary and counselling services should be provided.

Acknowledgements

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Table 1. Respondents demographic and clinical characteristics

	Patients (n = 31) % (No.)	Relatives (n = 40) % (No.)
Sex:		
Male	13 (4)	28 (11)
Female	87 (27)	72 (29)
Age:		
Mean (SD)	55.5 (12.8)	56.5 (11.7)
Range	25-77	24-78
Marital Status:		
Married	58 (18)	65 (26)
Single	13 (4)	3 (1)
Widowed/Divorced/Separated	29 (9)	33 (13)
Deprivation Category:		
Affluent	10 (3)	13 (5)
Middle	77 (24)	69 (28)
Deprived	13 (4)	18 (7)
Type of Cancer:*		
Breast	36 (11)	15 (6)
Lymphoma	20 (6)	5 (2)
Lung	7 (2)	18 (7)
Prostate	0	8 (3)
Bowel	0	10 (4)
Other	37 (12)	46 (18)
Time since diagnosis:		
Less than 1 year	19 (6)	20 (8)
1-5 years	42 (13)	40 (16)
More than 5 years	39 (12)	40 (16)
Receiving Treatment:		
Yes	36 (11)	13 (5)
No	64 (20)	87 (35)
Type of treatment:		
Radiotherapy	7 (2)	15 (6)
Chemotherapy	10 (3)	18 (7)
Surgery	29 (9)	28 (11)
Combined	55 (17)	25 (10)
Other	0	15 (6)

* This information identified by relatives are those refers to of the patients in their own family members.

Table 2. Satisfaction with care and support

	Patients (n = 31) % (No.)	Relatives (n = 40) % (No.)
Satisfaction with care:		
Very	58 (18)	38 (15)
Fairly	39 (12)	60 (24)
A little	3 (1)	2 (1)
Not at all	0	0
Support receiving:		
From one source (Tak Tent only)	84 (26)	85 (34)
From more than one source (Ta Tent and others)	16 (5)	15 (6)
Satisfaction with support:		
Very	52 (16)	70 (28)
Fairly	45 (14)	27 (11)
A little	3 (1)	0
Not at all	0	3 (1)

Table 3. Patients' and relatives' the most important concern at the time of diagnosis and the present time

	Concern at diagnosis % (No.)	Concern at present % (No.)
(a) Patients (n = 31):		
How to cope	19 (6)	0
Hopes	0	16 (5)
Fear of dying	36 (11)	0
Fear of recurrence	0	32 (10)
Life and health	16 (5)	0
Good life and living	0	32 (10)
Family	29 (9)	10 (3)
None	0	10 (3)
(b) Relatives (n = 40):		
Hopes	18 (7)	13 (5)
Worries	27 (11)	20 (8)
Fear of loss	13 (5)	0
Depression	0	25 (10)
Patients' ability to cope	25 (10)	0
Coping myself	0	20 (8)
Patients' suffering	15 (6)	0
Patients' well-being	0	15 (6)
Providing support	3 (1)	0
None	0	10 (4)

Appendix III
Letter sent to General Practitioners in Stobhill Hospital catchment area

STOBHILL
NHS TRUST

Stobhill NHS Trust
Balornock Road, Glasgow G21 3UW
Telephone: 0141-201 3000 Dr Milroy's secretary 0141 201 3715
Fax Number: 041.557.0468

DEPARTMENT OF RESPIRATORY MEDICINE

Consultant Physicians

Dr Gavin Boyd 0141 201 3716
Dr Robert Milroy 0141 201 3714

RM.EM
22nd December 1994

Dear

A survey of the needs and quality of life of patients with chronic respiratory problems and who attend the Stobhill Respiratory Department, is planned. The Department of Public Health, Glasgow University in association with the Health Gains Commissioning programme of GGHB and with support from the Area Clinical Audit Committee are helping Stobhill Hospital with this study. This prospective audit will act as a pilot for a broader assessment throughout Greater Glasgow of quality of life issues in patients with chronic respiratory disease, especially lung cancer.

We would like your assistance in this Stobhill audit project (protocol enclosed). With your permission, patients you consider to have chronic respiratory problems and who have been referred to the Respiratory Clinic at Stobhill Hospital will be asked to complete 3 questionnaires (samples enclosed).

Mr Ali Montazeri (BSc, MPH, Dept Public Health) has considerable insight into studying the problems with assessing quality of life. He will visit patients in their own homes to administer these questionnaires which take about 20 minutes to complete. He will be blind to the nature of their diagnosis.

In the case of patients who subsequently transpire to have lung cancer, further estimations of quality of life will be made immediately following diagnosis and 3 months after diagnosis, allowing the effects of diagnosis and treatment on quality of life to be assessed. These subsequent assessments will be performed at the Stobhill Hospital respiratory clinic or at the patients own home.

This prospective audit will be preceded by a pilot survey to determine the most practical arrangements for organising the logistics of the study.

Could you please indicate on the enclosed tear-off slip that you are happy for your patients to be included and return it to me in the envelope provided. If any of your patients are actually included then you will be contacted by our Research Coordinator, Mrs Jeanette Henderson, to obtain your approval.

Thank you very much in anticipation.

Yours sincerely,

[redacted]

ROBERT MILROY
Consultant Physician

To: Dr Robert Milroy
Consultant Physician
Stobhill NHS Trust

I agree ☐ / do not agree ☐ for my patients to be included in a prospective audit addressing quality of life issues in patients with chronic respiratory disease, including lung cancer. I understand I will be informed of any patients identified for inclusion in this study before the patients are asked to participate.

Please print
Name

_____

Signature

_____

Practice Address

_____

_____

_____

Appendix IV
Patient introductory format

Study Number:

QUALITY OF LIFE STUDY
Chronic Respiratory Disease

Consultant : Dr R Milroy / Dr G Boyd

Date of Referral:

Patient Information

Surname:

First Names:

Unit Number:

Date of Birth:

Address:

Post Code:

Telephone Number:

Date of Stobhill Appointment:

Name of General Practitioner:

Address:

Post Code:

Telephone Number:

Date GP contacted: Cleared Yes/No

Date patient contacted:

Date and time of Mr Montazeri Interview:

Date copy sent to Ali Montazeri:

Appendix V
The Nottingham Health Profile Part I

THE NOTTINGHAM HEALTH PROFILE

Please do
not write
in this margin

LISTED BELOW ARE SOME PROBLEMS PEOPLE MIGHT HAVE IN THEIR DAILY LIVES.

READ THE LIST CAREFULLY AND PUT A TICK IN THE BOX UNDER <u>YES</u> FOR ANY PROBLEM THAT APPLIES TO YOU <u>AT THE MOMENT</u>. TICK THE BOX UNDER <u>NO</u> FOR ANY PROBLEM THAT DOES NOT APPLY TO YOU.

<u>PLEASE ANSWER EVERY QUESTION</u>. IF YOU ARE NOT SURE WHETHER TO ANSWER YES OR NOT, TICK WHICHEVER ANSWER YOU THINK IS <u>MOST</u> TRUE AT THE MOMENT.

	YES	NO
I'm tired all the time	___	___
I have pain at night	___	___
Things are getting me down	___	___

	YES	NO
I have unbearable pain	___	___
I take tablets to help me sleep	___	___
I've forgotten what it's like to enjoy myself	___	___

	YES	NO
I'm feeling on edge	___	___
I find it painful to change position	___	___
I feel lonely	___	___

Please turn over

Please do not write in this margin

	YES	NO
I can only walk about indoors	___	___
I find it hard to bend	___	___
Everything is an effort	___	___

	YES	NO
I'm waking up in the early hours of the morning	___	___
I'm unable to walk at all	___	___
I'm finding it hard to make contact with people	___	___

REMEMBER IF YOU ARE NOT SURE WHETHER TO ANSWER "YES" OR "NO" TO A PROBLEM, TICK WHICHEVER ANSWER YOU THINK MORE TRUE AT THE MOMENT.

	YES	NO
The days seem to drag	___	___
I have trouble getting up and down stairs or steps	___	___
I find it hard to reach for things	___	___

	YES	NO
I'm in pain when I walk	___	___
I lose my temper easily these days	___	___
I feel there is nobody I am close to	___	___

Please turn over

Please do not write in this margin

	YES	NO
I lie awake for most of the night	____	____
I feel as if I'm losing control	____	____
I'm in pain when I'm standing	____	____

	YES	NO
I find it hard to dress myself	____	____
I soon run out of energy	____	____
I find it hard to stand for long (e.g. at the kitchen sink, waiting for a bus)	____	____

	YES	NO
I'm in constant pain	____	____
It takes me a long time to get to sleep	____	____
I feel I am a burden to people	____	____

	YES	NO
Worry is keeping me awake at night	____	____
I feel that life is not worth living	____	____
I sleep badly at night	____	____

Please turn over

Please do not write in this margin

	YES	NO
I'm finding it hard to get on with people	____	____
I need help to walk about outside (e.g. a walking aid or someone to support me)	____	____

	YES	NO
I'm in pain when going up and down stairs or steps	____	____
I wake up feeling depressed	____	____
I'm in pain when I'm sitting	____	____

NOW PLEASE GO BACK TO PAGE 1 AND MAKE SURE THAT YOU HAVE ANSWERED "YES" OR "NO" TO EVERY QUESTION, ON ALL FOUR PAGES OF THE QUESTIONNAIRE.

THANK YOU FOR YOUR HELP

Appendix VI
The EORTC QLQ-C30 and QLQ-LC13

EORTC QLQ-C30

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your inititals: _____

Your birthdate (Day, Month, Year): _____

Today's date (Day, Month, Year): _____

		No	Yes
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2
2.	Do you have any trouble taking a long walk?	1	2
3.	Do you have any trouble taking a short walk outside of the house?	1	2
4.	Do you have to stay in a bed or a chair for most of the day?	1	2
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2
6.	Are you limited in any way in doing either your work or doing household jobs?	1	2
7.	Are you completely unable to work at a job or to do household jobs?	1	2

During the past week:

		Not at All	A Little	Quite a Bit	Very Much
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4
16.	Have you been constipated?	1	2	3	4

Please go on to the next page

During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall physical condition during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

Patients sometimes report that they have the following symptoms. Please indicate the extent to which you have experienced these symptoms during the past week.

During the past week:	**Not at all**	**A little**	**Quite a bit**	**Very much**
31. How much did you cough?	1	2	3	4
32. Did you cough blood?	1	2	3	4
33. Were you short of breath when you rested?	1	2	3	4
34. Were you short of breath when you walked?	1	2	3	4
35. Were you short of breath when you climbed stairs?	1	2	3	4
36. Have you had a sore mouth or tongue?	1	2	3	4
37. Have you had trouble swallowing?	1	2	3	4
38. Have you had tingling hands or feet?	1	2	3	4
39. Have you had hair loss?	1	2	3	4
40. Have you had pain in your chest?	1	2	3	4
41. Have you had pain in your arm or shoulder?	1	2	3	4
42. Have you had pain in other parts of your body?	1	2	3	4
If yes, where?.....				
43. Did you take any medicine for pain?				
1 No 2 Yes				
44. If yes, how much did it help?	1	2	3	4

Please use the space below for additional comments you may have:

.....

.....

.....

.....

Appendix VII
Correspondence with the EORTC Quality Of Life Unit and user's agreement

UNIVERSITY
of
GLASGOW

26 July 1994

Dr Said Serbouti
Statistician
EORTC Data Centre
Ave E Mounier 83, Bte 11
1200 Brussels
Belgium

Dear Dr. Serbouti,

As a Ph.D. student in the Public Health Department, University of Glasgow, I am writing to request for materials on Quality of Life Studies. Based on advice I received from Dr. Cull I would like to ask your help. Would you please kindly send me relevant literature, supporting documents, and the EORTC QLQ-C30. My project is an unsponsored academic work. Therefore, I would be most grateful if you could arrange for me to be able to use EROTC QLQ-C30.

Thank you.

Yours sincerely

Ali Montazeri

DEPARTMENT OF PUBLIC HEALTH
University of Glasgow, 2 Lilybank Gardens, Glasgow G12 8RZ
Telephone: 0141–339 8855 *Ext* *Fax:* 0141–330 5018

EORTC
European Organization for Research and Treatment of Cancer
International Association under Belgian law

Saïd Serbouti, M.S.
Statistician Quality of Life Unit
Tel : 32.2.774.16.06

Mr. Ali Montazeri
University of Glasgow
Department of Public Health
2, Lilybank Gardens
GB - Glasgow G128RZ

EORTC Data Center

Brussels, 5 August 1994.

Dear Mr. Montazeri,

Thank you for your interest in the EORTC approach to quality of life assessment but we would like to have some more information about your unsponsored academic work and to know how you will utilize our information.

We have recently completed an international field study of the most recent version the EORTC quality of life questionnaire the EORTC QLQ-C30. This questionnaire is designed for use with a wide range of cancer patient populations, and is intended to be supplemented by tumor-specific questionnaire modules or supplements (e.g., lung cancer, breast cancer, head and neck cancer, etc.).

The empirical results to date are quite promising. The EORTC QLQ-C30 has proven to be a reliable and valid instrument and, importantly, appears responsive to changes in health status over time.
Please note that the QLQ-C30 is a copyrighted instrument, with all rights reserved. Written, prior consent of the EORTC Study Group on Quality of Life is required for its use. Conditions for its use are dependent on whether it will be employed in a university-based investigation, in which case its distribution is free. Or in a study that is carried out or sponsored by the pharmaceutical industry, its use is then subject to a royalty fee. The current fees are $2.500 for studies with less than 50 patients, $5.000 for studies with 50 patients and $10,000 for studies with 200 or more patients. The royalty fee is required per clinical study. The funds that are generated through the copyright arrangement will be used exclusively to support the on-going research of the Study Group on the development and refinement of quality of life instruments.

Enclosed please find the paper entitled "The EORTC QLQ-C30: A quality of life instrument for use in international clinical trials in oncology". In the appendix of this paper you will find the English-language version of the QLQ-C30. The questionnaire is available in most European languages.

Thank you again for your interest in our work and for your reply.

Sincerely yours,

[redacted]

Saïd Serbouti

encl. : 3

UNIVERSITY
of
GLASGOW

12 August 1994

Dr Said Serbouti
Statistician Quality of Life Unit
EORTC Data Centre
Ave E Mounier , 83 - Bte 11
1200 Brussels
Belgium

Dear Dr. Serbouti,

Thank you very much for your letter of 5 August 1994, and for the enclosed materials.

As I explained before I am doing my Ph.D., in the Public Health Department, University of Glasgow, on quality of life in patients with ovarian cancer. I am going to use the EORTC QLQ-C30 alongside the Nottingham Heath Profile (NHP) and the Rotterdam Symptom Checklist (RSCL) in a study which will be carried out in the West of Scotland. I will use these instruments as outcome measures (not in a clinical trial) to provide my thesis. These questionnaires are not going to be used other than for academic purposes. Thus, again I would like ask your permission to be able to use the EORTC QLQ-C30.

I hope to develop computer-based versions of these tools and compare them with a paper and pen method. I wonder if you have any information on computer-based quality of life studies in general, and about the EORTC QLQ-C30 in particular. If so I would be very grateful if you would forward it to me.

Thank you once more for your assistance.

Yours sincerely
Ali Montazeri

DEPARTMENT OF PUBLIC HEALTH
University of Glasgow, 2 Lilybank Gardens, Glasgow G12 8RZ
Telephone: 0141–339 8855 *Ext* *Fax:* 0141–330 5018

EORTC
European Organization for Research and Treatment of Cancer
International Association under Belgian law

Saïd Serbouti, M.S.
Statistician Quality of Life Unit
Tel : 32.2.774.16.06

Mr. Ali Montazeri
University of Glasgow
Department of Public Health
2, Lilybank Gardens
GB - Glasgow G128RZ

EORTC Data Center

Brussels, 30 August 1994.

Dear Mr. Montazeri,

We thank you for your letter dd. 12 August 1994 and in order to make the User's agreement we need the exact title of your PhD thesis.

We thank you in advance and remain,

Sincerely yours,

[redacted]

pp Saïd Serbouti

UNIVERSITY
of
GLASGOW

15 September 1994

Dr. Said Serbouti
Statistician Quality of Life Unit
EORTC Data Centre
Ave E Mounier , 83 - Bte 11
1200 Brussels
Belgium

Dear Dr. Serbouti,

Thank you very much for your letter of 30 August. I am writing to inform you about my new proposed study. After careful consideration I find that I am unable to recruit enough patients with ovarian cancer in the West of Scotland. Instead, I decided to continue my study with lung cancer patients. As you know the West of Scotland has the highest incidence of lung cancer in the world. Thus, I am going to use the EORTC QLQ-C30 and EORTC QLQ-LC13 alongside the Nottingham Heath Profile (NHP). I remind you that I will use these instruments as outcome measures (not in a clinical trial) for my Ph.D. thesis. These questionnaires are not going to be used other than for academic purposes. I would like to ask your permission to be able to use the EORTC QLQ-C30 and EORTC QLQ-LC13. Still I hope to develop computer-based versions of these tools and compare them with a paper and pen method.

The title of my Ph.D. thesis is: "The contribution of the clinical care to the quality of life in patients with cancer". In this study the process of care will be examined against outcome, with outcome measured in terms of quality of life instead of survival. Subjects are patients with lung cancer. Thank you for your assistance.

Yours sincerely
Ali Montazeri

DEPARTMENT OF PUBLIC HEALTH
University of Glasgow, 2 Lilybank Gardens, Glasgow G12 8RZ
Telephone: 0141–339 8855 *Ext* *Fax:* 0141–330 5018

EORTC
European Organization for Research and Treatment of Cancer
International Association under Belgian law

EORTC QLQ-C30 USER'S AGREEMENT

The EORTC Quality of Life Study Group grants permission to A. Montazeri to employ the EORTC QLQ-C30 in a study entitled "The contribution of the clinical care to the quality of life in patients with cancer ".

The Study Group will supply A. Montazeri with: (1) the QLQ-C30 in the currently available languages; and (2) the standard algorithms for scoring the QLQ-C30. Use of the EORTC QLQ-C30 in the above-mentioned investigation is subject to the following conditions:

1. A. Montazeri confirms that this study is being conducted without direct or indirect sponsorship or support from pharmaceutical, medical appliance or related, for-profit health care industries.

2. A. Montazeri will not modify, abridge, condense, translate, adapt or transform the QLQ-C30 or the basic scoring algorithms in any manner or form, including but not limited to any minor or significant change in wording or organization of the QLQ-C30.

3. A. Montazeri will not reproduce the QLQ-C30 or the basic scoring algorithms except for the limited purpose of generating sufficient copies for its own use and shall in no event distribute copies of the QLQ-C30 to third parties by sale, rental, lease, lending, or any other means. Reproduction of the QLQ-C30 as part of any publication is strictly prohibited.

4. Analysis and reporting of QLQ-C30 data by A. Montazeri should follow the written guidelines for scoring of the QLQ-C30 as provided by the EORTC Study Group on Quality of Life.

5. This agreement holds for the abovementioned study only. Use of the QLQ-C30 in any additional studies of A. Montazeri will require a separate agreement.

Signed and dated by:

Saïd Serbouti, for the
EORTC Quality of Life Group

S. Serbouti

22.9.94

Signed and dated by:

Ali Montazeri,for
Department of Public Health
University of Glasgow

30.9.94

Registered Office avenue E Mounier 83 Bte 11 • 1200 Brussels • Belgium • Phone: +32 2 774 16 11 • Fax. +32 2 772 35 45

UNIVERSITY
of
GLASGOW

7 October 1994

Dr. Said Serbouti
Statistician Quality of Life Unit
EORTC Data Centre
Ave E Mounier , 83 - Bte 11
1200 Brussels
Belgium

Dear Dr. Serbouti,

Thank you very much for your letter of 22 September, and for the enclosed materials. Please find enclosed one singed user's agreement. As I mentioned before I am going to use the EORTC QLQ-C30 and EORTC QLQ-LC13 alongside the Nottingham Heath Profile (NHP). Thus, would you please kindly let me know whether I need another user's agreement on QLQ-LC13 or not. I will collect data as soon as possible and hopefully I shall send you a copy of my proved protocol.

Thank you in advance.

Yours sincerely

Ali Montazeri

DEPARTMENT OF PUBLIC HEALTH
University of Glasgow, 2 Lilybank Gardens, Glasgow G12 8RZ
Telephone: 0141–339 8855 *Ext* *Fax:* 0141–330 5018

EORTC
European Organization for Research and Treatment of Cancer
International Association under Belgian law

Saïd Serbouti, M.S.
Statistician Quality of Life Unit
Tel : 32.2.774.16.06

EORTC Data Center

Mr. Ali Montazeri
University of Glasgow
Department of Public Health
2, Lilybank Gardens
GB-Glasgow G12 8RZ

Brussels, 12 October 1994.

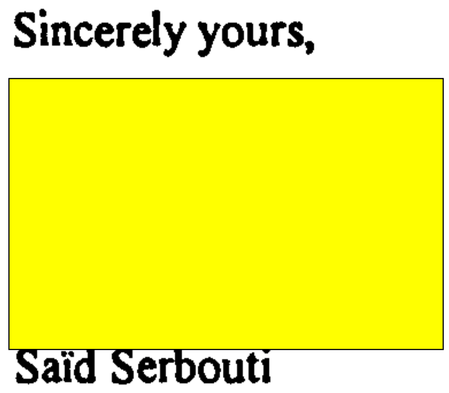
Dear Mr. Montazeri,

Please find enclosed the key-scoring algorithm for the analysis of the EORTC questionnaire QLQ-C30. No other user's agreement will be requested by us if you use the QLQ-LC13 as well.

Do not hesitate to contact me if you have any question regarding the use or interpretation of the QLQ-C30

I wish you great success with your project and I look forward to hearing from you as the study progresses.

Sincerely yours,



Saïd Serbouti

Enc. 1

UNIVERSITY
of
GLASGOW

16 February 1995

Dr. Said Serbouti
Statistician Quality of Life Unit
EORTC Data Centre
Ave E Mounier , 83 - Bte 11
1200 Brussels
Belgium

Dear Dr. Serbouti,

Since our last correspondence I was preparing for the study to begin. I started collecting data from 1st January 1995 and this will continue up to December. I wish to inform you that I received the key-scoring algorithm for the analysis of the EORTC QLQ-C30, but not for the QLQ-LC13. I would be most grateful if you could help me with a copy. Please fined enclosed, a copy of my study protocol. Your comments and assistance with further relevant literature will be most welcome.

Yours sincerely

Ali Montazeri

DEPARTMENT OF PUBLIC HEALTH
University of Glasgow, 2 Lilybank Gardens, Glasgow G12 8RZ
Telephone: 0141–339 8855 *Ext* *Fax:* 0141–330 5018

EORTC
European Organization for Research and Treatment of Cancer
International Association under Belgian Law

Gwendoline Kiebert
Head Quality of Life Unit
Tel : 32.2.774.16.61

Brussels, February 20, 1995

Dear Dr. Montazeri,

Thank you for your letter and outlines of your study. It seems a very interesting study to me. I did not know that Glasgow is the leading city I in the world with regard to the incidence of lung cancer. How sad.
I enclose a copy of the key scoring algorithm of the lung module. Good luck with your study, and please keep us informed about your study.
For your information, Dr. Said Serbouti has left the EORTC since last. January

Sincerely yours,

[redacted]

Gwendoline Kiebert

Registered Office: avenue E. Mounier 83 Bte 11 • 1200 Brussels • Belgium • Phone: + 32 2 774 16 11 • Fax: +32 2 772 35 45
E-mail: eortc @eortc.be

Appendix VIII
Study specific questionnaire

UNIVERSITY
of
GLASGOW

Quality of Life in Patients with Chronic Respiratory Disease
1995

Dear Sir/Madam,
We are trying to study how to improve the effectiveness of the health service in improving people's quality of life. But before any action can be taken we must know what people think about their own health and what they think their quality of life is.
The following questions and enclosed questionnaires are designed to seek your personal experiences. Your GP already has agreed with this investigation. It is hoped that data gained from you and other people who have agreed to help, will improve the delivery of health and enhance the quality of life. We hope you will be able to help us by co-operating with this research project and are grateful to you for doing so.

The information you give will be treated in confidence. Thank you.

No. | | | | | | |

Date of interview | | | |

Address

.....

.....Post code.....

Date of birth | | | |

Sex | M | F |

Marital status

Married	
Single	
Widowed	
Separated	
Divorced	
Living with a partner	

Employment

Employed (full time or part time)	
Unemployed	
Housewife	
Retired	
Other	

DEPARTMENT OF PUBLIC HEALTH
University of Glasgow, 2 Lilybank Gardens, Glasgow G12 8RZ
Telephone: 0141–339 8855 *Ext* *Fax:* 0141–330 5018

Education

No school leaving certificate
School certificate
College/University qualification
Other

House ownership

Owner occupied
Private rented
Rented from Council
Rented from Housing Association
Other

Type of accommodation

.....

Number of rooms available

.....

Number of children

.....

How often do your children who left home visit you?

Always (daily)
Almost always (2-3 times in a week/weekly)
Sometimes (monthly)
Almost never (yearly)
Never

Do they help you in any way (for example shopping, cooking, cleaning, etc.)

Always
Almost always
Sometimes
Almost never
Never

Do you see your other members of family or other relatives?

Always (daily)
Almost always (2-3 times in a week/weekly)
Sometimes (monthly)
Almost never (yearly)
Never

Do they help you in any way(for example shopping, cooking, cleaning, etc.)

Always
Almost always
Sometimes
Almost never
Never

How often do you contact/visit your neighbours?
Always (daily) ☐
Almost always (2 or 3 times in a week/weekly) ☐
Sometimes (monthly) ☐
Almost never (yearly) ☐
Never ☐

Do they help you in any way? (for example shopping, cooking, etc.)
Always ☐
Almost always ☐
Sometimes ☐
Almost never ☐
Never ☐

Home distance from Hospital Mile ☐

Have you been admitted to hospital for any treatment during the last year?
Yes ☐
No ☐

Do you have any problems travelling for your treatment?
Yes ☐
No ☐

What are they?
.....
Means of transport
.....

Do you have a car?
Yes ☐
No ☐

- *Thank you very much for your help.*

To be completed after interview:

Interview setting
Home ☐
Clinic ☐

Any comments
.....
.....
.....

Appendix IX
Acceptability questionnaire

Acceptability Questionnaire

Study Number:

Q1. Are the questions easy to understand in general?
Very easy
Moderately easy
Not very easy
Not at all

Q2. Please identify difficult questions?
.....
.....

Q3. Are the options provided as answers adequate?
Yes
No

Q4. Did you find the questions relevant to yourself?
Very relevant
Moderately relevant
Not very relevant
Not at all

Q5. Please identify questions you think are irrelevant:
.....
.....

Q6. Do you prefer to fill in a questionnaire or to be interviewed?
Fill in a questionnaire
To be interviewed
Either
Don't know

Q7. Do you find it difficult to fill in a questionnaire by yourself?
Very difficult
Quite difficult
Not very difficult
Not at all

Q8. Can you give reasons?
.....

Q9. Do you find being "interviewed" comfortable?
Very comfortable
Quite comfortable
Not very comfortable
Not at all

Q10. Can you give reasons?
.....

Q11. Do you prefer to be interviewed at home or clinic?
Home
Clinic
Either
Don't know

Q12. Any other comments?
.....
.....
.....
.....

Appendix X
Letter sent to lung cancer patients at follow-up by the chest physician

STOBHILL
NHS TRUST

DEPARTMENT OF RESPIRATORY MEDICINE

Consultant Physicians

Dr Gavin Boyd 0141 201 3716
Dr Robert Milroy 0141 201 3714

Stobhill NHS Trust
Balornock Road, Glasgow G21 3UW
Telephone: 0141-201 3000 Dr Milroy's secretary 0141 201 3715 (Direct line)
Fax Number: 0141.557.0468

RM.EM
7th April 1995
(Dictated 7.4.95)

Dear

You may remember completing a questionnaire with Mr Ali Montazeri around the time you first visited the Stobhill Chest Clinic about 3 months ago.

I am interested to know how you are feeling now. I would, therefore, like Mr Montazeri to see you again and assess how you are feeling.

If you have no objections I would like Mr Montazeri to intereview you again in the near future. If you do not want to see Mr Montazeri again please telephone Mrs Jeanette Henderson, our Research Co-ordinator, on 0141.201.3973. If we do not hear from you in the next week, Mr Montazeri will either telephone you or write to you to arrange an appointment to see you again. This appointment will, of course, be tailored for your convenience.

Thank you again for your help. We hope other patients will benefit in the future from your participation in this important research.

Yours sincerely,

[redacted]

ROBERT MILROY
Consultant Physician

Appendix XI
Letter sent to lung cancer patients at follow-up by the researcher

STOBHILL
NHS TRUST

Stobhill NHS Trust
Balornock Road, Glasgow G21 3UW.
Telephone: 041 558 0111

Dear .....

You will recently have received a letter from Dr. Robert Milroy regarding my proposed visit to assess how you are feeling. I am unable to contact you by telephone, but propose to visit you at home on ..... at ..... (a.m./p.m.).

If this arrangement does not suit you, please telephone me at ..... and we can arrange a more convenient time for you.
Thank you for your help.

Yours sincerely

Ali Montazeri
Clinical Research Assistant to Dr. Milroy

Appendix XII

The Nottingham Health Profile user's guide for data analysis

TABLE V. Weighted Scores for 'YES' Responses on Part I

Statement	Weight	Code
I'm tired all the time	39.20	EN1
I have pain at night	12.91	P1
I take tablets to help me sleep	22.37	SL1
Things are getting me down	10.47	EM1
I find it painful to change position	9.99	P3
I'm feeling on edge	7.22	EM3
I feel lonely	22.01	SO1
I can only walk about indoors	11.54	PM1
I have unbearable pain	19.74	P2
I find it hard to bend	10.57	PM2
Everything is an effort	36.80	EN2
I'm unable to walk at all	21.30	PM3
I'm waking up in the early hours of the morning	12.57	SL2
I've forgotten what is't like to enjoy myself	9.31	EM2
I'm finding it hard to make contact with people	19.36	SO2
I'm in pain when I walk	11.22	P4
The days seem to drag	7.08	EM4
I have trouble getting up and down stairs or steps	10.79	PM4
I find it hard to reach for things	9.30	PM5
I lose my temper easily these days	9.76	EM5
I lie awake for most of the night	27.26	SL3
I feel as if I'm losing control	13.99	EM6
I'm in pain when I'm standing	8.96	P5
I feel there is nobody I am close to	20.13	SO3
I find it hard to dress myself	12.61	PM6
I soon run out of energy	24.00	EN3
I find it hard to stand for long (eg at the kitchen sink, waiting for a bus)	11.20	PM7
I'm in constant pain	20.86	P6
It takes me a long time to get to sleep	16.10	SL4
I feel I am a burden to people	22.53	SO4
Worry is keeping me awake at night	13.95	EM7
I feel that life is not worth living	16.21	EM8
I sleep badly at night	21.70	SL5
I need help to walk about outside (eg a walking aid or someone to support me)	12.69	PM8
I'm in pain when going up and down stairs or steps	5.83	P7
I wake up feeling depressed	12.01	EM9
I'm finding it hard to get on with people	15.97	SO5
I'm in pain when I'm sitting	10.49	P8

NB It should be noted that the variable code is not related to the ordering of items on the questionnaire.

Coding of Part 1 Responses by Computer Programme (SPSS Format)

```
RECODE          EN1(1=39.2)/P1(1=12.91)/EM1(1=10.47)/P2(1=19.74)
                /SL1(1=22.37)/EM2(1=9.31)/EM3(1=7.22)/P3(1=9.99)
                /SO1(1=22.01)/PM1(1=11.54)/PM2(1=10.57)/EN2(1=36.8)
                /SL2(1=12.57)/PM3(1=21.3)/SO2(1=19.36)/EM4(1=7.08)
                /PM4(1=10.79)/PM5(1=9.3)/P4(1=11.22)

RECODE          EM5(1=9.76)/SO3(1=20.13)/SL3/(1=27.26)/EM6(1=13.99)
                /P5(1=8.96)/PM6(1=12.61)/EN3(1=24)/PM7(1=11.2)/P6
                (1=20.86)/SL4(1=16.1)/SO4(1=22.53)/EM7(1=13.95)/EM8
                (1=16.21)/SL5(1=21.7)/SO5(1=15.97)/PM8(1=12.69)/
                P7(1=5.83)/EM9(1=12.01)/P8(1=10.49)

COMPUTE         TEN=EN1+EN2+EN3

COMPUTE         TP=P1+P2+P3+P4+P5+P6+P7+P8

COMPUTE         TEM=EM1+EM2+EM3+EM4+EM5+EM6+EM7+EM8+EM9

COMPUTE         TSL=SL1+SL2+SL3+SL4+SL5

COMPUTE         TSO=SO1+SO2+SO3+SO4+SO5

COMPUTE         TPM=PM1+PM2+PM3+PM4+PM5+PM6+PM7+PM8

MISSING VALUES  EN1 to P8 (9)

ASSIGN MISSING  TEN TO TPM(200)

VARIABLES       EN1, TIRED ALL THE TIME/
                P1, PAIN AT NIGHT/
                EM1, THINGS ARE GETTING HIM DOWN/
                P2, UNBEARABLE PAIN/
                SL1, NEEDS TABLETS TO SLEEP/
                EM2, HAS FORGOTTEN HOW TO ENJOY HIMSELF/
                EM3, FEELING ON EDGE/
                P3, PAINFUL TO CHANGE POSITION/
                SO1, FEELS LONELY/
                PM1, CAN ONLY WALK INDOORS/
                PM2, HARD TO BEND/
                EN2, EVERYTHING IS AN EFFORT/
                SL2, WAKES UP EARLY/
                PM3, IS UNABLE TO WALK AT ALL/
                SO2, FINDS IT HARD TO CONTACT PEOPLE/
                EM4, THE DAYS DRAG/
                PM4, FINDS STAIRS OR STEPS DIFFICULT/
                PM5, FINDS IT HARD TO REACH FOR THINGS/
                P4, HAS PAIN WHEN WALKS/
                EM5, LOSES TEMPER EASILY/
                SO3, CANNOT GET CLOSE TO ANYONE/
                SL3, LIES AWAKE FOR MOST OF THE NIGHT/
                EM6, THINKS HE IS LOSING CONTROL/
                P5, HAS PAIN WHEN STANDING/
                PM6, FINDS IT HARD TO DRESS/
                EN3, SOON LOSES ENERGY/
                PM7, FINDS IT HARD TO STAND FOR LONG/
                P6, IS IN CONSTANT PAIN/
                SL4, TAKES A LONG TIME TO GET TO SLEEP/
                SO4, FEELS HE IS A BURDEN TO OTHERS/
                EM7, WORRY KEEPS HIM AWAKE/
                EM8, FEELS THAT LIFE IS NOT WORTH LIVING/
                SL5, SLEEPS BADLY AT NIGHT/
                SO5, FINDS IT HARD TO GET ON WITH OTHERS/
                PM8, NEEDS HELP TO WALK OUTSIDE/
                P7, HAS PAIN WHEN USING STAIRS OR STEPS/
                EM9, WAKES UP DEPRESSED/
                P8, HAS PAIN WHEN SITTING/
```

Appendix XIII
The EORTC Quality Of Life Questionnaires user's guide for data analysis

Scoring Procedures for the EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30)

I. Functional Scales

The questionnaire includes 6 functional scales:

- Physical functioning (PF)
- Role functioning (RF)
- Emotional functioning (EF)
- Cognitive functioning (CF
- Social functioning (SF)
- Global health status/quality of life (QL)

These 6 scales are all constructed in a similar manner: (1) the raw scores for the individual items within a scale are first summed, and then divided by the number of items within the scale; and (2) these scale scores are then linearly transformed such that all scales range from 0 to 100, with a higher scale score representing a higher level of functioning.

Following are the scoring algorithms for the 5 functional scales, including the SPSS computational language (note: the two-letter abbreviations employed for the various scales and items are arbitrary; alternative abbreviations can, of course, be used).

Physical functioning (questionnaire items 1 through 5)

1 Compute an additive scale (PF) by adding the questionnaire items 1-5 (Q1 to Q5) and dividing this sum by the number of items (5):

```
COMPUTE  PF=(Q1+Q2+Q3+Q4+Q5)/5.
```

2 Carry out a linear transformation to convert the physical functioning scale (PF) to a 0-100 scale (XPF):

```
COMPUTE  XPF=100-((PF-1)*100).
```

Role functioning (questionnaire items 6 and 7)

1 Compute an additive scale (RF) by adding the questionnaire items 6 and 7 (Q6 and Q7) and dividing this sum by the number of items (2):

```
COMPUTE  RF=(Q6+Q7)/2.
```

2 Carry out a linear transformation to convert the role functioning scale (RF) to a 0-100 scale (XRF):

```
COMPUTE  XRF=100-((RF-1)*100).
```

Emotional functioning (questionnaire items 21-24)

1 Compute an additive scale (EF) by adding the questionnaire items 21-24 (Q21 to Q24) and dividing this sum by the number of items (4):

```
COMPUTE  EF=(Q21+Q22+Q23+Q24)/4.
```

2 Carry out a linear transformation to convert the emotional functioning scale (EF) to a 0-100 scale (XEF):

```
COMPUTE  XEF=100-((EF-1)*100/3).
```

Cognitive functioning (questionnaire items 20 and 25)

1 Compute an additive scale (CF) by adding the questionnaire items 20 and 25 (Q20 and Q25) and dividing this sum by the number of items (2):

```
COMPUTE  CF=(Q20+Q25)/2.
```

2 Carry out a linear transformation to convert the cognitive functioning scale (CF) to a 0-100 scale (XCF):

```
COMPUTE  XCF=100-((CF-1)*100/3).
```

Social functioning (questionnaire items 26 and 27)

1 Compute an additive scale (SF) by adding the questionnaire items 26 and 27 (Q26 and Q27) and dividing this sum by the number of items (2):

```
COMPUTE  SF=(Q26+Q27)/2.
```

2 Carry out a linear transformation to convert the social functioning scale (SF) to a 0-100 scale (XSF):

```
COMPUTE  XSF=100-((SF-1)*100/3).
```

Global health status/quality of life (questionnaire items 29 and 30)

1 Compute an additive scale (QL) by adding the questionnaire items 29 and 30 (Q29 and Q30) and dividing this sum by the number of items (2):

```
COMPUTE  QL=(Q29+Q30)/2.
```

2 Carry out a linear transformation to convert the global quality of life scale (QL) to a 0-100 scale (XQL):

```
COMPUTE  XQL=(QL-1)*100/6.
```

II. Symptom Scales/Items

The questionnaire includes a number of multi-item scales and single items assessing a range of physical symptoms common among patients with cancer. An additional single item assesses the financial impact of the disease and treatment. These scales and single items are linearly transformed such that all scales/items range from 0 to 100, with a higher score representing a higher level of symptomatology/problems.

- Fatigue (FA)
- Nausea and vomiting (NV)
- Pain (PA)
- Dyspnea (DY)
- Sleep disturbance (SL)
- Appetite loss (AP)
- Constipation (CO)
- Diarrhea (DI)
- Financial impact (FI)

Fatigue (questionnaire items 10, 12 and 18)

1 Compute an additive scale (FA) by adding the questionnaire items 10, 12 and 18 (Q10, Q12 and Q18) and dividing this sum by the number of items (3):

```
COMPUTE  FA=(Q10+Q12+Q18)/3.
```

2 Carry out a linear transformation to convert the fatigue scale (FA) to a 0-100 scale (XFA):

```
COMPUTE  XFA=(FA-1)*100/3.
```

Nausea and vomiting (questionnaire items 14 and 15)

1 Compute an additive scale (NV) by adding the questionnaire items 14 and 15 (Q14 and Q15) and dividing this sum by the number of items (2):

```
COMPUTE  NV=(Q14+Q15)/2.
```

2 Carry out a linear transformation to convert the nausea and vomiting scale (NV) to a 0-100 scale (XNV):

```
COMPUTE  XNV=(NV-1)*100/3.
```

Pain (questionnaire items 9 and 19)

1 Compute an additive scale (PA) by adding the questionnaire items 9 and 19 (Q9 and Q19) and dividing this sum by the number of items (2):

```
COMPUTE  PA=(Q9+Q19)/2.
```

2 Carry out a linear transformation to convert the pain scale (PA) to a 0-100 scale (XPA):

```
COMPUTE  XPA=(PA-1)*100/3.
```

Single items (questionnaire items 8, 11, 13, 16, 17 and 28)

The remaining questionnaire items -- assessing dyspnea (DY), sleep disturbance (SL), appetite loss (AP), constipation (CO), diarrhea (DI), and financial difficulties (FI) are treated individually. These items should also be linearly transformed to a 0-100 scale.

```
COMPUTE  XDY=(DY-1)*100/3.
COMPUTE  XSL=(SL-1)*100/3.
COMPUTE  XAP=(AP-1)*100/3.
COMPUTE  XCO=(CO-1)*100/3.
COMPUTE  XDI=(DI-1)*100/3.
COMPUTE  XFI=(FI-1)*100/3.
```

Further inquiries regarding the scoring algorithms for the EORTC QLQ-C30 can be directed to: Saïd Serbouti, Head, Quality of Life Unit, The EORTC Data Center, Avenue Emmanuel Mounier 83/11, 1200 Brussels, Belgium. Telephone: 32-2-774-1606; Telefax: 32-2-772-3545.

Scoring procedures for the EORTC QUALITY OF LIFE QUESTIONNAIRE LONG CANCER MODULE

The questionnaire module includes twelve items in disease- and treatment-related symptoms, and one conditional item on effects of pain medication.
A multi-item scale on dyspneu is created, while the remaining symptoms and side-effects are measured by single items. All raw scores are linearly transformed to a score ranging from 0 to 100, with a higher score representing more complaints.

Dyspneu (items 33-35 in QLQ-LC13 + item 8 in QLQ-C30)

1. Compute an additive scale (DY) by adding the scores of items 33, 34, and 35 in QLQ-LC13, and item 8 in QLQ-C30. Divide the sum of the raw scores by the number of items. (4).

   COMPUTE DY = (LC33+LC34+LC35+C8) / 4

2. Carry out a linear transformation of the scale score (DY) to a 1-100 scale (XDY):

   COMPUTE XDY = (DY-1)* 100/3

Cough (CO-LC31), **Haemoptysis** (HP-LC32), **Sore mouth** (SM-LC36), **Trouble swallowing** (SW-LC37), **Peripheral_neuropathy** (PN-LC41), **Hair_loss** (HL-LC39), **Pain_in_chest** (PC-LC40), **Pain_in_shoulder** (PS-LC41), **Pain_elsewhere** (PE-LC42)

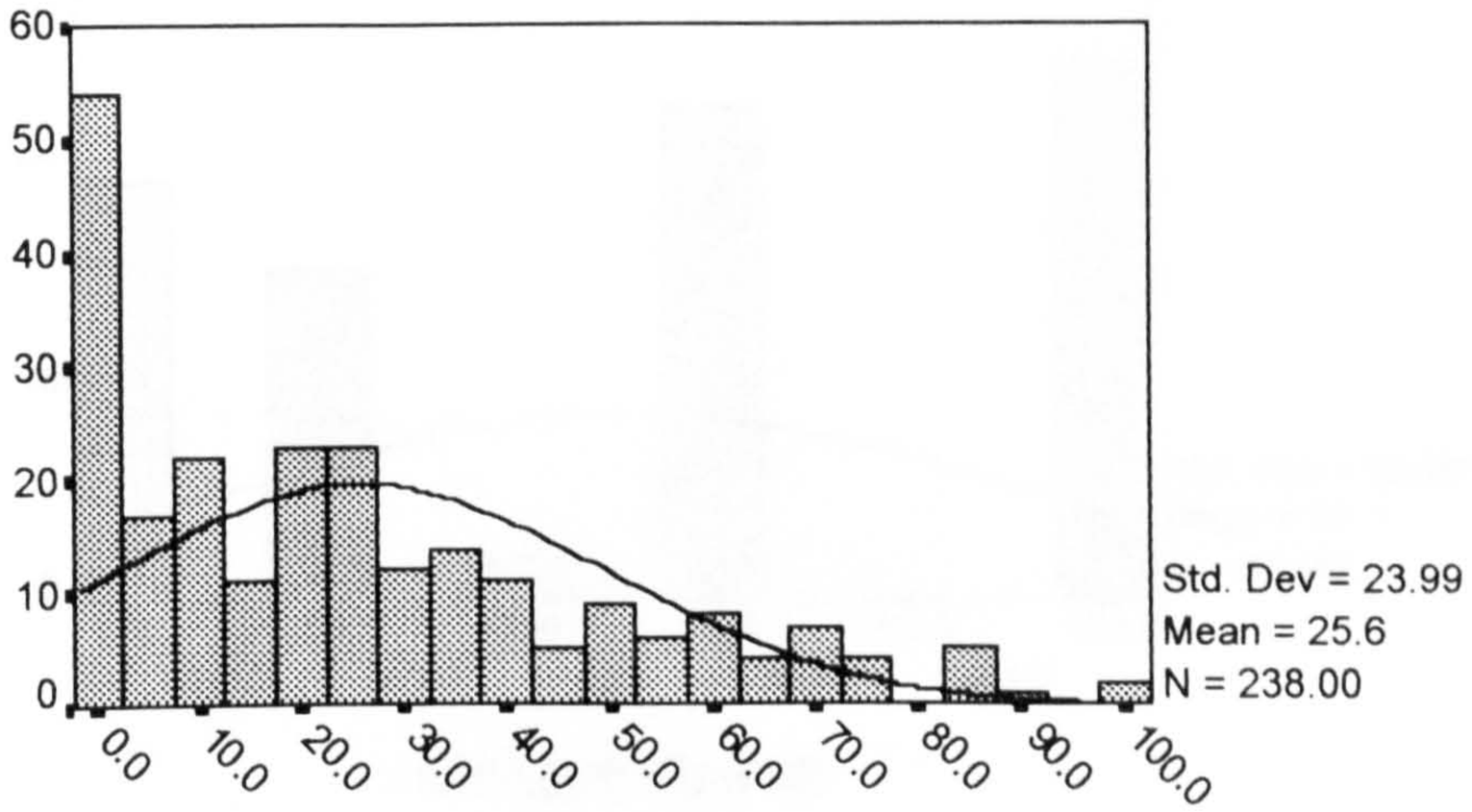
```
COMPUTE XCO = (CO-1)*100/3
COMPUTE XHP = (HP-1)*100/3
COMPUTE XSM = (SM-1)*100/3
COMPUTE XSW = (SW-1)*100/3
COMPUTE XPN = (PN-1)*100/3
COMPUTE XHL = (HL-1)*100/3
COMPUTE XPC = (PC-1)*100/3
COMPUTE XPS = (PS-1)*100/3
COMPUTE XPE = (PE-1)*100/3
```

Pain_medication (PMa -LC43, PMb - LC44)

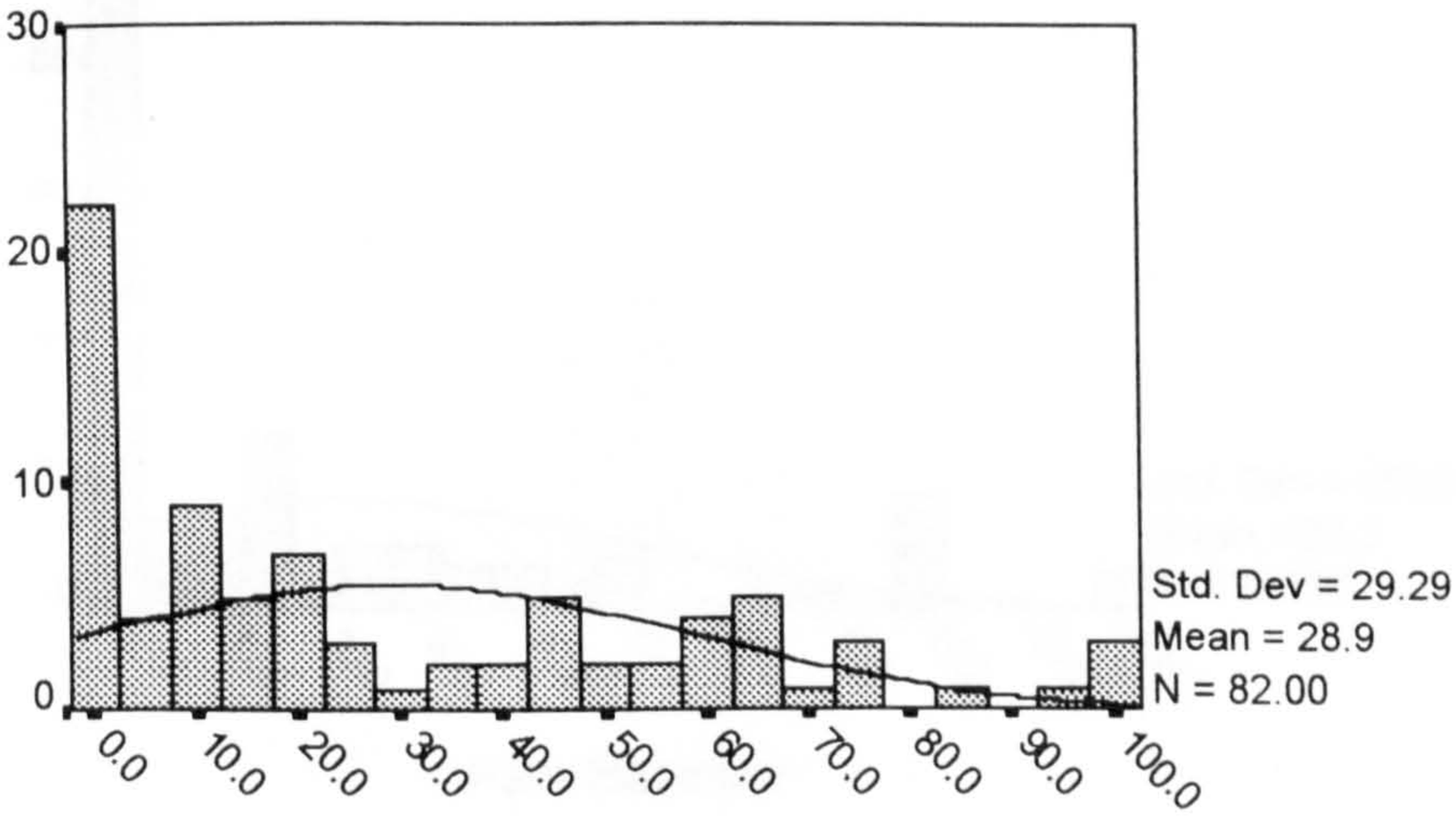
```
COMPUTE XPA = (PMa-1)*100
      if XPMa ≠ 0 (PMb ≠ 1):
COMPUTE  XPMb = 100-((PMb-1)*100/3)
```

Appendix XIV
Distribution of patients' scores on the NHP

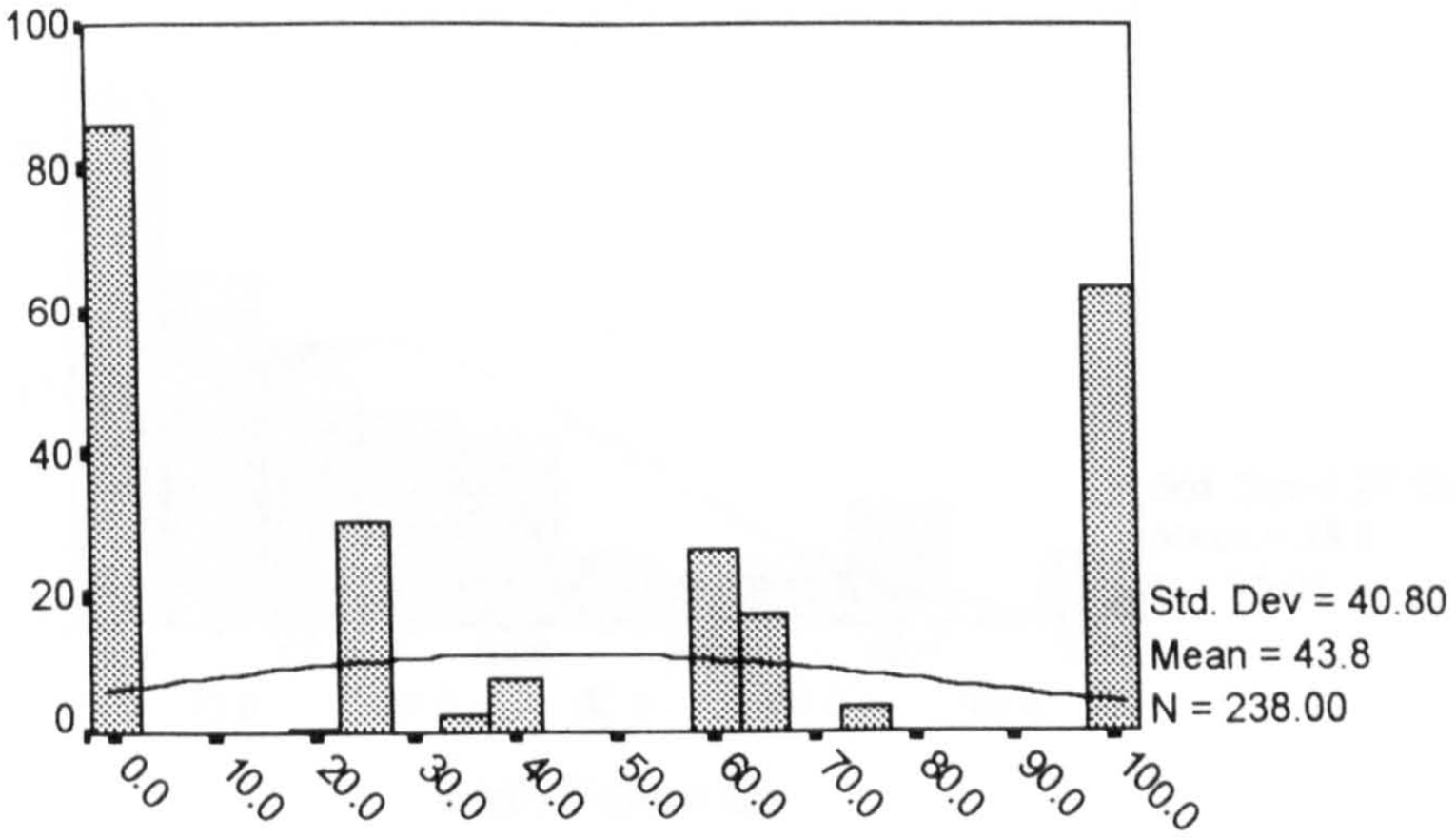
Key: vertical axis shows number of patients and horizantal axis indicates patients' scores



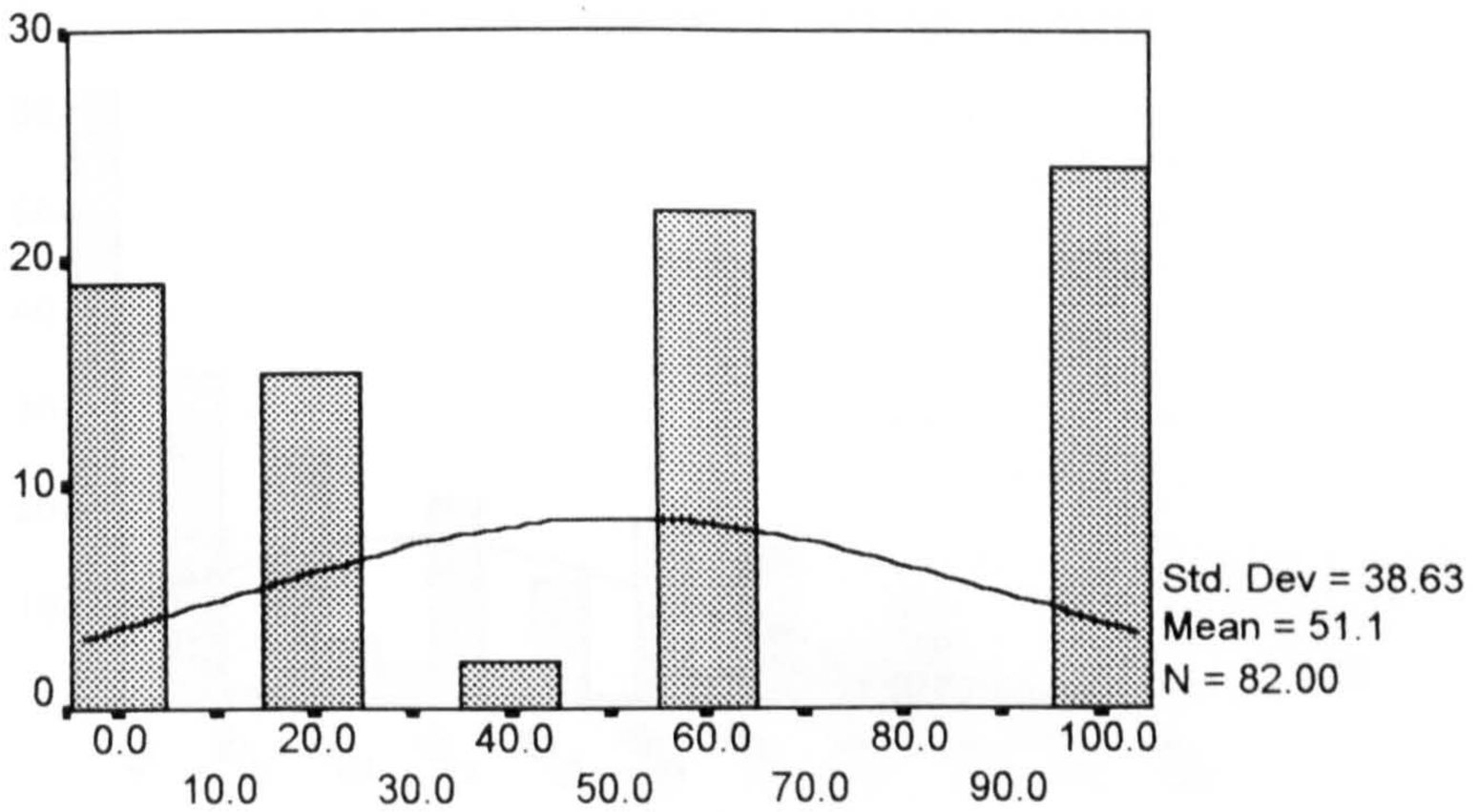
Emotional reactions-Baseline



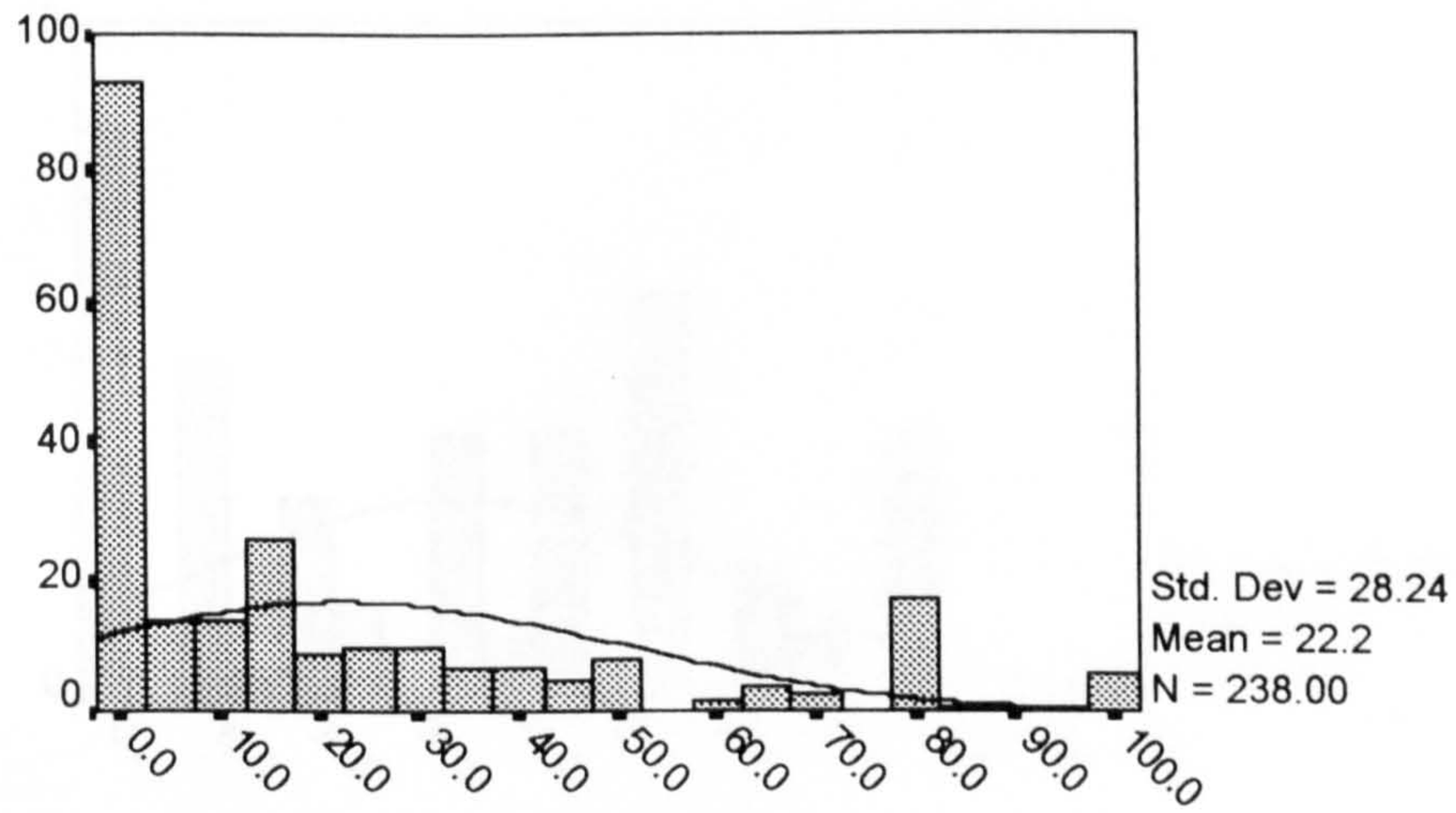
Emotional reactions-Follow up



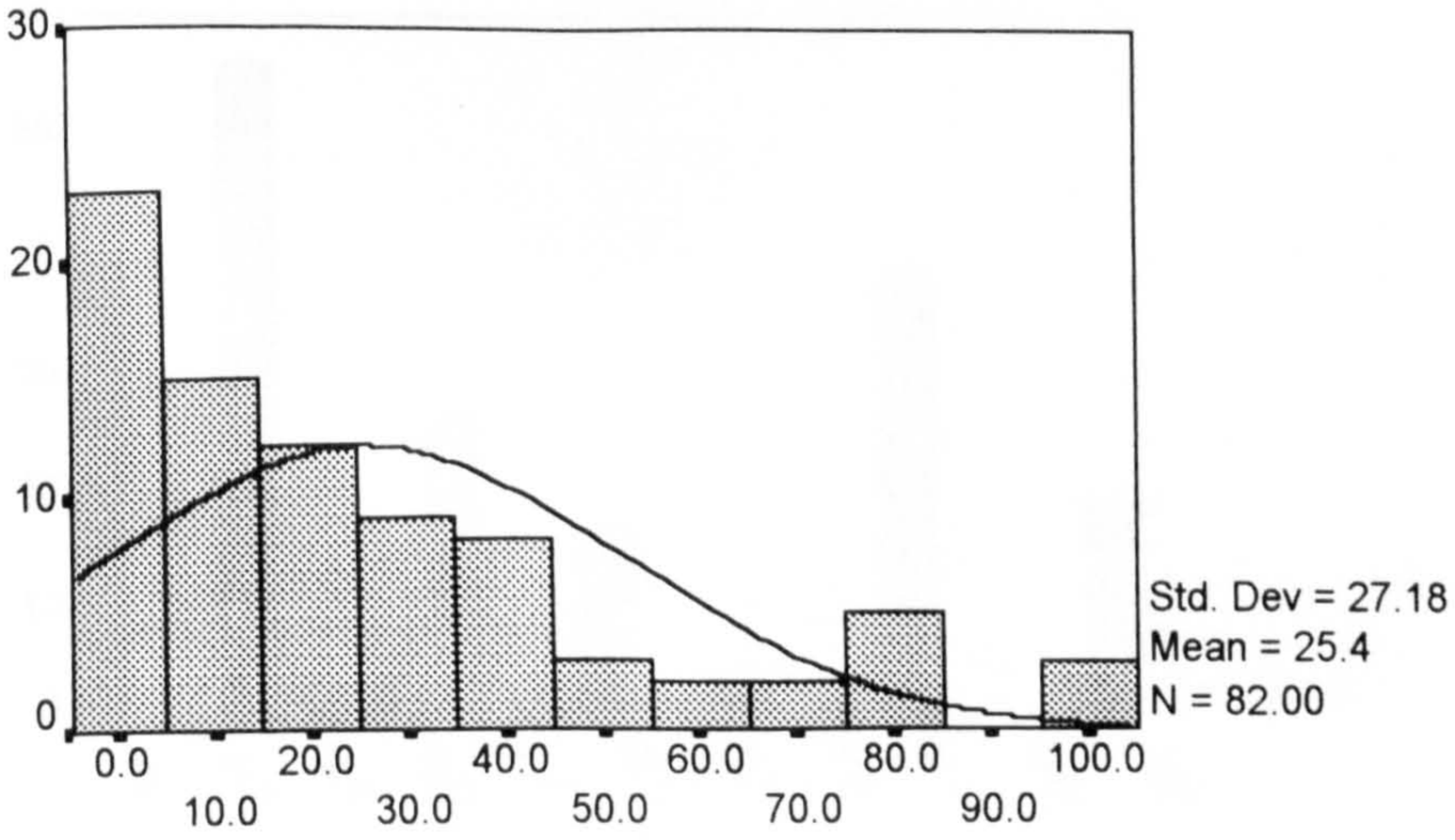
Energy-Baseline



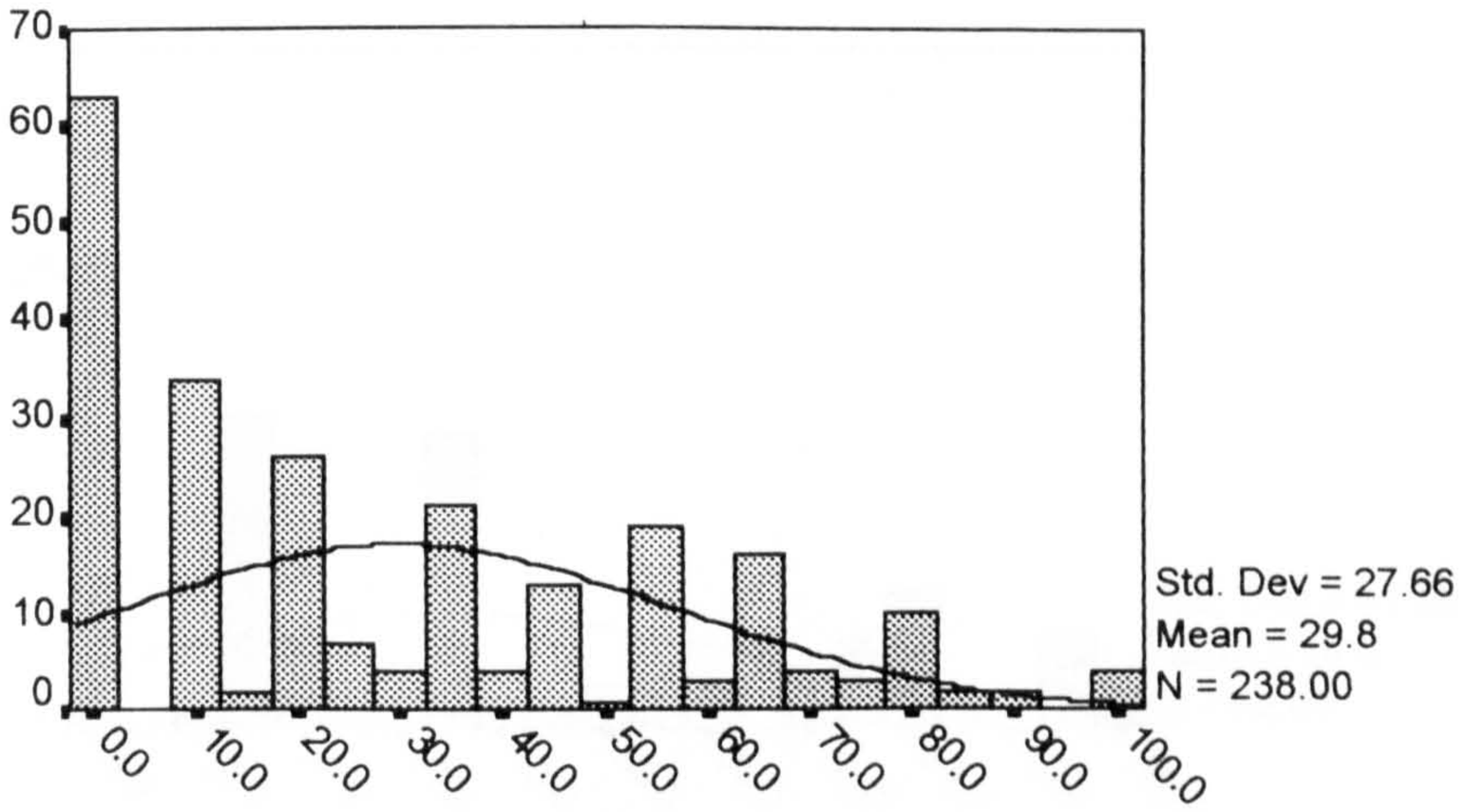
Energy-Follow up



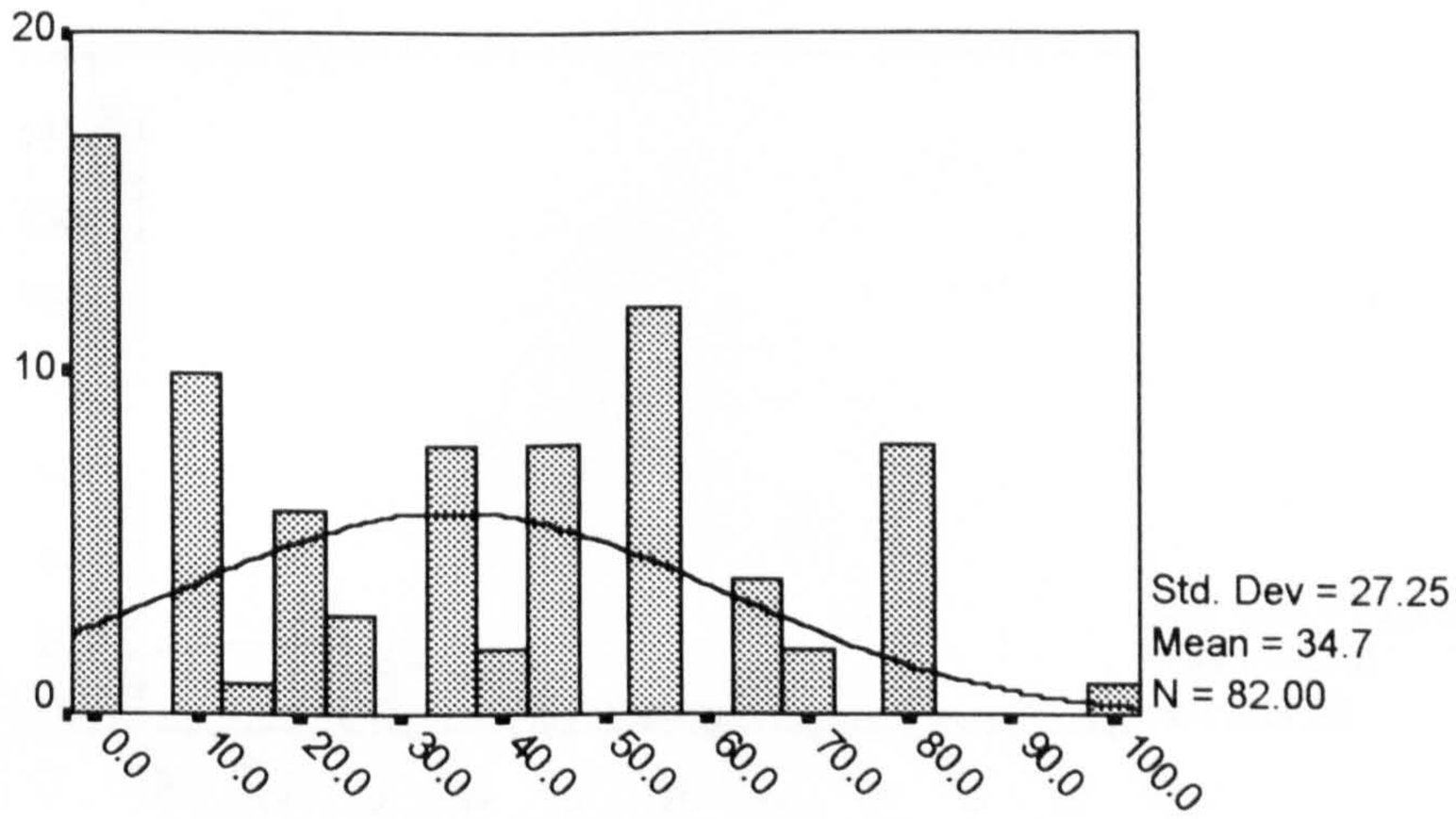
Pain-Baseline



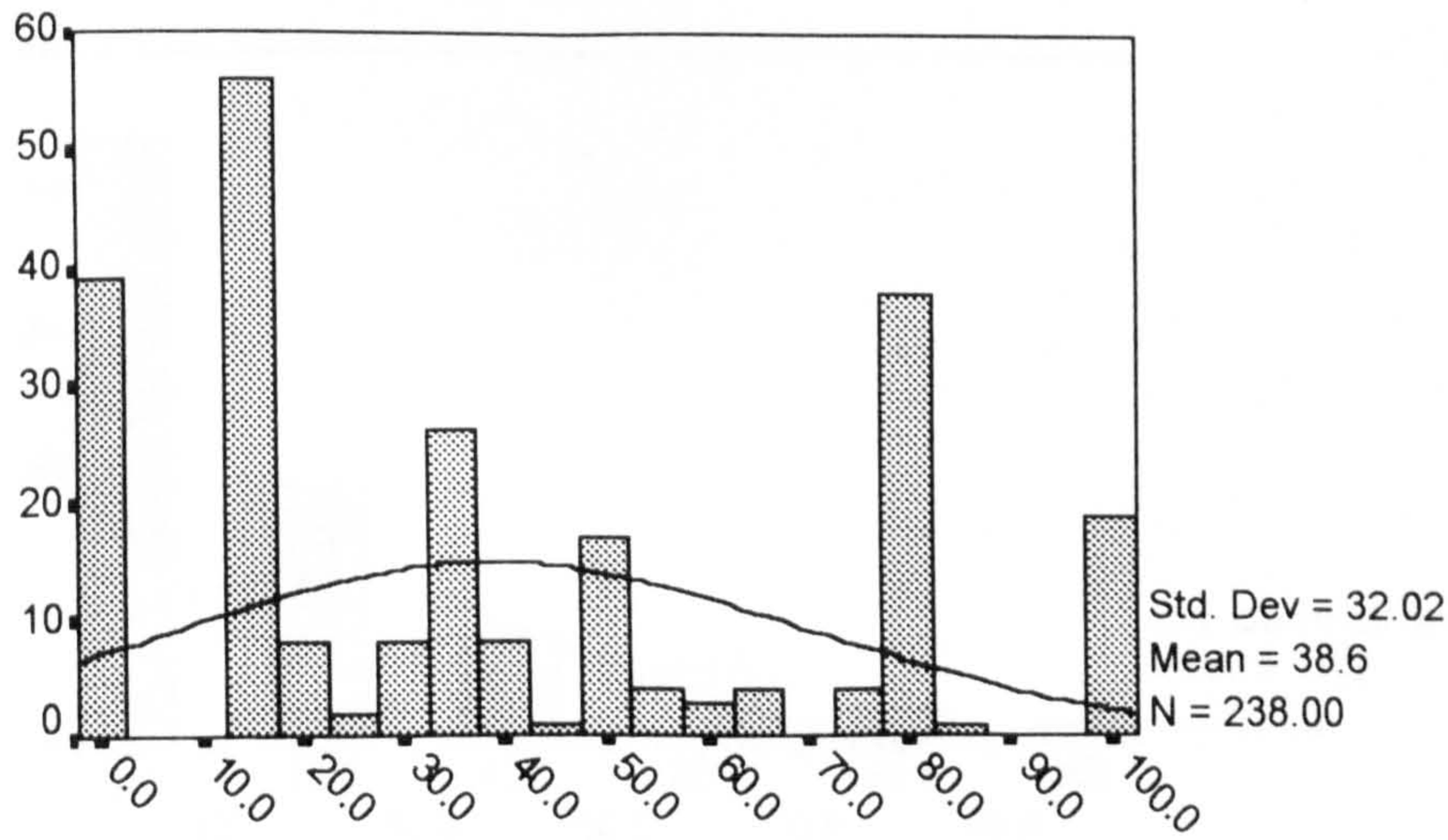
Pain-Follow up



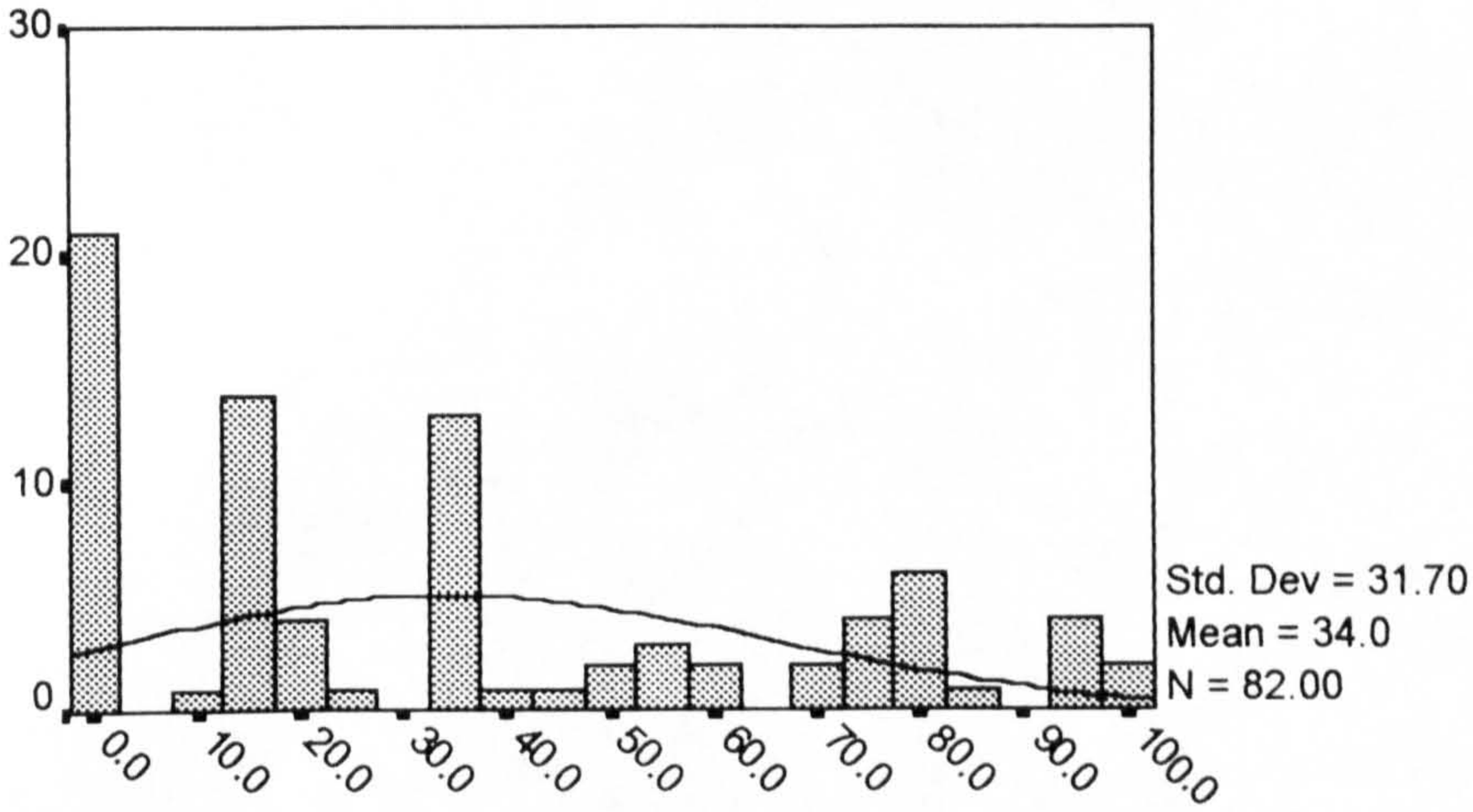
Physical mobility-Baseline



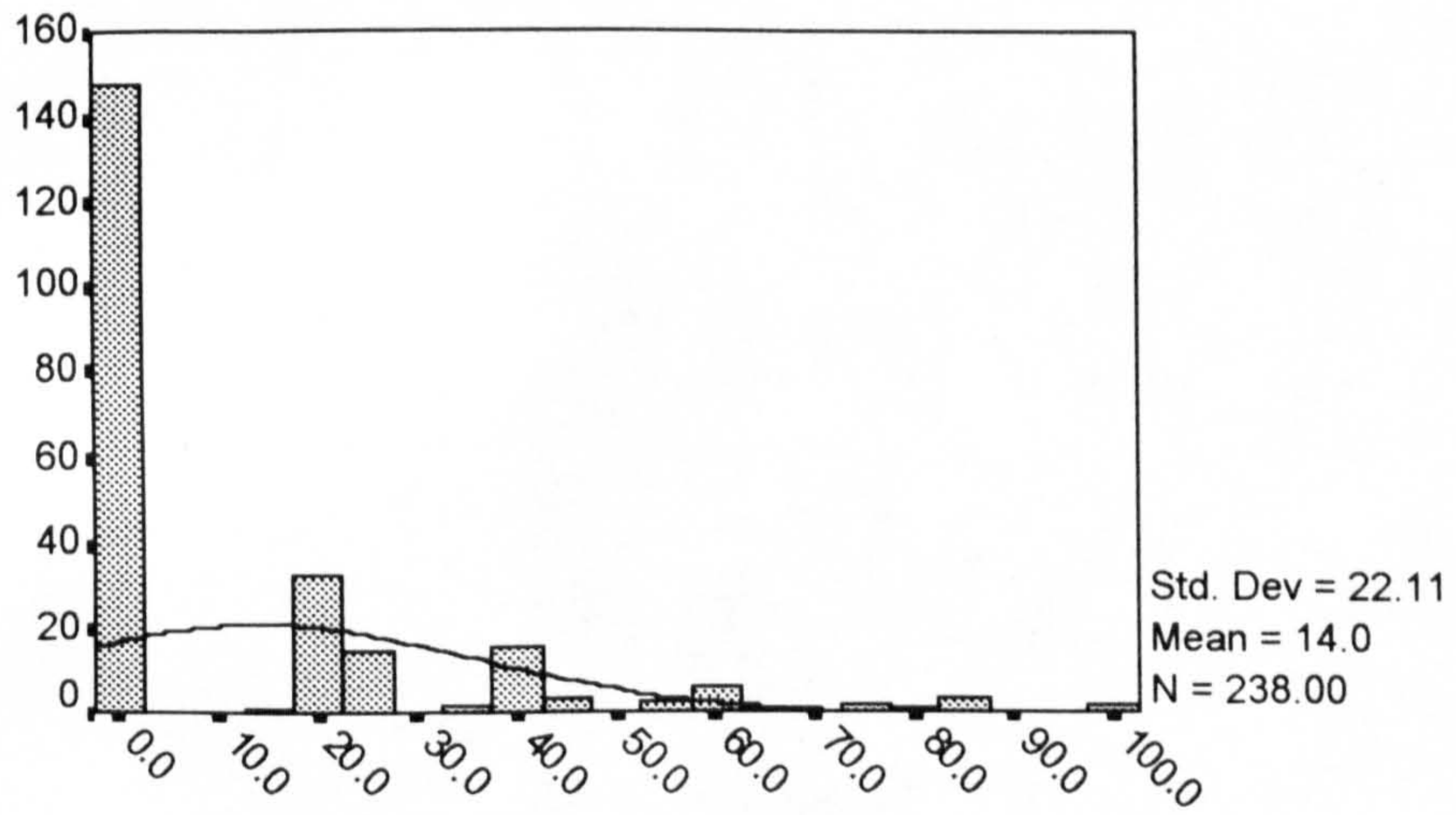
Physical mobility-Follow up



Sleep-Baseline



Sleep-Follow up



Social isolation-Baseline

Social isolation-Follow up