# Role of patient-reported symptoms and functioning in the care of patients with metastatic colorectal cancer

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The candidate confirms that the work submitted is her own, except where work which has formed part of jointly authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

Chapters 3, 4, 5, 6 and 7 are based on work from jointly authored publications.

Chapters 3 and 4: Harley, C; Takeuchi, E; Taylor, S; Keding, A; Absolom, K; Brown, JMB; Velikova, G. A mixed methods approach to adapting health-related quality of life measures for use in routine oncology clinical practice. Quality of Life Research, 2012. 21(3): p. 389-403.
I was responsible for the collection of data from majority of colorectal cancer patients, performing the analysis and commenting on the manuscript. Other authors contributed to the data collection, preparation of analysis plan, advice on analysis and preparation of the manuscript.

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I was responsible for performing the analysis and writing the manuscript. Other authors contributed to the data collection and content analysis of the oncology clinic consultations, advice on analysis and commenting on the manuscript.

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I was responsible for the development of the doctor training programme and was a facilitator in the training programme as part of the Pilot Study. I also commented on the manuscript. Other authors developed their own training programme to assist clinicians in how to use patient reported outcomes within their own clinical context and prepared the manuscript.

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My own contributions, fully and explicitly indicated in the thesis, have been recruitment of study participants, conducting the semi-structured interviews with oncologists and patients, management of study administration, data analysis and development of doctor training programme (Chapter 6). The development of the clinical scenarios for the doctor training facilitation DVDs was entirely my own work. I wrote the study protocol for the Doctor Training Pilot Study (Chapter 7) and obtained the necessary institutional approvals.

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# Abstract

Introduction

Regular assessment of patients' health related quality of life (HRQoL) with feedback to clinicians can play an important role in patient-doctor communication, problem detection and monitoring. Many cancer specific HRQoL instruments are available but their clinical utility in routine practice has not been systematically evaluated. The aim was to develop a HRQoL questionnaire for patients with advanced colorectal cancer (CRC) for use in routine practice and to explore ways to increase its' clinical utility.

Methods and results

A comprehensive development strategy was used to create CRC specific questionnaire for clinical practice. The strategy involved exploration of issues discussed in consultations of 17 CRC patients (68 consultations), review of literature, interviews with 7 oncologists and 10 patients, validation of the questionnaire in a sample of 155 CRC patients and validation in 448 patients as part of a wider study. A 55 item questionnaire, QuEST-Cr was created.

Exploratory work was performed to examine the longitudinal impact of patient reported HRQoL collection with feedback using data from 198 patients' oncology consultations over 4 consecutive visits. Impact of intervention on consultation content and communication preferences of patients and doctors were examined. Findings highlight lack of discussions about psychosocial issues even when patients reported poor functioning. Repeated assessment helped to maintain discussions of patients' symptoms over time but not psychosocial issues.

Training oncologists was considered a way of increasing the impact of patient reported HRQoL intervention. Review of literature identified barriers that needed to overcome. Conceptual models of adult learning guided the choice of teaching methods. Development of trigger DVDs provided valuable experiential learning opportunity.

Conclusion:

I developed and evaluated an instrument for screening and identifying the needs of CRC patients in routine clinical practice. I developed a training programme for oncologists which may help increase the clinical utility of patient reported HRQoL data.

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# Abbreviations

| | |
|---|---|
| ADL | Activities of Daily Living |
| CAT | Computer Adaptive Testing |
| CHA | Comprehensive Health Assessment |
| DT | Distress Thermometer |
| DVD | Digital video disc |
| EORTC | European Organisation for Research and Treatment of Cancer |
| EORTC QLQ-C30 | EORTC Quality of Life Questionnaire - Core 30 |
| EORTC QLQ-CR29 | EORTC Quality of Life Questionnaire - Colorectal cancer module CR29 |
| EORTC QLQ-CR38 | EORTC Quality of Life Questionnaire - Colorectal cancer module CR38 |
| EORTC QLQ-LMC21 | EORTC Quality of Life Questionnaire - Liver metastasis module |
| FACT | Functional Assessment of Cancer Therapy |
| FACT-C | Functional Assessment of Cancer Therapy - Colorectal |
| FACT-G | Functional Assessment of Cancer Therapy - General |
| GIQLI | Gastrointestinal Quality of Life Index |
| HADS | Hospital Anxiety and Depression Scale |
| HRQoL | Health related quality of life |
| IADL | Instrumental Activities of Daily Living |
| IRT | Item response theory |
| MHI-5 | Mental Health Inventory 5 items |
| MIC | Minimally important change |
| MIPS | Medical Interaction Process System |
| MPPC | Measure of Patient Centred Communication |
| MRC | Medical Research Council |
| NCCN | National Clinical Cancer Network |
| NHS | National Health Service |
| NICE | National Institute for Health and Care Excellence |
| PAF | Principal Axis Factoring |
| PCF | Principal Component Factoring |
| POCPRG | Psychosocial Oncology and Clinical Practice Research Group |
| PPC | Preferences and Perceptions of Communication questionnaire |
| PPM | Patient Pathway Manager |
| PPM | Patient Pathway Manager |
| PPPC | Patient Perception of Patient Centredness questionnaire |
| PRO | Patient reported outcomes |
| PROM | Patient reported outcome measures |
| QoL | Quality of life |
| QoL | Quality of life |
| QuEST-Br | Breast cancer specific questionnaire for routine clinical practice |

| | |
|---|---|
| QuEST-Cr | Colorectal cancer specific questionnaire for routine clinical practice |
| QuEST-Gy | Gynaecological cancer specific questionnaire for routine clinical practice |
| RIAS | Roter Interaction Analysis System |
| RSCL | Rotterdam Symptom Checklist |
| SEIQoL | Schedule for Evaluation of Individual Quality of Life |
| SF-36 | Medical Outcomes Study Short Form 36 |
| TSC | Touch Screen Computer |
| WHO | World Health Organization |

# Disseminations

## Peer Reviewed Journal Papers

Santana MJ, Haverman L, Absolom K, Takeuchi E, Feeny D, Grootenhuis M, Velikova G. Training clinicians in how to use patient-reported outcome measures in routine clinical practice. Quality of Life Research. 2015 Jul;24(7):1707-18. Epub 2015 Jan 15.

Taylor S, Harley C, Takeuchi E, Brown J, Velikova G. Detecting and discussing sexual problems during chemotherapy for breast cancer. The Breast Journal. 2013 Sep-Oct;19(5):566-7. Epub 2013 Jul 29.

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## Oral Presentations

Takeuchi EE, Absolom KL, Symons J, Lane R, Velikova G. Training oncologists in the use of patient reported outcome data in clinical practice: The development of a facilitation aid. British Psychosocial Oncology Society Annual Conference Dec 2010

Takeuchi EE, Harley C, Sheppard S, Velikova G. Cancer Specialists' Views on Assessing Psychosocial Issues in Routine Clinical Practice. Psycho-Oncology 2009, 18(3);307-330. British Psychosocial Oncology Society Annual Conference Dec 2008

Takeuchi EE, McCluskey S, Absolom K, Abhyankar P, Greenhalgh J, Symons J, Lane R, Velikova G. Development of communication skills training focused on patient-reported outcome measures in oncology practice. International Conference on Communication in Healthcare, Florida USA Oct 2009.

## Poster Presentations

Takeuchi EE, Keding A, Awad N, Hofmann U, Campbell L, Selby PJ, Brown JM and Velikova G. Impact of Patient Reported Outcome Measures in Oncology – A Longitudinal Analysis of Patient-Doctor Communication. National Cancer Research Institute Cancer Conference Nov 2010

# Chapter 1 Introduction

## 1.1 Health Related Quality of Life

The term “Quality of life (QoL)” has become a familiar phrase in everyday language as well as in academic literature. Although many people will have an intuitive understanding of what “Quality of Life” means to them, it may take on a different meaning to different people, depending on the context of the term being used.

In healthcare research, the term “Health Related Quality of Life (HRQoL)” is often used to distinguish between “quality of life” in its more general meaning and to focus the attention on how a person’s life may be affected by disease or its treatment (Fayers, 2007).

Cancer remains one of the most common causes of death in the UK (Cancer Research UK). Although there have been significant advances in diagnostics and treatments available for the disease leading to improvement in survival, cancer remains an incurable condition for many, if diagnosed at an advanced stage of the disease. Better understanding of how disease and its treatment impact on patients is important whatever the condition but this is particularly relevant for conditions which are chronic or incurable and for which treatment can have significant side effects. Cancer therefore provides a compelling model for examining the disease and its’ impact on patients’ lives.

The earliest attempts to examine the non biological aspects of cancer patients’ functional performance was made by Karnofsky (Karnofsky, 1949), who developed a clinical scale to quantify patients’ ability to perform routine self care activities and their level of independent living. Improvement on the Karnofsky Performance Scale rating was used to determine the clinical effectiveness of nitrogen mustards as a palliative therapy for cancer (Karnowsky et al., 1948). The functional assessment of patients was very much focused on their physical abilities or their health status. Very little attention was given by clinicians and researchers on some of the early non-clinical literature of surveys to evaluate happiness and psychological well-being which had been published by psychologists (Prutkin and Feinstein, 2002). However, in 1976, Priestman and Baum described the use of Linear Analogue Self Assessment (LASA) Scale in patients receiving treatment for breast cancer (Priestman and Baum, 1976). They used a visual

analogue scale on a 10 centimetre line labelled with extreme “anchors” at each end, where patients placed a mark which corresponded with how they felt. There were 10 questions in the scale ranging from feelings of well-being, pain and patients’ perception of treatment efficacy. The sum of the marks given became an overall measure of quality of life. They showed that their LASA Scale could be used to monitor the subjective benefit of treatment and to compare the subjective toxicities of different treatment regimens (Priestman and Baum, 1976). This type of instrument became popular tool for assessing quality of life in cancer patients; however, the next two decades saw the growth in the development of standardised instruments to measure quality of life in social sciences which became more widely used by researchers in the field of cancer medicine (Montazeri, 2008).

HRQoL research in cancer has expanded enormously over the last three decades, in association with growing concerns for the high symptom burden and unmet psychosocial needs of cancer patients receiving treatment (Aaronson, 1987, Cella and Tulsky, 1990, Fayers, 2007). The growth of HRQoL research has been seen particularly in clinical trials where quality of life end points are integrated into assessment of cancer therapies in addition to traditional endpoints such as tumour response or survival. It aims to gain better understanding of patients’ experience of their illness and the impact of the disease and treatment may have on their lives, which cannot be captured by biomedical parameters alone.

So what is meant by Health Related Quality of Life? There is a broad consensus that HRQoL is a multi-dimensional construct (The WHOQOL Group, 1998), which includes the three domains stated in the World Health Organization’s definition of “health” as its core (World Health Organization, 1946). These are physical functioning, psychological functioning and social well-being. However, the definitions of QoL or HRQoL have long been debated and there is no single definition that has been universally accepted. Many authors have proposed various definitions for the term, which also includes domains such as patient satisfaction, general health (Schumacher et al., 1991), physical symptoms and treatment related side effects (Aaronson et al., 1991), sexual functioning and existential issues. In addition, some authors have included indirect consequences of disease or treatment such as unemployment or financial difficulties (Fayers, 2007).

When considering a patient faced with treatment decisions for their cancer, QoL may be considered as the cost of treatment (e.g. side effects of treatment/toxicity) against the benefit it may bring to the patient (e.g. response to treatment and possible resultant

prolongation of life) (Cella and Tulsky, 1993). When the aim of the treatment is to cure the disease, then the decision to face potentially toxic therapy may be relatively straight forward, provided that the patient is well enough to receive the treatment. However, when the aim of the treatment is palliative, then the decision making process may become more complex. Patients will need to consider the potential benefit of the treatment against the impact the treatment may have on various aspects of their lives.

Researchers have used various HRQoL models to guide their research due to the multi-dimensional construct of HRQoL. A conceptual model is a schematic representation of a theory that acts as a practical tool to provide a better understanding of a phenomenon, such as HRQoL, by illustrating relationships between concepts (Bakas et al., 2012).

Wilson and Cleary have proposed a conceptual model for HRQoL (Wilson and Cleary, 1995) which integrates both the “biomedical” model of health and the “quality of life” model of health (Fig. 1.1). The “biomedical” model aims to better understand the disease processes in order to facilitate diagnosis and management of the disease and the “quality of life” model places its focus on the patients’ functioning and their overall well-being. Their model includes five main domains; biological, symptoms, function, general health perceptions and overall HRQoL. They are arranged from left to right according to increasing biological, social and psychological complexity. Their model also encompasses the characteristics of the patient, the social context in which the patient lives and any non medical factors which may impact on patients’ overall quality of life.

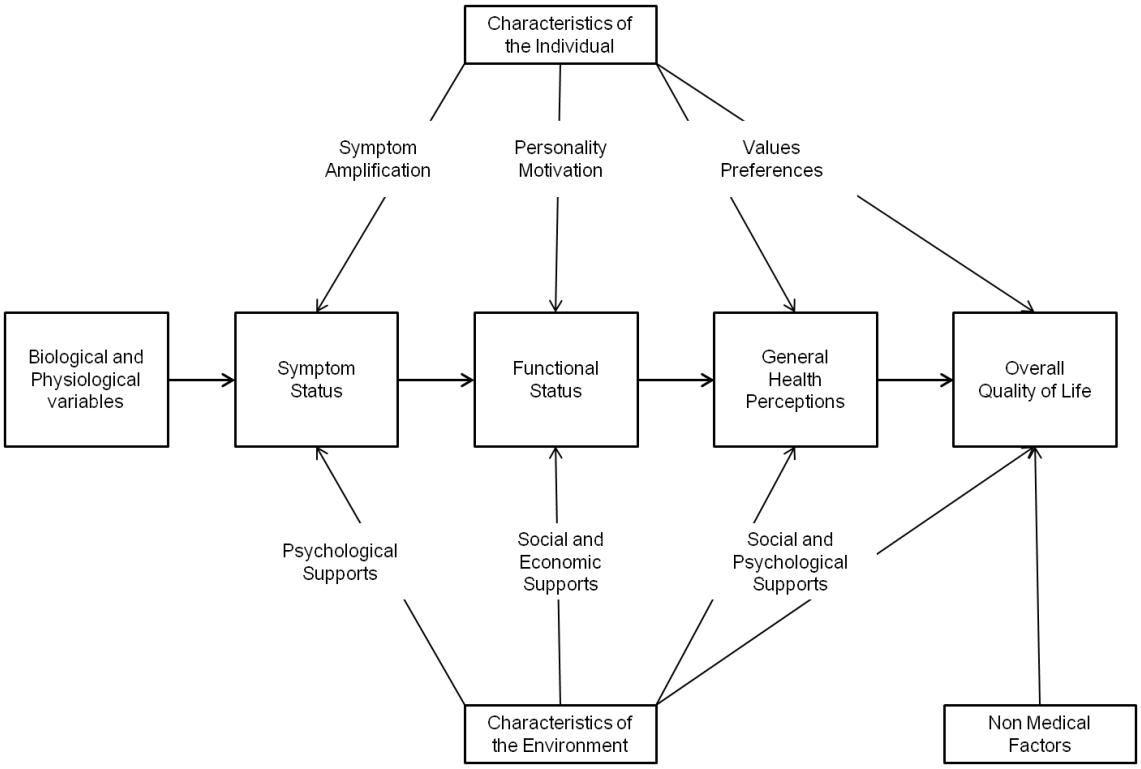


**Figure 1-1 Wilson and Cleary's model of health-related quality of life (Wilson and Cleary, 1995)**

Cella and Tulsky have proposed a model for HRQoL among cancer patients (Cella and Tulsky, 1993). Their model consists of four main domains; physical, functional, emotional and social (Fig. 1.2). They also specify a number of important areas which are not exclusively captured by the four domains listed. These are work, sexuality, leisure, spirituality and family functioning. They state that these secondary domains may be associated with aspects of two or more of the four main domains. For example, symptoms and side effects of the disease may impact on patients' physical functioning and their ability to work.

Many questionnaires or instruments have been developed which aims to measure HRQoL. These instruments allow patients to self report their experiences of in relation to their disease and associated healthcare interventions. This in turn allow researchers and healthcare professionals to gain insight into how the disease process impacts on patients' physical, social and emotional functioning, as well as symptoms of disease and treatment side effects.

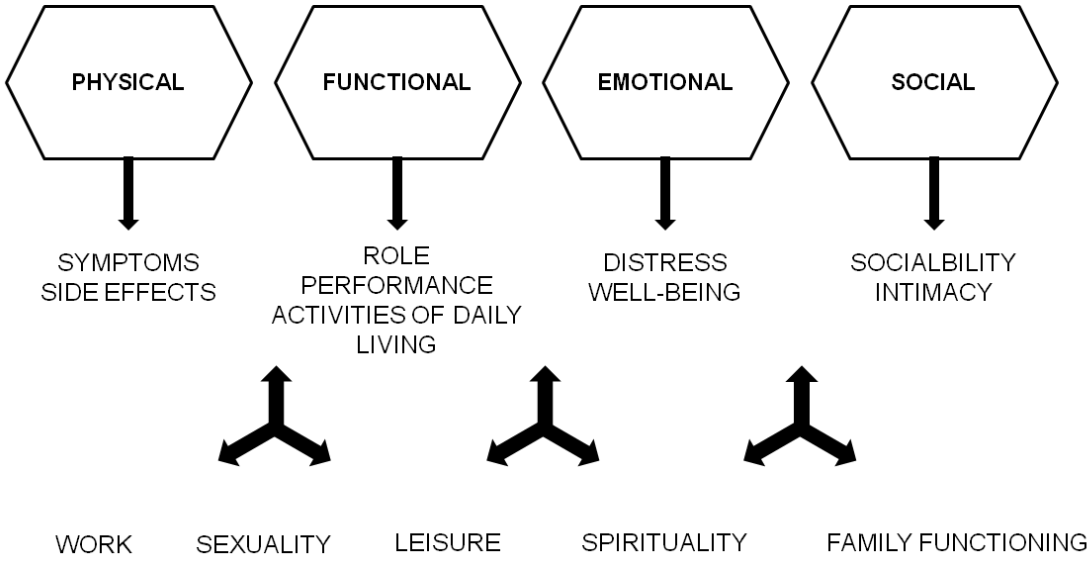


**Figure 1-2 Cella's model of quality of life (Cella and Tulsky, 1993)**

There is a broad consensus that HRQoL is subjective in that it derives from the individual patient and that it represents patients' experience from their own perspective (Bottomley, 2002). These patient self-reported measures have come to be known as Patient Reported Outcomes (PROs) and instruments used to obtain PROs as Patient Reported Outcome Measures (PROMs) or PRO instrument. PROs have been defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else" (Food and Drugs Administration, 2009). PROs can, therefore, relate to symptoms, signs, functional status and HRQoL. It may also include broader concepts such as patients' perceptions of satisfaction and preference.

## 1.2 Measuring HRQoL

There are now many HRQoL instruments which have been developed. These instruments are usually questionnaires consisting of a number of items or questions, often with several items grouped into domains (e.g. physical function, emotional function and social function). HRQoL instruments can be categorised broadly into two groups; generic and specific instruments. Generic HRQoL instruments are designed to

be applicable across a wide range of populations and interventions, whereas specific HRQoL instruments are designed to be relevant to a specific group of patients (e.g. patients with cancer) or to particular interventions (Patrick and Deyo, 1989).

Generic HRQoL includes Health Profiles and Utility Measures. Health profiles are instruments which attempt to measure all important aspects of HRQoL. They provide a range of scores representing individual domains of HRQoL, which may be useful to clinicians and researchers trying to measure differential impact of conditions or treatment on various aspects of HRQoL. Medical Outcomes Study 36-Item Short Form (SF-36) Health Survey (Ware and Sherbourne, 1992) is an example of a Health Profile. The SF-36 consists of eight sections which forms individual subscales within the questionnaire. These eight sections are vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health. It also includes an item which provides a suggestion of perceived change in health. Utility Measures of HRQoL, sometimes referred to as preference based measures, reflects patients' preferences for treatment process and outcome. These measures often provide a single number on a continuum of perfect health (1) to death (0), which is referred to as health index score. Utility based measures are used in pharmaco-economic research, particularly in cost utility analysis (Coons et al., 2000). An example of Utility Measures is EuroQol Instrument, EQ-5D (EuroQoL Group, 1990). EQ-5D has five dimensions which are mobility, self care, usual activity, pain/discomfort and Anxiety/depression. The questionnaire also consists of an overall assessment of the respondents' health on a visual analogue scale.

Specific HRQoL instruments focuses on aspects of health status that are specific to the area of primary interests. The instruments may be specific to the disease (such as cancer), to a certain function (such as emotional function) or to a problem (such as pain) (Guyatt et al., 1993). The EORTC QLQ-C30 (Aaronson et al., 1993) is an example of a disease specific HRQoL, which has been developed to measure HRQoL in cancer patients. Similar to SF-36, EORTC QLQ-C30 consists of a number of functional domains which are physical function, emotional function, social function, role function and cognitive function. It also contains items addressing some of the common symptoms and side effects attributable to the underlying disease and its treatment, such as pain, nausea and vomiting, diarrhoea and constipation. Disease specific instrument such as EORTC QLQ-C30 allows comparisons to be made across the cancer population. However, it may fall short of addressing issues or symptoms which are specific to those with particular types of cancer (Sprangers et al., 1993). The EORTC Quality of Life Group have therefore produced a number of cancer site specific

“modules” to complement the EORTC QLQ-C30 in order to improve relevance to particular type of cancer. The EORTC QLQ-CR38 (Sprangers et al., 1999) is an example of a colorectal cancer site specific questionnaire which is used in conjunction with the EORTC QLQ-C30. This approach of using the core questionnaire with primary disease site specific module can complement each other by retaining some generalisability across the cancer population whilst also ensuring that issues specific to the primary cancer site are also addressed (Sprangers et al., 1993, Bottomley and Aaronson, 2007).

Many HRQoL instruments have pre-defined set of domains. This means that domains which may be important for individual patient may be missing, while at the same time including domains that may be of less importance to that individual. Individualised measures have been developed which allows the individual respondent to choose the most important domains to be evaluated (McGee et al., 1991, Ruta et al., 1994). One of the commonly used individualised measures is the Schedule for Evaluation of Individual Quality of Life – Direct Weighting (SEIQoL-DW) (Hickey et al., 1996), an abbreviated form of SEIQoL (O'Boyle et al., 1992). It uses semi-structured interviews to collect the data. Participants are invited to nominate five domains they consider to be the most important in their life. Then the person is asked to rate how he/she is doing in each of the domains they have nominated on a visual analogue scale. In the third stage, the person is asked for the relative importance of each area, represented by five differently coloured areas on a pie chart with the greatest importance assigned to the largest pie area on the chart.

These instruments can be used in a number of applications; majority of these instruments have been developed for use in clinical trials and economic evaluations. However, there are some instruments which have been developed to assist healthcare professionals in caring for individual patients. Selection of HRQoL instrument may be based on a number of criteria including psychometric properties of the instruments such as reliability and validity, but also more general considerations such as the appropriateness of the instrument for a given application (Fitzpatrick et al., 1998).

## 1.3 Use of HRQoL in cancer clinical trials

Application of HRQoL assessment in cancer has been seen predominantly in the setting of clinical trials investigating the impact of variety of healthcare interventions, such as new anticancer therapies.

Development of reliable and valid self reported HRQoL questionnaires have allowed assessment of HRQoL to be increasingly incorporated into cancer clinical trials over the last four decades. This is reflected by growing recognition for the need to assess cancer treatments more broadly in addition to traditional endpoints, such as tumour response and survival. Measuring HRQoL can help to better understand the impact of various types of cancer and how the treatment may impact on patients' lives. HRQoL endpoints are particularly important when the intervention being investigated is palliative therapy for incurable cancer. In these situations, quality of survival may be just as important as the duration of survival (Joly et al., 2007). Assessment of HRQoL is now considered very much an integral part of the cancer clinical trial protocol. Clinical trial organizations such as EORTC and National Cancer Institute, all have designated quality of life working group, facilitating the integration of HRQoL assessments in clinical trials (Bottomley et al., 2005).

The HRQoL data derived from clinical trials or population based studies may be utilized in a number of ways. It may allow better understanding of the characteristics of the patient population of interest and enable comparisons to be made between different groups of patients (Osoba et al., 2005). Longitudinal assessment of HRQoL may provide how the intervention being investigated impacts on patients over time and provide insight into the patients' experiences. Many investigators are now utilising modular approach in measuring HRQoL (Aaronson et al., 1988, Sprangers et al., 1998, Brady et al., 1997). Several instruments have been developed specifically for a particular disease group, thus allowing more detailed assessment of the impact of a given intervention in a defined group of patients.

HRQoL data from clinical trials may also have an impact on clinical decision making. If there are different treatment options with similar efficacies, HRQoL data may help patients and oncologists choose the treatment which may have less detrimental impact on patients' functioning and symptoms (Osoba, 1999). HRQoL information may also assist involving patients in their decision making when there are trade-offs between

treatment efficacy and toxicities. It may also improve detection of impaired psychosocial functioning among patients (Lipscomb et al., 2005).

HRQoL measures, in conjunction with patients' clinical data, have also been shown to be prognostic indicator for survival in a number of studies (Gotay et al., 2008, Quinten et al., 2009, Montazeri, 2009). As HRQoL assessment includes multiple dimensions of patients' physical, psychological and social functioning, they may provide more sensitive information over clinical parameters such as performance status.

HRQoL data derived from clinical trials also play an important component of health technology assessment (European Medicines Agency, 2012). For example, The National Institute for Health and Care Excellence (NICE) provides guidance to the NHS in England on the clinical and cost effectiveness of new and well established health technologies. In the assessment of the cost effectiveness, HRQoL plays critical role in determining the Quality Adjusted Life Years (QALYs) of a medical intervention (National Institute for Health and Care Excellence, 2014), which can influence whether the intervention may be recommended and subsequently adopted as standard practice within the NHS.

## 1.4 Use of HRQoL in routine clinical practice

Increase in the integration of HRQoL assessments within cancer clinical trials has been associated with the greater appreciation for the importance of assessing the impact of cancer and its' treatments on the physical, psychological and social functioning of the individual patient. There is growing recognition that routine measurement of HRQoL in oncology practice has the potential to improve cancer care planning, monitoring and management of cancer patients (Donaldson, 2004). Routine assessment of patients' HRQoL may increase healthcare professionals' awareness of the issues which are important to their patients and facilitate delivery of a more patient-centred care, tailored to the needs of the individual patient (Boyes et al., 2006). Measuring individual patient's HRQoL routinely may allow patients to express their own experiences of their illness (Feldman-Stewart and Brundage, 2009), promote their involvement in medical decision making and enhance communication between patients and healthcare professionals (Greenhalgh and Meadows, 1999). Regular assessment of patients' health status may also help to identify adverse effects of cancer and its' therapy

(Higginson and Carr, 2001) and help monitor effects of treatment response or disease progression and inform decisions about treatment plans (Lipscomb et al., 2007).

### 1.4.1 Evidence for use of HRQoL in routine clinical practice

Use and efficacy of patient reported outcomes in routine clinical practice have been explored in four reviews (Greenhalgh and Meadows, 1999, Espallargues et al., 2000, Marshall et al., 2006, Valderas et al., 2008) conducted between 1999 and 2008. Between these reviews, 13 to 35 randomised controlled trials were identified evaluating the use of patient reported outcome interventions in a wide variety of clinical settings, with majority of the studies conducted in primary care. There was a trend, however, with more recent studies being conducted within the setting of specialist services, including cancer (Marshall et al., 2006).

Greenhalgh et al (Greenhalgh and Meadows, 1999) found evidence that most clinicians had positive attitudes about feasibility and utility of patient reported health assessment in routine clinical practice. Clinicians found the information derived from the measures useful in making an overall assessment of the patient and having a positive impact on patient-doctor relationship. There was a suggestion that patient reported measures improved detection of psychological issues although this did not necessarily translate into change in treatment or increased referral to other allied services. Similar findings about increased detection of psychological problems were also observed by other reviewers (Espallargues et al., 2000, Marshall et al., 2006). Most of the studies reviewed demonstrated effect of the patient reported outcome intervention on at least one aspect of the process of care when these were measured, such as patient education and counselling and increased detection of patient issues (Valderas et al., 2008). However, the impact of the interventions on more distal outcomes such as patients' health status and satisfaction with care were less convincing.

All of the reviews made remarks on the diversity of the interventions used in the studies identified; the clinical setting, instruments used, frequency of administration, unit of randomisation, mode of feedback to the healthcare professionals and the outcome measures of the studies. This heterogeneity or lack of comparability across the studies has limited the likelihood of performing formal quantitative meta-analyses in order to evaluate the impact of patient reported outcome intervention within routine clinical

practice. The reviews highlight the need for further research before patient reported outcome intervention is recommended for routine clinical practice. In particular, they emphasize the importance of building theoretical knowledge base regarding the impact of the intervention on patient outcomes and addressing any barriers to implementing patient reported measures in routine clinical practice.

### 1.4.2 Evidence for HRQoL in routine oncology practice

Marshall et all (Marshall et al., 2006) identified 4 randomised controlled studies specifically in the oncology setting (Trowbridge et al., 1997, McLachlan et al., 2001, Detmar et al., 2002, Velikova et al., 2004). Study by Trowbridge et al (Trowbridge et al., 1997) recruited patients with advanced or recurrent cancer from various primary sites including patients with haematological malignancies. Their study specifically focused on a single symptom of pain. Patients were asked to complete measures which described their experience of pain in the preceding 7 days, together with their satisfaction of their medication and the degree to which they provided pain relief. Patients whose doctors received the feedback of the questionnaire findings reported a lower incidence of pain at 4 week follow up. In addition, they found different prescribing patterns for analgesia between the two groups, with doctors more likely to make changes to patients' medications for patients in the intervention group. No analysis was performed to investigate the relationship between changes in the prescribing patterns and pain relief to provide an indication of likely causality.

McLachlan et al (McLachlan et al., 2001) evaluated self reported cancer needs, HRQoL and psychosocial information to screen for psychological distress in patients with different types of cancers. The measures were collected on touch screen computers and the results of the patient reported measures were fed back in real time so that the results were made available to the doctor during the consultation for those patients randomised to the intervention arm. Study utilized a designated care coordination nurse who was present during these consultations, who formulated an individualised management plan based on the issues raised in the patient reported measures. They found no significant differences between the two arms with respect to changes in cancer needs, HRQoL, or psychosocial functioning between baseline and follow up assessments, nor with respect to patients' satisfaction with care. However, for a subgroup of patients reporting moderate to severe emotional distress at baseline, there was a significant reduction in depression for the patients in the intervention group at 6

months follow up. They made no comment on the evidence linking screening for psychological issues and changes in the referral to allied services or management.

Detmar et al (Detmar et al., 2002) conducted a longitudinal study among patients receiving palliative chemotherapy treatment. Patients were asked to complete a standardised HRQoL instrument, EORTC QLQ-C30 immediately before the consultation with their doctor with results being made available for the consultation. The unit of randomisation was the doctors in this study which used a cross over design thus doctors provided their own controls. They found significant improvement in doctor-patient communication for those patients whose HRQoL questionnaire results were fed back to their oncologists with increased discussions of issues not commonly discussed, such as social functioning and fatigue. There was evidence for the intervention having an impact on patient satisfaction but this was limited to perceptions of increased emotional support from their doctors. They acknowledged that the cross over design may have carried with it the risk of contamination effect with doctors who began in the experimental condition and subsequently crossed over to the control condition having been made more aware of patients' HRQoL issues.

Velikova et al (Velikova et al., 2004) also conducted a longitudinal study in oncology out-patients receiving treatment for their underlying cancer. They aimed to examine the effects of regular HRQoL assessment, using standardised HRQoL measures with EORTC QLQ-C30 and HADS, on patient-doctor communication and patient well-being. As well as intervention and standard care arms, Velikova et al included an attention control arm in which patients completed the HRQoL measures but the results were not fed back to the doctors. The study found positive impact on patient-doctor communication and patient well-being for the patients in the intervention group. The study also indicated regular completion of HRQoL measures alone without feedback to the doctors may have a positive impact on patient well-being. The authors also acknowledged the possible contamination effect as the patients were the unit of randomisation and the same doctors saw patients from each of the study arms and doctors' practices may have been influenced by the exposure to the patient reported outcome intervention during the study.

### 1.4.3 From research to clinical practice

The above reviews of patient reported outcomes of HRQoL in routine clinical practice have highlighted that, whilst there has been some beneficial impact of patient reported outcomes on the processes of patient care, the anticipated benefits of the intervention on patient outcomes is yet to be realised.

Although the concept of measuring HRQoL in order to improve the care and management of individual patients seem a logical progression from measuring HRQoL in clinical trials to gain better understanding of the impact of disease and treatment on patients at a group level, there are a number of significant differences between these two contexts as well as the HRQoL measures serving different functions within them. Some of the key differences are outlined in Table 1.1.

**Table 1.1 Different utility of HRQoL: Clinical research vs Clinical practice**

| | **Research setting** | **Clinical practice** |
|---|---|---|
| Objectives | Characterisation of patient groups | Characterisation of individual patients<br>Screening for patient problems<br>Treatment decision guidance |
| Status of HRQoL instruments used | The descriptive capabilities (validity, reliability, responsiveness) of HRQoL measures are well established | The definitive impact of HRQoL data fed back to clinicians on patient outcomes has not yet been demonstrated consistently |
| Context | Defined within the clinical trial protocols | Routine patient care |
| Target population | Sampled/randomised/matched groups from the target population as appropriate to the study hypotheses and required power of the study | Unselected population within the care system |
| HRQoL instruments | Focused set of instruments determined by the trial protocol | Determined by aim of intervention<br>Instruments relevant to each individual patient's clinical condition |
| Frequency of HRQoL measurement | Defined by the trial protocol | Dependent on the aim of intervention:<br>Single collection or longitudinal |
| Analysis strategies | Data collected and analysed at defined time-points within the study | Real-time output needed for integration into clinical practice |

### 1.4.4 HRQoL instruments for clinical practice

HRQoL measures in the research setting perform a descriptive function of characterising a defined patient group. The descriptive capabilities (e.g. validity and reliability) of the HRQoL instruments used in this setting have been rigorously tested. The instruments are administered in a highly controlled manner for a defined group of patients in order to answer a specific research question.

HRQoL assessment within a routine clinical practice aims to characterise the experience of an individual patient and ultimately expect the process to change the behaviour of the patient and the healthcare professional. Many of the studies which have utilized patient reported measures have used the intervention to screen for any problems patients may be experiencing so that these issues are brought to the attention of the healthcare professionals, in the anticipation that this would lead to change in the management of the patients to address these issues.

There are several important considerations when choosing HRQoL instruments for clinical practice in terms of what kind of instruments should be used and what should be done to validate these tools further for use within the clinical practice (Arnould, 2006). Questionnaires which have been developed with the aim of making comparisons between different groups of patients within research setting may not necessarily be suitable for assessing patients on an individual basis (McHorney and Tarlov, 1995).

There are a number of characteristics that instruments for clinical practice need to have. It has to be of acceptable length for the patients to complete in routine clinical practice to reduce patient burden (Kirkova et al., 2006, Snyder et al., 2012). The instrument needs to be easy to use for the healthcare professionals. The scoring of the instruments need to be quick so that the results are readily available after patient has completed the questionnaire, unless technology for real time calculation of scores are available. The instrument needs to ask relevant questions for the clinical practice and support a judgment or trigger an action. It needs to address important issues for the patient, issues that patients would want assistance from the healthcare professionals and issues that healthcare professionals feel that they are able to offer their patients some help (Snyder et al., 2007). The instrument needs to meet the specification for use in routine practice (Feinstein, 1992) and may require items based on clinical

judgment or relevant to the context, not necessarily in accordance with psychometric theory (Feinstein, 1983).

Velikova et al conducted a focus group study in order to explore both patients and oncologists' views on the use and content of HRQoL questionnaire for routine oncology practice (Velikova et al., 2007a). They identified four key themes which were considered important to be included in the HRQoL instruments for use in clinical practice by the patients and oncologists. These were "common symptoms and problems", "disease site specific issues", "treatment specific issues" and "individual patient-specific issues". This study suggested that questionnaires for use in clinical practice needed to contain items which addressed disease site specific issues as well as those issues which may be common across all tumour sites. This is very similar to the approach already taken by the EORTC and FACT questionnaires, with a core set of items across all tumour sites with disease/condition specific modules. This study also suggested that a prompt list of issues may help patients to report any problems or concerns that they specifically wished to discuss, thus tailoring the instrument for individual patients.

In summary, instruments for clinical practice need to serve different functions compared to clinical research. New instruments may be necessary to meet the needs of clinical practice utility. Within the oncology practice, the HRQoL assessment may be expected to serve a number of different functions/purpose. First is to monitor common cancer and treatment related symptoms with patients' self report providing consistent measurement over time. This may help to provide evidence of treatment response or disease progression and facilitate clinical decision making regarding treatment. The second function is to screen or highlight any issues which may not be routinely addressed during consultations but are important and relevant to the patients, such as emotional distress, family/social issues and sexual functioning (Taylor et al., 2011, Anderson et al., 2008, Stead et al., 2003).

### 1.4.5 Conceptual framework for HRQoL assessment in routine clinical practice

Patient reported HRQoL information aims to convey their symptoms and functioning to the healthcare professionals in order to serve the functions as described above. It can therefore be considered a method of communication between patients and clinicians.

Indeed, there is evidence to suggest that provision of patient reported HRQoL information to healthcare professionals can have an impact on patient–doctor communication (Greenhalgh and Meadows, 1999). However, the mechanism by which this impact on communication leads to possible changes in patient outcomes is a complex staged process as illustrated below (Greenhalgh et al., 2005).

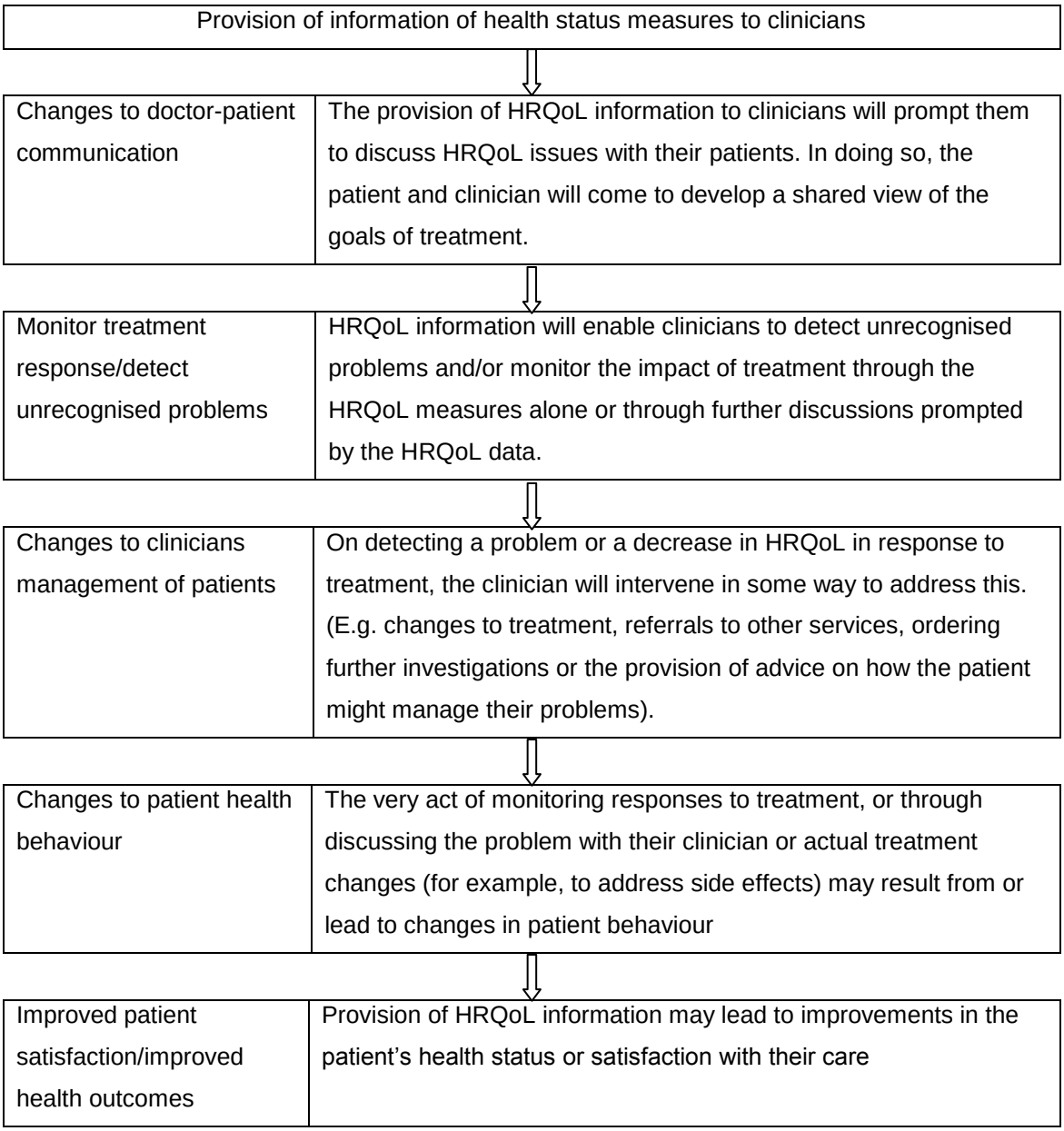


**Figure 1-3 Greenhalgh's description of the possible impact of HRQOL assessment in clinical practice (Greenhalgh et al., 2005)**

### 1.4.6 Barriers to implementation of HRQoL assessments in routine clinical practice

Integration of HRQoL assessment in routine clinical practice has been slow compared to its adoption in clinical research. Beyond the challenges of identifying the most appropriate instrument for use in routine clinical practice, a number of potential barriers have been proposed which may explain the relatively slow uptake of HRQoL assessment in this setting. These have been broadly categorised into three groups; 1) Healthcare professional/provider issues, 2) Healthcare delivery and organizational issues and 3) patient related issues (Deyo and Carter, 1992, Davis and Cella, 2002, McHorney and Earl Bricker, 2002).

#### 1.4.6.1 Healthcare professional issues

Healthcare professionals' endorsement for HRQoL assessment in routine clinical practice is essential for this intervention to be adopted into routine clinical practice (Davis and Cella, 2002). Healthcare professionals' lack of familiarity or experience with HRQoL assessments is considered to be one of the most important barriers for routine assessment of HRQoL (Morris et al., 1998a, Bezjak et al., 2001). There is considerable discrepancy between clinicians' perceptions of "usefulness" for routine HRQoL assessment and the reality of this assessment actually taking place within their practice (Taylor et al., 1996, Morris et al., 1998a, Bezjak et al., 2001).

Healthcare professionals are unlikely to have received any formal training in the use and interpretation of HRQoL instruments (Donaldson, 2004), therefore they may find it difficult to choose the most appropriate instrument, when these should be administered and how often and at what stage in the patients' disease trajectory such intervention would be most valuable. In addition, unlike laboratory or radiological investigations results, they may find it difficult to interpret the HRQoL information and use the information to influence patient management (Sutherland and Till, 1993, Giesler, 2000).

Another possible barrier is the healthcare professionals' perception that assessment of patients' HRQoL may unearth multiple problems to which the clinicians may not have effective solutions for. This may result in longer consultations in an already busy practice.

Many of the studies investigating the use of HRQoL assessment in routine oncology practice have focused on oncologists as the recipient of the HRQoL information from patients. However, clinical nurse specialists play an important role in supporting patients from diagnosis and through their treatment course and beyond (Taenzer et al., 2000). It may be that HRQoL information being made available to wider team members may be helpful in delivering the necessary care for the patients.

#### 1.4.6.2 Healthcare delivery and organizational issue

Routine data collection from patients requires commitment of significant resources, if the infrastructure for conducting such intervention is not already present. Unless the instrument is very short and easy to calculate the scores, it is likely that some form of technology will be necessary to assist with data collection and prompt scoring of the results so that it can be integrated into the normal work flow within the clinic. This is likely to require a member of staff to assist patients in completing the questionnaire, answer any queries and trouble shoot any technical issues. Such person may not be readily available. There also needs to be a mechanism whereby the HRQoL information from patients are stored securely and potentially be made available to other members of the clinical team to view. This will require robust mechanisms to ensure the patient reported information is linked with their case notes.

Consideration also needs to extend to the likely impact of the implementation of routine HRQoL assessment on the allied health services, such as referral to the palliative care team for symptom management, psychological intervention for emotional distress and other resources within the community which patients may need to access (Donaldson, 2004).

#### 1.4.6.3 Patient related issues

Just as the patient reported outcome measure intervention needs to be acceptable for the healthcare professionals, it also needs to be acceptable to the patients and that they feel the intervention has some utility and relevance in their care (Donaldson, 2004). Patient burden is a real concern for those with cancer diagnosis as some patients may be very ill and may not be able to complete a long questionnaire regularly.

Feasibility studies have shown that patients are willing and able to use a number of different devices for data input such as touch screen computers (Buxton et al., 1998, Goldman, 2000). New measurement approaches such as computer adaptive testing may help to make the data collection more efficient and precise and reduce burden for patients (Hays et al., 2000).

## 1.5 Training for healthcare professionals

Training healthcare professionals in the use of patient reported HRQoL measures have been suggested as one of the ways of overcoming the barriers concerning healthcare professional related issues as described above (Greenhalgh, 2009, Luckett et al., 2009). In the two randomised controlled studies within oncology setting (Detmar et al., 2002, Velikova et al., 2004), where training to the clinicians was provided, this was mainly on the explanation of the instruments used in the intervention and how they were scored. How the patient reported data was used, if at all, in the management of the patients was left to the clinicians' discretion.

For the routine assessment of patients' HRQoL to become more widely adopted, the training of clinicians should not only focus on the instruments to be used but also on the potential benefits of the intervention in the management of their patients (Luckett et al., 2009). The training would also provide opportunities to address clinicians' concerns that HRQoL assessments may have a significant impact on the consultation length and their worries that it may highlight issues which they are not able to manage themselves. There are a number of studies demonstrating that provision of patients' HRQoL data in clinic consultation do not lengthen consultations where this has been measured objectively (McLachlan et al., 2001, Detmar et al., 2002, Velikova et al., 2004). Moreover, there is suggestion that use of HRQoL information may make the consultations for effective and efficient (Newell et al., 1997, Velikova et al., 1999) by allowing the clinician to prioritise their discussions according to the patient reported information. Training should therefore emphasize on the time efficiency as one of the goals of the intervention (Luckett et al., 2009). In order for the clinicians to promptly manage issues reported by their patients, there needs to be a provision of guidelines and referral pathways so that patients may be given the necessary sign-posting (Rubenstein et al., Rosenbloom et al., 2007). Such guidelines should also be included as part of the training for the clinicians. The training should also highlight the evidence

for the reliability of the data generated by HRQoL assessment compared with other clinical measures (Hahn et al., 2007). The patient reported data may also help to augment the deficiency in the clinicians' awareness of their patients experience of cancer and its' treatment.

## 1.6 Summary

There are now many validated HRQoL instruments available, which have facilitated HRQoL assessments to be routinely incorporated in clinical trials in cancer. HRQoL assessments in routine clinical practice may be useful to facilitate communication between doctors and patients and help monitor individual patients symptoms and side effects. This may lead to improvement in patient care by allowing detection of problems which may not otherwise be realised, leading to improved outcomes for patients and their satisfaction with their care. However, evidence for the more distal outcomes of routine HRQoL assessment is still limited.

A number of barriers to implementing HRQoL assessments in routine clinical practice have been highlighted. One of these barriers is the potential lack of suitable instruments for this purpose. Existing instruments which have been developed for clinical trials may not be wholly suitable for use in clinical practice as they have not been developed with this use in mind. Instruments may need to be developed or adapted so that they are more suitable to be used in clinical practice for the assessment of individual patient. In addition, the instrument needs to be relevant to the clinical practice and address issues which are specific to the disease and treatment in order to increase the clinical utility.

Another key area for implementing routine assessment of HRQoL is the need for training for the clinicians in how to use the patient reported HRQoL information during their consultations with their patients and to highlight the potential benefits of using this information so that assessment of patients' HRQoL can become integral to routine clinical practice.

With my background in Medical Oncology, I felt I was well placed to focus my thesis on issues of clinician training and to develop a training programme for clinicians to facilitate the integration of routine HRQoL assessment in oncology practice.

In order to address the issues of using the most suitable measures for HRQoL assessment in clinical practice I have chosen to work in colorectal cancer (CRC), as it

is one of the most common cancers diagnosed in the UK, affecting both men and women, with recent expansion in systemic treatments, causing high symptom burden and psychological impact. Selecting one cancer type would allow me to explore relevant issues that affect this particular group of patients.

## 1.7 Colorectal Cancer

### 1.7.1 Incidence

Colorectal cancer is the fourth most common cancer diagnosed in the UK, accounting for 13% of all new cancer diagnosis. It is the third most common cancer in both men (after prostate and lung cancers) and women (after breast and lung cancers) separately (Cancer Research UK).

In 2011, there were 41,581 new cases of colorectal cancer in the UK; 23,171 (56%) in men and 18,410 (44%) in women (Cancer Research UK). Colorectal cancer is a disease of older age with approximately 43% colorectal cancer cases diagnosed in patients over the age of 75 years and over, and 95% of all cases were diagnosed in those aged 50 years and over. Incidence rates are significantly higher for men than in women in adults aged 45 years and over.

### 1.7.2 Mortality

Colorectal cancer is the second most common cause of death in the UK, accounting for 10% of all deaths from cancer. There were 16,187 deaths from colorectal cancer in UK in 2012 (Cancer Research UK).

Like many cancers, survival for colorectal cancer is dependent on the stage of disease at diagnosis; those presenting at stage I having the best chance of survival. Patients with stage IV disease or those with metastatic disease are incurable in majority of cases, with 5 year survival of 7%. There has, however, been a significant improvement in survival for patients with colorectal cancer over the last 40 years. One year age-standardised net survival for colorectal cancer has increased from 46% during 1971-1972 to 76% during 2010-2011 in England and Wales. This is likely due to advances in

surgical techniques, improvements in pre-operative radiological investigations and improvements in both adjuvant and palliative chemotherapy.

### 1.7.3 Diagnosis of colorectal cancer

Diagnosis of colorectal cancer is usually made on direct visualisation of the tumour by endoscopic (colonoscopy) examination, unless there are contraindications for performing this investigation. Biopsy is then taken during the endoscopic examination in order to make a definitive histological diagnosis. CT colonography may be used in centres where this is available or barium enema instead of colonoscopy. However, if a suspicious lesion is detected on these radiological investigations colonoscopy and biopsy are usually performed, unless there are any contraindications (National Institute for Health and Care Excellence, 2011).

### 1.7.4 Staging of colorectal cancer

Staging of cancer is important as it helps to predict survival. Staging also allows comparison of outcome in clinical trials and helps determine the most appropriate treatment for patients. Patients will usually undergo a contrast enhanced computed tomography (CT) of chest, abdomen and pelvis to determine the extent of the disease. Patients with rectal cancer will also undergo magnetic resonance imaging (MRI) of pelvis in order to assess their risk of local recurrence, as determined by anticipated resection margin, tumour and lymph node staging, unless this investigations is contraindicated. For patients who are unable to have MRI, endo-rectal ultrasound may be offered in order to obtain the necessary information (National Institute for Health and Care Excellence, 2011).

Tumour (T), Node (N), Metastasis (M) staging classification is used in colorectal cancer staging. T stage describes the extent of the primary tumour, N stage describes the involvement of loco-regional lymph nodes and M stage describes whether there is evidence of distant metastatic spread. Another staging classification commonly used by the doctors is the Dukes' staging (Dukes, 1932). Since the Dukes' staging has been proposed in 1932, it has undergone a number of modifications (Astler and Coller, 1954, Gabriel et al., 1935, Turnbull et al., 1967) as has the TNM staging, which is currently 7$^{th}$ edition (Edge, 2010). There are four stages in Dukes' classification; A, B, C and D. In

simplistic terms, Dukes' stage A means that the cancer is confined in the mucosa, Dukes' B means that the cancer has invaded the muscularis propria but no loco-regional lymph nodes are involved, Dukes' C means that the cancer has invaded the muscularis propria and loco-regional lymph nodes are involved and Dukes' D means that the cancer has spread to other part of the body such as liver.

### 1.7.5 Treatment

#### 1.7.5.1 Management of local disease

*Primary surgical therapy for colon cancer*

Standard therapy for patients with localised colon cancer has been open surgical resection of the primary and regional lymph nodes. However, laparoscopic surgery or laparoscopic assisted surgery is increasingly used which has been shown to be as effective as open surgery in a selected group of patients. (Clinical Outcomes of Surgical Therapy Study Group, 2004, Weeks et al., 2002) .

*Primary surgical therapy for rectal cancer*

The management of rectal cancer differs slightly from that of colon cancer due to the increased risk of local recurrence and a poorer overall prognosis. Differences include the surgical technique, and use of preoperative radiotherapy or chemo-radiotherapy (Berho et al., 2015, Sauer et al., 2012, Roh et al., 2009), depending on the risks for local recurrence as determined by the findings of staging MRI pelvis. There is also important consideration regarding therapeutic issues related to the maintenance or restoration of normal sphincter, genitourinary and sexual functions (Balch et al., 2006, Baxter and Garcia-Aguilar, 2007). The management of rectal cancer requires a multidisciplinary team approach in order to ensure best possible outcome for the patients (Berho et al., 2015).

The primary treatment for patients with localised rectal cancer is surgical resection of the tumour. The surgical approach used may vary according to the location of the tumour, stage of the disease, presence or absence of high risk features (positive margins, lymphovascular invasion and poorly differentiated histology). Types of surgical resection include polypectomy, transanal local excision, total mesorectal

excision with autonomic nerve preservation via low-anterior resection or total mesorectal excision via abdomino-perineal resection for patients who are not candidates for sphincter preservation, leaving patients with a permanent end-colostomy (Guillem and Cohen, 1999, Balch et al., 2006, Baxter and Garcia-Aguilar, 2007).

### 1.7.5.2 Adjuvant chemotherapy

Patients who have undergone potentially curative resection of their colon cancer may be offered adjuvant chemotherapy, aimed at reducing the risk of recurrence. Prior to 2000, 5-Fluorouracil was the only cytotoxic chemotherapy available in the adjuvant setting. There is evidence to suggest that patients with stage III colon cancer are the group of patients most likely to derive benefit from adjuvant chemotherapy (Laurie et al., 1989, Moertel et al., 1990, Wolmark et al., 1993, International Multicentre Pooled Analysis of Colon Cancer Trials (IMPACT) investigators, 1995). Subgroups of patients with stage II colon cancer may be at higher risk for recurrence (e.g. those with tumour adherence to neighbouring structures, perforation and obstruction) (Merkel et al., 2001), however, evidence for 5-Fluorouracil based adjuvant chemotherapy leading to improved overall survival for patients with stage II colon cancer is inconsistent (Moertel et al., 1995).

Capecitabine is an oral fluoropyrimidine that undergoes multiple enzymatic conversions to 5-Fluorouracil. Adjuvant Capecitabine provides equivalent outcome to intravenous 5-Fluorouracil and folinic acid (Twelves et al., 2005). More recently, addition of Oxaliplatin to the 5-Fluorouracil based chemotherapy regimen in the adjuvant setting has lead to improvement in the overall survival of patients with stage III colon cancer (Andre et al., 2004, Andre et al., 2009) and has now become the standard adjuvant chemotherapy regimen for many.

Unlike colon cancer, role of adjuvant chemotherapy with 5-Fluorouracil based chemotherapy in patients with rectal cancer is less well defined and more research is needed to identify patient group that may derive benefit from adjuvant chemotherapy (Petersen et al., 2012).

### 1.7.5.3 Treatment of metastatic or recurrent colorectal cancer

Surgical resection of local recurrence for both colon and rectal carcinoma may be feasible. In cases of rectal cancer, local recurrence alone after initial attempted curative resection, aggressive local therapy may lead to long term disease free survival (Ogunbiyi et al., 1997, Vermaas et al., 2007). Use of primary chemo-radiotherapy for previously non-irradiated rectal cancer patients with locally advanced pelvic recurrence may increase respectability and allow preservation of sphincter function (Lowy et al., 1996).

Patients with limited liver and pulmonary metastasis may be considered for surgical resection in highly selected patients (Coppa et al., 1985, Gayowski et al., 1994, Jaeck et al., 1997, Girard et al., 1996, Headrick et al., 2001). However, in majority of cases, patients with metastatic colorectal cancer are treated with palliative chemotherapy with the aim of reducing the volume of disease, alleviating some of the cancer related symptoms and prolong survival.

### 1.7.5.4 Chemotherapy drugs for the treatment of metastatic colorectal cancer

For many years, 5-Fluorouracil was the only active chemotherapy drug in the treatment of colorectal cancer. Studies have shown response to treatment and prolongation of the time to progression (TTP) of disease (Petrelli et al., 1989), as well as improved survival and quality of life for patients receiving chemotherapy compared with best supportive care (Scheithauer et al., 1993, Nordic Gastrointestinal Tumor Adjuvant Therapy Group, 1992, Buyse et al., 2000). Several trials have explored various regimens using different doses and schedules of 5-Fluorouracil. They have shown similar results in terms of median survival of the order of 12 months (Leichman et al., 1995).

As previously discussed, Capecitabine is an oral fluoropyrimidine drug which undergoes a number of conversions to become 5-Fluorouracil. Prior to the advent of multi-agent chemotherapy, two randomised controlled studies demonstrated equivalent efficacy between Capecitabine and 5-Fluorouracil given in a regimen called Mayo Clinic regimen (Van Cutsem et al., 2001, Hoff et al., 2001).

In addition to 5-Fluorouracil and Capecitabine, there are now two additional chemotherapy drugs available for the treatment of advanced colorectal cancer. These

are Irinotecan and Oxaliplatin. Randomised controlled studies in patients with advanced colorectal cancer have demonstrated improved response rates, progressions-free survival (PFS) and overall survival (OS) when Irinotecan or Oxaliplatin was combined with 5-Fluorouracil and folinic acid. (Saltz et al., 2000, de Gramont et al., 2000, Douillard et al., 2000, Braun et al., 2003). Two studies compared infusional 5-Fluorouracil regimens in combination with either Irinotecan or Oxaliplatin (Tournigand et al., 2004, Colucci et al., 2005). In both of these studies, patients were allowed to cross over upon progression of first line therapy. These trials showed no difference in the progression free survival and overall survival between the treatment arms.

Randomised studies have addressed the equivalence of substituting Capecitabine for infusional 5-Fluorouracil in combination with Oxaliplatin (Diaz-Rubio et al., 2007, Porschen et al., 2007). These studies have shown similar progression free survival between the two regimens. The Bolus, Infusional, or Capecitabine with Camptosar-Celecoxib (BICC-C) trial evaluated several different Irinotecan-based regimens in patients with advanced colorectal cancer in the first line treatment setting (Fuchs et al., 2007). Patients who received Irinotecan with infusional 5-Fluorouracil had better progression free survival compared to those who received Irinotecan with bolus 5-Fluorouracil or Irinotecan with Capecitabine. Patients who received Irinotecan with Capecitabine had the highest rates of toxicities (Fuchs et al., 2007).

Therefore, chemotherapy with 5-Fluorouracil based chemotherapy in combination with either Irinotecan or Oxaliplatin may be considered valid first line chemotherapy regimens for patients with advanced colorectal cancer, who are fit enough to have combination chemotherapy. 5-Fluorouracil may be substituted by Capecitabine for combination with Oxaliplatin but infusional 5-Fluorouracil is preferred when combined with Irinotecan. Patients may be offered Irinotecan based chemotherapy as second line treatment after Oxaliplatin based chemotherapy and vice versa.

Infusional 5-Fluorouracil with folinic acid or Capecitabine chemotherapy may be considered first line therapy for those patients who are not considered fit enough for combination chemotherapy. However, a randomised study has shown that combination chemotherapy with Oxaliplatin and either infusional 5-Fluorouracil or Capecitabine, if dose modified, may be feasible in elderly patients with borderline performance status. However, this study did not show overall survival benefit for those patients receiving combination chemotherapy (Seymour et al., 2007)

1.7.5.5 Side Effects of Colorectal Cancer Chemotherapy

Toxicity of 5-Fluorouracil changes significantly when the drug is used in different doses and schedules (Macdonald, 1999). The difference is particularly observed when bolus schedules are compared to infusional schedules (Levy et al., 1998). Bolus single agent of 5-Fluorouracil was, in the past, the standard method of administration for this drug in the treatment of colorectal cancer however, infusional regimens are favoured for their side effect profile. Bolus 5-Fluorouracil was associated with significant myelosuppresion. Major toxicities caused by infusional 5-Fluorouracil include mucositis, diarrhoea and palmar-plantar erythrodysesthesia, more commonly known and "hand-foot syndrome" (Levy et al., 1998). Infusional treatment requires patients to have indwelling central venous catheters which may cause additional problems for patients, such as thrombosis and infections.

Capecitabine has similar profile of toxicities as 5-Fluorouracil, which is not surprising given that it is ultimately converted to 5-Fluorouracil. Incidence of mucositis, diarrhoea and nausea are less common among patients receiving Capecitabine compared to those patients on bolus 5-Fluorouracil. However, incidence of hand-foot syndrome is significantly higher among patients on Capecitabine compared to bolus 5-Fluorouracil (Cassidy et al., 2002).

Rare side effects of 5-Fluorouracil and Capecitabine include their cardiac toxicities. These side effects include acute coronary syndrome, cardiomyopathy and arrhythmias (Sorrentino et al., 2012).

Irinotecan may be associated with a number of serious side effects. These include myelosuppresion, diarrhoea which can be severe, and hair loss (Fuchs et al., 2007). Oxaliplatin is also associated with risk of myelosuppresion but its' main troublesome side effect is sensory peripheral neuropathy (Saif and Reardon, 2005).

1.7.5.6 Biological treatments for colorectal cancer

The last decade has seen a number of biological treatments with activities in the treatment of colorectal cancer in combination with chemotherapy or as single agents. These include Bevacizumab, Cetuximab, Panitumomab, Aflibercept and Regorafenib.

Many of these treatments are currently not readily available within the National Health Service in the UK, although oncologists in England can apply for funding for some of these drugs via the Cancer Drugs Fund (NHS England).

### 1.7.6 HRQoL in colorectal cancer patients

Patients diagnosed with cancer will go through a number of stages during the course of their illness. Each stage of the disease trajectory will pose different challenges for the patients and impact on their HRQoL.

Diagnosis with a potentially life threatening disease is likely to instill fear and uncertainty for patients diagnosed with any cancer, including colorectal cancer. There is evidence to suggest that significant proportion of patients with colorectal cancer suffer from anxiety and depression (Strong et al., 2007). There is indication to suggest that younger patients with the disease are more like to have psychological distress compared to older patients (Cohen et al., 2014). It has been suggested that this may be in part due to younger patients potentially bearing more work and family related strains as a consequence of their cancer diagnosis (Arndt et al., 2004). On the other hand, older patients may have different expectations of life and of the future. They may anticipate developing various diseases as part of the aging process (Cohen et al., 2014, Phipps et al., 2008). Studies have indicated that those patients who have anxiety or depression at baseline are more likely to have on-going psychological issues long term (Chambers et al., 2012).

Surgical intervention for the primary cancer can have significant impact on patients, particularly for those patients diagnosed with rectal cancer. Patients with rectal cancer are more likely to receive pre-operative treatment such as radiotherapy or chemo-radiotherapy. These treatments can cause additional toxicities and higher rate of surgical complication for patients (Marijnen et al., 2002) and may result in long term sequelae in terms of bowel and sexual dysfunction (Birgisson et al., 2007). Rectal cancer patients are more likely to undergo surgical procedure which results in the formation of a permanent stoma. This can have an impact, not only on patients' bowel function, but also on how the patients adjust their life around managing the stoma and on their body image (Sprangers et al., 1995, Jansen et al., 2010). Rectal cancer patients are more likely than patient with colon cancer to report body image issues and

sexual dysfunction long term (Downing et al., 2015, Traa et al., 2012, Brown and Randle, 2005).

Chemotherapy treatment can cause a wide range of side effects as discussed earlier. Patients undergoing treatment will not only experience these toxicities but regular hospital visits to receive these treatments will undoubtedly have impact on their day to day activities. If the treatment is palliative for those with incurable disease then patients may have other symptoms attributable to their underlying disease as well as the treatment side effects. They are also more likely to have other health issues and concerns compared to those patients receiving the treatment as adjuvant therapy to the surgery with the aim of increasing the chance of cure. Fear of recurrence and uncertainty may be a significant on-going concern for those patients who may have received treatment with curative intent (Jansen et al., 2010, Downing et al., 2015). In addition, colorectal cancer affects older population; therefore these patients may have other significant co-morbidities which may have additive burden on their daily lives (Downing et al., 2015).

### 1.7.7 HRQoL instruments in colorectal cancer

A wide range of HRQoL instruments have been used in the assessment of HRQoL among colorectal cancer patients. These include both generic and cancer specific questionnaires but many studies employed colorectal cancer specific modules in order to capture issues which are specific to this group of patients. Review of the HRQoL instruments will be presented in Chapter 3 as part of the questionnaire development.

### 1.7.8 Summary

Colorectal cancer and its' treatments can pose significant symptom and psychosocial burden among patients. Evaluation of existing HRQoL instruments is necessary to examine if any of the existing measures are suitable for use in clinical practice.

## 1.8 Training programme for integration of patient reported HRQoL in routine consultations

The clinical consultation remains the foundation of all medical practice. During the course of a professional lifetime, most doctors will conduct between 160,000–300,000 medical interviews (Lipkin, 1996). Effective doctor-patient communication is a fundamental component in the delivery of high quality healthcare. It can facilitate positive effects for both patients and doctors, which include improved accuracy and understanding of patients' problems (Maguire et al.); patient satisfaction with their care and better understanding of their diagnosis/problems leading to adherence to therapy (Silverman et al., 2005); improved doctor-patient relationship and improved doctors' well-being (Fallowfield, 1995, Ramirez et al., 1995).

Communication is a skill which may be taken for granted. Some doctors are much better natural communicators than others. However, medical consultation requires skills which are different to how we may interact with other people socially. Different patients require different approaches and doctors need to be able to adjust their communication skills to meet the needs of the patient accordingly.

Good communication skills are particularly relevant in cancer medicine. Consultations about cancer may involve many difficulties, including breaking bad news about the diagnosis of cancer, or recurrence; treatment failure/disease progression and prognosis. Oncology consultations may also involve discussion of complex information about treatments and informed consent and participation into clinical trials.

The goal of effective communication between patients and doctors is to ensure patients receive the most optimal care. Communication needs of patients and doctors are therefore invariably linked to this goal. Optimal care for the patients includes not only the best medical management of the underlying cancer, but also optimal management of the patients' psychosocial adjustments in response to their disease. Eliciting these issues during the consultations, however, requires skill which not all clinicians may have.

Patient reported HRQoL would be expected to facilitate improved patient-doctor communication by providing clinicians with rich information about their patients, which can be used in a number of beneficial ways such as detection of problems and monitoring of patients' progress over time. However, adoption of patient reported

HRQoL collection in routine clinical practice has been slow due to a number of barriers described previously.

Training healthcare professionals has been suggested as one of the ways which may help overcome healthcare professional related barriers to implementation of routine patient reported HRQoL collection (Greenhalgh, 2009, Luckett et al., 2009). These barriers relate to clinicians' lack of expertise with the HRQoL assessments for individual patients (Morris et al., 1998a) and their concerns about the HRQoL highlighting problems for which clinicians feel unequipped to deal with (Donaldson, 2004). Another barrier may also be their reluctance for change (Locklear et al., 2014).

Descriptions of training provided to healthcare professionals within published studies of patient reported outcome interventions are brief where this information has been provided (Greenhalgh and Meadows, 1999). These training tended to focus on the HRQoL instruments used within the study and how these instruments were scored, without guidance on *how* healthcare professionals might use the data (Detmar et al., 2002, Velikova et al., 2004). Training, therefore, need to address these barriers so that doctors can respond to patient reported data in the way that would influence patient management.

In order to develop this training programme, I have explored the training methods used in the communication skills training to see if similar strategies may be feasible, as the patient reported outcomes intervention aims to impact on the communication between the patient and the healthcare professionals.

This developmental process will be discussed in detail in Chapter 6.

## 1.9 Research Hypothesis

My research hypothesis is that HRQoL questionnaires that have been developed primarily for assessing HRQoL of a group of patients (for example in clinical trials) may not wholly be suitable for use in clinical practice to assess individual patients. It may be possible to adapt existing questionnaires to ensure the instrument addresses all key areas relevant to the patient within the routine clinical practice setting. Training oncologists on how to integrate patient reported HRQoL data would further enhance the intervention by providing the oncologists with skills to incorporate patient data to assist clinical decision making.

My expectation is that a questionnaire developed specifically for use in clinical practice together with training for the doctors would serve the following functions:

1. Enhance doctor-patient communication; active involvement of patients' views and facilitating collaborative working relationship between the two parties.
2. Provide a reliable assessment of colorectal cancer specific physical symptoms and treatment toxicities. This may provide a way of monitoring treatment response and toxicities over time and help support clinical decision making.
3. Screen for and identify problems which are not always addressed by healthcare professionals, such as emotional distress and impact of treatment on daily activities. Training will allow doctors to respond to patient concerns more readily and integrate patient views during their clinic consultations.

My work on the questionnaire development was specifically for patients with colorectal cancer. However, it is important to have a consistent approach across different cancer sites in assessing patients' HRQoL. Therefore, questionnaire developmental processes were undertaken simultaneously with similar questionnaire developments in other cancer sites (breast and gynaecological). The training for the doctors was generic and intended for all oncologists with different cancer site expertise.
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### 1.9.1 Aims of thesis and outline of chapters

The main aim of my thesis was to develop (or adapt) a HRQoL questionnaire, specifically for patients with colorectal cancer to be used in routine clinical practice. The questionnaire was intended to facilitate patient care, based on the current colorectal cancer practice, available literature on HRQoL assessment in clinical practice, oncologists and patient opinions.

I have utilized a mixed methods approach which included review of literature, qualitative interviews with both oncologists and patients, and quantitative statistical methods. Methods used in this thesis are presented and discussed in detail in Chapter 2.

Objectives of my thesis and outline of the chapters are presented below:

Chapter 3: The details of the questionnaire developmental process are described in Chapter 3. This Chapter explored issues commonly discussed in real life clinic consultations of colorectal cancer patients. Review of the literature of questionnaires used to evaluate HRQoL of colorectal cancer patients was performed. This was followed by comparison of issues raised in clinic consultations and in the questionnaires. Further opinions were sought from oncologists specialising on colorectal cancer treatment and from their patients to assess relevance to routine clinical practice and also usability of the questionnaires.

Chapter 4: In this Chapter, I have tested the psychometric properties of the newly developed/adapted colorectal cancer specific questionnaire by administering it to a group of patients. The statistical analysis used helped to identify subscales and helped to reduce the number of items included in the questionnaire.

Chapter 5: In this Chapter, I have conducted exploratory analyses of the previous randomised controlled study conducted by the Leeds Psychosocial Oncology and Clinical Practice Research Group (Velikova et al., 2004). The aims of these analyses were to investigate what impact patient reported HRQoL had on doctor-patient communication and to explore whether the severity of patient reported symptoms and functions had any bearing on whether these issues were discussed during the clinic consultation. These analyses were aimed at identifying elements of the intervention that could be improved through training of the doctors.

Chapter 6: In this Chapter, conceptual models of knowledge acquisition and learning styles were explored which informed the structure of communication skills training in cancer. Teaching interventions used in communications skills training were reviewed to see what teaching methods would be suitable for training oncologists in using patient reported HRQoL data. This chapter also describes the developmental processes of “trigger” tapes used in the training programme to provide experiential learning opportunity for the oncologists.

Chapter 7 In this Chapter, I have described the Pilot Study of Doctor Training which aimed to evaluate the possible impact of doctor training. The

actual conduct of the study and patient recruitment were performed by the members of Leeds Psychosocial Oncology and Clinical Practice research Group (POCPRG).

### 1.9.2 Function of the thesis within a context of broader research programme

Cancer Research UK funded programme of research (C7775/A7424, 2008 – 2012) called Quality of Life, Enhanced Staff Training (QuEST), aimed to maximise the impact of patient reported HRQoL assessment on processes of patient care and outcomes.

The research programme consisted of two strands of work which were developed in parallel; these strands were questionnaire development and doctor training.

Questionnaire development strand aimed to evaluate and enhance existing HRQoL instruments by active engagement with both healthcare professionals and patients in making sure that issues relevant and important for patients were included in the questionnaire. It aimed for the questionnaires to be suitable for use within clinical practice.

The aim of the doctor training strand was to develop a training programme to assist healthcare professionals in responding to and facilitate integration of patient reported HRQoL information into clinic consultations in the way that patient reported data would play an active role in clinical decision making process.

In addition to these two strands within the Cancer Research UK funded programme of research, Leeds POCPRG are working on technology that enabled information collected from questionnaires completed on touch screen computers to be automatically scored and uploaded on to patients' electronic record system used in Leeds called the Patient Pathway Manager (PPM). This integrated system allowed results from questionnaire to be scored and presented in a graphical format immediately so that these results could be viewed by the oncologists during the clinic consultation.

As the questionnaire results were integrated into the patients' notes, they became part of the work flow for the oncologists, which enabled the clinicians to process the

information efficiently. The format of result presentation included graphs which were colour coded in traffic light schema according to cut off points to provide indication for more serious problems.

As part of the Cancer Research UK funded programme of research, three cancer site specific questionnaires for colorectal (QuEST-Cr), breast (QuEST-Br) and gynaecological cancers (QuEST-Gy) were adapted simultaneously. I was responsible for the adaptation processes for the development of QuEST-Cr. I was responsible for managing the recruitment of most of the colorectal cancer patients for the validation of the questionnaire items. Statistical analyses were conducted in parallel with other cancer sites but I was responsible for the analysis of the colorectal cancer patients' data. In order to create consistent function scales across the three cancer sites, group decisions were made on certain items which are described in detail in Chapter 4.

I was the key person in leading the development of doctor training programme. I explored the conceptual models of adult learning and learning styles to inform the types of teaching methods needed. I reviewed the teaching methods used in advanced communication skills training and used this as the framework on which the doctor training can be built on. I developed the "trigger tapes" to use as facilitation aid during the training to provide alternative experiential learning opportunity instead of role play.

# Chapter 2 Methodology

## 2.1 Introduction

Various methodologies were employed in order to address the aims of this thesis. Mixed methods approach, in which both quantitative and qualitative methods are combined, allows making the most of their respective strengths (Curry et al., 2009). Quantitative methods alone may not be sufficient in measuring complex aspects of how a medical care intervention may impact on patient outcomes. Qualitative methods are more exploratory in nature which may help to uncover beliefs and values of study participants which underpin their health behaviour (Malterud, 2001, Eccles et al., 2003, Green and Britten, 1998). The data generated from both methods may provide more complete data, thus offering supporting or complimentary information to facilitate better understanding of the research subject and provide broader perspective on the overall research question (Curry et al., 2009, Creswell JW, 2003).

Following methods were applied:

1. Evidence synthesis through structured review of literature
2. Qualitative methodology including semi structured interviews analysed using framework/thematic analysis
3. Quantitative methodology including descriptive statistics, regression analysis and psychometric methods

The thesis can be divided into the following key stages

1. Identifying the issues pertinent to patients with advanced colorectal cancer for inclusion in a colorectal cancer specific questionnaire package
2. Reviewing the questionnaire package with patients and oncologists
3. Refining the questionnaire package to facilitate its utility in the routine clinical oncology practice
4. Exploring the barriers for patient reported outcomes to be employed routinely in clinical practice
5. Developing training programme for oncologists to assist them in using the patient reported HRQoL data
6. Pilot study to test the potential benefits of doctor training

This chapter describes each of these key stages with references to available methodologies for data collection and analyses to meet their objectives, and the reasons behind decisions made regarding choice of methodologies utilized in this thesis.

## 2.2 Identifying relevant issues and topics for inclusion in the colorectal cancer specific questionnaire

One of the aims of this thesis was to explore whether existing health related quality of life (HRQoL) questionnaires, which have been developed for the purpose of capturing patients' quality of life in a specific group of patients/population (for example, in a clinical trial) would meet the needs of capturing such data for each individual patient within routine oncology practice.

It was envisaged that the questionnaire specific for colorectal cancer patients would address their symptoms, side effects of treatments and functional concerns. There would also be an additional concerns checklist which allowed patients to indicate whether they wished to discuss any specific issues.

It was expected that there would be some sections within the questionnaire which were generic to all cancers such as assessment of patients' physical function, emotional function and concerns checklist.

### 2.2.1 What topics are discussed in routine oncology clinic consultations?

In order to begin to answer the above question, it seemed natural to explore what topics or issues are actually raised and discussed in routine oncology clinic consultations.

There are a number of methods to gather such information. One method would be to review the patients' medical notes and document the issues written in the notes or in clinical correspondence. The problem with this method is that the doctor may not have written down all of the issues that were discussed. Doctors often summarise the consultation and document what was perceived to be the most pertinent issue from their perspective. Therefore, this method may not necessarily reflect the patients' viewpoint as the data would be obtained from documentation produced by the doctors.

Other methods include researchers making notes in real time during the consultation or using audio-visual equipment to capture such data. However, these methods can be considered intrusive and may potentially disrupt the flow of the clinic consultation. The most suitable method was considered to be the use of digital dictation devices. These are very small and can be left on the doctors' desk during the consultation. Leeds POCPRG has a wealth of experience in audio recording of clinic consultations and this was considered to be the favoured approach.

There are a number of methods for analysing patient-doctor communication and their interactions during a clinical encounter. Comprehensive consultation coding systems such as Roter Interaction Analysis System (RIAS) (Roter and Larson, 2002) or Medical Interaction Process System (MIPS) (Ford et al., 2000) can both provide detailed information about the complexity of patient-doctor interactions, through coding each utterance (any meaningful section of speech) during the consultation. These coding systems not only examine the discussion topics of the consultation but they also allow examination of the contributions made by the doctor and the patient and how they fulfill the purpose of the medical interview; gathering information and understanding the patient's problems, providing education and counseling, building a rapport and responding to patients' emotions and managing any problems identified. However, application of these coding systems can be very time consuming.

An alternative method is to use a simpler content analysis as a systematic analysis of the topics covered during patient-doctor interaction during the medical consultations. This method of analysis can be applied to a wide range of data, including text, videos and audio-recordings. It is a way of studying and analysing communication in a methodical, objective and quantitative manner for the purpose of measuring variables (Kerlinger, 1986). Content analysis has successfully been utilized in studies of patient-doctor communication in the oncology setting (Detmar et al., 2002, Fagerlind et al., 2008, Velikova et al., 2004) with good inter-rater reliability (Fagerlind et al., 2008).

As the aim of this part of the study was to capture the topics of discussion during a routine oncology clinic consultation, it was felt that the most suitable method of analysing the data was content analysis.

Leeds POCPRG has already conducted many studies utilising audio-recording of clinic consultations. Rather than collecting new audio-recording of clinic consultations,

previously recorded consultations of colorectal cancer patients were used for the purpose of this part of the study.

### 2.2.2 Examining the issues covered in existing quality of life questionnaires.

HRQoL questionnaires are developed by exploring issues which are relevant to the group of patients under investigation. This may be achieved by gathering such information directly from the patients. Another method used to generate items for inclusion in questionnaire is to conduct a review of literature to identify common symptoms and quality of life issues that are pertinent to the specified patient group (Johnson et al., 2011). Structured literature review of HRQoL instruments was performed to explore which topics or issues were already addressed by these existing instruments.

The finding from the above content analysis of consultation audio-recordings were compared to the findings of the review of the literature, in order to generate a comprehensive list of topics and issues relevant to the colorectal cancer patients.

## 2.3 Reviewing the questionnaire items with oncologists and patients

The aim of this stage of the project was to review the items of the questionnaire generated from measures described above, to ensure that the items were relevant to what is required for routine clinical practice and also to make sure that they reflected patients' experiences. This was also an opportunity to review the wording of the questions with healthcare professionals and patients and to rationalise which items should be included in the questionnaire.

There are both quantitative and qualitative methods available in achieving the aim of this stage of the study. The quantitative method would involve asking the healthcare professionals to provide their rating of each item according to how useful they find each item in routine clinical practice. Patients can also answer the questionnaire items which may provide indication as to the prevalence of the issue and to assess whether the questionnaire items are relevant to them. However, quantitative methods alone

may not address some of the other aims such as making sure that the wording of the items is appropriate.

Qualitative methods that may be applied here are interviews and focus group discussions. Interviews are among the most common methods for collecting qualitative data. They can be categorised into unstructured, semi-structured and structured (Fontana and Frey, 1994). Semi-structured interview is the most commonly used method in qualitative research. The interviewer will have a framework of the themes or topics to be explored but the questions can be left relatively open, allowing the interviewee to talk more openly about their experiences and thus enabling new ideas to be brought up.

Focus group discussions are a form of group interview (Kitzinger, 1995) in which a group of participants gather to discuss a specified topic to generate data. During focus group discussions, participants are encouraged to communicate with one another; asking questions and exchanging their experiences, allowing exploration of peoples' knowledge and experiences. The researcher acts more as a "moderator", rather than an "interviewer" in focus groups to keep the discussions flowing. Focus groups can involve a single group of participants meeting on a single occasion or it can involve many groups with repeated meetings. Typically, focus group discussions consist of four to eight participants but this number may vary (Wilkinson, 2004). The disadvantages of focus group discussions include the possibility that some of the participants may be hesitant to express their honest views if their thoughts oppose the views of others. There is also a risk that the discussion may become dominated by one or two people within the group, leading to bias. In addition, some participants may find it difficult to discuss sensitive topics amongst a group of people.

Using both quantitative and qualitative methods was considered the most appropriate approach for this part of the study. Oncologists specialising in the treatment of colorectal cancer patients were asked to go through the list of questionnaire items and provide their evaluation according to how useful they considered each item to be. This was coupled with a semi-structured interview around the questionnaire items, which also explored their views about using such questionnaires within routine clinical practice and how that may impact on patient care. Patients were also asked to complete the questionnaire items, which was then followed by a semi-structured interview. This helped to clarify whether the items were relevant to their experience

and also to check any issues around the wording of the items. Patients' views on using such questionnaire were also explored.

Semi-structured interviews were chosen over focus group discussions due to practical reasons of difficulties in arranging a convenient time for oncologists and patients to meet. Patient interviews were conducted when they attended for their planned out-patient appointments in order to avoid additional visits to the hospital.

Quantitative data generated from oncologists rating of the items and patients completing the questionnaire were analysed using descriptive statistics to explore the oncologists' assessment of the items and also to evaluate the prevalence of the issues amongst patients.

All of the semi-structured interviews conducted were audio-recorded and later transcribed prior to analysis.

Qualitative data analysis involves processes which converts the collected data into some form of explanation, understanding or interpretation of the subjects and situation being investigated. There are two main approaches for analysis; deductive and inductive approaches. The main difference between the two approaches is that deductive approach is aimed at testing a theory whilst inductive approach is concerned with generation of new theory or new phenomena emerging from the data.

Inductive analysis is the most common approach used to analyse qualitative data (Thomas, 2006). There are various analysis methods described associated with specific approaches or traditions, such as narrative analysis (Cortazzi, 2014), phenomenology (Giorgi, 1997), discourse analysis (Kinneavy, 1971) and grounded theory (Strauss and Corbin, 1994). More recently, some researchers have described more generic analysis methods for qualitative data collectively referred to as "general inductive approach" or framework/thematic analysis (Thomas, 2006).

Thematic content analysis is the most commonly used analysis method in qualitative research. It focuses on examining themes within the data. A theme represents a pattern of response or meaning from the data that is related to the research questions. Coding is the primary process for developing themes within the raw data by recognising important moments in the data and encoding it prior to interpretation (Braun and Clarke, 2006). This analysis method is strongly influenced by the data

rather than the researcher's preconceptions and theories about what themes may emerge. There are six key stages of thematic analysis: 1) familiarising yourself with the data; 2) generating initial codes; 3) searching for themes; 4) reviewing themes; 5) defining and naming themes and 6) producing the final report. The method allows relatively non technical way for analysing large volume of qualitative data in a comprehensive manner (Braun and Clarke, 2006).

Qualitative thematic analysis has therefore been used in analysing the data obtained through the semi-structured interviews conducted in this part of the study. The findings from the interviews were combined with the quantitative ratings for the items in order to gain a more complete understanding of the data.

## 2.4 Refining the questionnaire package

One of the most important steps in the development of questionnaires is the validation process, which consists of a series of procedures to determine the quality of the instrument as a tool for measurement. This would ensure that the questionnaire is valid and reliable.

Validity refers to how well the instrument measures what it is supposed to measure. Reliability refers to the degree to which an instrument produces repeatable or consistent results. In order to test the validity and reliability of the questionnaire, it needs to be tested in a group of patients for whom the questionnaire has been developed.

The main aim of this part of the study was to refine the questionnaire and to ensure its' suitability for use within routine clinical practice. Secondary aim of this study was to try and reduce the number of items within the questionnaire in order to reduce burden for patients completing the questionnaire but also to assist the healthcare professionals in interpreting the results.

There are two main theories leading the development and validation of rating scales and questionnaires: the classical test theory and the item response theory.
The main purpose of classical test theory within psychometric testing is to understand and improve the reliability of the instrument. Classical test theory assumes that any

score obtained from an instrument (the “observed” score) is composed of both the “true” score, which is unknown, and “error” in the measurement process (DeVellis, 2006). Errors can occur through a number of variables. These include the individuals completing the questionnaire, the items within the questionnaire and the timing of administering the questionnaire. The goal in classical test theory is to estimate errors in measurement and to suggest ways of improving the instrument so that errors are minimized. As there is no way to directly observe or calculate the “true” score, a variety of methods are used to estimate the reliability of a test. These include:

1. **Test-retest reliability** is a measure of reliability obtained by administering the same test to a group of individuals twice over a short period of time (when no change in status/scores is expected). The scores from Time 1 and Time 2 can then be correlated in order to evaluate the test for stability over time
2. **Parallel forms reliability** is a measure of reliability obtained by administering different versions of an assessment tool (both versions contain items that probe the same construct) to the same group of individuals. The scores from the two versions can then be correlated in order to evaluate the consistency of results across alternate versions.
3. **Inter-rater reliability** is a measure of reliability used to assess the degree to which different judges or raters agree in their assessment decisions.
4. **Internal consistency reliability** assesses the consistency of results across items within a test. The most common internal consistency measure is Cronbach's alpha

The classical test theory encompasses a number of methods which can be used to reduce the number of items within a questionnaire. Frequently employed methods include factor analysis, correlations and Cronbach’s alpha statistics per scale, or stepwise regression (Coste et al., 1997).

Factor analysis identifies the number of latent constructs and underlying structure of a set of variables. Items that measure the same construct should load onto the same factor which helps to form a sub-scale. Factor loading is based on correlation between items and range from -1 to 1. -1 indicates a negative correlation and 1 indicates a positive correlation, a score of 0 means that there is no correlation at all between the items.

Sub-scales identified through factor analysis can then be evaluated further by checking the internal consistency using Cronbach's alpha. The value of Cronbach's alpha ranges from 0 to 1.0; the closer the value of alpha to 1.0, the more reliable the scale. Cronbach's alpha may sometimes be improved by removing item(s) from the subscale, which may also assist in item reduction.

A number of limitations of classical test theory have been described. One of these is that the sample characteristics and test or instrument characteristics cannot be separated; each can only be interpreted in the context of the other. Classical test theory also assumes that there is equal measurement of error exists amongst the sample population. The classical test theory places its emphasis on the test score properties of the instrument rather than on the item parameters and it provides no basis for predicting the likelihood of a given response of a sample to a given test item, based on the response to other items (DeVellis, 2006).

Item response theory (IRT) is a more modern theory which was first proposed in the field of psychometrics for the purpose of ability assessment in education. It continues to be widely used in education setting to calibrate and evaluate items in tests, questionnaires, and other instruments and to score subjects on their abilities, attitudes, or other latent traits. The theory describes studies of test and item scores on assumptions concerning the mathematical relationship between abilities (or other hypothesized latent traits) and item responses (Hambleton et al., 1991).

The purpose of IRT is to provide a framework for evaluating how well assessments work and how well the individual items on assessments work, leading to more precise measurements. This allows IRT to construct scales that are short but still reliable and valid. IRT also enables applications such as computer adaptive testing (CAT), in which questions can be successively selected, based on the previous response given by the person completing the test/questionnaire. This tailored question selection can result in greater precision with only a relatively small number of questions (Gershon, 2005).

Disadvantages of IRT include the need for a large sample size for analysis (>500) for questions with multiple response options, such as the Likert scale (Reeve and Fayers, 2005). Other disadvantages include the need for standalone computer programmes to conduct the analyses, which are often complex, compared to the analysis methods used in classical test theory (Streiner, 2010).

For the colorectal cancer specific questionnaire presented in this thesis, classical test theory methodologies were applied. These are well established methods for questionnaire development outside of the education context (Aaronson et al., 1993, Trask et al., 2008) and analyses can be performed on smaller sample sizes (Hambleton and Jones, 1993). Future research may utilize item response theory methodologies to the classical test theory approach in order to enhance the instrument further.

## 2.5 Longitudinal analysis from the previous Randomised Controlled Trial

A previously conducted randomised control trial by the Leeds POCPRG demonstrated that regular feedback of patient reported outcomes of HRQoL to oncologists during cancer treatment led to improved doctor-patient communication and patient well being (Velikova et al., 2004). However, the impact observed was small. The published results were derived from pre-planned analysis of doctor-patient communication at a single time point, due to time and resource restrictions. Following the publication of the study, the members of the group continued to analyse all of the audio-recordings of the out-patient consultations collected as part of this study, resulting in the formation of a rich longitudinal dataset of doctor-patient communication in oncology. The consultations had been analysed using content analysis, employing a study specific framework. The analysis focused on the topics of discussion and dynamics of the communication (who initiated discussion of a specific topic). Approximately 75% of patients in the trial completed HRQoL questionnaire over time (4 consecutive consultations) and their consultations were audio-recorded and content analysed.

I was given access to this rich dataset in order to perform exploratory analysis of doctor-patient communication and how the completion and feedback to oncologists of HRQoL influenced the content of the discussions that took place during the consultations. The aim of the exploratory analysis was to identify elements of the questionnaire intervention which may be acted upon in order to enhance the process.

Regression analysis is a statistical method for investigating relationships between a dependent variable and one or more independent variables. Regression analysis is widely used for prediction or forecasting and can infer causality between the variables.

As the exploratory analysis was going to involve investigating the impact of questionnaire administration to various outcomes in doctor-patient communication during the consultations, regression analysis was considered to be the most appropriate approach.

The dataset obviously consisted of data collected from patients repeatedly over time (i.e. longitudinal data). One of the aims of the analysis was to investigate the impact of the questionnaire intervention on doctor-patient communication over time. There are a number of statistical methods available for analysing repeated measures. One method is repeated measures analysis of variance (ANOVA). It is used to compare three or more group means where the participants are the same in each group. The analysis requires a number of conditions to be met. One is that the dependent variable should be measured at a continuous level and this should be distributed normally. Another condition is the independent variable should consist of at least two categorical, "related" groups. This means that the same subjects are present in both groups. Another is the variances of the differences between all combinations of related groups must be equal (known as sphericity).

Another method is the mixed effects model. The model can accommodate both fixed effects and random effects within the model. Fixed effects represent population parameters, assumed to be the same each time data is collected. Estimating fixed effects is the traditional domain of regression modeling. Random effects, by comparison, are sample-dependent random variables. Mixed effects model offers flexible framework by which to model the sources of variation and correlation that occur from grouped data. There are a number of advantages to using mixed effects models. One advantage is the mixed effects model can handle missing data much better within the model compared to ANOVA. Another benefit of mixed effects model is that time can be incorporated as a truly continuous effect, whereas in ANOVA time is considered as a categorical variable. Mixed effects can also integrate any other important predictor variable that may change with time within the model.

Mixed effects method was chosen over the ANOVA method as it allowed better modeling of various variables including time as a continuous variable.

## 2.6 Development of doctor training

In order to develop the doctor training programme, it was necessary to explore conceptual models of knowledge acquisition and teaching methodologies to inform the structure and the content of the training programme. As the training was aimed primarily at facilitating oncologists to incorporate patient reported HRQoL information into their clinic consultations and impacting on patient-doctor communication, training methods used in advanced communication skills were reviewed and used as the framework for the training programme.

## 2.7 Pilot study to test the potential impact of doctor training

The objective of the pilot study was to gain an estimate of the impact of the doctor training programme on patient-doctor communication. There are a number of study designs that can be used to evaluate the impact of the doctor training. These designs vary in the extent to which they allow the observed effects to be attributed to the intervention. These study designs can be broadly grouped into 3 main categories; experimental, quasi-experimental or non-experimental.

Experimental designs or randomised experiments are considered to be the most rigorous and scientific approach to evaluating effectiveness of an intervention. Randomised controlled study is often considered as the “gold standard”. Quasi-experimental designs shares similarities with the experimental design but lack the random assignment to treatment or control. Quasi-experimental study designs are therefore commonly used in the evaluation of interventions when random assignment is not possible or practical. The non-experimental design only has an intervention group and lacks a control or comparison group, making it the weakest study design (Grimshaw et al., 2000).

Although randomised controlled study is the most rigorous study design to measure the impact of the doctor training, conducting a randomised study can be costly and time consuming. As the aim of the pilot study was to obtain an estimate of the impact of the training which would help inform sample size calculation for the future study investigating the combined effect of the cancer site specific questionnaires and doctor training, quasi-experimental pre-test/post-test design was considered most feasible study design for the pilot study.

# Chapter 3 Questionnaire Development

## 3.1 Introduction

### 3.1.1 Aim

The aim of this part of the study was to develop a HRQoL questionnaire (QuEST-Cr) for patients with advanced colorectal cancer, undergoing chemotherapy treatment, using a comprehensive development plan. The questionnaire was aimed specifically for use in routine clinical practice.

The plan included

1. Exploration of topics/issues discussed during clinic consultations of colorectal cancer patients
2. Literature review of existing HRQoL, including generic HRQoL, generic cancer HRQoL and colorectal cancer specific HRQoL instruments
3. Interviews with oncologists specialising in the treatment of colorectal cancer and with patients undergoing treatment for colorectal cancer

## 3.2 Questionnaire development

Many validated questionnaires have been developed with the aim of capturing patients' perspectives on how their illness and healthcare interventions impact on their lives (Ware, 1995, Fitzpatrick et al., 1998)

The process of developing a questionnaire usually involves several key stages. These have been described in a number of guidelines (Johnson et al., 2011, Food and Drugs Administration, 2009). Before the questionnaire development can begin, a conceptual framework must be formulated so that there is a clear description of the research question and the population for which the questionnaire is being developed.

The guidelines published by the EORTC Quality of Life Group describe four phases in the questionnaire development. This guidance specifically refers to the development of tumour site specific or disease distribution specific (e.g. patients with brain metastasis) modules. The four phases described are:

Phase 1. Generation of quality of life issues
Phase 2. Construction of item list
Phase 3. Pre-testing
Phase 4. Field-testing

During phase 1, quality of life issues that cover the area of interest are compiled from literature review, patients with relevant condition and healthcare professionals with clinical expertise within the specified area of interest. These quality of life issues are then presented as items or questions to be included in the questionnaire during phase 2. The EORTC Quality of Life Group has a bank of previously validated items from which they can select items to match the identified topic of interest. They also provide guidance on how item should be constructed when new items are required. The guidance recommends that the item list generated should be reviewed by healthcare professionals (ideally those that were not involved in the phase 1 of the questionnaire development) with clinical expertise of the target population or those with knowledge of questionnaire development prior to pre-testing phase with patients, in order to check for clarity of wording, removal any duplication and also to check the breadth of coverage. The pre-testing of the questionnaire is performed with a small group of patients to identify and solve any issues concerning administration of the questionnaire. This is followed by structured interviews with each of the patients to ensure completeness and questionnaire acceptability. The questionnaire is further refined by incorporating any modifications prior to field testing in a large group of patients.

The phases described in the EORTC guidelines were used as the framework for the development of the questionnaire within this study. Table 3.1 illustrates the comparison between the EORTC development phases and the methods used within this study.

**Table 3.1 EORTC module development phases vs QuEST-Cr development stages**

| EORTC module development phases | QuEST-Cr development stages |
|---|---|
| Phase 1: Generation of QoL issues:<br>Literature review<br>Views of patients and healthcare professionals | Stage 1. Generation of QoL issues:<br>Review of issues raised in routine oncology consultations<br>Literature review |
| Phase 2: Construction of item list:<br>Matching QoL issues generated from phase 1 to relevant items from EORTC Item Bank. New items created if existing item was not available. | Stage 2. Construction of item list:<br>Matching QoL issues generated from stage 1 to existing EORTC questions. New items were created if existing items were not available. |
| | Stage 3. Interviews with health professionals<br>Review of item list of items to check wording, remove duplications and check breadth of topic coverage |
| Phase 3. Pre-testing:<br>Small number of patients to complete the questionnaire, followed by interviews to check any issues with administration of questionnaire, check acceptability and relevance | Stage 4. Pre-testing<br>Small number of patients to complete the questionnaire, followed by interviews to check any issues with administration of questionnaire, check acceptability and relevance |
| Phase 4. Field-testing:<br>Psychometric testing of reliability, validity and sensitivity to change of the questionnaire | Stage 5. Validation:<br>To test the questionnaire in a large group of patients to perform psychometric testing of reliability and validity of the questionnaire |

Many questionnaires have been successfully developed using the above EORTC guidelines. However, the ultimate aim of the questionnaires developed in this manner has been for its use within clinical trials to compare groups of patients rather than in routine clinical practice for individual patients. In addition, some of the disease specific modules developed by the EORTC Quality of Life Group have been developed to assess patients' symptoms across a range of treatment modalities including surgery, radiotherapy and chemotherapy. As the aim within this study was to develop a questionnaire for use in chemotherapy review clinics, investigation of issues discussed

in such clinics for colorectal cancer patients was considered as useful starting point for the development of the questionnaire. This process has been used to substitute the interviews with patients and healthcare professionals described in the first phase of the EORTC guidelines.

Interviews were conducted later in the developmental stages. The interviews with the healthcare professionals were conducted in order to gather feedback regarding the items and their views on the usefulness of the individual items and questionnaire as a whole. This process also helped to ensure that the questionnaire had the necessary breadth of coverage of the topics. In addition, healthcare professionals were asked to comment on the wording of the items and to remove any redundant or duplicate items. Interviews with patients not only evaluated the questionnaire items but also tested any administrative issues as the questionnaire was delivered on touch screen computer.

Interviews were chosen over focus groups as interviews suited the process needed for this particular stage of the questionnaire development but also for practical reasons; difficulty in organising a convenient time for a group of healthcare professionals to meet and also preventing any additional hospital visit for patients. In addition, the questionnaire included items which were potentially sensitive or embarrassing for patients to discuss in a group setting and was considered better addressed on an individual basis.

Processes undertaken in the development of the colorectal cancer specific questionnaire, QuEST-Cr, for use in routine oncology practice is detailed in this chapter. The methods ensure all the issues important and relevant for the target population are included. This chapter details stages 1-4 of the developmental process (as presented in table 3.1) and stage 5 is presented in chapter 4.

## 3.3 Methods

### 3.3.1 Stage 1. Generation of quality of life topics

#### 3.3.1.1 Review of issues discussed in colorectal cancer patient consultations

The analysis was performed on a dataset previously collected by the Leeds POCPRG as part of a randomised controlled study which will be referred to as attention control

study (Velikova et al., 2008). The concept of this study arose from the previous randomised controlled study, which demonstrated that patients completing HRQoL questionnaires and feeding back the results from these questionnaires to the oncologists had a positive impact on patient well-being (Velikova et al., 2004). This study also demonstrated a trend for improved patient well-being within the attention control group, where patients completed the HRQoL questionnaires but the results were not feedback to the oncologists. The attention control study was conducted to further explore whether completing of HRQoL questionnaire alone had an impact on patients' well being. The patients were randomised to either the intervention group (completion of HRQoL questionnaires with no feedback to the oncologists) or control group (standard care). The two main outcomes of the study were patient well being and patient-doctor communication. A summary of the key elements of this study is shown in Table 3.2.

**Table 3.2 Summary of attention control study**

<table>
<tr><td>Study sample</td><td colspan="2">Patients with various cancer diagnoses<br>Commencing chemotherapy treatment and expected to attend at least three more times</td></tr>
<tr><td>Study setting</td><td colspan="2">Out-patient clinics in Leeds cancer centre and two district general hospitals in Yorkshire</td></tr>
<tr><td>Study design</td><td colspan="2">Randomised controlled trial with two arms:<br>Intervention arm (completion of HRQoL questionnaire, EORTC QLQ-C30, prior to each out-patient consultation)<br>Control arm (standard care)</td></tr>
<tr><td rowspan="2">Study measures</td><td colspan="2">Audio-recording of consultations</td></tr>
<tr><td>Patients:<br>FACT-G questionnaire<br>Preferences and perceptions of communication (PPC) questionnaire<br>Demographics</td><td>Doctors:<br>Preferences and perceptions of communication (PPC) questionnaire<br>Demographics</td></tr>
</table>

The results of the HRQoL questionnaires completed by the patients were not fed back to the doctors within this study, which may have had an impact on the content of the consultation discussion. The audio-recordings collected from the study were subjected to content analysis. This was performed by the members of the Leeds POCPRG,

using a study specific proforma that was devised in analysing the consultations. One of the key areas of this content analysis was investigating the topics or issues raised during the clinic consultations and the person initiating the subject (patient/relative or doctors). The content analysis proforma mapped onto the symptoms and quality of life domains of the questionnaire used within the study (EORTC QLQ-C30). Any other issues or symptoms raised which were outside of the questionnaire domains were also noted.

Review of the topics discussed in out-patient chemotherapy review consultations for colorectal cancer patients was considered a helpful starting point in the development of the questionnaire. This part of the study was assisted by Dr Sally Taylor, a member of the Leeds POCPRG, who was involved with the analysis of the attention control study, who was very familiar with the study database.

#### 3.3.1.2 Literature review

In order to explore HRQoL issues concerning patients with colorectal cancer, a literature search was performed. The literature search was conducted in PubMed using Medical Subject Headings (MeSH). The search terms used were “Intestinal Neoplasm” AND “Quality of Life” AND “Questionnaires”. References published up to end of 2012 were included. Non English references were removed. References concerning patients only with inflammatory bowel disease and those concerning genetic screening of hereditary condition increasing the risk of developing bowel cancer were also removed. Generated references were reviewed to see whether the study involved administration of patient self reported questionnaire in colorectal cancer patients. List of questionnaires was complied and reviewed to explore relevant issues for colorectal cancer patient population.

Comparing topics of discussion from consultation and HRQoL questionnaire items
The topics of discussions identified from the analysis of clinic consultation audio-recordings were tabulated. The questionnaires identified from the review of the literature were examined to see how well each of the questionnaires covered the topics identified from the clinic consultations and to see if there was a suitable existing questionnaire which covered these issues adequately. Review of the existing questionnaires also helped to identify any important or relevant issues which may not have been raised in the clinic consultations.

### 3.3.2 Stage 2. Construction of item list

Items from existing HRQoL questionnaires were mapped onto the topics identified from the clinic consultation analysis. Access to the items from EORTC Item Bank (Bottomley et al., 2002) was granted following request submitted by Prof Velikova. These items were used to augment any issues/topics which were not adequately addressed by items from questionnaires derived from above literature review. EORTC Item Bank holds many well validated items which have been tested by large patient population. Access to this resource helped to bridge any perceived gaps in the coverage of topics by existing instruments, resulting in the formation of a comprehensive list of items to be put forward towards the final questionnaire. Original response options were maintained for each item depending on the questionnaire they had originated from. Majority had Likert responses with four response options, ranging from “not at all” to “very much”.

Previous focus group feedback from patients and oncologists (Velikova et al., 2007a) have indicated the need for questionnaire items to encompass issues concerning functional impact of cancer. This included impact on patients’ daily activities, family life and sexuality. Items encompassing these topics were also sought from the EORTC item bank if these were not already covered by the existing questionnaires.

### 3.3.3 Stage 3. Interview with healthcare professionals

The aims of the interview with the healthcare professional were 1) to evaluate which of the items they considered useful as part of patient assessment in routine clinic review of patients, 2) to ensure the breadth of coverage of relevant topics and 3) to check the wording of items and to remove any overlapping items. The list of items was grouped into a number of sections. First section consisted of items concerning patients’ physical functioning, second section focused on symptoms and third section consisted on items addressing psychosocial issues. The list of items presented to the healthcare professionals is presented in Appendix 1.

### 3.3.3.1 Study sample and procedure

A list of oncologists working in Leeds Cancer Centre, specialising in the treatment of patients with colorectal cancer was compiled. All relevant consultant medical oncologists and their specialist registrars, and consultant clinical oncologists who treated colorectal cancer patients with chemotherapy were approached by an invitation letter. Arrangements were then made for the interview to take place at a convenient time for the oncologists. Clinical nurse specialists for bowel cancer patients are based in the surgical department and are not directly involved in oncology out-patient clinics at Leeds Cancer Centre. Therefore, the interviews were conducted only with doctors. Interviews were carried out by two researchers, so that one of the two researchers was able to make notes during the interview.

### 3.3.3.2 Data collection

The interviews were semi-structured according to a predefined interview schedule prepared around the questionnaire items. All questionnaire items were presented on paper. Firstly, oncologists were asked to comment about the physical functioning items and asked for their preference out of number of items listed. The oncologists were then asked to review the items in the questionnaire and to provide their rating on whether they considered each of the items “useful”, “somewhat useful” or “not useful” in the assessment of patients undergoing chemotherapy treatment in their clinics. For the purpose of the analysis, the ratings were scored 1-3, with 1 indicating “not useful”. They were asked to comment the reasoning behind their rating selection. The interview was audio-recorded and relevant sections were later transcribed.

### 3.3.3.3 Analysis

Rating provided by the oncologists for the questionnaire items were analysed using descriptive statistics. This helped to illustrate their level of endorsement for each item. This assisted with decisions about removal of items. Any discussions around items concerning psychosocial issues were transcribed verbatim from the audio-recordings of the interviews and analysed qualitatively using thematic analysis

### 3.3.4 Stage 4. Interview with patients

3.3.4.1 Study sample and procedure

The aims of the interviews with patients were 1) to address any administrative problems with the questionnaire, 2) to ensure items in the questionnaire were relevant to their experience and 3) to check clarity of wording. Interviews with patients not only served the purpose of the pre-testing of the questionnaire as described in the EORTC questionnaire development guidelines, but also provided opportunities for them to suggest any additional issues not already addressed in the item list presented to them. Eligible patients were those with advanced colorectal cancer, attending oncology out-patient clinics at Leeds Cancer Centre, undergoing chemotherapy treatment. Patients were purposively selected to ensure both gender were represented and to encompass patients on different chemotherapy treatment which may have different toxicity profiles.

The plan was to interview around 10 patients as suggested by the EORTC guidelines (Johnson et al., 2011) for this stage of the questionnaire development. The study was approved by the NHS Ethics Committee and written informed consent was obtained from all participating patients.

All consenting patients were interviewed on the days when they were scheduled to attend the hospital in order to minimize additional visits.

3.3.4.2 Data Collection

Interviews conducted were semi-structured using a predefined interview schedule prepared around the questionnaire items. All participating patients were initially asked to complete the questionnaire items on touch screen computer and respond to the questions according to their own experience. The questionnaire was uploaded and accessed through the Patient Pathway Manager (PPM), an electronic notes system used in the Leeds Cancer Centre. PPM has a research management module which allows recording of patient involvement in research studies within the oncology department. The questionnaire was devised so that patients did not have the option to return to the previous questions; therefore they were unable to change their response once entered.

Any issues regarding the use of touch screen was noted. Following completion of the questionnaire, patients were asked to comment about the questionnaire items and any issues concerning wording of the items using paper copies of the questionnaire they had just completed. They were also asked to provide suggestions for any issues not included in the questionnaire. All interviews were audio-recorded and later transcribed verbatim.

#### 3.3.4.3 Analysis

The scores derived from the completion of the questionnaire items were analysed using descriptive statistics. Majority of the questionnaire items had a Likert response, with four response options ranging from “not at all”, “a little”, “quite a bit” to “very much” scoring 1-4 respectively. Items with different response options were analysed individually. This provided indication as to the prevalence of the issue questioned and severity of any problems experienced by the study participants. A symptom/issue was considered to be present if the patient had responded to anything other than “not at all” or equivalent response. The results from the quantitative analysis were later used to assist decisions regarding item removal.

The interview transcripts were analysed qualitatively using thematic analysis to explore patients’ views on the questionnaire items, particularly in relation to their own experiences.

## 3.4 Results

### 3.4.1 Review of issues discussed in colorectal cancer patient consultations

17 patients with colorectal cancer took part in the attention control study. 12 patients (70.6%) were men and 5 patients (29.4%) were women with median age of 67 years (range 47 – 86 years). 15 patients (88.2%) were receiving palliative chemotherapy for metastatic or locally advanced colorectal cancer, whereas 2 patients (11.8%) were receiving adjuvant chemotherapy following surgical resection of high risk colorectal cancer. 9 patients (53%) were receiving oral single agent Capecitabine and 4 patients

(24%) were receiving combination chemotherapy with either Oxaliplatin or Irinotecan with 5-Fluorouracil and folinic acid.

There were total of 68 clinic consultations involving these 17 patients. Data from all 68 consultations was utilized in order to take full advantage of this valuable consultation data. The topics or issues raised during the consultation are listed in Table 3.3 in the order of frequency of discussion. Similar issues were grouped together, for example discussion of “weight” encompassed all discussions about weight including weight gain and loss.

**Table 3.3 Topics raised in oncology consultations**

| | Topic raised in consultation | Frequency | % |
|---|---|---|---|
| 1 | Overall functioning | 62 | 91.2 |
| 2 | Bowel function | 47 | 69.1 |
| 3 | Fatigue | 40 | 58.8 |
| 4 | Nausea | 33 | 48.5 |
| 5 | Pain | 33 | 48.5 |
| 6 | Social functioning | 33 | 48.5 |
| 7 | Sore mouth/tongue/ulcers | 29 | 42.6 |
| 8 | Appetite | 26 | 38.2 |
| 9 | Neuropathy | 22 | 32.4 |
| 10 | Infection - cough/catarrh/cold | 22 | 32.4 |
| 11 | Physical functioning | 20 | 29.4 |
| 12 | Sore hands | 19 | 27.9 |
| 13 | Skin - rash/dry/sore | 18 | 26.5 |
| 14 | Weight | 16 | 23.5 |
| 15 | Role functioning | 15 | 22.1 |
| 16 | Emotional functioning | 10 | 14.7 |
| 17 | Sleep | 8 | 11.8 |
| 18 | Stomach - bloated/upset | 8 | 11.8 |
| 19 | Dyspnoea | 7 | 10.3 |
| 20 | Sore eyes/watery eyes | 7 | 10.3 |
| 21 | Finance | 6 | 8.8 |
| 22 | Hair loss | 5 | 7.4 |
| 23 | Indigestion | 5 | 7.4 |
| 24 | Taste | 4 | 5.9 |
| 25 | Voice | 4 | 5.9 |
| 26 | Dizziness | 4 | 5.9 |
| 27 | Nose | 4 | 5.9 |
| 28 | Swallowing | 3 | 4.4 |
| 29 | Swollen legs/feet | 3 | 4.4 |

| | | | |
|---|---|---|---|
| 30 | Rectal bleeding | 3 | 4.4 |
| 31 | Temperature - feeling hot/cold | 3 | 4.4 |
| 32 | Throat issues | 3 | 4.4 |
| 33 | Cognitive functioning | 2 | 2.9 |
| 34 | Bleeding - general | 2 | 2.9 |
| 35 | Headache | 2 | 2.9 |
| 36 | Feet problems | 2 | 2.9 |
| 37 | Bladder function | 2 | 2.9 |
| 38 | Haemorrhoids | 2 | 2.9 |
| 39 | Rectal discharge | 1 | 1.5 |
| 40 | Genital discharge | 1 | 1.5 |
| 41 | Flatulence | 1 | 1.5 |
| 42 | Drinking | 1 | 1.5 |
| 43 | Chest tightness | 1 | 1.5 |

### 3.4.2 Literature review

The literature search returned 211 references. There were 24 non English references which were excluded from review. Further 24 references were removed as these specifically concerned patients with inflammatory bowel disease or they were concerned about genetic screening. Of the remaining 163 references, 42 specifically involved patients with rectal carcinoma, majority of these addressing the impact of surgical intervention for the disease. There were total of 34 questionnaires used in these references, which included a variety of questionnaires; some assessing general quality of life issues but others specifically focusing on a particular function such as continence. 64 references utilized the EORTC QLQ-C30 (Aaronson et al., 1993) together with EORTC QLQ-CR38 (Sprangers et al., 1999) as their quality of life instruments. They were by far the most commonly utilized instruments.

There were seven colorectal cancer specific questionnaires or questionnaires relevant to patients with colorectal cancer. These instruments were:

1. EORTC QLQ-CR38 (Sprangers et al., 1999)
2. EORTC QLQ-CR29 (Whistance et al., 2009)
3. FACT-C (Ward et al., 1999)
4. EORTC QLQ-LMC21 (Blazeby et al., 2009)
5. City of Hope Quality of Life – Ostomy (Grant et al., 2004)
6. Stoma Quality of Life Scale (Baxter et al., 2006)
7. Gastrointestinal Quality of Life Index (GIQLI) (Eypasch et al., 1995)

The items from these questionnaires were compared to the list of symptoms/issues raised during the routine clinic consultations as described above. City of Hope Quality of Life – Ostomy and Stoma Quality of Life Scale was excluded from this part of the analysis as the questions within these questionnaires were specifically in relation to patients having a stoma.

Table 3.4 lists the symptoms and issues discussed in routine clinic consultations and explores which questionnaires had the best coverage of these issues.
The combination of EORTC QLQ-C30 the disease specific modules provided the best coverage. EORTC QLQ-C30 plus QLQ-CR38, QLQ-CR29 and QLQ-LMC21 covered 21, 22 and 17 symptoms/issues respectively. There were some differences in the issues covered across these questionnaires but overall, EORTC QLQ-C30 plus above three modules covered 24 symptoms/issues. Table 3.4 illustrates how well the instruments covered the topics identified from consultation analysis. Therefore, it was felt that the EORTC instruments were most suited to be used as the core structure for the development of the colorectal cancer specific questionnaire, QuEST–Cr.

**Table 3.4 Comparison between topics raised in 68 oncology consultations and topics covered in existing questionnaires**

| Topic raised in consultation | Freq | (%) | QLQ-C30 +CR38 | QLQ-C30 +CR29 | QLQ-C30 +LMC21 | FACT-C | GIQLI |
|---|---|---|---|---|---|---|---|
| Overall functioning | 62 | (91.2) | x | x | x | x | x |
| Bowel function | 47 | (69.1) | x | x | x | x | x |
| Fatigue | 40 | (58.8) | x | x | x | x | x |
| Nausea | 33 | (48.5) | x | x | x | x | x |
| Pain | 33 | (48.5) | x | x | x | x | |
| Social functioning | 33 | (48.5) | x | x | x | x | x |
| Sore mouth/tongue/ulcers | 29 | (42.6) | | | x | | |
| Appetite | 26 | (38.2) | x | x | x | x | x |
| Neuropathy | 22 | (32.4) | | | x | | |
| Infection - cough/catarrh/cold | 22 | (32.4) | | | | | |
| Physical functioning | 20 | (29.4) | x | x | x | x | x |
| Sore hands | 19 | (27.9) | | | | | |
| Skin - rash/dry/sore | 18 | (26.5) | | | | | |
| Weight | 16 | (23.5) | x | x | x | x | |
| Role functioning | 15 | (22.1) | x | x | x | x | |
| Emotional functioning | 10 | (14.7) | x | x | x | x | x |
| sleep | 8 | (11.8) | x | x | x | x | |
| Stomach - bloated/upset | 8 | (11.8) | x | x | | x | x |
| Dyspnoea | 7 | (10.3) | x | x | x | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| sore eyes/watery eyes | 7 | (10.3) | | | | | |
| Finance | 6 | (8.8) | x | x | x | | |
| hair loss | 5 | (7.4) | x | x | | | |
| Indigestion | 5 | (7.4) | | | | | x |
| Taste | 4 | (5.9) | x | x | | | |
| Voice | 4 | (5.9) | | | | | |
| Dizziness | 4 | (5.9) | | | | | |
| Nose | 4 | (5.9) | | | | | |
| Swallowing | 3 | (4.4) | | | | | x |
| Swollen legs/feet | 3 | (4.4) | | | | | |
| Rectal bleeding | 3 | (4.4) | x | x | | | x |
| Temperature - feeling hot/cold | 3 | (4.4) | | | | | |
| Throat issues | 3 | (4.4) | | | | | |
| Cognitive functioning | 2 | (2.9) | x | x | x | | |
| Bleeding - general | 2 | (2.9) | | | | | |
| Headache | 2 | (2.9) | | | | | |
| Feet problems | 2 | (2.9) | | | | | |
| Bladder function | 2 | (2.9) | x | x | | | |
| piles | 2 | (2.9) | | | | | |
| rectal discharge | 1 | (1.5) | | x | | | |
| Genital discharge | 1 | (1.5) | | | | | |
| flatulence | 1 | (1.5) | x | x | | | x |
| drinking | 1 | (1.5) | | | | | |
| chest tightness | 1 | (1.5) | | | | | |
| Total number of topics covered | | | 21 | 22 | 17 | 13 | 13 |

### 3.4.3 Construction of the item list

The questionnaires identified from the literature review included important topics which were not raised during the routine consultations analysed above. As the aim of the colorectal cancer specific questionnaire was to raise any issues that patients may be having problems with, it was felt that these issues needed to be addressed.

#### 3.4.3.1 Stoma function

Some patients with colorectal cancer may have undergone an operation which may have resulted in a formation of a stoma. Having a stoma can have an impact on the life of a patient in a number of ways (Brown and Randle, 2005). Patients often require both psychological and social adjustments following a formation of a stoma (Brown and Randle, 2005). Although stoma function or issues were not raised in the content

analysis of the consultations, it was felt important that this topic was included in the colorectal cancer questionnaire, QuEST-Cr.

There were several questions related to stoma function from the questionnaires examined above. Items from QLQ-CR38, QLQ-CR29 and FACT-C were included in the list of items for review in the interview study. In addition to the questionnaires identified in the literature review, the comprehensive health assessment (CHA) questionnaires from Medical Research Council (MRC) FOCUS 2 Trial (Seymour et al., 2011) were reviewed. This study specifically looked at efficacy of modified dose palliative chemotherapy for patients with advanced colorectal cancer. This study specifically involved patients who were older and had borderline performance status. The CHA within this trial consisted on a number of questionnaires including Mini Mental Test examination (Folstein et al., 1975), Charlson Co-Morbidity Index (Charlson et al., 1987), EQ5D (EuroQoL Group, 1990), Nottingham Extended Activities of Daily Living Scale (Nouri and Lincoln, 1987) and some items from EORTC QLQ-C30. The authors had added their own stoma related questions and these were also included in the item list for review in the interview study. Questionnaires specifically looking at stoma related quality of life (City of Hope Quality of Life – Ostomy (Grant et al., 2004) and Stoma Quality of Life Scale (Baxter et al., 2006)) were considered too detailed to be included in QuEST-Cr.

#### 3.4.3.2 Sexual functioning and body image

Treatment of colorectal cancer may involve a combination of surgery, radiotherapy and chemotherapy. Treatment for rectal cancer patients in particular, often involves a type of surgery which may result in a formation of temporary or permanent stoma. Additional treatment with radiotherapy in combination with surgery may have a significant impact on patients' bowel, bladder and sexual functioning (Sprangers et al., 1995, Reese et al., 2014, Ho et al., 2011). Despite this, sexual dysfunction remains understudied and often not discussed in clinic consultations (Flynn et al., 2012). Body image disturbance may be an issue, particularly for those patients with a stoma. Presence of body image disturbance may be linked to higher prevalence of anxiety and depression among such patients (Sharpe et al., 2011).

All of the colorectal cancer specific questionnaires identified from the review of literature included questions on sexual functioning. QLQ-CR38, QLQ-CR29, FACT-C

and the two stoma specific questionnaires contained items concerning body image. As I had chosen to use the EORTC questionnaires as my core list of questionnaire items, I decided to retain the relevant items from the EORTC modules regarding these topics.

### 3.4.3.3 Physical functioning

Physical function is a topic covered in many questionnaires identified in the review of literature. It is one of the most commonly discussed functions in the oncology consultations as it can provide an indication as to how the patient may be responding to treatment, which may in turn have an impact on decisions about investigations and treatment.

Physical function has been defined as “the performance of or capability to perform a variety of physical activities normal for people in good health” (Stewart and Kamberg, 1992). This encompasses activities of daily living (ADL) and instrumental activities of daily living (IADL). ADL are basic tasks that we normally do such as self care, feeding ourselves and walking. IADL are tasks which allow a person to live independently such as preparing meals, house work, managing money and shopping.

World Health Organization (WHO) performance status is commonly used within clinical trials to describe the characteristics of patients’ physical ability and oncologists often use this as a surrogate measure of patients’ physical functioning in routine clinical practice. Definition of WHO performance status is shown in Table 3.5. Karnofsky Performance Status Scale (Karnofsky, 1949) is another measure used by the clinicians to rate patients physical ability. This scale is used less frequently compared to the WHO performance status but it also describes the patients’ physical ability using a 0-100 scale; 100 indicating the best possible physical ability.

**Table 3.5 WHO Performance Status**

| Grade | Explanation of activity |
|---|---|
| 0 | Fully active, able to carry on all pre-disease performance without restriction |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work |
| 2 | Ambulatory and capable of all self-care but unable to carry out any work activities. 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 any self-care. Totally confined to bed or chair |
| 5 | Dead |

As indicated in the review of literature, EORTC QLQ-C30 is one of the most commonly used HRQoL questionnaire used in oncology setting. In the previous focus group study (Velikova et al., 2007a), oncologists made suggestions that physical functioning and other items within the QLQ-C30 could be made more useful for use in clinical practice so that patients could rate their physical function in the way that would match with oncologists' assessments such as the WHO performance status. With this suggestion in mind, the WHO performance status was adapted into patient self report format to be presented to the oncologists for their view.

Physical function assessments are included in many HRQoL instruments. Rotterdam Symptom Checklist (RSCL) (de Haes et al., 1990) is another HRQoL instrument developed for assessment of QoL in cancer patients. This instrument also contains a physical function scale which encompasses activities of daily living (ADL) and instrumental activities of daily living (IADL) tasks. Unlike the EORTC QLQ-C30, RSCL items cover IADL tasks well such as patients' ability of perform housework and shopping. It was decided to retain physical function items from RSCL as well as those from the EORTC QLQ-C30 and the WHO performance status in patient self report format to be presented to the oncologists for review. They were separated from other functions and symptoms to specifically draw oncologists' attention during the interview. These three physical function items were presented to healthcare professionals as part of the questionnaire development plan across the three cancer sites within the wider research programme.

3.4.3.4 Other issues

There were several symptoms related to chemotherapy toxicities which were not covered by the existing questionnaires. These were “Infection”,” Sore hands”,” skin problems”,” sore eyes” and “indigestion”. Questionnaire items relating to these symptoms were identified from the EORTC Quality of Life Group Item Bank (Bottomley et al., 2002) and also from FOCUS 2 Comprehensive Health Assessment questionnaires (Seymour et al., 2011).

Chemotherapy treatment can cause lowering of the white blood cells which can make patients vulnerable to infection. Therefore, an additional item was created specifically asking whether the patient had experienced an infection episode.

Whilst discussing the items for consideration for the QuEST questionnaires with other researchers as part of the wider research programme, additional items were included from the EORTC Item Bank (Bottomley et al., 2002) concerning impact of the cancer treatments and patients’ future perspectives.

The resulting item list is shown below (Table 3.6) with details of where the items have originated from. This list of questionnaire items was taken forward for the interview with the oncologists. The first section consisted of physical function scales from EORTC QLQ-C30, Rotterdam Symptom Checklist (RSCL) and WHO performance status in patient self report format. This was followed by items concerning toxicities of treatment or disease related symptoms, which also included stoma related items from EORTC QLQ-CR38, QLQ-CR29, FACT-C and FOCUS 2 for comments from the oncologists. Next section consisted of items concerning psychosocial issues and functioning.

**Table 3.6 QuEST-Cr items and their origin (Full names of questionnaires with their references are presented in Appendix 2)**

| Item | Source |
|---|---|
| *Physical Function* | |
| Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? | QLQ-C30 |
| Do you have any trouble taking a long walk? | QLQ-C30 |
| Do you have any trouble taking a short walk outside of the house? | QLQ-C30 |
| Do you need to stay in bed or a chair during the day? | QLQ-C30 |
| Do you need help with eating, dressing, washing yourself or using the toilet? | QLQ-C30 |
| A number of activities are listed below. We do not want to know whether you actually do these, but only whether you are able to perform them presently. Would you please mark the answer that applies most to your condition of the past week?<br><br>Care for myself<br>Walk about the house<br>Light housework/household jobs<br>Climb stairs<br>Heavy housework/household jobs<br>Walk out of doors<br>Go shopping<br>Go to work | RSCL |
| Please select one of the following items that best describes your current level of physical ability<br><br>0 - I am fully active and more or less as I was before my illness<br>1 – I cannot carry out heavy physical work, but can do anything else<br>2 – I am up and about more than half the day; I can look after myself, but not well enough to work<br>3 – I am in bed or sitting in a chair for more than half the day; I need some help in self care<br>4 – I am in bed or a chair all the time and need a lot of looking after | WHO PS (adapted from CRUK Cancer Help website) |
| *Infection* | |
| Have you had any infection since your last cycle of chemotherapy? | New |
| Have you been bothered by fevers or chills? | QLQ-HDC29 |
| *Chemotherapy toxicity/disease related symptoms* | |
| Have you had sore mouth or tongue? | QLQ-LMC21 |
| Have you had dry mouth? | QLQ-CR29 |
| Have you had problems with sense of taste? | QLQ-CR29 |
| Did food and drink taste different from usual? | QLQ-CR38 |
| Have you lacked appetite? | QLQ-C30 |
| Have you had trouble with eating? | QLQ-LMC21 |
| Have you felt full up too quickly after beginning to eat? | QLQ-LMC21 |
| Have you worried about losing weight? | QLQ-LMC21 |
| Have you had indigestion or heartburn? | QLQ-OV28 |
| Have you felt nauseated? | QLQ-C30 |
| Have you vomited? | QLQ-C30 |
| Have you been constipated? | QLQ-C30 |
| Did you have bloated feeling in your abdomen? | QLQ-CR29 |
| Were you troubled by passing wind/gas/flatulence? | QLQ-OV28 |
| Have you had diarrhoea? | QLQ-C30 |
| Have you blood in your stools? | QLQ-CR29 |
| Have you had mucus in your stools? | QLQ-CR29 |
| Have your skin or eyes been yellow (jaundiced)? | QLQ-LMC21 |
| Have you had soreness or redness of your hands or feet? | FOCUS2 |
| Have you had any other skin problems (e.g. itching, dryness, sensitivity to sun)? | QLQ-OV28 |
| Have you had tingling or numbness in your hands or feet? | QLQ-CR29 modified |
| Are you concerned by any changes in your hearing? | QLQ-OV28 modified |
| Have you lost your hair as a result of your treatment? | QLQ-CR29 |
| Have you been upset by hair loss? | QLQ-OV28 |

| | |
|---|---|
| *Stoma* | |
| Do you have a stoma?<br>☐ Yes ☐ No<br><br>If yes, have you had any problems with it (for example soreness of skin, increased frequency, leakage)? | FOCUS2 |
| Do you have a stoma?<br>☐ Yes ☐ No<br><br><u>Only for patients WITHOUT a stoma</u><br>Did you have frequent bowel movements during the day?<br>Did you have frequent bowel movements during the night?<br>Did you feel the urge to move your bowel movements without actually producing any stools?<br>Have you had any unintentional release of stools?<br>Have you had any blood in your stools?<br>Have you had any difficulty in moving your stools?<br>Have your bowel movements been painful?<br><br><u>Only for patients WITH a stoma</u><br>Were you afraid that other people would be able to hear your stoma?<br>Were you afraid that other people would be able to smell your stoma?<br>Were you worried about possible leakage from the stoma?<br>Did you have problems caring for your stoma?<br>Was your skin around the stoma irritated?<br>Did you feel embarrassed because of your stoma?<br>Did you feel less complete because of your stoma? | QLQ-CR38 |
| Do you have a stoma bag (colostomy/ ileostomy)? Please circle the correct answer.<br>☐ Yes ☐ No<br><br>Answer these questions ONLY IF YOU HAVE A STOMA BAG<br>Have you had unintentional release of gas/flatulence from your stoma bag?<br>Have you had leakage of stools from your stoma bag?<br>Have you had sore skin around your stoma?<br>Did frequent bag change occur during the day?<br>Did frequent bag change occur during the night?<br>Did you feel embarrassed because of your stoma?<br>Did you have problems caring for your stoma?<br><br>Answer these questions ONLY IF YOU DO NOT HAVE A STOMA BAG<br>Have you had unintentional release of gas/flatulence from your back passage?<br>Have you had leakage of stools from your back passage?<br>Have you had sore skin around your anal area?<br>Did frequent bowel movements occur during the day?<br>Did frequent bowel movements occur during the night?<br>Did you feel embarrassed because of your bowel movement? | QLQ-CR29 |
| Do you have an ostomy appliance?<br>☐ Yes ☐ No<br><br>If yes, please answer the next two items:<br>I am embarrassed by my ostomy appliance<br><br>Caring for my ostomy appliance is difficult | FACT-C |
| *Fatigue* | |
| Have you had trouble sleeping? | QLQ-C30 |
| Did you need to rest? | QLQ-C30 |
| Have you felt weak? | QLQ-C30 |
| Were you tired? | QLQ-C30 |
| Have you been less active than you would like to be? | QLQ-LMC21 |
| Have you felt slowed down? | QLQ-LMC21 |
| Have you felt lacking in energy? | QLQ-LMC21 |
| *Pain* | |
| Have you had pain? | QLQ-C30 |
| Did pain interfere with your daily activities? | QLQ-C30 |
| Did you have abdominal pain? | QLQ-CR29 |

| | |
|---|---|
| Have you had pain in your stomach area? | QLQ-LMC21 |
| Have you had discomfort in your stomach area? | QLQ-LMC21 |
| Did you have pain in your buttocks/anal area/rectum? | QLQ-CR29 |
| Have you had pain in your back? | QLQ-LMC21 |
| *Bladder function* | |
| Did you urinate frequently during the day? | QLQ-CR29 |
| Did you urinate frequently during the night? | QLQ-CR29 |
| Have you had any unintentional release (leakage) of urine? | QLQ-CR29 |
| Did you have pain when you urinated? | QLQ-CR29 |
| *Others* | |
| Were you short of breath? | QLQ-C30 |
| Were your eyes painful, irritated or watery? | QLQ-Br23 |
| Did you feel ill or unwell? | QLQ-Br23 |
| *Emotional/Cognitive Function* | |
| Have you had difficulty in concentrating on things, like reading the newspaper or watching television? | QLQ-C30 |
| Did you feel tense? | QLQ-C30 |
| Did you worry? | QLQ-C30 |
| Did you feel irritable? | QLQ-C30 |
| Did you feel depressed? | QLQ-C30 |
| Have you had difficulty remembering things? | QLQ-C30 |
| Have you had trouble talking about your feelings to your family and friends? | QLQ-LMC21 |
| Have you felt stressed? | QLQ-LMC21 |
| Have you felt less able to enjoy yourself? | QLQ-LMC21 |
| *Body Image* | |
| Have you felt physically less attractive as a result of your disease or your treatment? | QLQ-CR29 |
| Have you been feeling less feminine/masculine as a result of your disease or your treatment? | QLQ-CR29 |
| Have you been dissatisfied with your body? | QLQ-CR29 |
| *Sexual Function* | |
| Has the disease or treatment affected your sex life (for the worse)? | QLQ-LMC21 |
| To what extent were you interested in sex? (Men) | QLQ-CR29 |
| Did you have difficulty getting or maintaining an erection? (Men) | QLQ-CR29 |
| To what extent were you interested in sex? (Women) | QLQ-CR29 |
| Did you have pain or discomfort during intercourse? (Women) | QLQ-CR29 |
| *Coping and Future Perspectives* | |
| How much has your disease been a burden to you? | QLQ-OV28 |
| How much has your treatment been a burden to you? | QLQ-OV28 |
| How much has your chemotherapy treatment interfered with your normal daily activities? | FOCUS2 |
| Have you worried about your health in the future? | QLQ-LMC21 |
| Were your worried about your family in the future? | QLQ-LMC21 |
| Did you feel uncertain about the future? | QLQ-BN20 |
| Were the side effects of treatment worse than you expected? | QLQ-HDC45 |
| Were you concerned about disruption of family life? | QLQ-BN20 |
| *Role and Social Function* | |
| Were you limited in doing either your work or other daily activities? | QLQ-C30 |
| Were you limited in pursuing your hobbies or other leisure time activities? | QLQ-C30 |
| Has your physical condition or medical treatment interfered with your family life? | QLQ-C30 |
| Has your physical condition or medical treatment interfered with your social life? | QLQ-C30 |
| Has your physical condition or medical treatment caused you financial difficulties? | QLQ-C30 |
| Have you had trouble having social contact with friends? | QLQ-LMC21 |
| *Treatment Worth* | |
| Since you started chemotherapy, how worthwhile do you think your treatment has been? | FOCUS2 |

Three physical function scales, four sets of stoma related items and 79 items encompassing symptoms and various functions were presented to the oncologists for review.

### 3.4.4 Interview with healthcare professionals

7 oncologists participated in the study. (Male=5). 4 were consultants and 3 were specialist registrars. As the target population for this questionnaire is patients with advanced colorectal cancer, receiving palliative chemotherapy, the interviews were conducted predominantly with Medical Oncologists who normally treat such cases in Leeds. However, one Clinical (or Radiation) Oncologist was invited to participate as her practice provides palliative chemotherapy for significant number of patients with advanced colorectal cancer. The median age of oncologists interviewed was 37 years (range 29–47 years) with varied length of experience in oncology practice (mean 9.6 years; range 2–18 years).

All oncologists were presented with the above list of questionnaire items on paper and asked to rate individual questionnaire item according to how useful they would find the responses from the questionnaire items in routine clinical practice. They had three response options, “not useful”, “somewhat useful” and “useful”

It was apparent that oncologists were able to provide rating for many of the symptom related questions with relative ease. However, regarding items concerning psychosocial issues, they often preferred to describe their thoughts and views about these issues rather than providing a rating as such.

#### 3.4.4.1 Physical function

All oncologists felt that the items in this section were simple for their patients to respond to. They were asked to choose their preference between EORTC QLQ-C30 and RSCL items; 4 preferred EORTC QLQ-C30 items and 3 preferred the RSCL items. One of the doctors commented that the QLQ-C30 items mirrored the WHO performance status to some extent. Doctors who preferred the RSCL commented that the activities listed were more relevant to their patients. Two of the doctors commented on the preamble of the RSCL, which asks patients whether they are able to carry out the tasks listed rather than whether they actually perform them. They felt that this may add a layer of complexity for the patients when they respond. In addition, they also commented that most of their patients are retired and “go to work” was irrelevant for their patients. Most of the doctors felt that WHO performance status would be a useful

addition to the physical function scale although some commented that this should be documented in the notes routinely anyway.

*Decisions made following the interview*

All three physical function scales were retained for review by the patients. RSCL preamble was removed and each task was made into a question format. For example, “Care for myself” was changed to “Are you able to care for yourself?”

3.4.4.2 Chemotherapy toxicities and disease related symptoms

There were 47 items in this section of the item list, covering treatment side effects and disease related symptoms. The highly endorsed items were those relating to chemotherapy toxicities; sore mouth, nausea, vomiting, bowel function, sensory neuropathy, hand foot syndrome, pain and eye problems. Table 3.7 lists the items in the order of oncologists’ endorsement as indicated by the mean score derived from their rating.

**Table 3.7 Oncologist rating of colorectal cancer symptom items sorted by mean rating**

| Symptoms | mean |
|---|---|
| 1. Have you had sore mouth or tongue? | 3.00 |
| 2. Have you felt nauseated? | 3.00 |
| 3. Have you vomited? | 3.00 |
| 4. Have you been constipated? | 3.00 |
| 5. Have you had diarrhoea? | 3.00 |
| 6. Have you had soreness or redness of your hands or feet? | 3.00 |
| 7. Have you had tingling or numbness in your hands or feet? | 3.00 |
| 8. Have you had pain? | 3.00 |
| 9. Were your eyes painful, irritated or watery? | 3.00 |
| 10. Have you had indigestion or heartburn? | 2.86 |
| 11. Did food and drink taste different from usual? | 2.71 |
| 12. Have you lacked appetite? | 2.71 |
| 13. Have you had trouble sleeping? | 2.71 |
| 14. Did pain interfere with your daily activities? | 2.71 |
| 15. Have you had any infection since your last cycle of chemotherapy? | 2.57 |
| 16. Were you short of breath? | 2.57 |
| 17. Were you tired? | 2.50 |
| 18. Have you been upset by hair loss? | 2.43 |

| | |
|---|---|
| 19. Did you feel ill or unwell? | 2.43 |
| 20. Have you been less active than you would like to be? | 2.33 |
| 21. Have you been bothered by fevers or chills? | 2.14 |
| 22. Have you worried about losing weight? | 2.14 |
| 23. Did you have bloated feeling in your abdomen? | 2.14 |
| 24. Were you troubled by passing wind/gas/flatulence? | 2.14 |
| 25. Have you blood in your stools? | 2.14 |
| 26. Have you had any other skin problems (e.g. itching, dryness, sensitivity to sun)? | 2.14 |
| 27. Did you need to rest? | 2.14 |
| 28. Have you had trouble with eating? | 2.00 |
| 29. Have you felt full up too quickly after beginning to eat? | 2.00 |
| 30. Have you had mucus in your stools? | 2.00 |
| 31. Have you felt weak? | 2.00 |
| 32. Have you felt slowed down? | 2.00 |
| 33. Have you felt lacking in energy? | 2.00 |
| 34. Did you have pain in your buttocks/anal area/rectum? | 2.00 |
| 35. Did you have pain when you urinated? | 2.00 |
| 36. Have you had dry mouth? | 1.86 |
| 37. Have your skin or eyes been yellow (jaundiced)? | 1.86 |
| 38. Are you concerned by any changes in your hearing? | 1.86 |
| 39. Have you had pain in your back? | 1.86 |
| 40. Have you had problems with sense of taste? | 1.71 |
| 41. Did you have abdominal pain? | 1.71 |
| 42. Have you had discomfort in your stomach area? | 1.71 |
| 43. Have you had any unintentional release (leakage) of urine? | 1.71 |
| 44. Have you had pain in your stomach area? | 1.57 |
| 45. Did you urinate frequently during the day? | 1.57 |
| 46. Did you urinate frequently during the night? | 1.57 |
| 47. Have you lost your hair as a result of your treatment? | 1.29 |
| Scoring:1="Not useful", 2="Somewhat useful", 3="useful" | |

Items with oncologists' mean rating score ≤ 2.0 were reviewed. Oncologists felt that pain was an important disease related issue to be raised during the consultation. However, they did not feel that enquiry about the specific sites of pain was necessary as this would be discussed in the consultation. Items directly relating to the primary tumour were considered perhaps less useful such as "blood and mucus in the stool". Items on micturition were considered unnecessary but if the question was to be raised then they suggested reducing to one question. Items such as jaundice and hair loss would be apparent when the doctor sees that patient so these were considered unnecessary. However, impact of hair loss was considered worth asking, although not

many chemotherapy regimens used in the treatment of colorectal cancer caused total hair loss.

Many oncologists agreed that fatigue is important to assess. However, they felt there were too many questions presented covering this topic and recommended item reduction. Infection was important as chemotherapy treatment can cause myelosuppresion making patients vulnerable to potentially serious infection. “Fevers and chills” question was considered non-specific and direct question about infection was thought to be more useful. Asking specifically whether the patient received antibiotics may be helpful in determining the severity of the infection episode. Enquiry about whether the patient has been admitted to hospital during a treatment cycle might be helpful as this may have been due to treatment toxicity. This may have impact on decisions about treatment.

*Decisions made following the interview*

Two items concerning antibiotics and hospital admission were created following comments by the oncologists. Items which scored less than or equal to 2.0 were removed, except for two items concerning “fatigue” and one item concerning “taste” which were retained for patients’ views. Items regarding problems with micturition/ bladder function were replaced by “Have you had any problems with your water works” as suggested by the oncologists. Two items were removed despite oncologists' mean score being >2.0 because of the comments they had made during the interviews (“troubled by wind/gas/flatulence” and “blood in stools”).

3.4.4.3 Stoma questions

Oncologists interviewed estimated that approximately 10-30% of their patients had a stoma. They all acknowledged that having a stoma may have wider implications for patients and that this topic should be covered in the questionnaire. Many considered items from QLQ-CR38 and QLQ-CR29 were too long and burdensome for patients. However, several doctors liked two items from QLQ-CR38; “Did you feel embarrassed because of your stoma?” and “Did you feel less complete because of your stoma?” They felt that these two items captured the body image issues experienced by the patients in relation to the stoma. In addition, some of the oncologists thought “Were you

afraid that other people would be able to smell your stools?" might be a genuine concern for patients. Of the two remaining sets of questions, all of the oncologists interviewed preferred the items from FOCUS2.

*Decisions made following the interview*

The stoma questions from FOCUS2 and the three items described above were retained to take forward to patient interviews.

### 3.4.4.4 Psychosocial issues

Although many oncologists provided some rating for the questions covering psychosocial issues, they provided their broader views about questionnaires raising issues listed in the item list. Audio-recording of this section of the interviews were transcribed verbatim and analysed using qualitative thematic analysis.
The discussions took place around the questionnaire items which were grouped according to the relevant topics such as emotional functioning, body image, sexual functioning and treatment impact on patients' social and role functioning. The key themes that have emerged from the analysis of the interviews were:

- Implications of raising issues through questionnaire
- Oncologists' beliefs about the relevance of questions
- Recommendations for the questionnaire including suggestions for wording/rephrasing of items

### 3.4.4.5 Emotional functioning

*Implications of raising issues through questionnaire*

All oncologists recognised the importance of assessing emotional functioning of their patients. Many welcomed routine assessment although two of the specialist registrars were concerned about how they may respond to a patient whose questionnaire scores indicated significant problems. They stated that they would welcome a specific guidance in managing such patients and having a defined pathway for further assessments by Psycho-Oncology team. One of the registrars stated that he would have a sense of patients' emotional state when you meet them in clinic and from their

general demeanour, particularly if there had been a previous encounter with that patient. He stated that questionnaire scores indicating poor emotional functioning, especially if this is observed repeatedly over time, may help support decisions about formal referral to allied services.

*Oncologists' beliefs about relevance of questions*

Many oncologists were not convinced that their patients may relate to some of the items listed, in particular, many did not like the word "depressed" as they felt that there was a significant stigma attached to this word. Majority felt that their patients would better relate to phrases such as "feeling low in mood".

*Decisions made following the interview*

Following the interview with the oncologists, it was decided to retain the QLQ-C30 emotional function scale so that patients' views can be obtained on these items. Additional items were added to encompass comments made by the oncologists. The MHI-5 (Berwick et al., 1991) is a 5 item measure of emotional distress which has been shown to be a useful screening tool (Cull et al., 2001). The MHI-5 utilizes everyday language such as 'downhearted and low" which may allow patients to better relate to the questions. The MHI-5 items were therefore included in the questionnaire to be presented to the patients in the interviews. In addition, two further items were added. These were "have you been bothered by mood changes?" and "Have you felt tearful?" It was felt that these may also be appropriate and relevant to the patients in describing their emotional state.

3.4.4.6 Cognitive function

*Implications of raising issues through questionnaire*

There were two items addressing patients' cognitive function. Majority of the oncologists liked the question concerning "concentration" as it linked with specific activities "reading the newspaper" or "watching the television". They all felt that patients would be able to relate to this question.

Oncologists generally considered cognitive function assessment to be important although they indicated that colorectal cancer patients are generally older and there may be a number of reasons for why their cognitive function may be impaired. There was a suggestion that perhaps they would not know what to do if the patient had reported poor cognitive functioning.

#### 3.4.4.7 Body Image

*Implications of raising issues through questionnaire*

Oncologist commented that they did not discuss about body image with their patients. They felt that body image is more likely to be a concern when patients are in follow up rather than when they are undergoing chemotherapy treatment when the focus of their clinic attendance would naturally be on managing and supporting patients through treatment. Some of the oncologists felt that there needed a specific referral pathway for patients if a problem was identified as asking the question would raise patients' expectations.

*Oncologists' beliefs about relevance of questions*

Several oncologists commented that many of the colorectal cancer patients are older men and body image issues are not as prevalent as other disease groups such as breast cancer. They felt that "attractive" or "less feminine or masculine" did not really capture body image issues which may be present among this group of patients.

*Recommendations for the questionnaire*

Some of the doctors felt that this topic should ideally be covered in a format where patients can specifically indicate whether they wished to discuss this topic with them. Phrases such as "feeling less complete", "embarrassed" and "disfigured" may be more suitable for this group of patients, particularly for those who have undergone a surgery which may have resulted in a formation of a stoma. It was also suggested that patients should be given the option not to respond to these questions.

*Decisions made following the interview*

The EORTC body image items were retained for discussion with patients. Two items "Feeling less complete" and "embarrassed" were retained as part of the stoma function assessments as described previously. Option to allow patients to skip these questions was implemented for the patient interview stage of the study.

3.4.4.8 Sexual function

*Implications of raising issues through questionnaire*

Many doctors felt that impact on patients' sexual function was an important issue for their patients. Some of the specialist registrars admitted that they would feel embarrassed to raise or discuss the subject unless it was brought up by the patient. Many felt that questionnaire was a good way of raising the topic for discussion. However, many oncologists felt that they were ill equipped in dealing such problems and indicted they would like a clear guidance on how this issue can be managed, although they appreciated that any treatment recommendation would be dependent on the specific problems experienced by the patient.

*Oncologists' beliefs about relevance of questions*

Some oncologists felt that many of their patients are probably not sexually active given the age of the population. In addition, oncologists suspected that their patients would not answer or respond to the questionnaire items concerning sexual function. However, many felt that this was a relevant topic particularly for patients with rectal carcinoma, who may have undergone surgical and/or radiotherapy treatments previously, which may have had significant impact on their sexual function. For those that are sexually active, oncologists felt that the questionnaire items presented were satisfactory.

*Recommendations for the questionnaire*

Oncologists suggested that patient should be given the option not to answer these questions on the touch screen computer. Suggestions were made about having an

opening question enquiring whether the patient had any issues concerning their sexual function and depending on their response this opener, further items may be presented to explore specific concerns. It was considered more helpful if the patient was given the option to indicate whether they specifically wished to discuss this area.

*Decisions made following the interview*

All the sexual function items were retained for review by the patients; however, specific message was inserted on the touch screen computer indicating that patients may skip these items if they did not wish to respond to them.

### 3.4.4.9 Treatment impact on patients' social and role functioning and future perspectives

*Implications of raising issues through questionnaire*

Many oncologists were interested to know about patients' expectations of chemotherapy and whether they had been adequately informed of all the possible toxicities. They also liked the item enquiring about the impact of treatment on patients' "normal daily activities" though this may overlap with the physical function items. They were also interested to know whether patients have found their treatment "worthwhile", despite of all the toxicities and inconvenience associated with their treatment. Some felt that this may assist in making decisions about future treatment for patients, particularly if a patient had equivocal response on radiological evaluation from previous treatments. Item on "finance" was generally well received as this is not a topic often raised in oncology consultations, yet it may have a huge impact on patients' day to day lives. Oncologists felt that referral to a social worker would be straight forward once any financial concerns are identified.

Many oncologists felt the future perspective items were not very helpful, stating that all patients with incurable cancer would be facing uncertainties. In particular the "worry about your future health" was not considered useful. They were unsure how they might handle patients' response to this question but considered this would link with discussions about prognosis.

**Table 3.8 Comments made by oncologists during interviews**

| | |
|---|---|
| **Emotional Function** | |
| Implications of raising issues | *"These are things that I don't know how to deal with"* |
| Relevance of questions | *"(poor emotional functioning) can have a huge impact on how patients cope with their treatment"*<br>*"it's the sort of thing you want to ask every time (to monitor)"* |
| Recommendation for wording | *"Would use phrases like - have you been worrying about things?"*<br>*"Low in mood better than depressed"*<br>*"(depressed) has a stigma attached to it as a medical term"*<br>*"need questionnaire to capture people who need help"* |
| **Cognitive** | |
| Implications of raising issues | |
| Relevance of questions | *"(Colorectal cancer patients are) older population in general and forgetfulness is part of the aging process"* |
| Recommendation for wording | |
| **Body Image/Sexual function** | |
| Implications of raising issues | *"The obvious problem with these questions is when the answers come out, we need tools to intercede and a referral network in place"*<br>*"I don't particularly feel qualified to deal body image – all I could do is to get in touch with someone that can help with that – maybe that's all I need to do"*<br>*"Many patients feel embarrassed to talk about these things (sexual function) but it can really worry them so questionnaire can help to raise these issues"*<br>*"I suspect it would be something that won't take the consultation anywhere"* |
| Relevance of questions | *"Physical attractiveness has not been an issue anyone has raised with me" "attractive may not be relevant but they can still have body image issues"*<br>*"I'm not sure that asking a 75 year old man whether he feels physically less attractive as a result of having colorectal cancer is appropriate or useful thing to do, quite frankly"*<br>*"patients may live several years on palliative chemotherapy so sexual function may be important"* |
| Recommendation for wording | *"a general opening question to the topic (sexual function) might be useful as a screening tool"*<br>*"you don't want to be asking these questions every 2-3 weeks"*<br>*"feeling embarrassed might be more relevant"* |
| **Role, social coping** | |
| Implications of raising issues | *"(side effects and treatment interfering with daily activities) are useful thing to ask as we never specifically ask this (though it may be inferred by going through other questions"*<br>*"Worry about family – there are two stems to that. Hereditary cancer risk to your children and family as a broad concept"*<br>*"it's useful to know (treatment worth) as it might help make decisions about future treatment if patients feel they got much out of it (chemotherapy) despite side effects"* |
| Relevance of questions | *"not sure how useful this information is (role and social) as it probably won't affect treatment decisions"*<br>*"Anybody feels uncertain about their future. It's just the whole uncertainty when you've got cancer"*<br>*"I would definitely keep the finance question"* |
| Recommendation for wording | *"better to say how has it (cancer and treatment)affected your life or changed your life (rather than burden)"* |

*Oncologists' beliefs about relevance of questions*

Oncologists anticipated that chemotherapy treatment would inevitably have impact on patients' social and role functions. Although patient reported data may provide further insight into the impact of patients' experience of their treatment, oncologists felt that this would not directly have an impact on decisions about treatment.

*Recommendations for the questionnaire*

There were several items covering similar topics within this section and suggestions were made to reduce the number of items. Many oncologists did not like the word "burden" in the two items enquiring about treatment and disease impact.

*Decisions made following the interview*

5 items were removed which had the least support from the oncologists from their comments and were considered to be overlapping. The role and social function items from EORTC QLQ-C30 were retained for patient interviews. Two items on future perspectives were retained for patient interviews for their opinion. All the changes made following the interviews with the oncologists are presented in Table 3.9.

**Table 3.9 Summary table of changes made after interview with oncologists**

| Items | Outcome after interview with oncologists |
|---|---|
| ***Physical Function*** | |
| Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? | ✓ |
| Do you have any trouble taking a long walk? | |
| Do you have any trouble taking a short walk outside of the house? | |
| Do you need to stay in bed or a chair during the day? | |
| Do you need help with eating, dressing, washing yourself or using the toilet? | |
| A number of activities are listed below. We do not want to know whether you actually do these, but only whether you are able to perform them presently. Would you please mark the answer that applies most to your condition of the past week?<br><br>Care for myself<br>Walk about the house<br>Light housework/household jobs<br>Climb stairs<br>Heavy housework/household jobs<br>Walk out of doors<br>Go shopping<br>Go to work | ✓<br>However, "Go to work" was removed.<br><br>Questions were modified into question format for each item. (e.g. "Are you able to care for yourself?") |

| | |
|---|---|
| Please select one of the following items that best describes your current level of physical ability<br><br>0 - I am fully active and more or less as I was before my illness<br>1 – I cannot carry out heavy physical work, but can do anything else<br>2 – I am up and about more than half the day; I can look after myself, but not well enough to work<br>3 – I am in bed or sitting in a chair for more than half the day; I need some help in self care<br>4 – I am in bed or a chair all the time and need a lot of looking after | ✓ |
| ***Infection*** | |
| Have you had any infection since your last cycle of chemotherapy? | ✓ |
| Were you admitted to hospital during your last cycle of chemotherapy? | New |
| Were you prescribed any antibiotics during your last cycle of chemotherapy? | New |
| Have you been bothered by fevers or chills? | X |
| ***Chemotherapy toxicity/disease related symptoms*** | |
| Have you had sore mouth or tongue? | ✓ |
| Have you had dry mouth? | X |
| Have you had problems with sense of taste? | ✓ |
| Did food and drink taste different from usual? | ✓ |
| Have you lacked appetite? | ✓ |
| Have you had trouble with eating? | X |
| Have you felt full up too quickly after beginning to eat? | X |
| Have you worried about losing weight? | X |
| Have you had acid indigestion or heartburn? | Modified |
| Have you felt nauseated (sick)? | Modified |
| Have you vomited? | ✓ |
| Have you been constipated? | ✓ |
| Did you have bloated feeling in your abdomen? | ✓ |
| Were you troubled by passing wind/gas/flatulence? | X |
| Have you had diarrhoea? | ✓ |
| Have you had blood in your stools? | X |
| Have you had mucus in your stools? | X |
| Have your skin or eyes been yellow (jaundiced)? | X |
| Have you had soreness or redness of your hands or feet? | ✓ |
| Have you had any other skin problems (e.g. itching, dryness, sensitivity to sun)? | ✓ |
| Have you had tingling or numbness in your hands or feet? | ✓ |
| Are you concerned by any changes in your hearing? | X |
| Have you lost your hair as a result of your treatment? | X |
| Have you been upset by hair loss? | ✓ |
| ***Stoma*** | |
| Do you have a stoma?<br>☐ Yes ☐ No<br><br>If yes, have you had any problems with it (for example soreness of skin, increased frequency, leakage)? | ✓ |

| | |
|---|---|
| Do you have a stoma?<br>☐ Yes ☐ No<br><br><u>Only for patients WITHOUT a stoma</u><br>Did you have frequent bowel movements during the day?<br>Did you have frequent bowel movements during the night?<br>Did you feel the urge to move your bowel movements without actually producing any stools?<br>Have you had any unintentional release of stools?<br>Have you had any blood in your stools?<br>Have you had any difficulty in moving your stools?<br>Have your bowel movements been painful?<br><br><u>Only for patients WITH a stoma</u><br>Were you afraid that other people would be able to hear your stoma?<br>Were you afraid that other people would be able to smell your stoma?<br>Were you worried about possible leakage from the stoma?<br>Did you have problems caring for your stoma?<br>Was your skin around the stoma irritated?<br>Did you feel embarrassed because of your stoma?<br>Did you feel less complete because of your stoma? | Removed except for three items<br>• Were you afraid that other people would be able to smell your stoma?<br>• Did you feel embarrassed because of your stoma?<br>• Did you feel less complete because of your stoma? |
| Do you have a stoma bag (colostomy/ ileostomy)? Please circle the correct answer.<br>☐ Yes ☐ No<br><br>Answer these questions ONLY IF YOU HAVE A STOMA BAG<br>Have you had unintentional release of gas/flatulence from your stoma bag?<br>Have you had leakage of stools from your stoma bag?<br>Have you had sore skin around your stoma?<br>Did frequent bag change occur during the day?<br>Did frequent bag change occur during the night?<br>Did you feel embarrassed because of your stoma?<br>Did you have problems caring for your stoma?<br><br>Answer these questions ONLY IF YOU DO NOT HAVE A STOMA BAG<br>Have you had unintentional release of gas/flatulence from your back passage?<br>Have you had leakage of stools from your back passage?<br>Have you had sore skin around your anal area?<br>Did frequent bowel movements occur during the day?<br>Did frequent bowel movements occur during the night?<br>Did you feel embarrassed because of your bowel movement? | X |
| Do you have an ostomy appliance?<br>☐ Yes ☐ No<br><br>If yes, please answer the next two items:<br>I am embarrassed by my ostomy appliance<br><br>Caring for my ostomy appliance is difficult | X |
| ***Fatigue*** | |
| Have you had trouble sleeping? | ✓ |
| Did you need to rest? | ✓ |
| Have you felt weak? | ✓ |
| Were you tired? | ✓ |
| Have you been less active than you would like to be? | ✓ |
| Have you felt slowed down? | X |
| Have you felt lacking in energy? | ✓ |

| | |
|---|---|
| ***Pain*** | |
| Have you had pain? | ✓ |
| Did pain interfere with your daily activities? | ✓ |
| Did you have abdominal pain? | X |
| Have you had pain in your stomach area? | X |
| Have you had discomfort in your stomach area? | X |
| Did you have pain in your buttocks/anal area/rectum? | X |
| Have you had pain in your back? | X |
| ***Bladder function*** | |
| Did you urinate frequently during the day? | X |
| Did you urinate frequently during the night? | X |
| Have you had any unintentional release (leakage) of urine? | X |
| Did you have pain when you urinated? | X |
| Have you had any trouble with your waterworks? | New |
| ***Others*** | |
| Were you short of breath? | ✓ |
| Were your eyes painful, irritated or watery? | ✓ |
| Have you felt ill or unwell? | Modified |
| | |
| ***Emotional/Cognitive Function*** | |
| Have you had difficulty in concentrating on things, like reading the newspaper or watching television? | ✓ |
| Did you feel tense? | ✓ |
| Did you worry? | ✓ |
| Did you feel irritable? | ✓ |
| Did you feel depressed? | ✓ |
| Have you had difficulty remembering things? | ✓ |
| Have you had trouble talking about your feelings to your family and friends? | ✓ |
| Have you felt stressed? | ✓ |
| Have you felt less able to enjoy yourself? | ✓ |
| Have you been tearful? | New |
| Have you been bothered by mood changed? | New |
| Have you felt calm and peaceful? | New (MHI-5) |
| Have you felt downhearted and low? | New (MHI-5) |
| Have you been a happy person? | New (MHI-5) |
| Have you felt so down in the dumps that nothing could cheer you up? | New (MHI-5) |
| Have you been a very nervous person? | New (MHI-5) |
| ***Body Image*** | |
| Have you felt physically less attractive as a result of your disease or your treatment? | ✓ |
| Have you been feeling less feminine/masculine as a result of your disease or your treatment? | ✓ |
| Have you been dissatisfied with your body? | ✓ |
| ***Sexual Function*** | |
| Has the disease or treatment affected your sex life (for the worse)? | ✓ |
| To what extent were you interested in sex? (Men) | ✓ |
| Did you have difficulty getting or maintaining an erection? (Men) | ✓ |
| To what extent were you interested in sex? (Women) | ✓ |
| Did you have pain or discomfort during intercourse? (Women) | ✓ |
| ***Coping and Future Perspectives*** | |
| How much has your disease been a burden to you? | X |
| How much has your treatment been a burden to you? | X |
| How much has your chemotherapy treatment interfered with your normal daily activities? | ✓ |
| Have you worried about your health in the future? | X |
| Were your worried about your family in the future? | ✓ |
| Did you feel uncertain about the future? | ✓ |
| Were the side effects of treatment worse than you expected? | ✓ |
| Were you concerned about disruption of family life? | X |

| | |
|---|---|
| ***Role and Social Function*** | |
| Were you limited in doing either your work or other daily activities? | ✓ |
| Were you limited in pursuing your hobbies or other leisure time activities? | ✓ |
| Has your physical condition or medical treatment interfered with your family life? | ✓ |
| Has your physical condition or medical treatment interfered with your social life? | ✓ |
| Has your physical condition or medical treatment caused you financial difficulties? | ✓ |
| Have you had trouble having social contact with friends? | X |
| ***Treatment Worth*** | |
| Since you started chemotherapy, how worthwhile do you think your treatment has been? | ✓ |
| ✓: Item retained, X: item removed | |

### 3.4.5 Interview with patients

Thirteen patients were approached to take part in the study. Three patients declined. Total of 10 patients completed the study; 6 were men and 4 were women. Their median age was 64.5 years (rage 58 – 70). 9 out of 10 patients were retired. They all had metastatic (stage 4) colorectal cancer. 9 out of 10 patients had liver metastasis. Patients' disease characteristics and treatment regimens are described in Table 3.10

**Table 3.10 Patient characteristics**

| | | Number |
|---|---|---|
| Primary disease site | Ascending colon | 1 |
| | Transverse colon | 1 |
| | Sigmoid colon | 5 |
| | Recto-sigmoid junction | 1 |
| | rectum | 2 |
| Extent of metastatic disease | One organ | 3 |
| | Two organs or more | 7 |
| Chemotherapy regimen | Oxaliplatin and 5 Fluorouracil (OxMdG*) | 6 |
| | Oxaliplatin and Capecitabine | 1 |
| | Irinotecan and 5 Fluorouracil (IrMdG*) | 1 |
| | Single agent Irinotecan | 1 |
| | 5 Fluorouracil (MdG*) + Cetuximab | 1 |
| *MdG: Modified de Gramont regimen | | |

3.4.5.1 Feasibility of accessing and completing the questionnaire through Patient Pathway Manager (PPM)

The questionnaire was easily accessible through PPM during the study. Patients were presented with three physical function scales (EORTC QLQ-C30, RSCL and WHO performance status in patient self report format) which consisted of 13 items, 3 items on infection and hospital admission, 26 items on symptom/treatment side effects, 5 items on stoma function and 32 items on psychosocial issues.

Average time taken for the patients to complete the questionnaire was 13 minutes (range 7 to 18 minutes). All patients found the touch screen computer (TSC) easy to use and stated that they would prefer to complete the questionnaire on TSC rather than on paper.

One patient reported that they had selected a wrong response option for one of the questions from Mental Health Inventory (MHI-5) where there are 6 response options to choose from.

There was a technical problem in accessing the results of the questionnaire on PPM for two patients who entered the study. This was later rectified by consulting with the information technology personnel for PPM. However, data for these two patients were unfortunately lost.

3.4.5.2 Physical functions and symptoms

*Quantitative Analysis*

Scores from patients' questionnaire responses for each item were collated; mean scores for each item were calculated and ranked from highest (indicating many patients experienced a problem) to lowest (indicating many patients did not experience a problem).

3 items on infection concerning hospital admission and antibiotic use were not included in this analysis as they had "yes" or "no" responses. WHO performance status item was also excluded as this item had a different format to all other questions. In addition, stoma items were excluded from this analysis as there were only responses from two

patients. Sexual function items were analysed separately as some patients opted not to answer the question as they had the option to skip.

Prevalence scores for each item was also calculated which indicated the presence of at least some degree of problem concerning a symptom/issue (i.e. any responses other than “not at all” or equivalent response).

**Table 3.11 Physical function**

| | Mean | Prevalence (%) |
|---|---|---|
| **EORTC QLQ-C30**<br>(Not at all = 1; A little = 2; Quite a bit = 3; Very much = 4) | | |
| Do you have any trouble taking a long walk? | 2.4 | 87.5 |
| Do you need to stay in bed or a chair during the day? | 2.1 | 62.5 |
| Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? | 2.0 | 75 |
| Do you have any trouble taking a short walk outside of the house? | 1.6 | 37.5 |
| Do you need help with eating, dressing, washing yourself or using the toilet? | 1.0 | 0 |
| **RSCL**<br>(Able without help = 1; Without help but with difficulty = 2; Only with help = 3; Unable = 4) | | |
| Can you perform heavy housework/household jobs? | 2.0 | 62.5 |
| Are you able to care for yourself? | 1.5 | 25 |
| Can you perform light housework/household jobs? | 1.4 | 25 |
| Are you able to do your shopping? | 1.4 | 25 |
| Can you climb stairs? | 1.3 | 25 |
| Are you able to walk outdoors? | 1.1 | 12.5 |
| Are you able to walk about the house? | 1.0 | 0 |

**Table 3.12 Symptom and treatment toxicities**

| Questions (Not at all = 1; A little = 2; Quite a bit = 3; Very much = 4) | Mean score | Prevalence (%) | Mean oncologist rating* |
|---|---|---|---|
| Have you had tingling or numbness in your hands or feet? | 3.0 | 100.0 | 3.0 |
| Have you been less active than you would like to be? | 2.9 | 87.5 | 2.3 |
| Were you tired? | 2.5 | 100.0 | 2.5 |
| Have you felt lacking in energy? | 2.5 | 100.0 | 2.0 |
| Have you had problems with sense of taste? | 2.5 | 87.5 | 1.7 |
| Did food and drink taste different from usual? | 2.5 | 87.5 | 2.7 |
| Have you felt weak? | 2.4 | 100.0 | 2.0 |
| Have you had sore mouth or tongue? | 2.4 | 87.5 | 2.3 |
| Did you need to rest? | 2.3 | 87.5 | 2.1 |
| Have you had diarrhoea (watery stools)? | 2.1 | 62.5 | 3.0 |
| Were you short of breath? | 2.0 | 62.5 | 2.6 |
| Have you felt nauseated (sick)? | 1.9 | 75.0 | 3.0 |
| Were your eyes painful, irritated or watery? | 1.9 | 50.0 | 3.0 |
| Have you had soreness or redness of your hands or feet? | 1.9 | 37.5 | 3.0 |
| Have you felt ill or unwell? | 1.6 | 62.5 | 2.4 |
| Did you have bloated feeling in your abdomen? | 1.6 | 50.0 | 2.1 |
| Have you had any other skin problems (e.g. itching, dryness, sensitivity to the sun)? | 1.6 | 50.0 | 2.1 |
| Have you had acid indigestion or heartburn? | 1.6 | 37.5 | 2.9 |
| Have you lacked appetite? | 1.5 | 37.5 | 2.7 |
| Have you had pain? | 1.5 | 37.5 | 3.0 |
| Have you been constipated? | 1.4 | 25.0 | 3.0 |
| Have you had trouble sleeping? | 1.4 | 25.0 | 2.7 |
| Have you vomited? | 1.3 | 25.0 | 3.0 |
| Did pain interfere with your daily activities? | 1.3 | 25.0 | 2.7 |
| Have you had any problems with your waterworks? | 1.1 | 12.5 | NA |
| Have you been upset by hair loss? | 1.1 | 12.5 | 2.4 |
| *1: ”not useful”, 2: ”somewhat useful” and 3: “useful” | | | |

As expected, patients found more strenuous tasks difficult to perform. In terms of physical symptoms, peripheral neuropathy was the most common and troublesome side effect as well as fatigue.

Table 3.11 and Table 3.12 illustrate the mean scores and the prevalence of symptoms/issues among the study population. Table 3.12 also lists oncologists’ rating for each of the questionnaire items derived from interviews described above.

3.4.5.3 Review of comments on physical functions and symptoms made by patients during the interview

*Physical functioning*

All patients found items in this section easy to answer. Only 2 patients were able to state their preference for one set of items over another. All patients stated that they found it easy to identify own level of physical ability on WHO performance status scale. One patient suggested that WHO performance status question was not necessary in addition to the other physical function items.

*Decision made after the interviews*

All physical function items were retained for further evaluation.

*Symptoms and side effects of chemotherapy*

All the patients identified with most of the symptoms covered in this section and felt that it was a very comprehensive list. One patient gave an account of a terrible time he had with severe vein pain and felt that this should be covered in the questionnaire. No other suggestions were made for additional issues to be included. All patients stated that fatigue was one of the most troublesome symptoms they had.

*Decision made after the interviews*

One item on taste was removed as this was considered duplication. “Did food and drink taste different from usual?” was retained as this had better rating by the oncologists. Item on bladder function was also removed in view of low prevalence and comments by made by oncologists in the previous interview study. Additional item on vein pain was added following patient comment.

3.4.5.3 Psychosocial Issues

*Quantitative Analysis*

Same analysis was performed with that of physical function and symptoms with tabulation of patients' mean scores for each item and the prevalence of the issue. MHI-5 was analysed separately as it had different response options from the other items. Sexual function was also analysed separately as some patients skipped items.

**Table 3.13 Mean score and prevalence of psychosocial issues among patients interviewed**

| Questions (Not at all = 1; A little = 2; Quite a bit = 3; Very much = 4) | Mean score | Prevalence (%) |
|---|---|---|
| Were you worried about your family in the future? | 2.9 | 87.5 |
| Did you feel uncertain about the future? | 2.6 | 75.0 |
| How much has your treatment interfered with your normal daily activities? | 2.3 | 87.5 |
| Were you limited in doing either your work or other daily activities? | 2.3 | 87.5 |
| Has your physical condition or medical treatment interfered with your social life? | 2.1 | 100.0 |
| Were you limited in pursuing your hobbies or other leisure time activities? | 2.1 | 75.0 |
| Have you felt less able to enjoy yourself? | 2.0 | 87.5 |
| Were the side effects of treatment worse than you expected? | 2.0 | 62.5 |
| Did you feel tense? | 1.9 | 87.5 |
| Did you feel irritable? | 1.8 | 75.0 |
| Have you felt stressed? | 1.8 | 62.5 |
| Have you had difficulty remembering things? | 1.6 | 50.0 |
| Did you worry? | 1.5 | 50.0 |
| Have you been tearful? | 1.5 | 50.0 |
| Since you started chemotherapy, how worthwhile do you think your treatment has been? | 1.5 | 25.0 |
| Have you had difficulty in concentrating on things, like reading the newspaper or watching television? | 1.5 | 25.0 |
| Since your diagnosis, have you been dissatisfied with your body? | 1.5 | 25.0 |
| Has your physical condition or medical treatment interfered with your family life? | 1.4 | 37.5 |
| Did you feel depressed? | 1.3 | 25.0 |
| Have you had trouble talking about your feelings to your family and friends? | 1.3 | 25.0 |
| Since your diagnosis, have you felt physically less attractive? | 1.3 | 12.5 |
| Has your physical condition or medical treatment caused you financial difficulties? | 1.1 | 12.5 |
| Have you been bothered by mood changes? | 1.0 | 0.0 |
| Since your diagnosis, have you been feeling less feminine/masculine? | 1.0 | 0.0 |

As anticipated by the oncologists, many patients admitted to future concerns and uncertainties. Many patients reported that their everyday lives had been impacted by their illness and treatment. Table 3.13 illustrates the mean patient scores and prevalence of psychosocial issues raised and Table 3.14 illustrate the same results for MHI-5 items.

**Table 3.14 Mean and prevalence of emotional distress (MHI-5)**

| **Mental Health Inventory (MHI-5) (None of the time = 1, A little of the time = 2, Some of the time = 3, A good bit of the time = 4, Most of the time = 5, All of the time = 6)** | **Mean score** | **Prevalence (%)** |
|---|---|---|
| Have you felt calm and peaceful? (scores reversed) | 2.4 | 75.0 |
| Have you felt downhearted and low? | 1.8 | 62.5 |
| Have you been a happy person? (scores reversed) | 1.8 | 62.5 |
| Have you felt so down in the dumps that nothing could cheer you up? | 1.4 | 37.5 |
| Have you been a very nervous person? | 1.3 | 25.0 |

3.4.5.4 Sexual Function

Available responses were from 5 men and 3 women. 1 patient skipped all the items in this section. 4 out of 7 patients stated that their sex life had been affected by their illness or their treatment and these 4 patients all indicated that they were “not at all” interested in sex. From the responses from this small group of patients, erectile dysfunction did seem to be a relevant issue for the male patients.

**Table 3.15 Patient responses to sexual function items**

| Questions (Not at all = 1; A little = 2; Quite a bit = 3; Very much = 4) | Responses available | No. skipped | mean | Prevalence (%) |
|---|---|---|---|---|
| During the past 4 weeks, has the disease or treatment affected your sex life (for the worse)? | 7 | 1 | 2 | 57.1 |
| During the past 4 weeks, to what extent were you interested in sex? (score reversed) | 7 | 1 | 3.8 | 100.0 |
| During the past 4 weeks, did you have difficulty getting or maintaining an erection? (men) | 4 | 1 | 3.25 | 100.0 |
| Did you have pain or discomfort during intercourse? (women) | 1 | 2 | 1 | 0 |

### 3.4.6 Qualitative analysis of psychosocial issues

All interviews were audio-recorded and transcribed verbatim. The interviews were conducted in a similar manner to that of those with the oncologists; where discussions took place around items covering relevant topics. Data from all 10 patients were available for this part of the analysis. Sections on psychosocial items were analysed using qualitative thematic analysis. The main themes arising from the analysis were:

- Relevance of the issues being questioned to themselves or to others with similar diagnosis
- Opinions about questionnaire items including suggestions for wording/rephrasing of items

Emotional Function

*Relevance of the issues*

Many patients admitted that they had occasions when they felt “low” or “down” at times but generally stated that they had positive attitudes which helped them to cope on a day to day basis. Several patients commented that support from family and friends were vital in getting them through each day and expressed concerns for those people who may be lacking such support.

*Opinions about the questionnaire items*

Many stated that they would identify better with feeling “low” or “down” rather than “depressed”. Some stated that there was a negative connotation and stigma attached with this word. Some patients liked the MHI-5 items as there were more response options and also because some of the items were positively phrased.

*Decision made after the interviews*

Item on “mood changes” was removed as the MHI-5 contained an item on feeling “downhearted and low”. Other items were retained. Although some of the oncologists and patients had made remarks about the item feeling “depressed”, this item was

retained for further testing, particularly because it formed a part of a scale within the EORTC QLQ-C30.

Cognitive Function

*Relevance of the issues*

Not many patients made remarks on these items but those that did, commented that they have become aware of their memory being affected since starting chemotherapy and identified well with the items covering this issue.

*Decision made after the interviews*

Both items were retained.

Body image

*Relevance of the issues*

Many patients stated that “body image” issues were irrelevant to them personally. Some stated that it may be more relevant to those who are younger. However, one patient was particularly troubled by a hernia and he felt very unhappy with his appearance.

*Opinions about the questionnaire items*

None of the patients were offended by the items in this section. However, one patient specifically stated that “dissatisfied” did not seem the right word to describe body image issues but had no other suggestions.

*Decision made after the interviews*

All three items on body image were retained for further testing.

Sexual function

*Relevance of the issues*

Some patients very much welcomed sexual function being included in the questionnaire. These patients had been experiencing various issues but felt embarrassed to raise it in clinic consultations. In addition, they stated that they felt very embarrassed about talking regarding these issues with doctors of opposite gender to them. Several patients stated that these issues were not relevant to them as they were not sexually active or because they did not have a partner.

*Opinions about the questionnaire items*

All patients felt that this was an important topic to be included in the questionnaire to allow patients to raise the issues. However, they all agreed that patients be given the option not to respond. One patient suggested that the questionnaire could ask more detailed questions about specific problems but appreciated that these issues may not necessary be relevant to everyone.

*Decision made after the interviews*

It was decided that there should be a screening question. If the patient reports no issues with their sexual function then they would not be shown further questions. If however, the patient reports an issue then they would be presented with further questions on the matter. Additional items were added from EORTC OV28 (“sexually active”, “sex enjoyable”, “pain and discomfort” for men and “dry vagina” for women) to specify the problem they may be experiencing

Treatment impact on patients’ social and role functioning and future perspectives

*Relevance of the issues*

Most patients admitted that treatment and associated hospital visits had a significant impact on their daily lives. Several patients stated they had given up their hobbies because of treatment side effects. Majority of the patients expressed overwhelming support from their family and friends, who in turn helped them cope with their cancer diagnosis and treatment. Several patients expressed their concern for their family in

the future more than for themselves. One patient stated that he felt isolated as his immediate family lived far away.

*Opinions about the questionnaire items*

One patient stated that raising financial issues was important as he had been given advice about entitlement to benefits which was helpful.

*Decision made after the interviews*

All the items in this section were retained for further testing as there was no strong evidence for removal. New items “have you felt lonely” and “have you had support from family and friends?” were added to identify patients who may be feeling socially isolated.

Treatment worthwhile?

*Opinions about the questionnaire items*

Many patients did not feel that they could respond truthfully to the question “how worthwhile” their treatment had been, as this would depend on how effective the treatment has been in controlling their cancer

*Decision made after the interviews*

This item was retained but response option was modified by giving patients option to respond “I don’t know”

3.4.5.5 Summary of results from the interviews with patients

As a result of the interviews with patients, 7 new items were added while 3 items were removed. Some items were modified; changes to phrasing of questions, changes in response options and branching of questions dependent on the screening or opening question. Changes made are summarized in Table 3.17. Remaining 82 items were taken forward to the next stage of the development of QuEST-Cr.

**Table 3.16 Comments made by patients during interviews**

| | |
|---|---|
| Emotional Function | |
| Relevance of issue | *"I do tend to feel depressed and down, particularly when I am by me self"*<br>*"I get tearful at times"* |
| Opinions about the item | *"(Depressed) seems to be a "bad" word"*<br>*"Mood swings better than depressed"*<br>*"(Questionnaire) can help to keep an eye on things. Doctors can pick things up if things are not going right"*<br>*"Felling low is something I would identify with (rather than depressed)"*<br>*"Have you been a nervous person is a very strange question"* |
| Cognitive Function | |
| Relevance of issue | *"Chemotherapy does make me lose my mind a little bit"*<br>*"I need to write everything down, otherwise I forget what to tell the doctor"* |
| Opinions about the item | |
| Body Image and Sexual Function | |
| Relevance of issue | *"they are not really an issue for me"*<br>*"it might be more of an issue for younger people"*<br>*"I would talk to my GP about it (sexual function) rather than Dr ...(Hospital doctor"*<br>*"There are doctors that I would find it easier to talk to about these things"*<br>*"I was talking to another patient and he had the same problem (with sexual function) as I did"*<br>*"I'm not very happy with my body image at all. I feel very embarrassed (with a hernia)"*<br>*"I always get the feeling that everybody is looking at me"*<br>*"People can get embarrassed by their stoma and emotionally scarred by it"* |
| Opinions about the item | *"For some people (sexual function questions) would be very helpful – if doctors see it, they can respond"*<br>*"(Sexual function questions) should definitely be in the questionnaire"*<br>*"I think it's good to be asked"*<br>*"I am embarrassed to bring it up (about sexual function). This (Questionnaire) might help"*<br>*"I'd like people to have a choice (of answering questions)"*<br>*"(Questionnaire) gives opportunity for people to raise it"* |
| Role, Social and Coping | |
| Relevance of issue | *"You need a lot of support, or you can go down very easily"*<br>*"(Treatment) really interferes with my social life. I don't like to go out with my pump on"*<br>*"I can't pursue my hobbies"*<br>*"I really worry about my family"*<br>*"I miss my family and friends. I get a little bit feeling sorry for myself cos I'm long way from my family"* |
| Opinions about the item | *"I didn't know I was entitled to disability living allowance. (Finance question) is a good thing to draw attention"*<br>*"(Treatment worth) you don't know until you've had your scan at the end of treatment"* |

**Table 3.17 Changes made to QuEST-Cr following interviews with patients**

| Items | Outcome after interview with patients |
|---|---|
| ***Physical Function*** | |
| Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? | ✓ |
| Do you have any trouble taking a long walk? | |
| Do you have any trouble taking a short walk outside of the house? | |
| Do you need to stay in bed or a chair during the day? | |
| Do you need help with eating, dressing, washing yourself or using the toilet? | |
| Are you able to care for myself | ✓<br>Modified so that each task made into a question |
| Are you able to walk about the house | |
| Can you perform light housework/household jobs | |
| Can you climb stairs | |
| Can you perform heavy housework/household jobs | |
| Are you able to walk out of doors | |
| Are you able to do your shopping | |
| Please select one of the following items that best describes your current level of physical ability<br><br>0 - I am fully active and more or less as I was before my illness<br>1 – I cannot carry out heavy physical work, but can do anything else<br>2 – I am up and about more than half the day; I can look after myself, but not well enough to work<br>3 – I am in bed or sitting in a chair for more than half the day; I need some help in self care<br>4 – I am in bed or a chair all the time and need a lot of looking after | ✓ |
| ***Infection*** | |
| Have you had any infection since your last cycle of chemotherapy? | ✓ |
| Were you admitted to hospital during your last cycle of chemotherapy? | ✓ |
| Were you prescribed any antibiotics during your last cycle of chemotherapy? | ✓ |
| ***Chemotherapy toxicity/disease related symptoms*** | |
| Have you had sore mouth or tongue? | ✓ |
| Have you had problems with sense of taste? | X |
| Did food and drink taste different from usual? | ✓ |
| Have you lacked appetite? | ✓ |
| Have you had acid indigestion or heartburn? | ✓ |
| Have you felt nauseated (sick)? | ✓ |
| Have you vomited? | ✓ |
| Have you been constipated? | ✓ |
| Did you have bloated feeling in your abdomen? | ✓ |
| Have you had diarrhoea? | ✓ |
| Have you had soreness or redness of your hands or feet? | ✓ |
| Have you had any other skin problems (e.g. itching, dryness, sensitivity to sun)? | ✓ |
| Have you had tingling or numbness in your hands or feet? | ✓ |
| Have you been upset by hair loss? | ✓ |
| Have your veins been sore or irritated? | New |
| ***Stoma*** | |
| Do you have a stoma?<br>☐ Yes ☐ No<br><br>If yes, have you had any problems with it (for example soreness of skin, increased frequency, leakage)? | ✓ |
| Were you afraid that other people would be able to smell your stoma? | ✓ |
| Did you feel embarrassed because of your stoma? | ✓ |
| Did you feel less complete because of your stoma? | ✓ |

| | |
|---|---|
| ***Fatigue*** | |
| Have you had trouble sleeping? | ✓ |
| Did you need to rest? | ✓ |
| Have you felt weak? | ✓ |
| Were you tired? | ✓ |
| Have you been less active than you would like to be? | ✓ |
| Have you felt lacking in energy? | ✓ |
| ***Pain*** | |
| Have you had pain? | ✓ |
| Did pain interfere with your daily activities? | ✓ |
| ***Bladder function*** | |
| Have you had any trouble with your waterworks? | X |
| ***Others*** | |
| Were you short of breath? | ✓ |
| Were your eyes painful, irritated or watery? | ✓ |
| Have you felt ill or unwell? | ✓ |
| ***Emotional/Cognitive Function*** | |
| Have you had difficulty in concentrating on things, like reading the newspaper or watching television? | ✓ |
| Did you feel tense? | ✓ |
| Did you worry? | ✓ |
| Did you feel irritable? | ✓ |
| Did you feel depressed? | ✓ |
| Have you had difficulty remembering things? | ✓ |
| Have you had trouble talking about your feelings to your family and friends? | ✓ |
| Have you felt stressed? | ✓ |
| Have you felt less able to enjoy yourself? | ✓ |
| Have you been tearful? | ✓ |
| Have you been bothered about mood changes? | X |
| Have you felt calm and peaceful? (scores reversed) | ✓ |
| Have you felt downhearted and low? | ✓ |
| Have you been a happy person? (scores reversed) | ✓ |
| Have you felt so down in the dumps that nothing could cheer you up? | ✓ |
| Have you been a very nervous person? | ✓ |
| ***Body Image*** | |
| Have you felt physically less attractive as a result of your disease or your treatment? | ✓ |
| Have you been feeling less feminine/masculine as a result of your disease or your treatment? | ✓ |
| Have you been dissatisfied with your body? | ✓ |
| ***Sexual Function*** | |
| Has the disease or treatment affected your sex life (for the worse)? | ✓ |
| To what extent were you interested in sex? (Men + Women) | ✓ |
| To what extent were you sexually active? (Men + Women) | New |
| To what extent was sex enjoyable for you? (Men + Women) | New |
| Did you have difficulty getting or maintaining an erection? (Men) | ✓ |
| Did you have pain or discomfort during intercourse? (Men + Women) | New for men |
| Did you have a dry vagina during sexual activity? (Women) | New |
| ***Coping and Future Perspectives*** | |
| How much has your chemotherapy treatment interfered with your normal daily activities? | ✓ |
| Were your worried about your family in the future? | ✓ |
| Did you feel uncertain about the future? | ✓ |
| Were the side effects of treatment worse than you expected? | ✓ |
| Have you felt lonely? | New |
| Have you had support from your family and friends? | New |

| | |
|---|---|
| ***Role and Social Function*** | |
| Were you limited in doing either your work or other daily activities? | ✓ |
| Were you limited in pursuing your hobbies or other leisure time activities? | ✓ |
| Has your physical condition or medical treatment interfered with your family life? | ✓ |
| Has your physical condition or medical treatment interfered with your social life? | ✓ |
| Has your physical condition or medical treatment caused you financial difficulties? | ✓ |
| ***Treatment Worth*** | |
| Since you started chemotherapy, how worthwhile do you think your treatment has been? | ✓<br>New response option "I don't know" |
| ✓: item retained, X: item removed | |

## 3.5 Discussion

The aim of this chapter was to describe in detail the initial developmental phases of a questionnaire, QuEST-Cr, which intends to measure symptoms, toxicities of cancer therapy and their impact upon patients' functioning within routine oncology practice to help support the care of patients with colorectal cancer.

The processes undertaken were broadly guided by the framework outlined by the EORTC Quality of Life Group module development guidelines (Johnson et al., 2011). Interviews with patients and healthcare professionals in the in the first phase of "generating quality of life issues" were substituted by the content analysis of routine oncology consultations of patients with colorectal cancer. This ensured that commonly discussed issues or topics within real life consultations were included in the questionnaire; which helped to make the questionnaire relevant to clinical practice and specific to the patient group. It was felt that this substitution was acceptable given that EORTC guidelines are aimed at developing a new questionnaire for a group of patients where there are no other comparable existing questionnaires. Brown et al (Brown et al., 2001b) used similar approach in the development of their chemotherapy toxicity questionnaire for use in routine practice. They had used an established questionnaire which explored chemotherapy toxicities and used this as the starting point in their questionnaire adaptation in order to develop a tool which was more relevant in everyday practice. Remainder of the questionnaire developmental phases followed the EORTC guidance and used similar strategies as other authors developing modular instruments (Chow et al., 2009)

Review of the literature identified 5 questionnaires which were considered relevant to patient with colorectal cancer, although only 3 of these were specific to colorectal cancer with one for patients with liver metastasis and the other for gastrointestinal diseases in general. There were differences among the instruments identified in terms of the number of symptoms and issues covered, with some covering extensive range of bowel related symptoms. The EORTC QLQ-C30 plus QLQ-CR29 (Whistance et al., 2009) provided the best coverage of the topics raised in the clinic consultations. However, there were several symptoms which were not included in the questionnaires which were commonly discussed in clinics such as “sore mouth”, “tingling and numbness in fingers and toes” and “sore and red hands and feet”. This may in due to the fact that these symptoms are due to chemotherapy treatments which were not available at the time of questionnaire development. For example, Oxaliplatin, the common side effect of which is sensory peripheral neuropathy, was shown to prolong progression free survival when combined with 5-fluorouracil and folinic acid in a phase III study, which was published in 2000 (de Gramont et al., 2000). This study led to Oxaliplatin being used as standard chemotherapy regimen for patients with colorectal cancer. Similarly, Capecitabine was shown to have equivalent efficacy to 5 Fluorouracil and folinic acid in a phase III study, which was published in 2001 (Van Cutsem et al., 2001). One of the common side effects of Capecitabine is hand foot syndrome, which manifests as sore and red swollen hands and feet. Capecitabine can cause more mucosal toxicities compared to 5-Fluorouracil and folinic acid which may increase patients experiencing sore mouth and indigestion (Van Cutsem et al., 2001).

There are a number of biological treatments which are being incorporated into the treatment of colorectal cancer. These agents have different side effect profile compared to cytotoxic chemotherapy. It is likely that further modules will need to be developed or existing modules to be updated once these agents are incorporated into standard treatment algorithm for patients with colorectal cancer.

Many doctors considered this questionnaire to provide a “trigger” for discussion of certain issues, particularly if the patients were experiencing problems. They felt that this should, by no means, replace the conversation with the patients. Questions about specific sites of pain, detailed bowel/abdominal and bladder symptoms were therefore considered unnecessary as these issues would be discussed with the patient. Many of these items were therefore removed following interview with oncologists.

Oncologists recognised that a diagnosis of an incurable cancer would have a significant impact on patients and their families' lives. They appreciated that patients may become emotionally distressed because of the diagnosis, which can in turn have an impact on how patients might cope with their treatment. Emotional functioning was therefore considered an important issue to look out for. Many oncologists felt that the questionnaire could act as a screening tool but wanted some guidance as to how best to manage the patient if he/she reports problems here. Oncologists suggested that patients had both good and bad days like all of us, and feeling "low" from time to time was probably quite common for their patients and wanted the questionnaire to be reasonably sensitive in identifying patients that needed further intervention.

There were a number of issues which are routinely addressed in existing instruments but were not included in the consultation analysis (indicating lack of discussion of the topic). These were body image, sexual function and stoma issues. These issues are included in the questionnaires because some of the treatment for colorectal cancer, such as surgery, may lead to a formation of a stoma (Cunningham et al., 2010), which can lead to patients having to make adjustments both physically and psychologically (Brown and Randle, 2005). In addition, surgical intervention together with other modalities of cancer treatment such as preoperative radiotherapy and chemo-radiotherapy can have a direct impact on patients' sexual functioning (Ho et al., 2011). There is a large body of evidence that colorectal patients do indeed experience these concerns (Sharpe et al., 2011, Sprangers et al., 1995, Bullen et al., 2012, Traa et al., 2012), although they may not readily be brought up in a routine chemotherapy review consultations. Both oncologists and patients considered these issues, particularly sexual function, to be important for this group of patients.

Although many of the oncologists interviewed recognized sexual function was probably important for their patients, their sexual health care needs were poorly understood. Some felt uncomfortable or embarrassed to raise these topics during the consultations. This sentiment was echoed by the patients. Oncologists expressed concerns about what should be done when a problem might be identified through the questionnaire and the impact such discussions may have on the consultation length. These are well recognized barriers to discussing these topics (Traa et al., 2014, Park et al., 2009). Some oncologists commented using a questionnaire would give them permission to ask about these issues and allow more open discussion with patients. In addition, it can make patients realize that these are relevant and appropriate issues for them to discuss in outpatient clinics (Flynn et al., 2012, Traa et al., 2014). This may help to

determine the scale of the need among the patients, which can lead to developing any additional services required.

Existing instruments also covered issues about the uncertainty and the future perspectives. These issues were again not identified in the consultation analysis. However, these issues are likely to be particularly relevant when patients receive the outcome of tests to assess response to treatment. The consultations used in the content analysis may not have captured discussion of these issues due to the timing of the audio-recording. During the interview with the oncologists, many indicated that items concerning future perspectives are not helpful as patients with incurable cancer would inevitably be faced with many uncertainties. Nevertheless, it was felt important to retain items addressing these concerns.

Many oncologists wanted the questionnaire to be able identify when patient specifically wished to discuss certain topics. Additional concerns checklist was considered very helpful, particularly in addressing issues such as body image, sexual function and discussion about future and prognosis.

There were a number of limitations to this study. Although 68 consultations were analysed, these came from 17 patients, rather than 68 different patients. If a patient was experiencing a particular symptom or an issue then this may have been repeated several times over the four visits, potentially distorting the prevalence of the problem. In addition 9 patients were in the attention control group of the study from which the consultations have been obtained. One of the aims of this study was to see whether patients completing the EORTC QLQ-C30 were more likely to raise issues covered by this questionnaire. Therefore, patients in the attention control group may have raised more symptoms and function issues addressed in QLQ-C30, although independent samples t-tests confirmed that patients in the attention-control arm were no more likely to discuss symptoms and functions covered by the EORTC QLQ-C30 questionnaire items.

Another limitation is the relatively small number of oncologists and patients interviewed. In addition, these oncologists and patients were all recruited from one hospital. However, the numbers were largely in line with the recommendations from the guideline used in this process (Johnson et al., 2011). Although saturation was not reached in terms of generation of quality of life issues, both oncologists and patients were discussing similar issues during the interviews.

Furthermore, the interviews with healthcare professionals were limited to oncologists as they do not have a clinical nurse specialist based in their department in Leeds. A nurse may have provided a different perspective and opinions about the questionnaire items and inform the issues patients report to them as opposed to oncologists. Further limitation was the loss of questionnaire data from 2 patients, although audio-recording of the whole interview were available, which may have skewed the mean and prevalence of the symptoms and issues covered in the questionnaire.

## 3.6 Summary

This chapter has described and presented the key stages of the development of QuEST-Cr, a colorectal cancer specific questionnaire for routine clinical practice. QuEST-Cr at this stage consisted of 82 items; 13 items on physical function, 3 items on infection/hospital admission, 25 items on symptoms and side effect of treatment, 5 items on stoma, 3 items on body image, 6 items (for both men and women with 5 items common to both gender), and 27 items on other psychosocial issues. Items on Physical function and some of the symptoms/treatment toxicity items were common to all three cancer sites as part of the questionnaire development within the wider programme of research.

For QuEST-Cr to be useful in everyday clinical practice, it needs to be quick and easy to administer, collect relevant information from patients and easily interpreted by the recipient of the questionnaire results. This was not possible with an 82 item questionnaire and QuEST-Cr needed further refinement.

The next chapter describes the testing of QuEST-Cr for its validity and reliability, using psychometric techniques. The QuEST-Cr has been administered to a large number of patients to collect the necessary data for the analysis. Results from psychometric analysis and interviews will be used to further improve QuEST-Cr

# Chapter 4 Questionnaire Validation Study

## 4.1 Introduction

The aim of this chapter was to assess the psychometric properties of the colorectal cancer specific questionnaire, QuEST-Cr, in a larger patient population, using classical psychometric theory. In order to achieve this, individual item performance, measurement properties (including scale structure), reliability and clinical validity of the questionnaire were tested. Attempts were made to reduce the number of items included in the questionnaire in the analysis process to improve its clinical utility. In order to make the questionnaire useful for healthcare professionals to use the patient reported information in their clinical decision making, cut off score analysis was also performed.

Previous chapter described the development of a questionnaire which consisted of 82 items, which included assessment of physical function, emotional function and symptoms and issues specific to patients with colorectal cancer. It was envisaged that QuEST-Cr would include subscales in addition to single items, as seen in the EORTC questionnaires on which the QuEST-Cr was based. The aim was to develop a questionnaire with strong psychometric properties but also one that was clinically useful. 82 item questionnaire is a long questionnaire to be used in routine clinical practice. It was, therefore, necessary to reduce the number of items included in the questionnaire to decrease patient burden in completing the questionnaire but also for the clinicians to be able to interpret the information efficiently. Several key issues were considered in order to improve the psychometric properties of the questionnaire whilst ensuring its utility in the clinical context. These were reliability, validity, assessment of subscales and item reduction.

### 4.1.1 Psychometric analysis

A number of different measurement theories have been developed to test the psychometric properties of assessment instruments such as questionnaires; these include classical test theory (DeVellis, 2006) and item response theory (Hambleton et al., 1991). Key concepts within the classical test theory are reliability and validity. A

reliable measure is one that measures a construct consistently across time, individuals and situations. A valid measure is one that measure what is intended to measure.

There are different types of reliability assessments. The most relevant in terms of subscale development is internal consistency reliability, which assesses the consistency of results across items within a test. One of the most common ways to demonstrate internal consistency reliability is Cronbach's alpha statistics (Cronbach, 1951), which uses inter-item correlations to determine whether the constituent items within the questionnaire or individual subscales are measuring the same concept (Edgar, 1998).

There are three main types of validity; these are content, criterion and construct validity. Content validity (or face validity) refers to expert opinion concerning whether the items within the test or the scale represents the concept the questionnaire is intended to measure. For QuEST-Cr, this is addressed during the questionnaire development stages detailed in chapter 3, which included review of content of oncology consultations, review of the literature and interviews with patients and oncologists. Criterion validity compares the test with other measures or outcomes already considered to be valid. Therefore, criterion validity assessment involves comparing the new instrument with existing questionnaires which measure a similar concept and evaluate whether they produce similar results. Construct validity refers to how well a test measures the constructs that it was designed to measure. Construct validity often divided into three types; known groups validity, convergent validity and discriminant validity. Known groups validity is based on the assumption that certain specified groups of subjects may be expected to score differently from other groups. Convergent validity refers to how well a test agrees with other previously validated tests that measure the same construct and discriminant validity refers whether constructs or measurements that are supposed to be unrelated are indeed unrelated. Multi-trait analysis can be performed to investigate this concept.

### 4.1.2 Clinimetrics

Psychometric approaches require multiple items to measure a single construct or domain. Therefore developing a questionnaire which aims to capture multiple dimensions of an individual's HRQoL can result in a long questionnaire with multiple items. This can present as a challenge for implementation in a routine clinical practice,

where such assessments need to be made in a relatively short time to keep both patients and healthcare professionals engaged. Another approach used for developing a clinically useful instrument is to apply principles of clinimetrics (Feinstein, 1983), which includes selection of items based on clinical rather than statistical criteria; scoring to be simple and readily interpretable; and easy for clinicians to use (Feinstein, 1983). The clinimetric method aims to ensure clinical validity of measures which quantify patient experiences, such as symptoms and severity of illness. Example of clinimetric instrument includes the Apgar score (Apgar, 1953), which was developed to assess the health status of the newborn. The Apgar score is determined by evaluating five simple criteria, (appearance, pulse rate, reflex, activity and respiratory effort) on a scale of zero to two and summating the scores. Scales commonly used to describe performance status of an individual, such as the WHO performance status (Oken et al., 1982) and Karnofsky performance scale (Karnofsky, 1949) both utilize clinimetric approach. However, many clinimetric instruments consist of single items, which may fail to communicate the complexity behind the domain being measured. Therefore, there are calls for integration of psychometric and clinimetric approaches for developing patient outcome measures (Maruish, 2014).

Development of QuEST-Cr planned to use both psychometric and clinimetric approach to ensure its utility within the clinical setting. The questionnaire was anticipated to consist of subscales and individual symptom items which would complement each other and provide broad assessment of patients' HRQoL. Individual item performance was planned to be assessed using descriptive data obtained as part of the validation study as well as using the data collected during the interviews with the oncologists.

### 4.1.3 Cut off score analysis

In order to make the questionnaire useful in the clinical setting, it is necessary for the clinicians to be able to use the data derived from the patients in their clinical decision making. For example, results derived from laboratory test usually have reference ranges which assist clinicians to interpret the data and help them decide whether the results need acting upon. However, the meaning of the (changes in) scores from health status questionnaires may not be inquisitively apparent to clinicians (Juniper et al., 1994). There is a need to define (changes in) scores which can represent clinical

relevance in order to assist clinicians to interpret the data. This is referred to as the minimally important change (MIC) of health status questionnaires (Jacobson and Truax, 1991).

Different approaches to determine the MIC on the scale of health status instruments have been proposed and includes distribution based and anchor based methods (Lydick and Epstein, 1993, Crosby et al., 2003). Distribution based methods are based on distributional characteristics of the sample, and express the observed change to some form of variation to obtain a standardised metric. Examples are the effect sizes (ES) which relate observed change to the sample variability, or standardised response mean (SRM) which relate observed change to the variability of change. Another distribution based measure is the standard error of measurement (SEM), which links the reliability of the instrument to the standard deviation of the population (Crosby et al., 2003). The disadvantage of the distribution based methods is that they do not provide a good indication of the importance of the observed change.

Anchor based methods uses an external measure, or anchor (which should correlate with the health status instrument being studied), to determine clinical important improvement or deterioration. The advantage of this approach is that “minimal importance” is explicitly defined and incorporated. However, the limitation of the anchor based method is that they do not take into account the variability of the instrument or the sample (Crosby et al., 2003). It is therefore recommended that both approaches are considered.

These approaches were explored to evaluate the optimum cut off scores for the subscales within QuEST-Cr.

## 4.2 Methods

### 4.2.1 Study sample and procedure

This was a cross sectional survey study. Eligible patients were those with colorectal cancer (CRC), attending oncology clinics at Leeds Cancer Centre, who were currently receiving chemotherapy or had received chemotherapy in the past three months. Patients were approached to take part in the study at their planned out-patient clinic appointments. Consenting patients completed the questionnaire on touch screen computer either on the day or whilst receiving chemotherapy. Paper questionnaires

were offered to minority of patients if they were unable to stay to complete the questionnaire during their hospital visit or if there were no plans for them to return to clinic within few weeks. Paper questionnaires were returned either by post or at their next clinic visit.

Participating patients were asked to complete the CRC specific questionnaire QuEST-Cr, followed by FACT-G (Cella et al., 1993), the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983) and Distress Thermometer (Roth et al., 1998) as validated measures of cancer-related quality of life and anxiety/depression respectively. Participating patients were also asked to complete a socio-demographics questionnaire which included their age, gender, marital status, education and employment status. Patients' clinical details including current extent of disease and chemotherapy regimens were collected from their medical notes. The project was approved by the Local NHS Research Ethics Committee. Written informed consent was obtained from patients and their oncologists to approach their patients.

#### 4.2.1.1 Study Measures

*QuEST-Cr*

The colorectal cancer specific questionnaire QuEST-Cr at this stage consisted on 82 items, which covered symptoms and side effects of treatment specific to this group of patients as well as broader functional and psychosocial issues. The questionnaire is presented in table 4.1. The items within QuEST-Cr can be divided into the following broad categories: physical function (13 items), infection (3 items); symptoms and side effects (25 items); stoma (5 items); body image (3 items); sexual function (6 items each for men and women); and psychosocial functioning 27 items). Response options from the original questionnaires were used, from which the items were derived. Response options for the majority of the items were: not at all; a little; quite a bit; very much. Response option of "don't know" was added for the item about patients' perception of treatment worth. 7 items in the physical function category had response options: unable; only with help; alone but with difficulty; alone easily. 5 items in the emotional function (from MHI-5) had response options: None of the time; a little of the time; some of the time; a good bit of the time; most of the time; all of the time. Patients were asked to consider their experience over the past week when responding to the questions. Appearance and body image items asked patients to reflect on their experience since their diagnosis and the sexual function items over the past 4 weeks. Patients were

given option to skip all body image and sexual function items. Patients were presented with an opening question to the sexual function section which asked whether their sex life had been affected for the worse. If the patient reported no issues then they were screened from the remaining questions.

As the study allowed patients who had received chemotherapy within the past 3 months to participate, an additional item “Have you had chemotherapy in the last 4 weeks?” was added. The questionnaire items were numbered in such a way that some of the sexual function items were separated between men and women as shown in Table 4.1.

**Table 4.1 QuEST-Cr questionnaire**

| Question No | Questionnaire Item |
|---|---|
| Q01 | Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? |
| Q02 | Do you have any trouble taking a long walk? |
| Q03 | Do you have any trouble taking a short walk outside of the house? |
| Q04 | Do you need to stay in bed or a chair during the day? |
| Q05 | Do you need help with eating, dressing, washing yourself or using the toilet? |
| Q06 | Are you able to care for yourself? |
| Q07 | Are you able to walk about the house? |
| Q08 | Can you perform light housework/household jobs? |
| Q09 | Can you climb stairs? |
| Q10 | Can you perform heavy housework/household jobs? |
| Q11 | Are you able to walk outdoors? |
| Q12 | Are you able to do your shopping? |
| Q13 | Please place a tick in the box next to the statement that best describes your current level of physical ability |
| | ☐ I am fully active and more or less as I was before my illness<br>☐ I cannot carry out heavy physical work, but can do anything else<br>☐ I am up and about more than half the day; I can look after myself, but not well enough to work<br>☐ I am in bed or sitting in a chair for more than half the day; I need some help in self care<br>☐ I am in bed or a chair all the time and need a lot of looking after |
| | |
| Q14 | Have you had chemotherapy in the past 4 weeks? |
| Q15 | Have you had any infection during your last cycle of chemotherapy? |
| Q16 | Were you admitted to hospital during your last cycle of chemotherapy? |
| Q17 | Were you prescribed any antibiotics during your last cycle of chemotherapy? |
| | |
| Q18 | Have you felt ill or unwell? |
| Q19 | Have you had sore mouth or tongue? |
| Q20 | Did food or drink taste different from usual? |
| Q21 | Have you lacked appetite? |
| Q22 | Have you had indigestion or heartburn? |
| Q23 | Have you felt nauseated (sick?) |
| Q24 | Have you vomited? |
| Q25 | Have you been constipated? |
| Q26 | Did you have a bloated feeling in your abdomen? |
| Q27 | Have you had diarrhoea (or watery stools)? |
| Q28 | Were you short of breath? |
| Q29 | Have you had tingling or numbness in your hands or feet? |

| | |
|---|---|
| Q30 | Have you had soreness or redness of your hands or feet? |
| Q31 | Have you had any other skin problems (e.g. itching, dryness, sensitivity to the sun)? |
| Q32 | Were your eyes painful, irritated, or watery? |
| Q33 | Have you been upset by hair loss? |
| Q34 | Have you had pain? |
| Q35 | Did pain interfere with your daily activities? |
| Q36 | Have your veins been sore or irritated? |
| | |
| Q37 | Do you have a stoma? |
| Q38 | Have you had any problems with it (for example, soreness of skin, increased frequency, leakage)? |
| Q39 | Were you afraid that other people would be able to smell your stools? |
| Q40 | Did you feel embarrassed because of your stoma? |
| Q41 | Did you feel less complete because of your stoma? |
| | |
| Q42 | Have you had trouble sleeping? |
| Q43 | Did you need to rest? |
| Q44 | Have you felt weak? |
| Q45 | Were you tired? |
| Q46 | Have you been less active than you would like to be? |
| Q47 | Have you felt lacking in energy? |
| Q48 | Have you had difficulty in concentrating on things, like reading the newspaper or watching television? |
| Q49 | Did you feel tense? |
| Q50 | Did you worry? |
| Q51 | Did you feel irritable? |
| Q52 | Did you feel depressed? |
| Q53 | Have you been a very nervous person? |
| Q54 | Have you felt so down in the dumps that nothing could cheer you up? |
| Q55 | Have you felt calm and peaceful? |
| Q56 | Have you felt downhearted and low? |
| Q57 | Have you been a happy person? |
| Q58 | Have you felt stressed? |
| Q59 | Have you had difficulty remembering things? |
| Q60 | Have you felt lonely? |
| Q61 | Have you had support from family or friends? |
| Q62 | Have you had trouble talking about your feelings to family or friends? |
| Q63 | Have you felt less able to enjoy yourself? |
| Q64 | Have you been tearful? |
| | |
| Q65 | Have you felt physically less attractive? |
| Q66 | Have you been feeling less feminine/masculine? |
| Q67 | Have you been dissatisfied with your body? |
| | |
| Q68 | Has the disease or treatment affected your sex life (for the worse)? |
| Q69 | To what extent were you interested in sex? |
| Q70 | To what extent were you sexually active? |
| Q71 (men) | To what extent was sex enjoyable for you? |
| Q72 (men) | Did you have difficulty getting or maintaining an erection? |
| Q73 (men) | Did you have pain or discomfort during intercourse? |
| Q74 (women) | To what extent was sex enjoyable for you? |
| Q75 (women) | Did you have a dry vagina during sexual activity? |
| Q76 (women) | Did you have pain or discomfort during intercourse? |
| | |
| Q77 | How much has your treatment interfered with your normal daily activities? |
| Q78 | Were the side effects of your treatment worse than you expected? |
| Q79 | Were you worried about your family in the future? |
| Q80 | Did you feel uncertain about the future? |
| Q81 | Were you limited in doing either your work or other daily activities? |
| Q82 | Were you limited in pursuing your hobbies or other leisure time activities? |
| Q83 | Has your physical condition or medical treatment interfered with your family life? |
| Q84 | Has your physical condition or medical treatment interfered with your social activities? |
| Q85 | Has your physical condition or medical treatment caused you financial difficulties? |
| Q86 | Since you started chemotherapy, how worthwhile do you think your treatment has been? |

*FACT-G*

FACT-G (Cella et al., 1993) is a quality of life instrument intended for use in a variety of chronic illness conditions, which was originally validated in a general cancer populations. It has four scales: Physical well-being (FWB), Social/family well-being (SFWB), Emotional well-being (EWB) and Functional well-being (FWB). A total score or individual subscale score can be calculated. There are five response options to each item within the questionnaire: not at all, a little, somewhat, quite a bit or very much, scoring 0 – 4 respectively. Subscale scores range from 0-24 or 0-28 depending on the number of items within the subscale. Higher scores indicate better functioning. FACT-G has been validated in various cancer populations and has been shown to be reliable across many studies which have used this instrument (Victorson et al., 2008).

*Hospital Anxiety and Depression Scale (HADS)*

The HADS (Zigmond and Snaith, 1983) is a 14 item self report scale which consists of a depression and an anxiety scale, each with 7 items. The scale was designed to screen for mood disorders in general (non-psychiatric) medical outpatients. It focuses on subjective disturbances of mood rather than physical signs and aims to distinguish depression from anxiety. There are four response options for each item scored on 0-3 scale. Scores range from 0-42 with higher scores indicating greater anxiety or depression. Score for each subscale range from 0-21. A score of 0-7 is considered normal, 8-10 mild, 11-14 moderate and 15-21 severe anxiety or depression (Zigmond and Snaith, 1983). The measure has been tested and shown to be valid and reliable in cancer patients (Vodermaier et al., 2009).

*Distress Thermometer (DT)*

DT (Roth et al., 1998) consists of a single item self report measure of psychological distress, followed by a symptom/problem checklist which was added by the National Comprehensive Cancer Network (NCCN) (National Comprehensive Cancer Network, 2003). Patients grade the level of distress they have experienced on 0 (No distress) – 10 (Extreme distress) visual analogue scale. The symptom/problem list consists of 39 items which are divided into 5 groups (practical problems, family problems, emotional problems, physical problems, spiritual/religious concerns). Cut off score of 4 is

suggested to be most sensitive and specific in cancer patients (Jacobsen et al., 2005, Gessler et al., 2008).

## 4.3 Analysis

The analysis had 5 key stages

1. Individual item performance

2. Principal axis factoring

3. Internal consistency reliability

4. Assessment of construct validity

5. Cut off score analysis

Item performance analysis included patient responses in terms of mean score, prevalence and spread of responses together with rating of items by the oncologists were tabulated to formulate evidence to support removing or retaining items. Comments made by patients and oncologists were reviewed prior to any decisions about item removal. The analyses performed were iterative and exploratory in nature with various stages of principal axis factor and reliability analysis being performed before definitive decisions being made about item inclusion/removal. Subscales strength were examined by comparing with validated questionnaires (FACT-G, HADS and DT).

### 4.3.1 Sample size

The sample size was calculated as part of a larger study validating breast, colorectal and gynaecological cancer site specific questionnaires, conducted by the Leeds POCPRG. There were 72 items common across the three disease site specific questionnaires and 9 items specific to colorectal cancer questionnaire and 2 items which were common with either breast or gynaecological cancer questionnaire.

For multivariate analysis, a sample size of at least 200 participants or a subject to item ratio of 5-10 participants per item is typically recommended (Tabacknick and Fidell, 2007). With a ratio of 5 patients per item, it was estimated that a sample size of 370

patients would be required to analyse the 72 core (common across all questionnaires) items. It was anticipated that between the three tumour groups, this target will be met. The planned sample size for the colorectal cancer questionnaire was 120 patients, which would also allow the measurement properties of the CRC specific items to be explored.

### 4.3.2 Data preparation

The data from the questionnaires were automatically imported from Patient Pathway Manager (PPM) into a Microsoft Access database for those patients who completed the questionnaires on touch screen computer. Data from patients who completed the paper questionnaires were entered into the Microsoft Access database manually. Majority of the questionnaire items had 4 point response scale. Data were recoded to avoid '0' categories and to reflect high scores as universally indicating worse outcomes where necessary. Any items which did not have the standard 4 point response scale, such as the MHI5 questions which had 6 point response scale, were transformed to a 1-4 scale so that they can be compared equally with other items during the analysis. Final dataset was imported into SPSS (PASW Statistics 17 for Windows, IBM Corporation, NY, USA).

### 4.3.3 Individual item performance

Descriptive statistics was applied to the data collected from the current study to calculate the mean, prevalence scores (proportion of patients who reported having problems) and spread of patient responses for each item. Items were considered to have problem distributions if

1. Mean scores displaying floor or ceiling effect (mean score <1.5 or >3.0 respectively)

2. Prevalence of experiencing at least some problem/symptom in question was <20% or >80%

3. At least two response categories contained fewer than 10% of responses, indicating poor spread. (An item was considered to have "fair" spread of responses if one category included less than 10% of patient responses)

The descriptive analysis data was tabulated alongside ratings provided by the oncologists (Chapter 3). Items with oncologists' mean ratings of less than 2.5 were considered poor (mean score of 3 indicates an item is useful and mean score of 1 indicates an item is not useful). Any other comments made by patients and oncologists during the interview studies were also considered as part of the assessment of item performance.

### 4.3.4 Exploratory factor analysis

The measurement properties of the CRC questionnaire were studied using exploratory factor analysis. Questionnaire items were initially reviewed in order to select most appropriate items for this analysis. Several items were excluded during this initial item selection. These were 1) Items requiring clinical information from patients (questions concerning infection and antibiotic use); 2) Questions which contained branching items that filtered respondents according to "null" responses (stoma and sexual functioning questions) and 3) Items that were considered to be important clinical question (toxicity questions) which should be retained as single items. The remaining items were broadly divided into "Physical" and "Psychosocial" items. Although physical and psychosocial issues were considered to be two separate concepts, physical symptoms may also have a causal relationship with psychosocial issues. For example, "trouble sleeping" may be manifestation of underlying depressive illness. Any items which were uncertain as to whether they were physical symptoms or psychosocial issues were included in both groups of analyses.

Principal axis factoring (PAF) was used for the analysis. PAF is a type of exploratory factor analysis, which is directed at understanding the correlations among variables by understanding the constructs that underlie them, whereas other forms of factor analysis, such as principal components analysis (PCA), is directed at reduction of variables to summarise the data (Costello and Osborne, 2005). PAF is considered to provide a more accurate reflection of the population factors compared to other types of factor analysis (Snook and Gorsuch, 1989). Promax rotation was applied as this allows the factors to correlate with other items within that factor (Costello and Osborne, 2005).

Various factor models were examined iteratively and items were removed at different stages. Physical issues and psychosocial issues were analysed separately, although there were items included in both analyses as described above. Standard diagnostic

tests were performed in order to ensure appropriateness for factor analysis. These were Kaiser-Meyer-Olkin Measure of Sampling Adequacy and Bartlett's test of sphericity. The number of factors extracted by the models was restricted to those with Kaiser-Guttman Eigenvalue of >1. Factors identified were given appropriate labels. Item loading values ($> \pm 0.3$) were tabulated and variance accounted for by each factor was recorded.

### 4.3.5 Internal consistency and reliability

The scales identified by the exploratory factor analysis and previously existing subscales (from their validated questionnaires) were explored for optimal item reduction. The internal consistency and reliability of the hypothesised subscales was examined using Cronbach's alpha correlation coefficients. Alpha value between 0.7 and 0.9 is generally considered acceptable (Fitzpatrick et al., 1998). Reliability analysis was performed in conjunction with principal axis factor analysis in order to identify the best fit model.

### 4.3.6 Assessment of construct validity

Multi-trait scaling analysis was performed to explore item convergent and discriminate validity. To ensure item convergent validity an item should have a correlation of 0.4 or greater with its own scale (Howard and Forehand, 1962) Item discriminate validity was confirmed if an item did not correlate higher with another scale.

Known groups analysis was conducted using one-way between groups analysis of variance (ANOVA) to explore the subscales' ability to differentiate between particular demographic and clinical characteristics of patients; and to see how they performed with respect to patients' responses to HADS and FACT-G questionnaires. Patients were divided into groups according their gender, disease stage, age (three equal tertiles), HADS total score (divided into four groups using the cut scores provided by the developers of this instrument (Snaith and Zigmond, 1994)) and FACT-G total score quartiles. Quartiles were used for the FACT-G as there are no published cut-points for this instrument.

### 4.3.7 Cut off score analysis

4.3.7.1 Distribution based methods

*Percentage of study population*

Score for each subscale identified from the above exploratory factor analysis and reliability analysis were calculated. Lowest scores of the 10% and 25% (values chosen after discussion with the statistician of Leeds POCPRG) of patients with the poorest scores were calculated to represent severe and moderate impairment respectively.

*Minimally important change (MIC)*

Mean score differences corresponding to small, medium and large effect sizes were calculated by scaling the standard deviation of each scale by the effect size. The standard errors of measurement (SEM) was calculated as a function of the function of the standard deviation and reliability ($\alpha$) of each subscale. The SEM provides an indication of the expected range of a patient's true score.

*Anchor based methods*

FACT-G, HADS, and WHO performance status were used as anchors for the questionnaire subscales. Specific anchors were chosen a priori, based on which measures were expected to be related. Previously published cut points for the anchors were identified where possible, otherwise distribution based cut points were derived. Each of the chosen anchors was used to predict the questionnaire subscale in question using linear regression. The regression formula was applied to calculate equivalent cut off scores and accuracy of such grouping was assessed. Receiver Operator Characteristics curve analysis was also performed using the same anchors. The best cut off score was derived which gave sensitivity above 0.8 or nearest for each of the subscales. Results from the above analyses were compared and most optimal cut off scores for each subscale were selected.

Statistical analyses were guided by the POCPRG statistician, Miss Ada Keding. However, all analyses were performed by myself. All statistical analyses were performed using SPSS (PASW Statistics 17 for Windows, IBM Corporation, NY, USA).

## 4.4 Evaluation of the CRC questionnaire as part of the POCPRG programme of research

This study was a part of a wider study conducted by the POCPRG as part of their programme of research, evaluating cancer site specific questionnaires for breast and gynaecological cancer, as well as colorectal cancer (Harley et al., 2012).

## 4.5 Results

### 4.5.1 Patient characteristics

Of the 168 eligible colorectal cancer patients, 159 patients (92%) consented to take part in the study. However, 4 patients failed to return the paper questionnaires. Therefore, 155 colorectal cancer patients who had recently received or were currently receiving chemotherapy treatment completed the study. 97 were male (62.6%) and 58 were female (37.4%). Their median age was 64 years (range 31 – 88; SD 10.37). 100 patients were receiving the chemotherapy with palliative intent, 51 patients were receiving chemotherapy as adjuvant therapy following potentially curative resection of their disease and 4 patients were receiving the chemotherapy as primary or neo-adjuvant therapy to with the intention of down-staging their disease with the aim of definitive surgery.

#### 4.5.1.1 Chemotherapy regimens

All the chemotherapy agents known to be active in the treatment of bowel cancer were represented in the study population. These are Oxaliplatin, Irinotecan, Fluoropyrimidines (5 Fluorouracil and Capecitabine) and Mitomycin. Most common chemotherapy regimen was Oxaliplatin with 5 Fluorouracil and folinic acid (45.8%), followed by Oxaliplatin with Capecitabine (14.8%) and single agent Capecitabine (11%). 113 patients (72.9%) in the study were receiving intravenous chemotherapy; 17 patients (11.0%) were on oral chemotherapy and 25 patients (16.2%) were on combination of intravenous and oral chemotherapy.

### 4.5.2 Feasibility of questionnaire completion

131 patients (84.5%) completed the questionnaire on touch screen computer (TSC) and 24 patients (15.5%) completed on paper. None of the patients reported difficulty in completing or understanding the questionnaires. Missing data was minimal as majority of patient completed the questionnaire on TSC where they were not given the option to "skip" questions, except for the body image and sexual function items. There were 28 items with at least 1 missing response (excluding body image and sexual function items). This was due to one of the patients who completed paper questionnaire returning it with multiple missing responses. There were only 4 items which had more than one missing data.

2 patients reported that they selected the wrong response option when completing the MHI5 emotional function questions on the touch screen computer. This is likely to have occurred as the wording for these items are different to the standard 4 point responses. As there were only 2 patients who reported this, no specific changes were made to the questionnaire, in particular, option to return to previous items was not instituted.

No specific comments were made for the inclusion of sexual functioning items. 129 patients (83.2%) responded at least to the first item concerning general sexual function. 24 patients (15.5%) responded to all of the items in this section.

### 4.5.3 Item distributions

#### 4.5.3.1 Descriptive statistics

Questionnaire responses were summarised in terms of mean, prevalence and spread. Items with problem distribution were identified according to the criteria set a priori. Questionnaire items with distribution issues is shown in Table 4.2 and summarised in Table 4.3.

**Table 4.2 Questionnaire items with distribution issues**

| Item No. | | Floor effect (mean) | Ceiling effect (mean) | Low prev % | High prev % | Poor spread |
|---|---|---|---|---|---|---|
| 3 | Do you have any trouble taking a short walk outside of the house? | 1.38 | | | | ✓ |
| 5 | Do you need help with eating, dressing, washing yourself or using the toilet? | 1.19 | | 13.5 | | ✓ |
| 6 | Are you able to care for yourself? | 1.45 | | | | ✓ |
| 7 | Are you able to walk about the house? | 1.14 | | 9.7 | | ✓ |
| 8 | Can you perform light housework/household jobs? | 1.40 | | | | ✓ |
| 9 | Can you climb stairs? | 1.25 | | 18.1 | | ✓ |
| 11 | Are you able to walk outdoors? | 1.26 | | 19.4 | | ✓ |
| 12 | Are you able to do your shopping? | | | | | ✓ |
| 13 | Please place a tick in the box next to the statement that best describes your current level of physical ability<br>a. I am fully active and more or less as I was before my illness<br>b. I cannot carry out heavy physical work, but can do anything else<br>c. I am up and about more than half the day; I can look after myself, but not well enough to work<br>d. I am in bed or sitting in a chair for more than half the day; I need some help in self care<br>e. I am in bed or a chair all the time and need a lot of looking after | 1.19 | | | | |
| 15 | Have you had any infection during your last cycle of chemotherapy? | | | 13.7 | | |
| 16 | Were you admitted to hospital during your last cycle of chemotherapy? | | | 12.1 | | |
| 19 | Have you had sore mouth or tongue? | | | | | ✓ |
| 21 | Have you lacked appetite? | | | | | ✓ |
| 22 | Have you had indigestion or heartburn? | | | | | ✓ |
| 24 | Have you vomited? | 1.14 | | 11.6 | | ✓ |
| 25 | Have you been constipated? | 1.41 | | | | ✓ |
| 28 | Were you short of breath? | | | | | ✓ |
| 30 | Have you had soreness or redness of your hands or feet? | 1.37 | | | | |
| 31 | Have you had any other skin problems (e.g. itching, dryness, sensitivity to the sun)? | | | | | ✓ |
| 32 | Were your eyes painful, irritated, or watery? | 1.47 | | | | ✓ |
| 33 | Have you been upset by hair loss? | 1.22 | | 18.1 | | ✓ |
| 34 | Have you had pain? | | | | | ✓ |
| 35 | Did pain interfere with your daily activities? | 1.37 | | | | ✓ |
| 36 | Have your veins been sore or irritated? | 1.18 | | 16.1 | | ✓ |
| 38 | Have you had any problems with it (for example, soreness of skin, increased frequency, leakage)? (stoma) | | | | | ✓ |
| 43 | Did you need to rest? | | | | 83.1 | |
| 45 | Were you tired? | | | | 87.7 | |
| 46 | Have you been less active than you would like to be? | | | | 83.1 | |
| 47 | Have you felt lacking in energy? | | | | 85.6 | |
| 50 | Did you worry? | | | | | ✓ |
| 52 | Did you feel depressed? | | | | | ✓ |
| 53 | Have you been a very nervous person? | | | | | ✓ |
| 54 | Have you felt so down in the dumps that nothing could cheer you up? | | | | | ✓ |

| | | | | | | |
|---|---|---|---|---|---|---|
| 55 | Have you felt calm and peaceful? | | | | 89.0 | |
| 56 | Have you felt downhearted and low? | | | | | ✓ |
| ✓57 | Have you been a happy person? | | | | 80.6 | |
| 58 | Have you felt stressed? | | | | | ✓ |
| 60 | Have you felt lonely? | 1.30 | | | | ✓ |
| 61 | Have you had support from family or friends? | 1.24 | | 1.9 | | ✓ |
| 62 | Have you had trouble talking about your feelings to family or friends? | 1.42 | | | | ✓ |
| 64 | Have you been tearful? | | | | | ✓ |
| 65 | Have you felt physically less attractive? | | | | | ✓ |
| 66 | Have you been feeling less feminine/masculine? | | | | | ✓ |
| 67 | Have you been dissatisfied with your body? | | | | | ✓ |
| 69 | To what extent were you interested in sex? | | 3.22 | | | |
| 70 | To what extent were you sexually active? | | 3.59 | | | ✓ |
| 71 | To what extent was sex enjoyable for you? (Men) | | | 6.7 | | |
| 73 | Did you have pain or discomfort during intercourse? (Men only) | | | | | ✓ |
| 74 | To what extent was sex enjoyable for you? (Women) | | | 18.8 | | |
| 77 | How much has your treatment interfered with your normal daily activities? | | | | 83.9 | |
| 80 | Did you feel uncertain about the future? | | | | 81.3 | |
| 84 | Has your physical condition or medical treatment interfered with your social activities? | | | | 82.6 | |
| 86 | Since you started chemotherapy, how worthwhile do you think your treatment has been? | | 3.07 | | | ✓ |

**Table 4.3 Summary of items with distribution issues**

| **Characteristics of distribution issues** | **Number of items with identified distribution issues (Total number of items 86 – sexual function items divided according to gender)** |
|---|---|
| Items with floor effect (mean <1.5) | 18 |
| Items with ceiling effect (mean >3.0) | 3 |
| Items with low prevalence (<20%) | 12 |
| Items with high prevalence (>80%) | 9 |
| Poor item response spread | 37 |
| Total number of items with some score distribution concerns | 53 |

The distribution properties were used as a decision aid for item inclusion/exclusion following further analyses.

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## 4.5.4 Exploratory factor analysis

Table 4.4 illustrates the initial questionnaire item categorization prior to exploratory factor analysis. The following items were excluded from the analysis at the outset;

these were; items concerning infection which required clinical information and branching items (stoma and sexual function items). Remaining items were broadly divided into “Physical” and “Psychosocial” groups. Item concerning treatment worth was also excluded from the factor analysis as it did not fit in with either category.

**Table 4.4 Categorisation of questionnaire items in preparation for exploratory factor analysis**

| Question number | Abbreviated question | Item category |
|---|---|---|
| Q01 | strenuous activities | Phys |
| Q02 | long walk | Phys |
| Q03 | short walk | Phys |
| Q04 | in bed | Phys |
| Q05 | eat/wash/dress | Phys |
| Q06 | self care | Phys |
| Q07 | walk about the house | Phys |
| Q08 | light housework | Phys |
| Q09 | stairs | Phys |
| Q10 | heavy housework | Phys |
| Q11 | walk outdoors | Phys |
| Q12 | shopping | Phys |
| Q13 | physical activity (WHO) | Phys |
| Q14 | chemo | Clinical |
| Q15 | infection | Clinical |
| Q16 | hospital | Clinical |
| Q17 | antibiotics | Clinical |
| Q18 | ill / unwell | Phys |
| Q19 | sore mouth | Phys |
| Q20 | taste | Phys |
| Q21 | appetite | Phys |
| Q22 | indigestion / heartburn | Phys |
| Q23 | nauseated | Phys |
| Q24 | vomited | Phys |
| Q25 | constipated | Phys |
| Q26 | bloated | Phys |
| Q27 | diarrhoea | Phys |
| Q28 | short of breath | Phys |
| Q29 | hand/feet tingling | Phys |
| Q30 | hand/feet sore | Phys |
| Q31 | skin problems | Phys |
| Q32 | painful eyes | Phys |
| Q33 | hair loss upset | Phys/Psych |
| Q34 | pain | Phys |
| Q35 | pain interference | Phys |
| Q36 | sore veins | Phys |
| Q37 | stoma | Stoma |
| Q38 | stoma - problems | Stoma |
| Q39 | stoma - smell stools | Stoma |
| Q40 | stoma - embarrassment | Stoma |
| Q41 | stoma - feeling complete | Stoma |
| Q42 | sleep | Phys/Psych |

| | | |
|---|---|---|
| Q43 | rest | Phys/Psych |
| Q44 | weak | Phys/Psych |
| Q45 | tired | Phys/Psych |
| Q46 | less active | Phys/Psych |
| Q47 | lacking energy | Phys/Psych |
| Q48 | concentration | Phys/Psych |
| Q49 | tense | Psych |
| Q50 | worry | Psych |
| Q51 | irritable | Psych |
| Q52 | depressed | Psych |
| Q53 | nervous | Psych |
| Q54 | down in dumps | Psych |
| Q55 | calm | Psych |
| Q56 | downhearted | Psych |
| Q57 | happy | Psych |
| Q58 | stressed | Psych |
| Q59 | memory | Phys/Psych |
| Q60 | lonely | Psych |
| Q61 | family support | Psych |
| Q62 | talk about feelings | Psych |
| Q63 | enjoyment | Psych |
| Q64 | tearful | Psych |
| Q65 | attractive | Psych |
| Q66 | feminine/masculine | Psych |
| Q67 | body dissatisfaction | Psych |
| Q68 | sex life | Sexual |
| Q69 | sex interest | Sexual |
| Q70 | sexually active | Sexual |
| Q71/Q74 | enjoyable men / women | Sexual |
| Q72 | erection | Sexual |
| Q75 | dry vagina | Sexual |
| Q73/Q76 | intercourse discomfort men/women | Sexual |
| Q77 | treatment and daily activities | Phys/Psych |
| Q78 | side effects | Phys/Psych |
| Q79 | family future | Psych |
| Q80 | uncertain future | Psych |
| Q81 | limited work or activities | Phys/Psych |
| Q82 | hobbies | Phys/Psych |
| Q83 | family life - interference | Phys/Psych |
| Q84 | social activities | Phys/Psych |
| Q85 | financial difficulties | Psych |
| Q86 | treatment worthwhile | Psych |

Phys: Physical; Psych: Psychosocial

4.5.4.1 Initial factor analysis - Physical items

*Round 1*

46 items belonging to the “physical” category were subjected to principal axis factoring. The Keyser-Meyer-Olkin value was 0.853 exceeding required levels (Tabacknick and Fidell, 2007) and Bartlett’s Test of Sphericity was significant ($p<.05$). The principal axis factoring revealed 13 factors with Eigenvalues above 1, which accounted for 60.4% of the variance (Table 4.5). 12 of these factors were logical and could be given meaning names. These were: Treatment impact, everyday tasks, fatigue, strenuous activities, pain, toxicity, constipation, hands and feet, eyes, hair loss and sore mouth.

**Table 4.5 Round 1 factor analysis of physical items. Dark grey indicates which factor the item correlates most highly with and light grey indicates which factors the item co-loads with (>0.3 or within 0.1 of the highest loading item).**

| | Treatment impact | Everyday tasks | Fatigue | Strenuous activities | Pain | Toxicity | Constipation | Cognitive function | Hands and feet | Eyes | Hair loss | 12 | Sore mouth |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Strenuous activities | .563 | .501 | .557 | .801 | .420 | .286 | | .527 | .350 | .229 | .235 | .376 | -.370 |
| Long walk | .548 | .577 | .505 | .709 | .298 | .247 | | .451 | .337 | .266 | .224 | .416 | -.314 |
| Short walk | .501 | .822 | .500 | .555 | .362 | .301 | | .362 | .373 | .225 | | .467 | -.449 |
| Stay in bed/chair | .468 | .493 | .650 | .430 | .349 | .254 | | .335 | .121 | .177 | | .381 | -.389 |
| Help with eating/dressing | .354 | .744 | .369 | .434 | .497 | .153 | | .348 | .192 | | | .186 | -.282 |
| Care for yourself | .360 | .647 | .220 | .367 | .289 | | | .129 | .139 | | .111 | .433 | |
| Walk about the house | .297 | .696 | .256 | .133 | .309 | | | | .135 | | -.127 | .273 | |
| Light housework | .493 | .627 | .482 | .622 | .277 | .162 | | .385 | .322 | | | .643 | -.204 |
| Stairs | .277 | .766 | .338 | .509 | .147 | .166 | | .348 | .231 | .100 | .201 | .285 | -.183 |
| Heavy housework | .586 | .515 | .518 | .837 | .232 | .205 | | .249 | .181 | | .262 | .509 | -.190 |
| Walk outdoors | .442 | .782 | .384 | .584 | .329 | .352 | | .368 | .308 | .224 | .433 | .419 | -.425 |
| Shopping | .498 | .625 | .453 | .714 | .298 | .274 | | .301 | .284 | .135 | .191 | .442 | -.302 |
| WHO PS | .594 | .454 | .621 | .536 | .315 | .218 | | .351 | .185 | | | .455 | -.158 |
| Ill or unwell | .508 | .316 | .515 | .347 | .416 | .677 | .144 | .459 | .356 | .263 | .347 | .466 | -.315 |
| Sore mouth tongue | .175 | | .141 | .156 | | .203 | | .271 | .269 | .349 | .166 | .154 | .364 |
| Taste different | .358 | | .223 | .107 | | .359 | .290 | .331 | .271 | .277 | .184 | .457 | .142 |
| Lacked appetite | .426 | .216 | .416 | .364 | .259 | .370 | .240 | .345 | .230 | .246 | .332 | .580 | -.211 |
| Indigestion | .102 | .123 | .301 | | .114 | .292 | .387 | | .307 | | | .382 | .132 |
| Nausea | .172 | | .293 | | | .792 | .271 | .239 | | .291 | .108 | .215 | |
| Vomiting | | | | | | .567 | .149 | | .120 | | .127 | | -.112 |
| Constipated | | | | | .237 | .225 | .630 | | .159 | | | .183 | .104 |
| Bloated abdo | .211 | | .188 | .133 | .182 | .285 | .876 | .221 | .220 | | .227 | .223 | |
| Diarrhoea | .192 | .106 | .191 | .144 | | .225 | | | | .145 | | .222 | .119 |
| Short of breath | .511 | .418 | .538 | .301 | .471 | .466 | | .451 | .464 | .352 | .159 | .335 | -.360 |
| Numb hands/feet | .216 | .119 | .101 | .140 | | | .161 | | .784 | | .138 | .221 | .138 |
| Sore hands feet | | | | | | | | .180 | .333 | .204 | -.145 | | |
| other skin probs | | | .137 | | .147 | .127 | .149 | .303 | | .149 | | | |
| Eyes painful | .109 | | .119 | .130 | | .183 | | .246 | .102 | .759 | .141 | .165 | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Upset hair loss | | | | .107 | | | | .102 | | .101 | .544 | .117 | |
| Pain | .392 | .354 | .393 | .277 | .871 | .223 | .157 | .354 | .159 | .148 | | .281 | -.211 |
| Pain interfere with activities | .430 | .464 | .445 | .358 | .911 | .236 | .150 | .418 | .247 | .167 | | .245 | -.316 |
| Veins sore | .295 | | .171 | .104 | .104 | .140 | | .134 | .101 | | | | |
| Trouble sleeping | .360 | | .330 | | .234 | .146 | .314 | .118 | .299 | -.106 | | .325 | .297 |
| Need to rest | .543 | .283 | .839 | .324 | .341 | .327 | | .413 | .280 | .177 | | .342 | |
| Felt weak | .677 | .384 | .819 | .583 | .317 | .403 | .180 | .514 | .416 | .185 | .411 | .599 | -.327 |
| Tired | .605 | .294 | .850 | .513 | .315 | .345 | .120 | .515 | .249 | .145 | .255 | .470 | -.133 |
| Less active | .714 | .431 | .718 | .627 | .311 | .220 | | .383 | .340 | | .296 | .600 | -.271 |
| Lacking in energy | .732 | .421 | .844 | .659 | .398 | .336 | | .503 | .338 | .106 | .412 | .587 | -.349 |
| Concentrating | .558 | .362 | .553 | .483 | .323 | .228 | .112 | .628 | .259 | | .227 | .473 | -.281 |
| Difficulty remembering | .363 | .214 | .364 | .297 | .257 | .149 | | .661 | .238 | .162 | .174 | .277 | -.123 |
| Treatment interfere with daily activities | .824 | .407 | .582 | .478 | .324 | .127 | | .335 | .252 | | .168 | .504 | |
| Treatment side effects | .577 | .264 | .371 | .467 | .264 | .347 | .186 | .381 | .303 | .166 | .277 | .300 | -.277 |
| Limited in work | .781 | .391 | .562 | .475 | .353 | .128 | | .371 | .202 | .148 | | .415 | |
| Limited in hobbies | .793 | .481 | .487 | .540 | .335 | .169 | | .386 | .239 | .102 | .163 | .547 | |
| Interfere with family life | .748 | .209 | .500 | .343 | .286 | .252 | | .222 | .274 | | .118 | .394 | -.221 |
| Interfere with social activities | .834 | .444 | .556 | .464 | .303 | .194 | | .361 | .367 | | .143 | .407 | -.164 |

*Round 2*

The questionnaire items were reviewed with members of the Leeds POCPRG as part of the process of developing cancer site specific questionnaires across three different disease groups to see whether any of the items which did not fit in well with the named factor were considered clinically useful single items rather than item within a subscale. For example, item on sensory peripheral neuropathy would be considered important chemotherapy toxicity question, which can have an impact on clinical decision making. Therefore, items on sensory neuropathy, sore eyes and sore veins were removed from subsequent subscale analysis and retained as clinically meaningful single items. Principal axis factoring with remaining 43 items revealed 11 factors with Eigenvalues above 1, which accounted for 59.3% of the variance. The Keyser-Meyer-Olkin value was 0.87 and Bartlett's Test of Sphericity was significant (.000). The factors could each be given meaningful names, which were: everyday tasks, fatigue, treatment impact, nausea and vomiting, pain, constipation, strenuous activities, appetite, sore mouth, skin and hair loss.

*Round 3*

Further review of the items was carried out following the above analysis. Gastrointestinal symptoms are of particular relevance for patients receiving chemotherapy treatment, especially for those with colorectal cancer. Constipation and diarrhoea were both considered to be important clinically important individual items. In addition, the WHO performance status was also removed as this item did not correlate well with other physical function items. The WHO performance status item is also different from other items in a sense that it tries to capture the overall physical ability of a patient in one question, rather than exploring a particular side effect or ability to perform a specific activity. Remaining 40 items were subjected to principal axis factoring. The Keyser-Meyer-Olkin value was 0.87 and Bartlett's Test of Sphericity was significant (.000). Principal axis factoring revealed 10 factors with Eigenvalues above 1 which accounted for 58.5% of the variance. The factors were each given names, which were: everyday tasks, impact on activities, fatigue, strenuous activities, nausea and vomiting, pain, non-specific bowel symptoms, skin/cognitive function, sore mouth and hair loss. The result of this factor analysis is shown in Table 4.6.

**Table 4.6 Round 3 factor analysis of physical items (six items removed). Dark grey indicates which factor the item correlates most highly with and light grey indicates which factors the item co-loads with (>0.3 or within 0.1 of the highest loading item).**

| | Everyday tasks | Impact on activities | Fatigue | Strenuous activities | Nausea/ vomiting | pain | Non-specific GI symptoms | Skin/ cognitive | Sore mouth | Hair loss |
|---|---|---|---|---|---|---|---|---|---|---|
| Strenuous activities | | | .126 | .809 | | .187 | | | .134 | -.102 |
| Long walk | .255 | .106 | | .553 | | | -.222 | | .195 | |
| Short walk | .725 | | | | .129 | | -.131 | .116 | | -.101 |
| Stay in bed/chair | .224 | | .527 | | | | -.148 | | -.241 | |
| Help with eating/dressing | .631 | | | | | .251 | | .103 | | |
| Care for yourself | .705 | .130 | -.173 | | -.225 | | .171 | | | .115 |
| Walk about the house | .859 | .183 | | -.405 | | | .116 | -.222 | | |
| Light housework | .454 | | | .332 | -.101 | | | .222 | | -.268 |
| Stairs | .815 | -.251 | | .141 | | -.128 | | .106 | .162 | |
| Heavy housework | .170 | .132 | | .821 | | | | -.341 | | |
| Walk outdoors | .721 | | -.146 | .116 | .130 | | | | | .250 |
| Shopping | .397 | | | .568 | | | | -.176 | | |
| Ill or unwell | | .201 | | | .509 | .133 | | .119 | | .155 |
| Sore mouth or tongue | | | | .176 | .143 | | | .208 | .778 | .199 |
| Taste different | | .294 | -.158 | | .195 | -.235 | .237 | .360 | .239 | |
| Lacked appetite | | | | .111 | | | .244 | .168 | -.139 | .104 |
| Indigestion | .184 | -.261 | .268 | -.125 | .198 | | .542 | | | |
| Nausea | | | | | .836 | | .159 | -.102 | .171 | -.131 |
| Vomiting | | | | .106 | .731 | | | -.315 | | |
| Bloated abdomen | | | -.126 | | | .101 | .625 | | -.169 | |
| Short of breath | .162 | .171 | .150 | -.135 | .277 | .109 | | .224 | | |
| Sore hands or feet | .106 | -.136 | | -.109 | | | | .434 | .213 | -.156 |
| other skin problems | | -.211 | | -.192 | -.110 | .194 | | .547 | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Upset by hair loss | | | | -.131 | | | | | .228 | .804 |
| Pain | | | | .131 | | .739 | | .141 | | |
| Pain interfere with activities | | | | .190 | | .801 | | .168 | | |
| Trouble sleeping | | .293 | .127 | -.187 | | .167 | .452 | | .178 | |
| Need to rest | | | .860 | -.152 | | | | .105 | .131 | |
| Felt weak | | | .542 | .105 | | | .137 | | | .129 |
| Tired | -.130 | | .880 | .187 | | | | | .103 | |
| Less active | | .294 | .413 | .278 | | | | -.128 | -.109 | |
| Lacking in energy | | .155 | .624 | .233 | | | | | -.116 | |
| Concentrating | | .128 | .192 | | -.207 | | .138 | .394 | -.150 | |
| Difficulty remembering | | | .106 | | -.217 | | -.116 | .713 | .137 | |
| Treatment interfere with daily activities | | .817 | | | -.102 | | | | | |
| Treatment side effects | | .432 | -.164 | .251 | .128 | | | | | |
| Limited in work | | .732 | | | -.108 | | | | | |
| Limited in pursuing hobbies | .146 | .748 | -.104 | .174 | | | | | .112 | |
| Interfere with family life | -.179 | .982 | | -.129 | | | -.123 | -.122 | -.167 | |
| Interfere with social activities | | .895 | | | | | -.113 | | | |

4.5.4.2 Reliability analysis – Physical items

Reliability analysis was performed for each of the subscales identified from the factor analysis using Alpha reliability statistics. The results from this analysis are shown in Table 4.7. 10 factors emerged from the final principal axis factoring. Name given to each factor is written in bold at the top of each section and below are the individual items which formed that factor. The loading column describes the correlations each item had within the factor. If any of the items co-loaded with another factor then this is detailed in the “co-loader”. The best alpha column indicates which items combined to create the best possible alpha. The initial alpha score and the percentage of variance explained by the factor or presented below the list of items for each factor.

Each of the subscales was analysed individually to determine whether the alpha could be improved by removal of items. The reliability statistics were repeated until the best alpha was achieved. For example, removing “Treatment side effects” and “Interfere with family life” improved the alpha for the impact on activities subscale.

**Table 4.7 Reliability analysis for physical items.**

| **Factor 1** | **Everyday Tasks** | | | |
|---|---|---|---|---|
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | short walk | 0.725 | n | ✓ |
| | Help with eating/dressing | 0.631 | n | ✓ |
| | Care for yourself | 0.705 | n | ✓ |
| | Walk about the house | 0.859 | -.405 strenuous activities | ✓ |
| | Light housework | 0.454 | .332 strenuous activities | ✓ |
| | Stairs | 0.815 | n | ✓ |
| | Walk outdoors | 0.721 | n | ✓ |
| Cronbach's α | 0.871 | | | 0.871 |
| % Variance explained | 31.7 | | | |
| | | | | |
| **Factor 2** | **Impact on Activities** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Treatment interfere | 0.817 | n | ✓ |
| | Treatment side effects | 0.432 | n | X |
| | Limited in work | 0.732 | n | ✓ |
| | Limited pursuing hobbies | 0.748 | n | ✓ |
| | Interfere with family life | 0.982 | n | X |
| | Interfere with social activities | 0.895 | n | ✓ |
| Cronbach's α | 0.888 | | | 0.902 |
| % Variance explained | 6.6 | | | |
| | | | | |

| **Factor 3** | **Fatigue** | | | |
|---|---|---|---|---|
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Stay in bed/chair | 0.527 | n | X |
| | Need to rest | 0.860 | n | ✓ |
| | Felt weak | 0.542 | n | ✓ |
| | Tired | 0.880 | n | ✓ |
| | Less active | 0.413 | n | ✓ |
| | Lacking energy | 0.624 | n | ✓ |
| Cronbach's α | 0.910 | | | 0.914 |
| % Variance explained | 4.4 | | | |
| | | | | |
| **Factor 4** | **Strenuous Activities** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Strenuous activities | 0.809 | n | ✓ |
| | Long walk | 0.553 | n | ✓ |
| | Heavy housework | 0.821 | -.341 skin/cognitive | ✓ |
| | Shopping | 0.568 | .397 everyday tasks | ✓ |
| Cronbach's α | 0.856 | | | 0.856 |
| % Variance explained | 2.9 | | | |
| | | | | |
| **Factor 5** | **Nausea & Vomiting** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Ill / unwell | 0.509 | n | ✓ |
| | Nausea | 0.836 | n | ✓ |
| | Vomiting | 0.731 | -.315 skin/cognitive | ✓ |
| | Short of breath | 0.277 | .224 skin/cognitive | ✓ |
| Cronbach's α | 0.684 | | | 0.684 |
| % Variance explained | 3.5 | | | |
| | | | | |
| **Factor 6** | **Pain** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Pain | 0.739 | n | ✓ |
| | Pain interfere with activities | 0.801 | n | ✓ |
| Cronbach's α | 0.886 | | | 0.886 |
| % Variance explained | 2.5 | | | |
| | | | | |
| **Factor 7** | **Non-specific GI symptoms** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Lacked appetite | 0.244 | .168 skin/cognitive | ✓ |
| | Indigestion | 0.542 | n | ✓ |
| | Bloated abdomen | 0.625 | n | ✓ |
| | Trouble sleeping | 0.452 | n | ✓ |
| Cronbach's α | 0.556 | | | 0.556 |
| % Variance explained | 2.2 | | | |
| | | | | |

| **Factor 8** | **Skin / Cognition** | | | |
|---|---|---|---|---|
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Taste different | 0.360 | 4 co-loaders | X |
| | Sore hands or feet | 0.434 | n | X |
| | Other skin problems | 0.547 | n | X |
| | Concentrating | 0.394 | n | ✓ |
| | Difficulty remembering | 0.713 | n | ✓ |
| Cronbach's α | 0.512 | | | 0.603 |
| % Variance explained | 1.8 | | | |
| | | | | |
| **Factor 9** | **Sore Mouth** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Sore mouth or tongue | 0.778 | n | - |
| Cronbach's α | - | | | - |
| % Variance explained | 1.5 | | | |
| | | | | |
| **Factor 10** | **Hair Loss** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | Upset by hair loss | 0.804 | n | - |
| Cronbach's α | - | | | - |
| % Variance explained | 1.4 | | | |

4.5.4.3 Secondary factor analysis

Everyday tasks, impact on activities, fatigue, strenuous activities and pain all formed reliable subscales in the initial factor analysis as described above. These items were removed from the factor analysis model for the physical and symptom items and further factor analysis was performed on the remaining 15 items. These items were subjected to principal axis factoring. The Keyser-Meyer-Olkin value was 0.742 and Bartlett's Test of Sphericity was significant (.000). Principal axis factoring revealed 6 factors with Eigenvalues above 1 which accounted for 41.9% of the variance. The result of this analysis is shown in Table 4.8. Four of the factors were logical and could be given names, which were: nausea and vomiting, mouth problems, hair loss and skin problems.

**Table 4.8 Factor analysis of leftover physical items. Dark grey indicates which factor the item correlates most highly with and light grey indicates which factors the item co-loads with (>0.3 or within 0.1 of the highest loading item).**

| | 1 | Nausea/ vomiting | 3 | Mouth problems | Hair loss | Skin problems |
|---|---|---|---|---|---|---|
| Ill or unwell | .501 | .387 | | | | |
| Sore mouth or tongue | -.122 | | | .701 | .146 | .210 |
| Taste different | .185 | | | .624 | | -.182 |
| Lacked appetite | .420 | | .112 | .117 | .100 | -.207 |
| Indigestion | -.151 | | .636 | | | .138 |
| Nausea | | .717 | | .182 | -.108 | |
| Vomiting | | .712 | | -.127 | | |
| Bloated abdo | .133 | | .651 | -.196 | | |
| Shortness of breath | .537 | .173 | | | | |
| Sore hands or feet | | | .119 | .159 | | .367 |
| other skin problems | .163 | | .166 | | | .301 |
| Upset by hairloss | | | | .101 | .700 | |
| Trouble sleeping | | -.101 | .462 | .148 | | .202 |
| Concentrating | .660 | -.118 | | | | |
| Difficulty remembering | .749 | -.102 | -.188 | | | .279 |

Physical activity items were also explored individually as the initial factor analysis and reliability analyses did not reduce the number of items within the subscale significantly, particularly for the subscale “Everyday tasks”. The 12 physical activity items were subjected to principal axis factoring. The Keyser-Meyer-Olkin value was 0.897 and Bartlett’s Test of Sphericity was significant (.000). The items separated into 2 factors with Eigenvalues above 1, which accounted for 55.5% of the variance. The result from this analysis is shown in Table 4.9.

**Table 4.9 Factor analysis of physical activity items. Dark grey indicates which factor the item correlates most highly with and light grey indicates which factors the item co-loads with (>0.3 or within 0.1 of the highest loading item).**

| | Strenuous activities | Everyday tasks |
|---|---|---|
| Strenuous activities | .962 | -.228 |
| Long walk | .782 | |
| Short walk | .361 | .523 |
| Stay in bed/chair | .399 | .181 |
| Help with eating/dressing | .157 | .598 |
| Care for yourself | | .667 |
| Walk about the house | -.305 | .917 |
| Light housework | .525 | .267 |
| Stairs | .228 | .558 |
| Heavy housework | .839 | |
| Walk outdoors | .314 | .542 |
| Shopping | .641 | .17 |

The factors could broadly be described as “strenuous activities” and “everyday tasks” although “stay in bed/chair” and “light housework” both loaded onto the factor which generally described activities which required more effort. In the previous factor analysis, “stay in bed/chair” loaded onto the factor which described symptoms of fatigue and “light housework” co-loaded between “everyday tasks” and “strenuous activities” (Table 4.5).

### 4.5.4.4 Secondary reliability analysis

The reliability analysis of the 15 remaining physical and symptoms items (nausea and vomiting, mouth problems and skin problems) did not demonstrate good reliability. These subscales were disregarded but they were retained for decision whether they should be considered as single items. For example, nausea and vomiting are both important toxicity symptoms of chemotherapy and therefore they were retained as clinically meaningful question as part of this questionnaire

The strenuous activity scale had a reliability of 0.870. Two items “stay in bed/chair” and “light housework” were removed as they were considered not to fit in conceptually with “strenuous activity scale”. The reliability was not significantly affected with alpha of 0.86 for the remaining four items in the subscale.

The everyday tasks scale had best reliability of 0.871 if all seven items, including “light housework” was included in the scale. Conceptually, “short walk” and “walk about the house” seemed to encompass similar activity. Removal of “walk about the house” had little impact on the alpha, which was 0.863; removal of “short walk” resulted in alpha of 0.838. Similarly, “care for yourself” and “help with eating/washing and dressing” seemed to address similar activities. Removal of “care for yourself” improved the alpha to 0.868.

#### 4.5.4.5 Final decisions made regarding physical items with wider programme of research in mind

Regular meetings took place with other members of the Leeds POCPRG so that common subscales can be developed for questionnaires across the three cancer sites.

The analyses of factor analyses and reliability analyses were reviewed and occasionally changes were made to produce the best combination of items for the three cancer groups. . For example, inclusion of “walk about the house” improved the alpha of the “everyday tasks” subscale for the breast and gynaecological cancer questionnaires over “short walk”. This did not impact significantly on the alpha of the colorectal questionnaire, which was still 0.815. Table 4.10 illustrates the final decision made on the physical items.

**Table 4.10 Final decisions about physical items**

| Abbreviated item description | Decisions made (scale, single item, remove) | Reasons |
|---|---|---|
| short walk | Remove | Similar item within everyday task scale No detriment to alpha |
| walk about the house | Everyday Tasks | Included to streamline with other questionnaires |
| light housework | Remove | Good reliability |
| stairs | Everyday Tasks | Good reliability |
| walk outdoors | Everyday Tasks | Good reliability |
| eat/wash/dress | Everyday Tasks | Good reliability |
| strenuous activities | Strenuous activities | Good reliability |
| long walk | Strenuous activities | Good reliability |
| heavy housework | Strenuous activities | Good reliability |
| shopping | Strenuous activities | Good reliability |
| rest | Fatigue | Best alpha |
| weak | Fatigue | Best alpha |

| | | |
|---|---|---|
| tired | Fatigue | Best alpha |
| less active | Fatigue | Best alpha |
| lacking energy | Fatigue | Best alpha |
| treatment and daily activities | Impact on Activities | Removed to streamline with other questionnaires |
| limited work or activities | Impact on Activities | Good reliability |
| hobbies | Impact on Activities | Good reliability |
| family life - interference | Impact on Activities | Good reliability |
| social activities | Impact on Activities | Good reliability |
| pain | Pain | Best alpha |
| pain interference | Pain | Best alpha |
| in bed | Remove | Did not fit conceptually with strenuous activities |
| self care | Remove | Better reliability if removed.<br>Similar to another item in everyday tasks |
| ill / unwell | Remove | Poor doctor rating, too generic |
| skin problems | Remove | Not specific enough |
| concentration | Single item | Of clinical interest |
| memory | Single item | Of clinical interest |
| side effects | Remove | Question is good, but more about managing expectations |
| physical activity (who) | Single item | Of clinical interest |
| sore mouth | Single item | Of clinical interest |
| taste | Single item | Of clinical interest |
| appetite | Single item | Of clinical interest |
| indigestion / heartburn | Single item | Of clinical interest |
| nauseated | Single item | Of clinical interest |
| vomited | Single item | Of clinical interest |
| constipated | Single item | Of clinical interest |
| bloated | Single item | Of clinical interest |
| diarrhoea | Single item | Of clinical interest |
| short of breath | Single item | Of clinical interest |
| hand/feet tingling | Single item | Of clinical interest |
| hand/feet sore | Single item | Of clinical interest |
| hair loss upset | Remove | Not often applicable in colorectal cancer |
| sore veins | Single item | Of clinical interest |
| painful eyes | Single item | Of clinical interest |
| sleep | Single item | Of clinical interest |

4.5.4.6 Initial factor analysis – Psychosocial Items

The 36 psychosocial items were subjected to principal axis factoring. The Keyser-Meyer-Olkin value was 0.911 exceeding required levels and Bartlett's Test of Sphericity was significant ($p<.000$) supporting the use of this type of analysis. Principal axis factoring revealed 8 factors with Eigenvalues above 1 which accounted for 58.7% of the variance. The result from the principal axis factoring is shown in Table 4.11. The names given to the 8 factors were: emotional functioning, impact on activities, fatigue, body image, future worries, depression, support and hair loss.

There were 15 items which overlapped between physical and psychosocial items. These items generally fell into the same factors as previously identified during the exploratory factor analysis of the physical items.

**Table 4.11 Initial factor analysis of psychosocial items. Dark grey indicates which factor the item correlates most highly with and light grey indicates which factors the item co-loads with (>0.3 or within 0.1 of the highest loading item).**

| | Emotional functioning | Impact on activities | Fatigue | Body image | Future worries | depression | support | Hair loss |
|---|---|---|---|---|---|---|---|---|
| Upset by hairloss | -.124 | -.289 | .220 | .181 | | -.179 | | .651 |
| Trouble sleeping | | | | | | .724 | | -.253 |
| Need to rest | -.126 | | .729 | | | .342 | .156 | |
| Felt weak | | | .820 | | | | | .284 |
| Tired | -.101 | | .943 | | | | | |
| Less active | | .374 | .538 | | | | | |
| Lacking in energy | | .242 | .682 | | | | | .182 |
| Concentrating | .271 | .160 | .434 | | | -.169 | -.191 | |
| Feel tense | .527 | -.170 | .280 | | | .239 | -.227 | |
| Worry | .888 | | | | .112 | | -.263 | -.125 |
| Irritable | .394 | | .188 | | | .174 | | .268 |
| Depressed | .772 | .144 | -.109 | | -.174 | | | .203 |
| Nervous person | .490 | -.141 | | | | -.141 | .146 | -.261 |
| Down in the dumps | .802 | -.204 | .146 | | | -.134 | .351 | |
| Calm and peaceful | .477 | | | | | | .127 | .220 |
| Downhearted and low | .761 | | | | | | | |
| Happy person | .447 | .171 | | -.176 | | | .223 | .221 |
| Felt stressed | .500 | -.116 | | | .187 | .262 | | |
| Difficulty remembering | .456 | | .205 | | | | | |
| Felt lonely | .836 | | | | | | | -.284 |
| Support from family and friends | | | | | -.159 | | .558 | |
| Trouble talking about feelings | .237 | | | | | .216 | .248 | -.131 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Less able to enjoy | .398 | .257 | .363 | | | -.129 | | -.126 |
| Tearful | .177 | | | | | .478 | | |
| Physically less attractive | | | | .969 | | | | .123 |
| Less feminine/masculine | .106 | .244 | | .552 | | | | |
| Dissatisfied with body | | .117 | | .671 | | .146 | | .205 |
| Treatment interfere with daily activities | | .764 | .192 | | | | | -.121 |
| Treatment side effects | .171 | .524 | | | | | | |
| Worried about family | -.122 | | | | .959 | | -.174 | |
| Uncertain about future | .207 | .211 | -.179 | | .608 | | | .146 |
| Limited in work | -.134 | .749 | .161 | | .100 | .133 | | -.232 |
| Limited in pursuing hobbies | | .849 | | .160 | -.126 | | | -.110 |
| Interfere with family life | | .743 | | | .150 | | | |
| Interfere with social activities | | .773 | .131 | | .103 | | | -.186 |
| Finance | | .235 | | | .240 | .190 | | -.176 |

4.5.4.7 Initial reliability analysis

In a similar manner to the physical items, reliability analysis was performed on each of the 8 subscales identified from the factor analysis. The result is shown in Table 4.12.

**Table 4.12 Reliability analysis of psychosocial items**

| **Factor 1** | **Emotional functioning** | | | |
|---|---|---|---|---|
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | tense | *0.527* | n | ✓ |
| | worry | 0.888 | n | ✓ |
| | irritable | 0.394 | n | ✓ |
| | depressed | 0.772 | n | ✓ |
| | nervous | 0.490 | n | X |
| | down in the dumps | 0.802 | 0.351 Support | ✓ |
| | calm and peaceful | 0.477 | n | ✓ |
| | downhearted | 0.761 | n | ✓ |
| | happy person | 0.447 | n | ✓ |
| | felt stressed | 0.500 | n | ✓ |
| | memory | 0.456 | n | ✓ |
| | lonely | 0.836 | n | X |
| | less able to enjoy | 0.398 | 0.363 Fatigue | ✓ |
| | | | | |
| Cronbach's α | 0.910 | | | 0.915 |
| % Variance explained | 36.3 | | | |
| **Factor 2** | **Impact on activities** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | treatment interfere with daily activities | 0.764 | n | ✓ |
| | Treatment side effects | 0.524 | n | X |
| | limited in work | 0.749 | n | ✓ |
| | limited in hobbies | 0.849 | n | ✓ |
| | interfere with family life | 0.743 | n | X |
| | interfere with social activities | 0.773 | n | ✓ |
| | | | | |
| Cronbach's α | 0.888 | | | 0.902 |
| % Variance explained | 6.7 | | | |

| **Factor 3** | **Fatigue** | | | |
|---|---|---|---|---|
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | need to rest | 0.729 | 0.342 Depression | ✓ |
| | felt weak | 0.820 | n | ✓ |
| | tired | 0.943 | n | ✓ |
| | less active | 0.538 | 0.374 Impact of activities | ✓ |
| | lacking in energy | 0.682 | n | ✓ |
| | concentrating | 0.434 | n | X |
| | | | | |
| Cronbach's α | 0.911 | | | 0.914 |
| % Variance explained | 4.7 | | | |
| **Factor 4** | **Body image** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | less attractive | 0.969 | n | ✓ |
| | less feminine/masculine | 0.552 | n | ✓ |
| | dissatisfied with body | 0.671 | n | ✓ |
| | | | | |
| Cronbach's α | 0.870 | | | 0.870 |
| % Variance explained | 3.0 | | | |
| **Factor 5** | **Future worries** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | worried about family | 0.959 | n | ✓ |
| | uncertain about future | 0.608 | n | ✓ |
| | finance | 0.240 | 0.235 Impact on activities | X |
| | | | | |
| Cronbach's α | 0.728 | | | 0.814 |
| % Variance explained | 2.9 | | | |
| **Factor 6** | **Depression** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | sleep | 0.724 | n | ✓ |
| | tearful | 0.478 | n | ✓ |
| | | | | |
| Cronbach's α | 0.578 | | | 0.578 |
| % Variance explained | 1.9 | | | |
| **Factor 7** | **Support** | | | |
| | *Initial Items* | *Loading* | *Co-Loader?* | *Best α* |
| | family support | 0.558 | n | ✓ |
| | talk about feelings | 0.248 | 2 co-loaders | ✓ |
| | | | | |
| Cronbach's α | 0.292 | | | 0.292 |
| % Variance explained | 1.7 | | | |

| **Factor 8** | **Hair loss** | | | |
|---|---|---|---|---|
| | *Initial items* | *Loading* | *Co-Loader?* | *Best α* |
| | upset by hair loss | 0.651 | n | |
| | | | | |
| Cronbach's α | | - | | |
| % Variance explained | 1.6 | | | |

The emotional distress scale initially consisted of 13 items with Cronbach alpha reliability of 0.910. After removal of two items, this could be improved to 0.915. However, 11 items within the subscale was considered too lengthy. Further reliability analyses were performed to examine how far the number of items within the subscale could be reduced, whilst maintaining acceptable reliability ($\alpha$ >0.8). It was possible to reduce the scale to 5 items (Feel tense, worry, irritable, depressed and stressed) and still retain reliability of 0.902. These items, with the exception of "stressed" derives from EORTC QLQ-C30 (Aaronson et al., 1993). Reliability of the four emotional functioning items from EORTC QLQ-C30 was found to be 0.889 and reliability of five items from MHI-5 (Berwick et al., 1991) was 0.756.

Items for "impact on activities" and "Fatigue" formed reasonable subscales, as found from previous factor analyses of "physical" items. The three body image items showed good reliability with alpha of 0.870.

#### 4.5.4.8 Secondary factor analysis – Psychosocial items

Principal axis factoring was performed on the remaining psychosocial items after items on "impact on activities", "fatigue" and "body image" were removed as they had formed subscales with good reliability. The emotional function items were retained in the analysis. This analysis, however, failed to show any new meaningful factor which had not been identified previously.

#### 4.5.4.9 Final decisions made regarding psychosocial items with wider programme of research in mind

In a similar manner to the decisions made for the "physical" items, regular meetings were held with other members of the Leeds POCPRG so that common subscales can be developed for the three cancer sites. Table 4.13 illustrates the decisions made on

the psychosocial items. There were two additional subscales identified which have been retained for the QuEST-Cr questionnaire; emotional distress and body image.

The emotional functioning items from the MHI-5 was retained over the EORTC QLQ-C30 emotional functioning subscale, despite the latter having better reliability, as the interview study suggested that both clinicians and patients did not necessarily feel that the wording from the EORTC QLQ-C30 items reflected patients' experiences.

Although two items concerning "uncertain about future" and "worried about family in the future" seemed to form a subscale according to the factor analysis, these items were considered to address different issues. These items were removed as clinicians considered "uncertainty about future" was something that they expected their patients to experience and not a helpful question for the purpose of this questionnaire.

**Table 4.13 Final decisions about psychosocial items**

| Abbreviated item description | Decisions made (scale, single item, remove) | Reasons |
|---|---|---|
| attractive | Body Image | Best alpha |
| feminine/masculine | Body Image | Best alpha |
| body dissatisfaction | Body Image | Best alpha |
| nervous | Emotional Distress | MHI-5 items, good scale for clinical management |
| down in dumps | Emotional Distress | MHI-5 items, good scale for clinical management |
| calm | Emotional Distress | MHI-5 items, good scale for clinical management |
| downhearted | Emotional Distress | MHI-5 items, good scale for clinical management |
| happy | Emotional Distress | MHI-5 items, good scale for clinical management |
| family future | Family/ Future Worries | Though good alpha with "uncertain future", these were considered two separate issues |
| rest | Fatigue | Best alpha |
| weak | Fatigue | Best alpha |
| tired | Fatigue | Best alpha |
| less active | Fatigue | Best alpha |
| lacking energy | Fatigue | Best alpha |

| | | |
|---|---|---|
| uncertain future | Future Worries | Though good alpha with “family future”, these were considered two separate issues |
| limited work or activities | Impact on Activities | Good reliability |
| hobbies | Impact on Activities | Good reliability |
| family life - interference | Impact on Activities | Good reliability |
| social activities | Impact on Activities | Good reliability |
| tense | Remove | Potential Anxiety question, but due to poor factoring of emotional items MHI-5 instead |
| worry | Remove | Potential Anxiety question, but due to poor factoring of emotional items MHI-5 instead |
| irritable | Remove | Potential Anxiety question, but due to poor factoring of emotional items MHI-5 instead |
| depressed | Remove | Potential Depression question, but due to poor factoring of emotional items MHI-5 instead |
| stressed | Remove | Potential Anxiety question, but due to poor factoring of emotional items MHI-5 instead |
| lonely | Remove | Did not fit well into any emotional construct |
| family support | Remove | Did not fit well into any emotional construct |
| talk about feelings | Remove | Did not fit well into any emotional construct |
| enjoyment | Remove | Potential Depression question, but due to poor factoring of emotional items MHI-5 instead |
| tearful | Remove | Potential Depression question, but due to poor factoring of emotional items MHI-5 instead |
| future health | Remove | Did not fit well into any emotional construct |
| treatment and daily activities | Remove | Good question but data only for colorectal questionnaire |
| side effects | Remove | Question is good, but more about managing expectations |
| hair loss upset | Remove | Of clinical interest for breast and gynae, did not fit well with other items |
| sleep | Single Item | Of clinical interest, did not fit well with other items |
| concentration | Single Item | Of clinical relevance |
| memory | Single Item | Of clinical relevance |
| financial difficulties | Single Item | Anticipated to be single item, did not group meaningfully with other items |

Table 4.14 summarises the final subscales derived from the above factor analyses of physical and psychosocial items and single items retained for QuEST-Cr.

**Table 4.14 Subscales derived from factor analyses and retained single items for QuEST-Cr**

| |
|---|
| **Strenuous activities** |
| Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase? |
| Do you have any trouble taking a long walk? |
| Can you perform heavy housework/household jobs? |
| Are you able to do your shopping? |
| |
| **Everyday Tasks** |
| Do you need help with eating, dressing, washing yourself or using the toilet? |
| Are you able to walk about the house? |
| Can you perform light housework/household jobs? |
| Can you climb stairs? |
| Are you able to walk outdoors? |
| |
| **Pain** |
| Have you had pain |
| Did pain interfere with your daily activities? |
| |
| **Fatigue** |
| Did you need to rest? |
| Have you felt weak? |
| Were you tired? |
| Have you been less active than you would like to be? |
| Have you felt lacking in energy? |
| |
| **Impact on activities** |
| Were you limited in doing either your work or other daily activities? |
| Were you limited in pursuing your hobbies or other leisure time activities? |
| Has your physical condition or medical treatment interfered with your family life? |
| Has your physical condition or medical treatment interfered with your social activities? |
| |
| **Emotional Distress (MHI-5)** |
| Have you been a very nervous person? |
| Have you felt so down in the dumps that nothing could cheer you up? |
| Have you felt calm and peaceful? |
| Have you felt downhearted and low? |
| Have you been a happy person? |
| |
| **Body Image** |
| Have you felt physically less attractive? |
| Have you been feeling less feminine/masculine? |
| Have you been dissatisfied with your body? |
| |
| **Single Items** |
| Have you had sore mouth or tongue? |
| Did food or drink taste different from usual? |
| Have you lacked appetite? |
| Have you had indigestion or heartburn? |
| Have you felt nauseated (sick?) |

| |
|---|
| Have you vomited? |
| Have you been constipated? |
| Did you have a bloated feeling in your abdomen? |
| Have you had diarrhoea (or watery stools)? |
| Were you short of breath? |
| Have you had tingling or numbness in your hands or feet? |
| Have you had soreness or redness of your hands or feet? |
| Have your veins been sore or irritated? |
| Were your eyes painful, irritated, or watery? |
| Have you had trouble sleeping? |
| Has your physical condition or medical treatment caused you financial difficulties? |

#### 4.5.4.10 Sexual function and stoma items

Items for sexual function and stoma issues were retained as they were without any alterations in the QuEST-Cr as it was not feasible to analyse these items in the similar way as the other times in the questionnaire.

### 4.5.5 Assessment of construct validity

#### 4.5.5.1 Multi-trait scaling analysis

Table 4.15 illustrates the multi-trait scaling analysis performed to explore the item convergent validity, which was above 0.4 for all subscales. No item discriminate scaling errors were identified.

**Table 4.15 Multi-trait scaling analysis. (Figures in bold represent item convergent validity)**

| | strenuous activities | everyday tasks | pain | fatigue | impact on activities | emotional distress (MHI-5) | body image |
|---|---|---|---|---|---|---|---|
| Strenuous activities | **0.847** | 0.548 | 0.465 | 0.601 | 0.511 | 0.318 | 0.298 |
| Long walk | **0.805** | 0.581 | 0.345 | 0.531 | 0.490 | 0.293 | 0.271 |
| Heavy housework | **0.876** | 0.582 | 0.294 | 0.586 | 0.543 | 0.301 | 0.350 |
| Shopping | **0.822** | 0.678 | 0.372 | 0.492 | 0.454 | 0.216 | 0.279 |
| Help with eating/dressing | 0.512 | **0.777** | 0.491 | 0.365 | 0.366 | 0.136 | 0.223 |
| Walk about the house | 0.283 | **0.643** | 0.228 | 0.210 | 0.317 | 0.028 | 0.063 |
| Light housework | 0.659 | **0.768** | 0.361 | 0.516 | 0.493 | 0.243 | 0.278 |
| Stairs | 0.558 | **0.817** | 0.220 | 0.352 | 0.262 | 0.190 | 0.223 |
| Walk outdoors | 0.631 | **0.818** | 0.390 | 0.445 | 0.393 | 0.266 | 0.278 |
| Pain | 0.374 | 0.363 | **0.950** | 0.362 | 0.350 | 0.173 | 0.334 |
| Pain interfere with activities | 0.450 | 0.475 | **0.945** | 0.431 | 0.402 | 0.150 | 0.301 |
| Need to rest | 0.403 | 0.336 | 0.350 | **0.807** | 0.541 | 0.391 | 0.362 |
| Felt weak | 0.603 | 0.474 | 0.359 | **0.873** | 0.599 | 0.430 | 0.423 |
| Tired | 0.519 | 0.378 | 0.363 | **0.886** | 0.561 | 0.405 | 0.330 |
| Less active | 0.644 | 0.489 | 0.329 | **0.844** | 0.644 | 0.380 | 0.383 |
| Lacking in energy | 0.645 | 0.513 | 0.411 | **0.919** | 0.651 | 0.484 | 0.411 |
| Limited in work | 0.527 | 0.429 | 0.366 | 0.619 | **0.864** | 0.352 | 0.386 |
| Limited in pursuing hobbies | 0.577 | 0.499 | 0.371 | 0.583 | **0.860** | 0.333 | 0.445 |
| Interfere with family life | 0.388 | 0.248 | 0.285 | 0.528 | **0.788** | 0.434 | 0.403 |
| Interfere with social activities | 0.522 | 0.468 | 0.316 | 0.629 | **0.876** | 0.407 | 0.454 |
| Nervous person | 0.210 | 0.195 | 0.003 | 0.154 | 0.123 | **0.564** | 0.160 |
| Down in the dumps | 0.215 | 0.202 | 0.092 | 0.434 | 0.333 | **0.806** | 0.384 |
| Calm and peaceful | 0.299 | 0.193 | 0.191 | 0.361 | 0.386 | **0.734** | 0.421 |
| Downhearted and low | 0.188 | 0.152 | 0.172 | 0.416 | 0.373 | **0.725** | 0.338 |
| Happy person | 0.269 | 0.122 | 0.136 | 0.369 | 0.375 | **0.748** | 0.262 |
| Physically less attractive | 0.307 | 0.247 | 0.265 | 0.356 | 0.389 | 0.367 | **0.933** |
| Less feminine/masculine | 0.420 | 0.324 | 0.353 | 0.479 | 0.526 | 0.417 | **0.852** |
| Dissatisfied with body | 0.245 | 0.216 | 0.288 | 0.348 | 0.425 | 0.391 | **0.886** |

4.5.5.2 Known groups analysis

Results of the one-way between groups analysis of variance are presented in Table 4.16. There was a statistically significant difference ($p < .05$) for all the subscales when evaluated against the HADS and FACT-G total scores. Poorer scale scores from QuEST-CR corresponded with poorer scores on both HADS and FACT-G.

Age did not have significant impact on the subscales, apart from body image with younger patients reporting more problems. Female patients reported more problems with strenuous activities than male patients but otherwise gender impact was not observed. There was a trend for younger patients reporting body image issues. No significant differences were seen between patients with different stages of disease, although the number of patients with early stage disease (stages 1 to 3) was small.

**Table 4.16 Differences in subscale scores by disease stage, HADS and FACT-G Total score groups, age and gender**

| | Disease Stage (Total n=155) | | | | p | HADS Total Score (Total n=154) | | | | p | FACT-G Total Score (Total n=155) | | | | p | Age (Total n=155) | | | p | Gender (Total n=155) | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | | 0-7 | 8-10 | 11-15 | 16-42 | | 108-90 | 89-80 | 79-69 | 68-0 | | 31-60 | 61-68 | 69-88 | | Male | Female | |
| | n=2 Mean (SD) | n=9 Mean (SD) | n=34 Mean (SD) | n=110 Mean (SD) | | n=84 Mean (SD) | n=17 Mean (SD) | n=24 Mean (SD) | n=29 Mean (SD) | | n=39 Mean (SD) | n=40 Mean (SD) | n=38 Mean (SD) | n=38 Mean (SD) | | n=54 Mean (SD) | n=52 Mean (SD) | n=49 Mean (SD) | | n=97 Mean (SD) | n=58 Mean (SD) | |
| Strenuous Activities | 2.38 (1.94) | 2.19 (0.75) | 1.88 (0.68) | 2.10 (0.91) | .524 | 1.76 (0.78) | 2.33 (0.78) | 2.41 (0.81) | 2.45 (0.92) | .000 | 1.37 (0.44) | 1.86 (0.73) | 2.48 (0.80) | 2.57 (0.85) | .000 | 1.96 (0.81) | 2.10 (0.86) | 2.13 (0.94) | .564 | 1.91 (0.83) | 2.3 (0.88) | .006 |
| Everyday Tasks | 1.00 (0.00) | 1.25 (0.66) | 1.15 (0.30) | 1.23 (0.45) | .750 | 1.11 (0.30) | 1.26 (0.51) | 1.22 (0.38) | 1.44 (0.64) | .004 | 1.02 (0.12) | 1.08 (0.18) | 1.31 (0.5) | 1.44 (0.6) | .000 | 2.06 (0.87) | 1.18 (0.38) | 1.19 (0.41) | .598 | 1.19 (0.43) | 1.22 (0.45) | .653 |
| Pain | 1.00 (0.00) | 1.28 (0.44) | 1.32 (0.49) | 1.53 (0.77) | .293 | 1.32 (0.57) | 1.38 (0.76) | 1.48 (0.52) | 1.88 (0.97) | .003 | 1.17 (0.37) | 1.26 (0.42) | 1.63 (0.79) | 1.80 (0.9) | .000 | 1.53 (0.63) | 1.44 (0.82) | 1.41 (0.65) | .673 | 1.47 (0.71) | 1.44 (0.70) | .768 |
| Fatigue | 2.20 (0.28) | 2.42 (0.59) | 2.22 (0.67) | 2.25 (0.77) | .911 | 1.92 (0.56) | 2.25 (0.73) | 2.68 (0.68) | 2.89 (0.65) | .000 | 1.65 (0.45) | 2.05 (0.52) | 2.37 (0.57) | 2.99 (0.65) | .000 | 2.26 (0.70) | 2.31 (0.70) | 2.20 (0.76) | .727 | 2.22 (0.74) | 2.30 (0.73) | .536 |
| Emotional Distress | 2.32 (0.34) | 1.65 (0.55) | 1.68 (0.51) | 1.77 (0.55) | .352 | 1.46 (0.38) | 1.72 (0.31) | 1.93 (0.34) | 2.45 (0.47) | .000 | 1.38 (0.37) | 1.55 (0.34) | 1.80 (0.5) | 2.29 (0.46) | .000 | 1.84 (0.52) | 1.71 (0.58) | 1.60 (0.51) | .287 | 1.73 (0.55) | 1.77 (0.53) | .638 |
| Body Image | 1.67 (0.94) | 1.67 (0.47) | 1.49 (0.63) | 1.78 (0.86) | .343 | 1.33 (0.48) | 1.94 (0.88) | 2.07 (0.76) | 2.35 (0.95) | .000 | 1.25 (0.42) | 1.49 (0.63) | 1.75 (0.66) | 2.36 0.95 | .000 | 1.94 (0.84) | 1.63 (0.77) | 1.52 (0.75) | .022 | 1.65 (0.84) | 1.80 (0.73) | .234 |
| Impact on Activities | 2.13 (0.18) | 2.17 (0.81) | 2.12 (0.80) | 2.24 (0.81) | .638 | 1.81 (0.62) | 2.40 (0.78) | 2.71 (0.66) | 2.81 (0.77) | .000 | 1.58 (0.54) | 1.96 (0.56) | 2.25 (0.56) | 3.07 (0.68) | .000 | 2.33 (0,81) | 2.16 (0.78) | 2.13 (0.82) | .386 | 2.15 (0.79) | 2.31 (0.82) | .240 |
| [3]Sexual Function | n=2 | n=7 | n=30 | n=89 | | n=67 | n=14 | n=23 | n=24 | | n=31 | n=31 | n=33 | n=33 | | n=48 | n=43 | n=37 | | n=83 | n=45 | |
| | 2.00 (1.41) | 2.71 (1.11) | 1.87 (1.01 | 2.31 (0.29) | .243 | 1.85 (1.13) | 2.50 (1.16) | 2.61 (1.27) | 2.75 (1.23) | .003 | 1.68 (0.98) | 2.00 (1.25) | 2.27 (1.23) | 2.91 (1.18) | .000 | 2.35 (1.18) | 2.21 (1.23) | 2.08 (1.32) | .598 | 2.22 (1.31) | 2.24 (1.09) | .904 |

*One person did not complete the HADS questionnaire therefore excluded from known groups analysis using HADS. [1]HADS Total Score: range of scores 0-42, higher scores represent greater emotional distress; [2]FACT-G Total Score: range of scores 0-108, lower scores represent poorer functioning; [3]Sexual Function: only the first item in the scale was evaluated in order to maximize the responses available

## 4.5.6 Cut off score analysis

### 4.5.6.1 Distribution base methods

*Percentage of study population*

Score for the subscale identified from the above factor analyses were calculated for the whole study population. As majority of patients (83.2%) responded to the screening question concerning impact on their sexual function, this was included in the cut score analysis.

The lowest score of the 10% and 25% (values chosen after discussion with the wider research group to represent severe and moderate impairment, respectively) of patients with the poorest scores is shown in Table 4.17.

**Table 4.17 Top percent of patients with worse scores**

| Subscale (Mean Raw Score) | 25% Cut off (Moderate Approximation) | 10% Cut off (Severe Approximation) |
|---|---|---|
| Strenuous Activities | 2.75 | 3.35 |
| Everyday Tasks | 1.25 | 2.00 |
| Pain | 2.00 | 2.50 |
| Fatigue | 2.80 | 3.40 |
| Impact on Activities | 2.75 | 3.25 |
| Emotional Distress (MHI-5) | 2.08 | 2.49 |
| Body Image | 2.00 | 3.00 |
| Sex Life | 3.00 | 4.00 |

### 4.5.6.2 Minimally important differences (MIDs)

Mean score differences corresponding to small, medium and large effect sizes (d=0.2, 0.5 and 0.8 respectively) were calculated by scaling the standard deviation (s) of each scale by the effect size.

The standard error of the mean (SEM) is calculated as a function of the standard deviation of the sample scores and reliability (α) of each subscale. (SEM = s $\sqrt{}$(1 - $\alpha$)). The SEM gives an indication of the expected range of a patient's true score (Crosby et

al., 2003). Low levels of SEM indicate high levels of score accuracy and conversely, high levels of SEM indicate low levels of score accuracy. The thresholds of 1.0 SEM (68% confidence interval) and the more conservative 1.96 SEMs (95% confidence interval) are reported.

Quality of Life data is expected to be positively skewed with the majority of patients being well. In order to make estimates of the changes in quality of life more meaningful for these patients, MIDs was calculated as above using the variability of the total sample as well as the 75% best scoring sub-sample. The result of this analysis is shown in Table 4.18.

**Table 4.18 Distribution based estimates of Minimally Important Differences**

| Subscale | | MID for Total Sample | MID adjusted for 75% best scoring sample* |
|---|---|---|---|
| Strenuous Activities | d=0.2 | .17 | .10 |
| | d=0.5 | .43 | .25 |
| | d=0.8 | .69 | .39 |
| | 1.00 * SEM | .33 | .19 |
| | 1.96 * SEM | .64 | .36 |
| Everyday Tasks | d=0.2 | .09 | .02 |
| | d=0.5 | .23 | .04 |
| | d=0.8 | .36 | .06 |
| | 1.00 * SEM | .19 | .03 |
| | 1.96 * SEM | .38 | .06 |
| Pain | d=0.2 | 14 | .04 |
| | d=0.5 | .35 | .11 |
| | d=0.8 | .56 | .17 |
| | 1.00 * SEM | .24 | .08 |
| | 1.96 * SEM | .47 | .16 |
| Fatigue | d=0.2 | 15 | .09 |
| | d=0.5 | .37 | .22 |
| | d=0.8 | .59 | .35 |
| | 1.00 * SEM | .21 | .12 |
| | 1.96 * SEM | .42 | .25 |

| | | | |
|---|---|---|---|
| Impact on activities | d=0.2 | .16 | 07 |
| | d=0.5 | .40 | .17 |
| | d=0.8 | .64 | .28 |
| | 1.00 * SEM | .29 | .17 |
| | 1.96 * SEM | .57 | .34 |
| Emotional distress | d=0.2 | .11 | .06 |
| | d=0.5 | .27 | .15 |
| | d=0.8 | .43 | .24 |
| | 1.00 * SEM | .27 | .15 |
| | 1.96 * SEM | .52 | .29 |
| Body Image | d=0.2 | 16 | .09 |
| | d=0.5 | .40 | .24 |
| | d=0.8 | .64 | .28 |
| | 1.00 * SEM | .29 | .10 |
| | 1.96 * SEM | .57 | .20 |
| Impact on sex life | d=0.2 | 25 | .09 |
| | d=0.5 | .62 | .23 |
| | d=0.8 | .98 | .37 |
| | 1.00 * SEM | n/a | n/a |
| | 1.96 * SEM | n/a | n/a |
| * Number of patients may exceed stated percentile where more patients have the same scale score | | | |

4.5.6.3 Anchor based methods

*Anchor selection*

Hospital Anxiety and Depression Scale (HADS), FACT-G, the Distress Thermometer and WHO Performance Status were used as anchors for the questionnaire subscales. Specific anchors were chosen a priori, based on which measures were expected to be related.

Cut off scores derived from the developers of the instruments were available for the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) and the Distress Thermometer (Jacobsen et al., 2005). Razavi et al investigated the use of HADS specifically as a tool to screen for depressive disorders in cancer population (Razavi et al., 1990). They have proposed a slightly different cur off scores compared to Snaith

and Zigmond, whose study sample consisted of patients in general medical out-patient clinics. Therefore, both sets of cut off scores were examined.

**Table 4.19 Chosen anchors and cut points**

| | Approximate Impairment Categories | | | |
|---|---|---|---|---|
| | Non-Case | | Case | |
| | Normal | Mild | Moderate | Severe |
| HADS Total[1] | 0 - 7<br>0 - 7 | 8 - 10<br>8 - 10 | 11 - 15<br>11 - 18 | 16 – 42*<br>19 – 42** |
| HADS Anxiety[1] | 0 - 7 | 8 - 10 | 11 - | 21 |
| HADS Depression[1] | 0 - 7 | 8 - 10 | 11 - | 21 |
| WHO Performance Status[2] | 1 - | 2 | 3 - | 5 |
| FACT-G Total[2] | 108 - | 65 | 64 - 55 | 54 - 0 |
| FACT-G PWB[2] | 28 - | 18 | 17 - 13 | 12 - 0 |
| FACT-G EWB[2] | 24 - | 14 | 13 - 10 | 9 - 0 |
| FACT-G SFWB[2] | 28 - | 19 | 18 - 15 | 14 - 0 |
| FACT-G FWB[2] | 28 - | 12 | 11 - 8 | 7 - 0 |
| FACT-G Fatigue Item[2] | 0 - | 2 | 3 | 4 |
| FACT-G Pain Item[2] | 0 - | 0 | 1 - 2 | 3 - 4 |
| FACT-G Sex Item[2] | 0 - | 3 | 4 - | 4 |
| Distress Thermometer[1] | 0 - | 3 | 4 - | 10 |

[1] Published cut points available (* scores based on Zigmond and Snaith, ** scores based on Razavi et al)

[2] No published cut points available. Worst scoring 25% and 10% chosen as approximates for moderate and severe cases respectively. Where both scores are equivalent, only a moderate cut point is specified.

PWB: Physical well-being, EWB: Emotional well-being, SFWB: Social/Family well-being, FWB: Functional well-being

For FACT-G and WHO performance status, Worst scoring 25% and 10% chosen as approximates for moderate and severe cases respectively. For WHO performance status, scale of 1-5 was used rather than 0-4, to avoid null values. Table 4.19 illustrates the chosen anchors and approximate impairment categories and their respective questionnaire/item scores.

Anchor-based measures require them to be least moderately correlated with the instrument being explored. Pearson correlation coefficients were examined between the anchor measures and the respective subscales. As all data originated from the same source, correlations between all measures were only used to assess the suitability of the chosen anchors, but not to select them. Table 4.20 illustrates the correlation between the anchor measures and the QuEST-Cr subscales. This showed that the FACT-G Social/Family well-being scale did not correlate well with the subscale "Impact on activities".

**Table 4.20 Pearson's Correlation Coefficients with Chosen Anchors**

| | HADS Total | HADS Anx | HADS Dep | WHO Performance Status | FACT-G Total | FACT-G PWB | FACT-G EWB | FACT-G SFWB | FACT-G FWB | FACT-G Q4 (Pain) | FACT-G Q1 (Energy) | FACT-G Q14 (Sex Life) | Distress Therm. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | r | r | r | r | r | r | r | r | r | r | r | r | r |
| Strenuous Activities | | | | .583 | | -.538 | | | | | | | |
| Everyday Tasks | | | | .489 | | -.470 | | | | | | | |
| Pain | | | | | | | | | | .821 | | | |
| Fatigue | | | | | | | | | | . | .783 | | |
| Impact on Activities* | | | | | | | | -.255 | -.696 | | | | |
| Emotional Distress (MHI-5) | .752 | .658 | .677 | | | | -.416 | | | | | | .561 |
| Body Image | | | | | | | | | | | | | |
| Impact on Sex Life | | | | | | | | | | | | -.394 | |

r: Pearson correlation coefficient, PS: performance status
* Due to low correlations, FACTG-SFWB will not be used as an anchor for Impact on Activities

4.5.6.4 Linear regression

Each of the chosen anchors was used to predict the questionnaire subscale in question using linear regression. The regression formula was then applied to calculate equivalent cut-off scores (where equivalent values before and at the cut point were more than one decimal apart, the mean was taken as the new cut point) and the accuracy of such groupings was assessed. Table 4.21 summarizes the cut off score analysis by linear regression.

**Table 4.21 Cut-offs predicted by Linear Regression**

| | Matched Cut-Offs | | | | Under-estimate | Correct Assignment | Over-estimate | Positive Predictive Value | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Moderate | Severe |
| **Strenuous Activities** | | | | | | | | | |
| WHO PS | 1-2 | - | 3-5 | - | | | | | |
| Strenuous Activities | 1.0-2.2 | | 2.3-4.0 | | 24 (15.5%) | 105 (67.7%) | 26 (16.8%) | 57.4% | |
| FACT-PWB | 28-18 | - | 17-13 | 12-0 | | | | | |
| Strenuous Activities | 1.0-2.4 | | 2.5-2.9 | 3.0-4.0 | 7 (4.5%) | 108 (69.7%) | 40 (25.8%) | 48.1% | 16.7% |
| **Everyday Tasks** | | | | | | | | | |
| WHO PS. | 1-2 | - | 3-5 | - | | | | | |
| Everyday Tasks | 1.0-1.2 | | 1.3-4.0 | | 35 (22.6%) | 104 (67.1%) | 16 (10.3%) | 60.0% | |
| FACT-PWB | 28-18 | - | 17-13 | 12-0 | | | | | |
| Everyday Tasks | 1.0-1.3 | | 1.5-1.6 | 1.7-4.0 | 18 (11.6%) | 121 (78.1%) | 16 (10.3%) | 62.5% | 22.2% |
| **Pain** | | | | | | | | | |
| FACTG Pain | 0 | - | 1-2 | 3-4 | | | | | |
| Pain | 1.0-1.4 | | 1.4-2.5 | 2.6-4.0 | 15 (9.7%) | 129 (83.8%) | 10 (6.5%) | 86.6% | 83.3% |
| **Fatigue** | | | | | | | | | |
| FACTG Fatigue | 0-2 | - | 3 | 4 | | | | | |
| Fatigue | 1.0-2.5 | | 2.6-3.0 | 3.1-4.0 | 14 (9.1%) | 118 (76.6%) | 22 (14.3%) | 72.5% | 58.3% |
| **Impact on Activities** | | | | | | | | | |
| FACTG FWB | 28-12 | - | 11-8 | 7-0 | | | | | |
| Impact on Activities | 1.0-2.6 | | 2.7-3.0 | 3.1-4.0 | 7 (4.5%) | 121 (78.1%) | 27 (17.4%) | 53.3% | 34.6% |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Emotional Distress (MHI-5)** | | | | | | | | | |
| HADS Total (1) | 0-7 | 8-10 | 11-15 | 16-42 | | | | | |
| Emotional Distress | 1.0-1.6 | 1.7-1.8 | 1.9-2.1 | 2.2-4.0 | 24 (15.6%) | 100 (64.9%) | 30 (19.5%) | 72.7% | 60.5% |
| HADS Total (2) | 0-7 | 8-10 | 11-18 | 19-42 | | | | | |
| Emotional Distress | 1.0-1.6 | 1.7-1.8 | 1.9-2.3 | 2.4-4.0 | 24 (15.6%) | 96 (62.3%) | 34 (22.1%) | 72.7% | 35.0% |
| HADS Anxiety | 0-7 | 8-10 | 11-21 | - | | | | | |
| Emotional Distress | 1.0-2.0 | 2.1-2.3 | 2.4-4.0 | | 11 (7.1%) | 114 (74.0%) | 29 (18.8%) | 46.5% | 30.0% |
| HADS Depression | 0-7 | 8-10 | 11-21 | - | | | | | |
| Emotional Distress | 1.0-2.0 | 2.1-2.3 | 2.4-4.0 | | 14 (9.0%) | 112 (72.3%) | 29 (18.7%) | 38.6% | 35.0% |
| FACTG EWB | 24-14 | - | 13-10 | 9-0 | | | | | |
| Emotional Distress | 1.0-1.9 | | 2.0-2.1 | 2.2-4.0 | 11 (7.1%) | 95 (61.3%) | 49 (31.6%) | 28.6% | 13.2% |
| Distress Therm. | 0-3 | - | 4-10 | - | | | | | |
| Emotional Distress | 1.0-1.9 | | 2.0-4.0 | | 11 (7.1%) | 114 (73.5%) | 30 (19.4%) | 46.4% | |
| **Impact on Sex Life** | | | | | | | | | |
| FACTG Sex Life | 0-3 | - | 4 | - | | | | | |
| Impact on Sex Life | 1.0-2.3 | | 2.4-4.0 | | 20 (22.2%) | 32 (35.6%) | 38 (42.2%) | 7.3% | |

4.5.6.5 Receiver Operating Characteristic Curves

Cut off scores were further explored using the Receiver Characteristic Operating (ROC) curves using the same anchor measures. ROC curves compare sensitivity versus specificity across a range of values for the ability to predict a dichotomous outcome and provide another measure of test performance.

The anchor measures were converted into dichotomous variables according to the cut off scores outlined previously in order to perform the analysis using SPSS.

Cut off scores were chosen based on the score which provided sensitivity greater than or nearest to 0.8 with best specificity. Positive predictive value for the cut off score identified was also calculated for each subscale. Table 4.22 summarizes the ROC curve analysis performed.

**Table 4.22 ROC curve analysis**

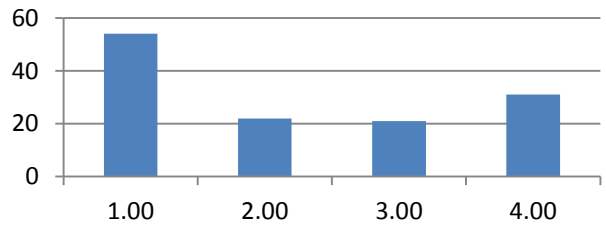
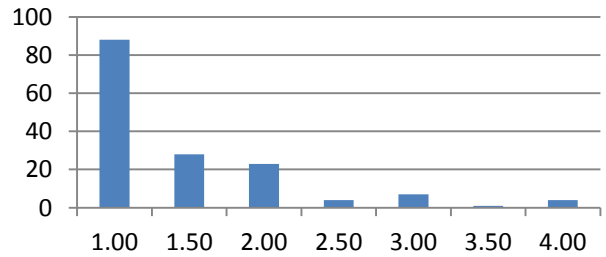
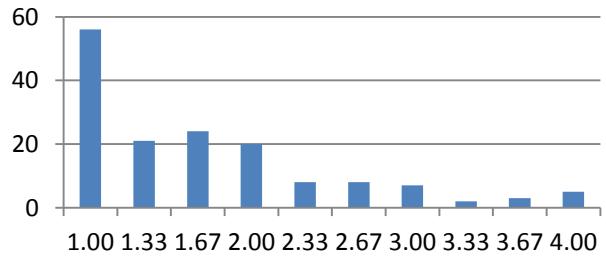
| | Anchor | | positive case n | AUC* (standard error) *p* | p | Best Cut-off | Sensitivity above 0.8 or nearest | Specificity | Positive Predictive Value |
|---|---|---|---|---|---|---|---|---|---|
| Strenuous Activities | WHO PS | ≥ 3 | 59 | .758 (.039) | .000 | 1.6 | 81.4% | 51.0% | 50.5% |
| | FACTG-PWB | ≤ 17 | 31 | ..839 (.036) | .000 | 2.4 | 80.6% | 78.2% | 48.1% |
| | | ≤ 12 | 7 | .875 (.038) | .001 | 2.9 | 85.7% | 79.7% | 16.7% |
| Everyday Tasks | WHO PS | ≥ 3 | 59 | .720 (.044) | .000 | 1.1 | 66.1% | 78.1% | 65.0% |
| | FACTG-PWB | ≤ 17 | 31 | .777 (.051) | .000 | 1.1 | 64.5% | 71.0% | 40.0% |
| | | ≤ 12 | 7 | .910 (.039) | .000 | 1.5 | 85.7% | 87.8% | 25.0% |
| Pain | FACTG Pain | ≥ 1 | 70 | .879 (.031) | .000 | 1.3 | 82.9% | 89.3% | 86.6% |
| | | ≥ 3 | 14 | .930 (.050) | .000 | 1.8 | 92.9% | 81.4% | 33.3% |
| Fatigue | FACTG Fatigue | ≥ 3 | 46 | .925 (.022) | .000 | 2.5 | 80.4% | 87.0% | 72.5% |
| | | ≥ 4 | 20 | .935 (.021) | .000 | 2.9 | 85.0% | 86.6% | 48.6% |
| Impact on Activities | FACTG FWB | ≤ 11 | 31 | .869 (.034) | .000 | 2.4 | 839% | 72.6% | 43.3% |
| | | ≤ 7 | 12 | .845 (.065) | .000 | 2.1 | 83.3% | 54.5% | 13.3% |
| Emotional Distress (MHI-5) | HADS-T | ≥ 8 | 70 | .859 (.030) | .000 | 1.7 | 81.4% | 77.4% | 75.0% |
| | | ≥ 11 | 53 | .884 (.027) | .000 | 1.8 | 84.9% | 78.2% | 67.2% |
| | | ≥ 16 | 29 | .921 (.023) | .000 | 1.9 | 89.7% | 76.8% | 47.3% |
| | | ≥ 19 | 11 | .915 (.039) | .000 | 2.1 | 90.9% | 80.4% | 26.3% |
| | HADS Anxiety | ≥ 8 | 29 | .857 (.033) | .000 | 1.8 | 86.2% | 66.4% | 37.3% |
| | | ≥ 11 | 8 | .935 (.027) | .000 | 2.1 | 100.0% | 79.5% | 21.1% |
| | HADS Depression | ≥ 8 | 25 | .853 (.035) | .000 | 1.9 | 84.0% | 73.1% | 37.5% |
| | | ≥ 11 | 15 | .881 (.038) | .000 | 2.1 | 80.0% | 81.4% | 31.6% |
| | FACTG EWB | ≤ 13 | 27 | .738 (.049) | .000 | 1.5 | 85.2% | 46.9% | 25.3% |
| | | ≤ 9 | 7 | .801 (.084) | .007 | 1.5 | 100.0% | 43.2% | 7.7% |
| | Distress Thermometer | ≥ 4 | 37 | .784 (.046) | .000 | 1.8 | 81.1% | 67.8% | 44.1% |
| Impact on Sex Life | FACTG Sex Life | ≥ 4 | 60 | .301 (.047) | .000 | 1.5 | 41.7% | 26.9% | 33.8% |

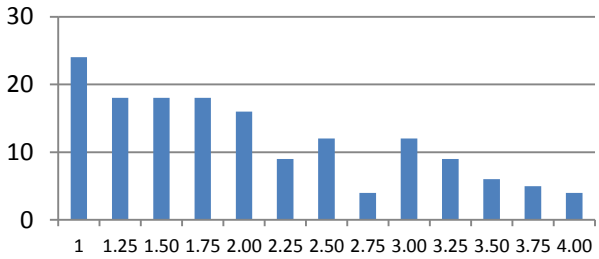
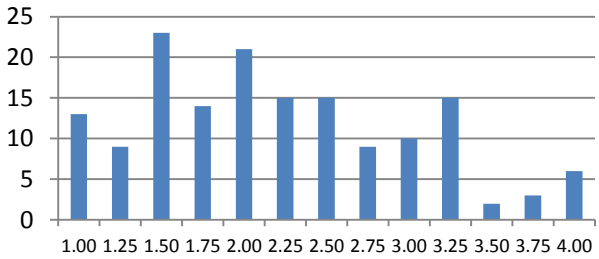
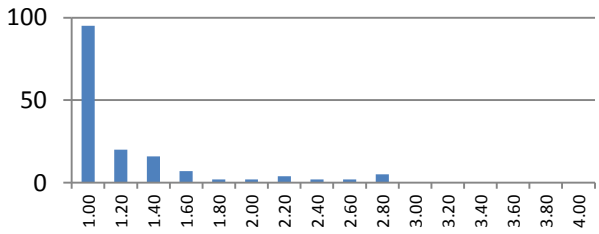
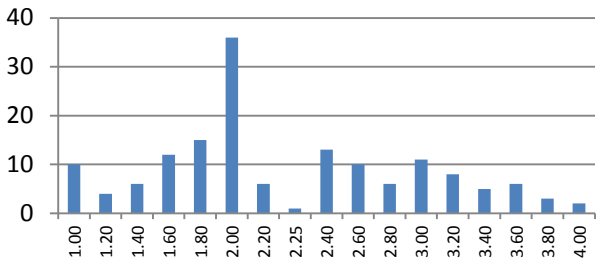
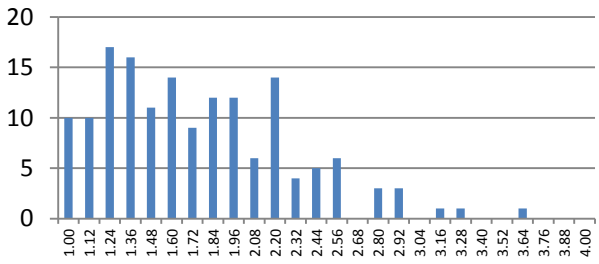
*AUC: Area under the curve, PS: performance status

4.5.6.6 Scale Representation

Prior to decisions being made on the cut off scores for the respective subscales, it was necessary to determine the smallest feasible difference between two scores for each subscale. Table 4.23 illustrates the relationship between the number of scale items and response options together with minimal possible increment for each subscale. The table also illustrates the frequency of scores obtained from the study population from the Questionnaire Validation Study.

**Table 4.23 Response Options and Minimal Possible Increment**

| Scale Items | Number of possible responses | Range | Minimum Possible Increment | Response Frequencies |
|---|---|---|---|---|
| 1 | 4 | 1 - 4 | 1.00 | Impact on Sex Life   |
| 2 | 7 | 1 - 4 | 0.50 | Pain   |
| 3 | 10 | 1 - 4 | 0.33 | Body Image   |

| Scale Items | Number of possible responses | Range | Minimum Possible Increment | Response Frequencies |
|---|---|---|---|---|
| 4 | 13 | 1 - 4 | 0.25 | Strenuous Activities   |
| | | | | Impact on Activities   |
| 5 | 16 | 1 - 4 | 0.20 | Everyday Tasks   |
| | | | | Fatigue   |
| 5 | 26 | 1 - 4 | 0.12 | Emotional Functioning (MHI-5)   |

4.5.6.7 Summary of the cut off score analysis

All of the analyses performed for exploring the optimal cut off score for the subscales within QuEST-Cr are summarised in Table 4.24.

The cut off scores for the “moderate impairment” for respective subscales obtained from the above analyses with the highest positive predictive value have been highlighted in red font within Table 4.24. The actual cut off score for the moderate impairment category used will be the closest score that can be obtained within the subscale. The cut off for the severe impairment category will be cut off for the moderate impairment category plus the minimally important difference for the medium effect size of the total population derived from the validation study.

**Table 4.24 Summary of Results and Cut Point Decisions (preferred options marked in red)**

| Scale | Smallest possible change | Source / Anchor | r | Analysis | PPV % for Moderate Cut-Off | Estimated Cut-Offs | | | MIDs Effect Size total population (75% most well population) | | | Best Moderate Cut-off for scale | Best Severe Cut-off for scale |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Mild | Mod | Severe | Small | Med | Large | | |
| Strenuous Activities | .25 | Distribution | | Top 25/10% | | | 2.8 | 3.4 | .17 (.10) | **.43** (.25) | .69 (.39) | 2.25 | 2.75 |
| | | WHO Perf. Stat | .583 | **Regression** | **57.4** | | **2.3** | | | | | | |
| | | | | ROC | 50.5 | | 1.6 | | | | | | |
| | | FACT-G PWB | -.538 | Regression | 48.1 | | 2.5 | 3.0 | | | | | |
| | | | | ROC | 48.1 | | 2.4 | 2.9 | | | | | |
| Everyday Tasks | .20 | Distribution | | Top 25/10% | | | 1.4 | 2.0 | .09 (.02) | **.23** (.04) | .36 (.06) | 1.20 | 1.40 |
| | | WHO Perf. Stat | .489 | Regression | 60.0 | | 1.3 | | | | | | |
| | | | | **ROC** | **65.0** | | **1.1** | | | | | | |
| | | FACT-G PWB | -.470 | Regression | 62.5 | | 1.5 | 1.7 | | | | | |
| | | | | ROC | 45.5 | | 1.1 | 1.5 | | | | | |
| Pain | .50 | Distribution | | Top 25/10% | | | 2.0 | 2.5 | .14 (.04) | **.35** (.11) | .56 (.17) | 1.50 | 2.00 |
| | | FACTG Pain | .821 | **Regression** | **86.6** | | **1.4** | 2.6 | | | | | |
| | | | | **ROC** | **86.6** | | **1.3** | 1.8 | | | | | |
| Fatigue | .20 | Distribution | | Top 25/10% | | | 2.8 | 3.4 | .15 (.09) | **.37** (.22) | .59 (.35) | 2.60 | 3.00 |
| | | FACTG Fatigue | .783 | **Regression** | **72.5** | | **2.6** | 3.1 | | | | | |
| | | | | **ROC** | **72.5** | | **2.5** | 2.9 | | | | | |
| Impact on Activities | .25 | Distribution | | Top 25/10% | | | 2.8 | 3.3 | .16 (.07) | **.40** (.17) | .64 (.28) | 2.75 | 3.00 |
| | | FACTG FWB | -.696 | **Regression** | **53.3** | | **2.7** | 3.1 | | | | | |
| | | | | ROC | 43.3 | | 2.4 | 2.1 | | | | | |
| Emotional Distress | .12 | Distribution | | Top 25/10% | | | 2.1 | 2.5 | .11 (.06) | **.27** (.15) | .43 (.24) | 1.96 | 2.20 |
| | | HADS-T | .752 | **Regression** | **72.7** | 1.7 | **1.9** | 2.2/2.4 | | | | | |
| | | | | **ROC** | **67.2** | 1.7 | 1.8 | 1.9/2.1 | | | | | |
| | | HADS-Anx | .658 | Regression | 46.5 | 2.1 | 2.4 | | | | | | |
| | | | | ROC | 37.3 | 1.8 | 2.1 | | | | | | |
| | | HADS-Dep | .677 | Regression | 38.6 | 2.1 | 2.4 | | | | | | |
| | | | | ROC | 37.5 | 1.9 | 2.1 | | | | | | |
| | | FACT EWB | -.416 | Regression | 28.6 | | 2.0 | 2.2 | | | | | |
| | | | | ROC | 25.3 | | 1.5 | 1.5 | | | | | |
| | | Dist. Thermometer | .561 | Regression | 46.4 | | 2.0 | | | | | | |
| | | | | ROC | 44.1 | | 1.8 | | | | | | |
| Body Image | .33 | Distribution | | Top 25/10% | | | **2.0** | 3.0 | .16 (.09) | **.40** (.24) | .64 (.28) | 2.00 | 2.33 |
| Impact on Sex Life | 1.00 | Distribution | | Top 25/10% | | | 3.0 | 4.0 | .25 (.09) | **.62** (.23) | .98 (.37) | 2.00 | 3.00 |
| | | FACTG Sex | -.623 | Regression | 7.3 | | 2.4 | | | | | | |
| | | | | **ROC** | **33.8** | | **1.5** | | | | | | |

## 4.6 Discussion

This study has allowed exploration of 155 CRC patients' experience of going though chemotherapy treatment for their underlying cancer. Majority of patients were receiving palliative treatment for their underlying disease. The results of the questionnaires indicate that these patients were physically functioning well with reasonable performance status. This is not unexpected as they need to have reasonable reserve to be deemed fit to have chemotherapy treatment. The findings from the questionnaire suggest cancer and treatment have varied impact on their symptoms and functions. The most prevalent symptom was fatigue in this population.

The exploratory factor analysis identified 7 subscales which were common to the three disease groups investigated as part of this study. These are strenuous activities, everyday tasks, pain, fatigue, impact on activities, emotional distress and body image. The subscales contain between 2 and 5 items. All had good internal consistency (Cronbach alpha >0.7). . QuEST-Cr also contains 16 single items which address symptoms patients may experience as a result of their underlying cancer or from their treatment.

Findings from previous research suggested that the EORTC QLQ-C30 physical functioning scale would benefit from adjustment in order to make the scale more suitable for clinical practice. The two physical function scales, everyday tasks and strenuous activities, separated basic activities of daily living and more strenuous activities which may be useful in better defining different groups of patients with varied physical capabilities. The everyday tasks scale reflects activities of daily living (ADL) for self care activities; for example, eating, washing and dressing. The strenuous activities scale reflects instrumental activities of daily living (IADL) which represents activities that allow individuals to live independently within a community, such as housework, and shopping. It would be expected that a patient undergoing chemotherapy would have good levels of basic physical functioning; however, it would be relevant for the clinicians to monitor this, particularly with patients with colorectal cancer, as they are often elderly patients.

The EORTC QLQ-C30 (Aaronson et al., 1993) includes two items on role and 2 items of social functioning. The role functioning questions explore patients' perception of their limitations to work, perform daily activities and limitations in pursuing hobbies and

leisure time activities. The social functioning questions explore patients' perceptions of how their disease or treatment has interfered with their family life or social activities. Patients and clinicians may interpret "hobbies", "leisure time activities" and "social activities" as very similar concepts and clinicians in particular, may have difficulty in differentiating between the two subscales. Within the above factor analysis, the four role and social items converged into one factor, with good levels of reliability, suggesting that these issues are actually underpinned by one concept; assessing the impact of disease and/or treatment on various activities patients may engage with. It is likely that this description of the scale would assist clinicians to better understand what this scale is trying to measure.

Selecting the most suitable set of items for Emotional Function was difficult. It was felt that retaining the scales form original questionnaires was the most sensible approach. It was decided that the MHI-5 subscale would be retained for all three disease groups as there was evidence from a previous study which had indicated MHI-5 to be a useful tool for step wise screening for emotional distress in oncology practice (Cull et al., 2001). In addition, oncologists and patients expressed their unease about some of the wording in the EORTC QLQ-C30 items. However, the adaptation of the MHI-5 time frame from "during the past month" to "during the past week" may be a limitation, as we are yet to explore how this change may impact on the validity of patient responses.

Sexual function and stoma function items were retained within the questionnaire as they were considered important topics to address in the questionnaire from the previous interview studies with oncologists and patients. 83.2% of patients responded to the initial sexual function question. 42% of those patients who responded to this question stated that they had not experienced negative impact on their sex life and would have been screened from the remaining sexual function items. It may be that the first question about general sexual function may be used as a screening question to prompt a discussion where needed. The additional items may help facilitate discussion about specific problems experienced by the patients. No changes were made to these items as more data is required to evaluate these items. Similarly, items relating to stoma function require further data to evaluate the utility of these items.

Known group differences were explored to see if QuEST-Cr was able to distinguish between different characteristics; this analysis illustrated that the QuEST-Cr questionnaire distinguished relevant groups based on HADS and FACT-G total scores. Female patients reported more problems with strenuous activities than male patients

and younger patients reported more issues with their body image. Overall, QuEST-Cr did not perform well based on patients' age, gender and disease stage, however, majority of patients (71%) in this study had metastatic disease with only 11 patients with stage 1 or 2 disease.

There are a number of limitations to the study. Although, the validation study managed to recruit more than the target patient population sample overall, it was still a relatively small sample of patients, all recruited in a single cancer centre. As the study participation was optional, it may have biased more patients with better performance status to be included in the study compared to the general oncology population. Patients completed the questionnaire only once during the study; therefore there is no data on how the questionnaire may perform over a period of time or to ensure test-retest reliability. More data is needed to further validate the shortened QuEST-Cr and examine the psychometric properties, and the cut off scores.

Rigorous developmental processes involving mixed qualitative and quantitative methods have been pursued in the development of the QuEST-Cr questionnaire. These involved review of discussion topics within routine oncology out-patient clinics; review of literature; interviews with both oncologists specialising in the treatment of colorectal cancer and their patients; assessment of individual item performance, exploratory factor analysis; internal consistency reliability, multi-trait scaling and cut off score analysis. The focus was always on developing an instrument specifically for use within clinical practice to provide means of assessing patients' health related quality of life. Qualitative data from the interview studies helped to ensure the questionnaire to be clinically relevant and provide clinimetric perspective to the questionnaire development.

The processes undertaken thus far have resulted in a formation of a colorectal cancer specific questionnaire, QuEST-Cr, which is clinically relevant with acceptable psychometric properties. The questionnaire needs to be utilized in oncology clinics to further explore its psychometric performance, but more importantly, to assess its' utility in clinical practice and patient care.

The cut off scores aim to assist the clinicians to act upon the questionnaire results during their clinic encounter with their patients. The cut off scores are expected to serve an important function to assist oncologists to use the data from QuEST-Cr as

part of patient management.  Future studies will investigate how this questionnaire might impact on patient – doctor communication and decision making.

# Chapter 5 Longitudinal Analysis of Patient-Physician Communication

## 5.1 Introduction

The aim of this exploratory analysis was to investigate the impact the patient reported HRQoL data had on the patient-doctor communication and to see whether the repeated intervention had an impact over time. I particularly wanted to explore whether the intervention made the doctors enquire more about patients' symptoms and problems and to investigate whether scores of the questionnaires made doctors act upon them The purpose of this exploratory analysis was also to glean from the results whether there were any specific aspects that may help to increase the utility of the patient reported data.

## 5.2 Randomized controlled study conducted by POCPRG

The analyses were performed on a data set from a study previously conducted by the Leeds POCPRG (Velikova et al., 2004). This was a randomized controlled prospective longitudinal study with repeated measures, investigating the impact of patients completing health related quality of life (HRQoL) questionnaires as part of their routine oncology care. Eligible patients were those attending the Medical Oncology Out-Patient clinics at St. James's University Hospital, Leeds, who were starting cytotoxic chemotherapy or biological therapy for their underlying cancer diagnosis; who were expected to attend the clinic for review for at least four times. Other eligibility criteria included those who were able to read and understand English and able to provide written informed consent. Out-patient clinics were delivered by team approach whereby patients saw a variety of different doctors working within teams. Therefore, all Consultant Medical Oncologists and Specialist Registrars working within the Medical Oncology Department during the study period took part in the study. The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from participating patients and physicians.

286 patients and 28 physicians took part in this study. The patients were randomly assigned to one of three arms; 1) Intervention, 2) Attention Control and 3) Control. All patients had a baseline consultation followed by three study consultations. Patients in the Intervention Arm were asked to complete EORTC QLQ-C30 (Aaronson et al., 1993) and HADS (Zigmond and Snaith, 1983) prior to their consultation on a touch-screen computer. The results of the questionnaires were tabulated in real time and presented in a graphical format to the physicians so that they were available during their clinic encounter with the patient. Patients in the Attention Control Arm were asked to complete the same questionnaires but the results were not fed back to the physicians. Patients in the Control Arm received standard care (i.e. no questionnaire intervention). All consultations were audio-recorded.

All oncologists received individual one to one meeting/training with the members of the POCPRG prior to the study commencement. They were provided with explanation for the questionnaire scoring and graphical output. They were also given a manual containing information about the questionnaires which were made readily available in their consultation rooms. Oncologists were asked to use the data provided by the questionnaires where applicable without any further instructions as to how they might use the patient reported HRQoL data in their clinic consultation. The clinical utility of patient reported data include detection of problems which would not otherwise be identified. Other ways in which the patient reported information might help doctors would be to allow the consultation to be focused around problems reported by patients and use the patient data to structure the consultation accordingly. However, such information was not provided.

The study had predetermined outcomes for which audio-recordings of the clinic consultations at specified time points were analysed using a study specific checklist developed by the POCPRG to analyse the content of the consultations. This content analysis checklist noted discussions of symptoms/psychosocial functioning covered in the EORTC QLQ-C30 and HADS. Symptoms covered in EORTC QLQ-C30 are Fatigue, Dyspnoea (shortness of breath), Insomnia, Pain, Nausea and Vomiting, Bowel Function (Constipation and Diarrhoea) and appetite. Functions covered in QLQ-C30 are Physical, Social, Role, Emotional (also covered by HADS) and Cognitive functions. Any other symptoms or issues raised were also noted. The person (patient/relative or oncologists) initiating the discussion of each topic was documented. Content analysis was performed directly from the audio-recordings. Each consultation was coded by two raters. Weekly meetings were held to achieve consensus.

Basic demographic data were collected from both patients and oncologists as part of the study. This included age, gender, diagnosis, extent of disease, performance status for patients and age, gender, grade (consultants/specialist registrars) for oncologists.

Following the publication of the above study, further work was performed to code all of the 4 consecutive clinic consultation audio-recordings collected during this study, which has resulted in the formation of a rich database of consecutive real life oncology clinic consultations of patients undergoing cancer therapy. This provided longitudinal database of consultations which took place within a defined period of time.

All of the content analyses were performed by the members of the Leeds POCPRG. However, I performed all of the exploratory statistical analyses with guidance from the Leeds POCPRG statistician.

## 5.3 Analysis planning

The randomized study had indicated that patients completing the questionnaires and feeding back the result to the oncologists had contributed to improvements in patient well being. The mechanism by which this intervention resulted in improvement in patient well being remains uncertain. There was, however, some evidence that the intervention had an impact on patient-doctor communication.

This analysis aimed to investigate the impact on the use of the patient reported measures/questionnaires and the feedback of the results to the physicians on the clinic consultations. It may be anticipated that patients' well being may be linked with improvement in patients' health-related quality of life (HRQoL). If the questionnaire or patient reported outcome intervention had contributed to improvement in patients' HRQoL then it would be anticipated that such issues may have be brought to the consultation for discussion. Therefore, analysis of communication between oncologists and patients and how this was impacted by the questionnaire feedback were considered important. Particular attention was given to the communication on the issues that were specifically covered in the questionnaires to assess the impact of the intervention and whether the scores from the patient reported HRQoL had any relationship as to whether these issues were, in fact, raised during the consultation. In addition, the longitudinal nature of the consultation database allowed exploration of the intervention impact over time.

## 5.4 Aims and hypotheses

The aims and hypotheses for these analyses were

1. To investigate whether repeated collection of patient reported outcomes of HRQoL and feedback of the results to the oncologists in clinic consultations had an impact on patient-physician communication over time.

   It was hypothesized that collecting patient reported HRQoL and feeding back the results to the oncologists would lead to increased discussion of patients' HRQoL issues. It was also hypothesized that repeated intervention would help maintain the level of discussion of such issues at subsequent clinic consultations.

2. To investigate whether feedback of patient reported HRQoL had an impact on oncologists to initiate the discussion of highlighted HRQoL issues.

   The hypothesis was that feedback of the patient reported HRQoL may have an impact on the dynamics of the patient-physician communication and prompt oncologists to initiate discussions about problems patients have highlighted in the questionnaire.

3. To investigate the relationship between the severity of the problems reported by patients and the content of the clinic consultation discussion.

   It was hypothesized that clinic discussion will be reflected by the severity of the problems reported by patients through the questionnaire and that feedback of the results to the oncologists would prevent important issues being missed (i.e. any severe problems would be noticed by the oncologists and therefore discussed during the clinic encounter).

4. To identify elements within the intervention that may enhance the impact of patient reported outcome intervention to inform the content of the doctor training programme.

## 5.5 Methods

### 5.5.1 Data preparation

The content analyses performed on the audio-recording of clinic consultations were stored on Microsoft Access database. Data necessary for the analysis was extracted from this database and exported to excel file. The information extracted is shown in table 5.1. In order to perform an analysis which took effect of time into consideration, it was felt that data from all four clinic consultations (baseline plus three study consultations) were necessary. Therefore patients who did not have complete dataset from all four consultations were excluded. In addition, patients whose audio-recordings were of poor quality, thus limiting the quality of the content analysis was also excluded.

Final dataset was imported on SPSS for analysis.

**Table 5.1 Data extracted for analysis**

| |
|---|
| Patient details<br>1. Study ID<br>2. Study Arm<br>3. Age<br>4. Gender<br>5. Disease site<br>6. Extent of disease<br>7. Performance status<br>8. Date of diagnosis<br>9. Response at 3 months |
| Physician details<br>1. Study ID<br>2. Age<br>3. Gender<br>4. Grade (consultant or specialist registrars) |
| Consultation details<br>1. Dates<br>2. QLQ-C30 and HADS scores from each clinic visit where applicable<br>3. Topics of clinic consultation discussion<br>4. Person initiating the discussion of a certain topic/symptom (oncologist or patient/relatives) |

## 5.6 Analyses

### 5.6.1 Longitudinal impact of study intervention

Mixed effects models were employed to assess whether number of symptoms/functions discussed differed between study arms over time. This model requires the outcome variable to be an ordinal data. Therefore a summated score was calculated for the total number of symptoms (0-7) and functions (0-5) discussed at each consultation. Potential covariates (age, gender, diagnosis, response at 3 months, performance status, extent of disease, time in study, months since diagnosis and a measure of extent to which patients have seen the same oncologist) were identified by univariate regression (the number of issues discussed at first consultation as the outcome variable and each covariate as the predictor, controlling for baseline). Covariates meeting the inclusion criterion ($p<0.1$) were entered in multivariate mixed effects models.

The models' outcome variable was the number of symptoms/functions discussed. Fixed effects were the number of symptoms/functions discussed at baseline, study arm, time (consultation 1, 2 or 3), arm by time interaction (only retained in the final model if significant) and any identified covariates. Patients were entered as a random effect. A significance level of $p<0.05$ was used for this primary hypothesis testing analysis.

### 5.6.2 Dynamics of communication between patients and oncologists

Descriptive statistics were used to analyse the proportion of clinic consultations in which topics from EORTC QLQ-C30/HADS were raised, and who initiated the discussion.

Multivariate logistic regression was used to explore predictors for who initiated discussions of symptoms /functions (oncologists versus patients/relatives).

In order to identify potential covariates for inclusion into the multivariate regression models, univariate regression analyses were performed for each symptom and function for each visit; the person initiating the discussion (oncologists or patients/relatives) as the outcome and potential covariate (patients' gender, age, diagnosis, performance

status, extent of disease, oncologists' gender and oncologists' grade) as single explanatory variable. It was planned that covariates which met significance level of $p<0.1$ at least on two out of the three study visits would be entered in the multivariate analysis.

In the multivariate regression model, the outcome variable was the person initiating the discussion at each visit, and the independent variables were study arm and significant covariates. This was repeated for all symptoms and functions.

The significance level was set at $p<0.01$ for the multivariate analysis to take into account for multiple tests.

### 5.6.3 Relationship between the severity of patient-reported symptoms and functions and content of the clinic discussions

Subgroup analyses were performed on the data from patients in the Intervention and Attention-Control arms of the study who completed the two questionnaires (n=146). Multivariate logistic regression was again used to investigate the relationship between the severity of patients' symptoms/functions as determined by the questionnaire scores and the content of the clinic discussions.

Potential covariates (patients' gender, age, diagnosis, performance status, extent of disease, discussion of respective symptom/function at baseline, oncologists' gender and oncologists' grade) were determined by univariate regression, with a particular symptom or function discussed or not as the outcome variable. This was repeated for each symptom/function at each of the three study visits.

In the multivariate regression model, the outcome variable was whether a symptom/function was discussed or not and the independent variables were questionnaire score for the relevant symptom/function, study arm and significant covariates. Covariates which met significance level of $p<0.1$ at least on two out of the three study visits were planned to be included in the multivariate analysis.

Analyses were repeated for all symptoms and functions at each consultation. A significance level of $p<0.01$ was again used to adjust for multiple testing.

Statistical analysis for the mixed effects model was assisted by the POCPRG statistician, Miss Ada Keding. I performed all the regression analysis under her

supervision. All statistical analyses were carried out using SPSS (PASW Statistics 17 for Windows, IBM Corporation, NY, USA).

## 5.7 Results

### 5.7.1 Patient population

286 patients participated in the study. Of these, 222 patients completed the planned four consecutive clinic consultations within the study. 7 patients withdrew consent after the baseline consultation and 57 patients dropped out during the study at various time points. More male patients (p=0.002) and those with poorer performance status (p=0.003) failed to complete the study.

After review of the content analysis of the clinic consultations, further 24 patients were excluded because of poor quality of audio recordings, resulting in 198 patients with complete data set. The characteristics of these 198 patients are shown in Table 5.2.

**Table 5.2 Patient characteristics**

| | Study Arm | | |
|---|---|---|---|
| | **Intervention** n = 100 | **Attention Control** n = 46 | **Control** n = 52 |
| Age (years) | | | |
| Median | 56 | 56 | 56 |
| Range | 23-85 | 27-78 | 23-75 |
| Gender | | | |
| Female, n (%) | 78 (78) | 37 (80) | 41 (79) |
| Diagnosis | | | |
| Gynaecological Cancer | 37 | 21 | 20 |
| Breast Cancer | 20 | 9 | 11 |
| Renal Cancer | 17 | 6 | 9 |
| Bladder Cancer | 5 | 2 | 2 |
| Sarcoma | 9 | 3 | 3 |
| Melanoma | 6 | 3 | 3 |
| Other | 6 | 2 | 4 |
| Extent of disease, n (%) | | | |
| Disease free/localised | 20 (20) | 12 (26) | 6 (12) |
| Metastatic | 80 (80) | 34 (74) | 46 (88) |
| Performance Status | | | |
| 0+1 | 71 (71) | 23 (50) | 32 (61) |
| 2+3 | 29 (29) | 23 (50) | 20 (39) |

### 5.7.2 Oncologist population

All 28 oncologists working in the Medical Oncology Department at St. James's University Hospital at the time of the study participated. There were 17 male and 11 female oncologists with median age of 33.5 years (range, 26 to 51 years). 6 were consultants and 22 were specialist registrars, with varied oncology experience (range, 0 to 24 years).

## 5.8 Longitudinal analysis

Table 5.3 presents the results of the mixed effects models for number of symptoms and functions discussed. A time by arm interaction was not significant for either model. Patients in the intervention arm discussed more symptoms during consultations than those in the Attention-Control (p=0.008) and Control arms (p=0.040). There was also a significant effect of time with fewer symptoms being discussed between the first and third consultations (p=0.004). The results of the univariate regression analysis to identify potential covariates are shown in Appendix 3.

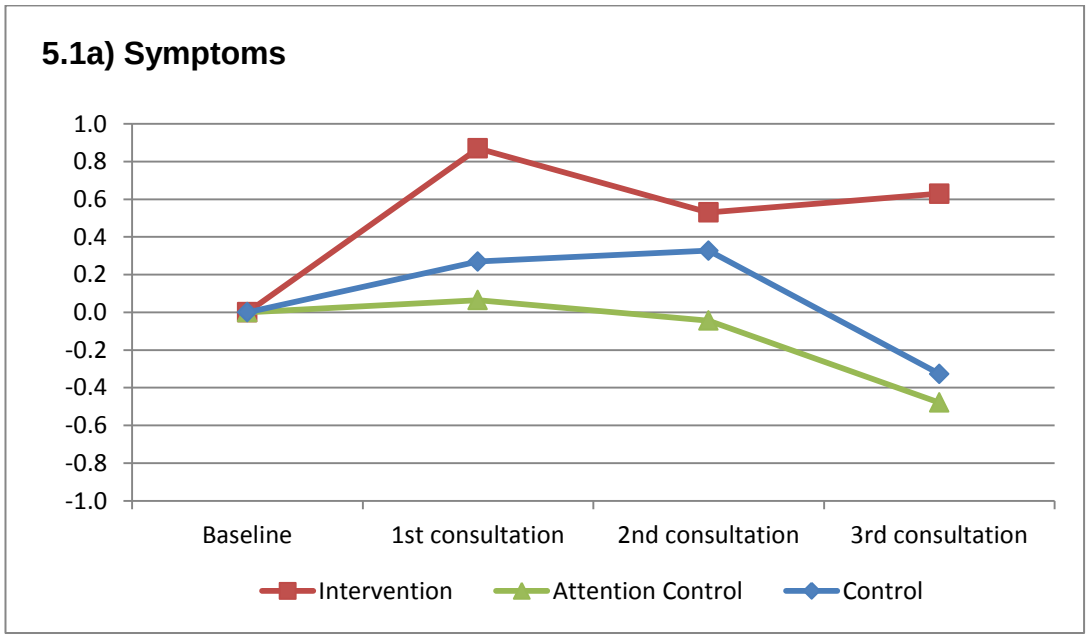
Figure 5.1 graphically represents the change in number of issues discussed compared to baseline, at first, second and third consultations. The increase in symptoms discussions was largest the first time PROs were provided to the physicians and was maintained over time. There were no differences between arms for the discussion of functions and no time effect. Of the identified covariates only diagnosis remained significant in the functions model. In particular, melanoma patients discussed more and bladder cancer patients discussed fewer functional issues than patients in other disease groups. However, the numbers of patients with these cancers were small.

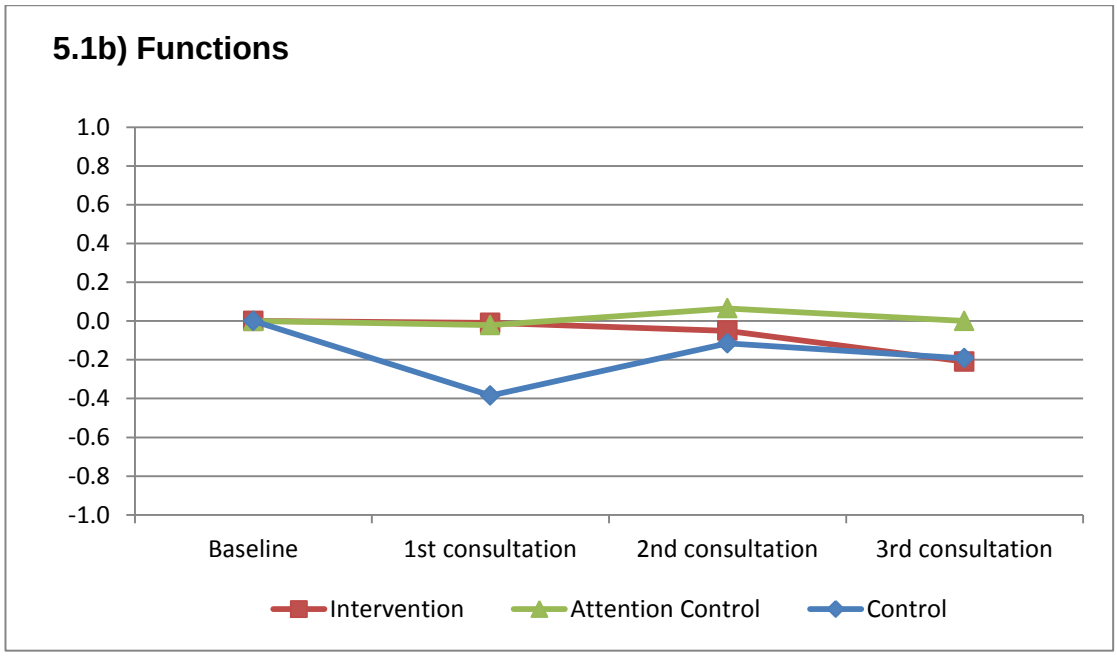
**Table 5.3 Mixed effects model results**

| Variables | Estimate of effect | Standard error | 95% Confidence Interval | | | p |
|---|---|---|---|---|---|---|
| **Number of symptoms discussed** | | | | | | |
| Intercept | 2.57 | (0.437) | | | | |
| Discussion at baseline | 0.26 | (0.048) | 0.16 | - | 0.35 | <0.001 |
| Arm | | | | | | 0.014 |
| Intervention v Control | -0.41 | (0.197) | -0.79 | - | -0.02 | 0.040 |
| Intervention v Attention Control | -0.55 | (0.207) | -0.96 | - | -0.14 | 0.008 |
| Time | | | | | | 0.016 |
| Consultation 1 v Consultation 3 | 0.40 | (0.140) | 0.13 | | 0.68 | 0.004 |
| Consultation 2 v Consultation 3 | 0.22 | (0.140) | -0.05 | - | 0.50 | 0.113 |
| Gender | -0.16 | (0.277) | -0.71 | - | 0.38 | 0.562 |
| Diagnosis* | | | | | | 0.880 |
| Response at 3 months* | | | | | | 0.851 |
| **Number of functions discussed** | | | | | | |
| Intercept | 1.09 | (0.339) | | | | |
| Discussion at baseline | 0.16 | (0.041) | 0.08 | - | 0.24 | <0.001 |
| Arm | | | | | | 0.172 |
| Intervention v Control | -0.22 | (0.125) | -0.46 | - | 0.03 | 0.084 |
| Intervention v Attention Control | -0.16 | (0.130) | -0.42 | - | 0.09 | 0.210 |
| Time | | | | | | 0.547 |
| Consultation 1 v Consultation 3 | 0.05 | (0.106) | -0.16 | - | 0.25 | 0.670 |
| Consultation 2 v Consultation 3 | 0.12 | (0.106) | -0.09 | - | 0.33 | 0.276 |
| Diagnosis* | | | | | | 0.001 |
| Extent of Disease | 0.02 | (0.137) | -0.25 | - | 0.29 | 0.873 |
| Time Since Diagnosis | -0.002 | (0.002) | -0.01 | - | 0.001 | 0.261 |
| Time on Study | 0.002 | (0.001) | -0.0006 | - | 0.004 | 0.154 |

*Only p value of overall F test is given for categorical covariates with more than two levels

**Figure 5-1 Change in the number of issues discussed compared to baseline**



## 5.9 Dynamics of communication

The discussion frequency of symptoms and functions at each consultation, together with person initiating the topic (oncologists or patients/relatives) are shown in Table 5.4 a-c.

Frequencies of symptom discussion were similar at all three time points; 26% to 63% at first consultation, 27% to 59% at second consultation and 27% to 59% at third consultation. Discussions about pain, fatigue, nausea and vomiting were common at all three consultations.

Frequencies of function discussion were less than symptom discussions; ranging 4% to 41%, 6% to 42% and 6% to 37% at first, second and third consultations respectively. Most commonly discussed function was physical function at all three time points.

**Table 5.4 (a-c) Person initiating discussions of symptoms/functions**

| Table 5.4 a Person Initiating Discussion of Symptoms/Functions During First Consultation | | | | | | |
|---|---|---|---|---|---|---|
| | No. of consultations in which issue was discussed (n=198) | | Oncologist initiating | | Patient initiating | |
| | No. | % | No. | % | No. | % |
| Symptom | | | | | | |
| Fatigue | 117 | 59 | 26 | 22 | 91 | 78 |
| Dyspnoea | 52 | 26 | 36 | 69 | 16 | 31 |
| Insomnia | 64 | 32 | 22 | 34 | 42 | 66 |
| Pain | 125 | 63 | 46 | 37 | 79 | 63 |
| Nausea/Vomiting | 108 | 55 | 40 | 37 | 68 | 63 |
| Bowels | 98 | 49 | 64 | 65 | 34 | 35 |
| Appetite | 94 | 47 | 40 | 43 | 54 | 57 |
| Function | | | | | | |
| Physical | 81 | 41 | 24 | 30 | 57 | 70 |
| Social | 70 | 35 | 16 | 23 | 54 | 77 |
| Role | 52 | 26 | 13 | 25 | 39 | 75 |
| Emotional | 74 | 37 | 25 | 34 | 49 | 66 |
| Cognitive | 8 | 4 | 1 | 13 | 7 | 88 |
| | | | | | | |

| Table 5.4 b Person Initiating Discussion of Symptoms/Functions During Second Consultation | | | | | | |
|---|---|---|---|---|---|---|
| | No. of consultations in which issue was discussed (n=198) | | Oncologist initiating | | Patient initiating | |
| | No. | % | No. | % | No. | % |
| Symptom | | | | | | |
| Fatigue | 111 | 56 | 24 | 22 | 87 | 78 |
| Dyspnoea | 53 | 27 | 36 | 68 | 17 | 32 |
| Insomnia | 71 | 36 | 24 | 34 | 47 | 66 |
| Pain | 116 | 59 | 37 | 32 | 79 | 68 |
| Nausea/Vomiting | 106 | 54 | 39 | 37 | 67 | 63 |
| Bowels | 94 | 47 | 59 | 63 | 35 | 37 |
| Appetite | 80 | 40 | 38 | 48 | 42 | 53 |
| Function | | | | | | |
| Physical | 83 | 42 | 27 | 33 | 56 | 67 |
| Social | 75 | 38 | 15 | 20 | 60 | 80 |
| Role | 52 | 26 | 12 | 23 | 40 | 77 |
| Emotional | 78 | 39 | 38 | 49 | 40 | 51 |
| Cognitive | 11 | 6 | 3 | 27 | 8 | 73 |
| | | | | | | |

| Table 5.4 c Person Initiating Discussion of Symptoms/Functions During Third Consultation | | | | | | |
|---|---|---|---|---|---|---|
| | No. of consultations in which issue was discussed (n=198) | | Oncologist initiating | | Patient initiating | |
| | No. | % | No. | % | No. | % |
| Symptom | | | | | | |
| Fatigue | 100 | 51 | 33 | 33 | 67 | 67 |
| Dyspnoea | 54 | 27 | 34 | 63 | 20 | 37 |
| Insomnia | 53 | 27 | 23 | 43 | 30 | 57 |
| Pain | 117 | 59 | 44 | 38 | 73 | 62 |
| Nausea/Vomiting | 101 | 51 | 30 | 30 | 71 | 70 |
| Bowels | 88 | 44 | 44 | 50 | 44 | 50 |
| Appetite | 75 | 38 | 35 | 47 | 40 | 53 |
| Function | | | | | | |
| Physical | 73 | 37 | 16 | 22 | 57 | 78 |
| Social | 70 | 35 | 10 | 14 | 60 | 86 |
| Role | 46 | 23 | 13 | 28 | 33 | 72 |
| Emotional | 76 | 38 | 30 | 39 | 46 | 61 |
| Cognitive | 11 | 6 | 3 | 27 | 8 | 73 |
| | | | | | | |

## 5.10 Regression analyses

Discussion of symptoms and functions were predominantly initiated by patients/relatives with the exception of dyspnoea and bowel function.

Results (p values) from univariate logistic regression analyses to identify potential covariate for the multivariate analyses are shown in Appendix 4.

Variables which were significant at minimum of two time points were planned to be included in the multivariate model. However, no variable fulfilled this criterion for this model. Therefore only univariate logistic regression was applied. Table 5.5 a and b illustrate the results of the analyses of the communication dynamics concerning discussion of symptoms and functions at three time points.

**Table 5.5 (a-b) Regression analysis of dynamics of communication of symptoms and functions**

| a). Symptom | Consultation 1 | Consultation 2 | Consultation 3 |
|---|---|---|---|
| | p | p | p |
| Fatigue | 0.474 | 0.387 | 0.551 |
| Dyspnoea | 0.468 | 0.315 | 0.444 |
| Insomnia | 0.354 | 0.43 | 0.395 |
| Pain | 0.654 | 0.437 | 0.29 |
| Nausea + Vomiting | 0.416 | 0.003 | 0.136 |
| Bowels | 0.605 | 0.912 | 0.605 |
| Anorexia | 0.9 | 0.566 | 0.282 |

| b). Function | Consultation 1 | Consultation 2 | Consultation 3 |
|---|---|---|---|
| | p | p | p |
| Physical | 0.234 | 0.599 | 0.893 |
| Social | 0.519 | 0.571 | 0.768 |
| Role | 0.769 | 0.269 | 0.348 |
| Emotional | 0.219 | 0.35 | 0.982 |
| Cognitive* | NA | NA | NA |
| *There were too few discussions of cognitive function for analysis | | | |

Study arm effect was not observed in the above analyses, indicating that feedback of the questionnaire results to the oncologists did not increase inquiry about patients' problems by the oncologists at all three time points in the study.

### 5.10.1 Association between severity of patient reported symptoms/ functions and content of clinic discussion

Analyses were performed on patients in the Intervention and Attention Control arms, in which patients were asked to complete the two study questionnaires (n=146).

For illustrative purposes, the EORTC QLQ-C30 scores were divided into four groups. In this questionnaire, higher scores represent better functioning but worse symptoms. For symptoms, three equally spaced score ranges (1 to 33.3, 33.4 to 66.7 and 66.8 to 100) were categorised as “mild”, “moderate” and “severe” respectively. For those patients scoring zero were grouped separately as having “no symptom”. Similarly for functions, three equally spaced score ranges (0 to 33.3, 33.4 to 66.7 and 66.8 to 99.9) were categorised as “poor”, “moderate” and “good” respectively. Patients scoring 100 was grouped separately as having “excellent functioning”. HADS scores were also categorised into four groups, using cut off scores suggested by HADS developers. Score 0 as “no anxiety/depression”, scores 1 to 7 as “mild”, scores 8 to 10 as “moderate” and scores 11 or above as “severe” anxiety/depression (Zigmond and Snaith, 1983).

The figures below (Fig 5.2 a-c) illustrate the prevalence and severity of symptoms and functions reported by this subgroup of patients at the first consultation. Results for the second and third consultations are shown in Appendix 5.

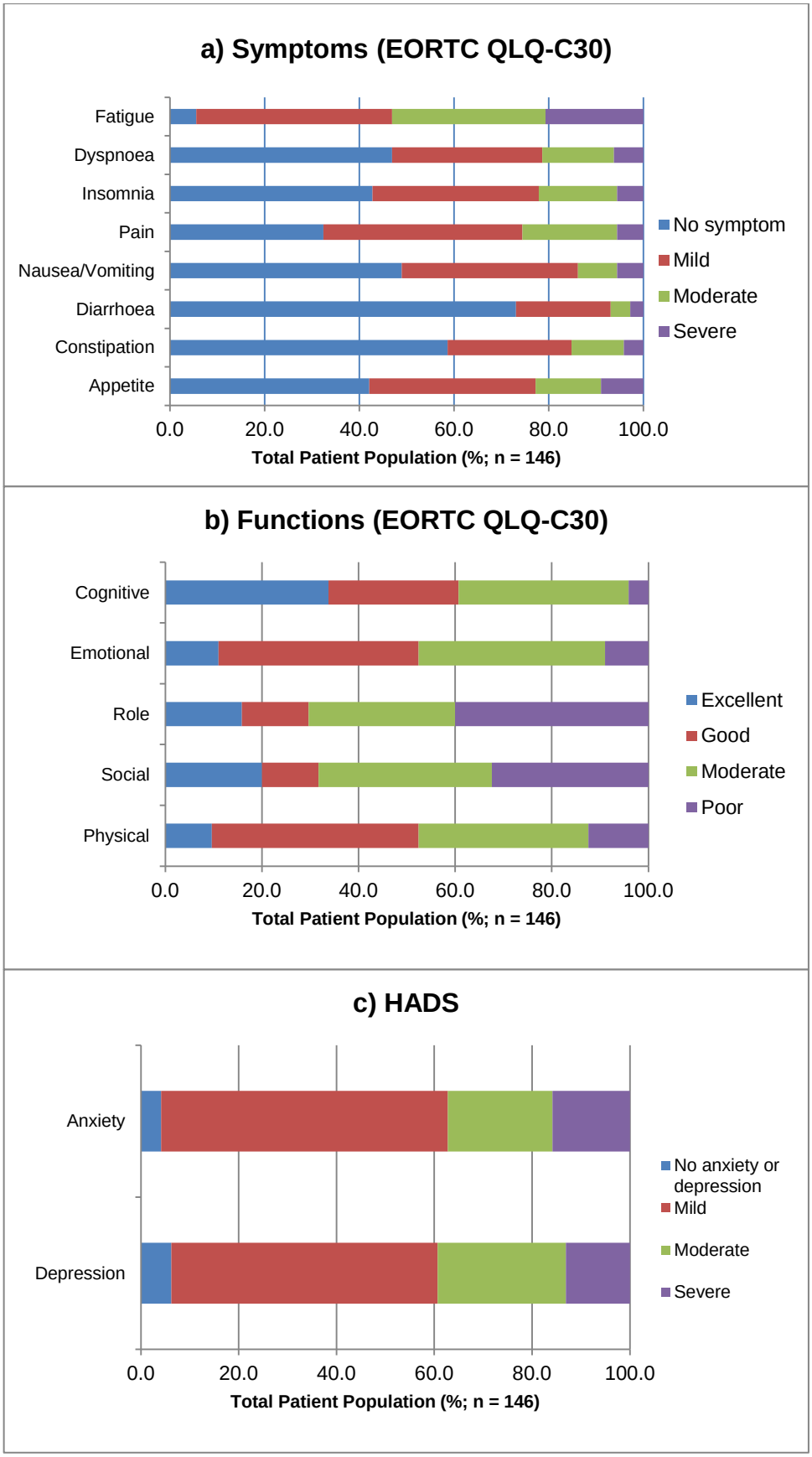
With the exception of fatigue, a large proportion of patients denied the presence of the symptoms listed (32% to 73%). Where present, symptoms were generally mild with only a minority of patients reporting severe symptoms (3% to 9%). Fatigue, on the other hand was very common, with 21% of patients reporting severe fatigue.

A substantial proportion of patients reported poor role and social functioning (40% and 32% respectively). However, physical and cognitive functioning was generally good with poor functioning reported only by 12% and 4 % respectively.

Although 9% of patients reported poor emotional functioning on EORTC QLQ-C30, “severe” anxiety and depression were reported on HADS by 16% and 13% of patients respectively.

Similar results were seen at subsequent consultations.

**Figure 5-2 (a-c) Prevalence and Severity of Symptoms and Functions Reported by Patients (at first consultation)**



### 5.10.2 Association between questionnaire results and clinic discussion

In the multivariate regression analyses, symptom and function discussions were predicted by relevant questionnaire score, study arm and significant covariates.

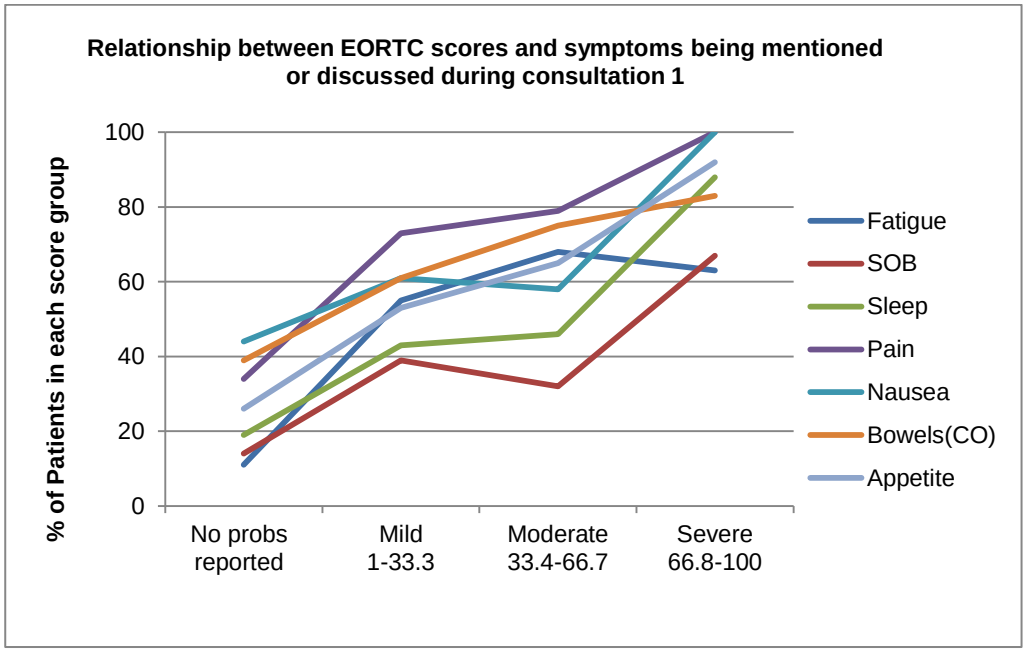
Results (p values) from univariate logistic regression analyses to identify potential covariate for the multivariate analyses are shown in Appendix 6.

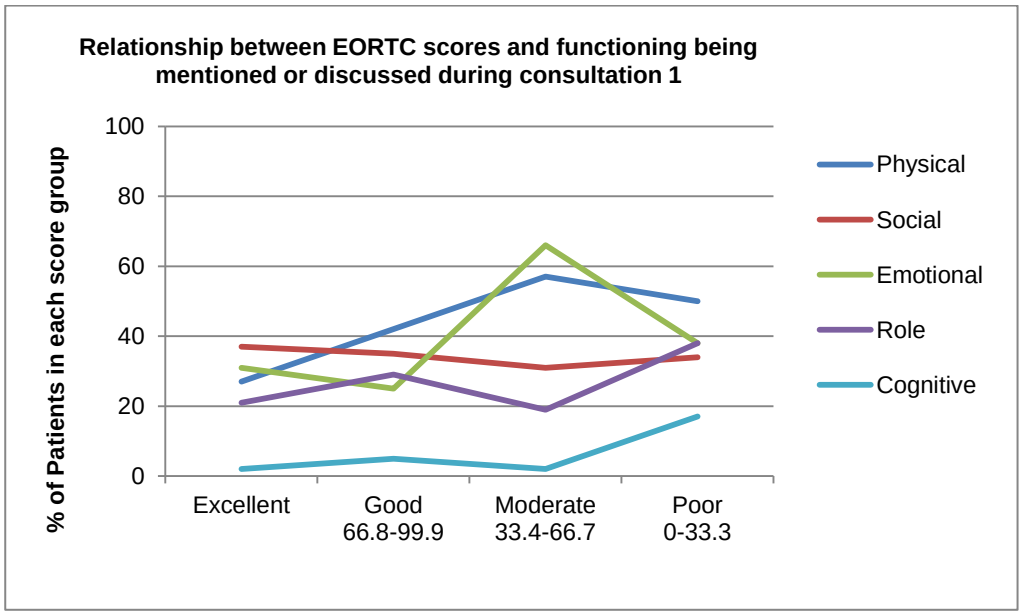
The analyses indicated that patients reporting severe symptoms were more likely to have a discussion about those symptoms during their clinic consultation (Fig. 5.3). Severity was predictive of discussion about shortness of breath, and pain at all three clinic encounters. Severity of fatigue, nausea and vomiting, anorexia and insomnia were significant predictors for discussion at two out of the three clinic encounters. Severity of constipation was a significant predictor for discussion of bowel function at first consultation, however, there was a positive trend at second and third consultations ($p=0.015$ and $p=0.030$ respectively). There was no significant impact of the study arm on whether a specific symptom was discussed; indicating that the feedback of the questionnaire results to the oncologists did not influence the discussion of patients' symptoms.

In contrast to the symptoms, there was no clear relationship between severity of patients' functional impairment and clinic discussions (Fig 5.3). The frequency of discussion about cognitive function was too small for multivariate analysis. Study arm effect was again not observed.

Similar results were observed in the second and third consultations (Appendix 7)

**Figure 5-3 Relationship between Severity of Symptoms/Functions and Clinic Discussion**



## 5.11 Discussion

The findings from these analyses have highlighted the differences in the communication of symptoms and functions in oncology clinics. The discussions during consultations seemed to focus on patient symptoms rather than how the symptoms and their underlying cancer may impact on patients' functioning.

The intervention of patients regularly completing HRQoL questionnaires and feeding the results back to the oncologists had an impact on the range of symptoms being discussed during the clinic consultations. This effect was maintained over time. It is not clear from these analyses how the intervention impacted on the communication of patients' symptoms in this way. The analysis illustrated that discussions about symptoms were predominantly initiated by patients (or by their relatives) and not by the oncologists, irrespective of whether the patients completed the questionnaires or whether the results were fed back to the oncologists. Discussions of symptoms were appropriate to the severity of the problems experienced by the patients; patients experiencing severe symptoms were more likely to have such issues discussed during their clinic consultations. The feedback of the results to the oncologists did not influence the discussion of these symptoms but the main trigger seemed to be the severity of the problems experienced by the patients.

The patients in this study were undergoing cytotoxic chemotherapy or biological therapy for their underlying cancer; therefore, the discussion topics during clinic consultations would have naturally focused on how the patients were tolerating their treatment. Assessment of toxicity would have been expected to be one of the primary purposes of these clinic consultations. It is therefore not surprising that the consultations were more focused on patients' symptoms for this reason. It is possible that the for those patients who completed the questionnaire and the results given to their oncologist, the physical presence of the questionnaire results being available during their consultation may have acted as a prompt for both patients and oncologists, resulting in a more thorough discussion of patients' symptoms. However, the mechanism by which the questionnaire feedback impacted on the symptom discussion in the clinic consultation in these analyses remains speculative.

In contrast, the patient reported outcome intervention had no impact on the communication of patients' functions. Similar to the symptom discussions, patients were more likely to raise these issues during the consultations themselves. However, there was no clear relationship between the severity of their problems reported on the

questionnaires and the content of the clinic consultations, indicating that patients were possibly held back from raising such issues during the consultations. Furthermore, the analyses indicated that oncologists failed to explore these issues even when the questionnaire results demonstrating poor functioning were presented to them. Discussions of social and role functions were particularly low with respect to the proportion of patients reporting poor functioning.

It was anticipated that feedback of the questionnaire results to the oncologists may influence the dynamic of the communication between patients and oncologists by increasing exploration of both symptoms and functions initiated by the oncologists. This did not appear to be the case from these analyses, which indicated that the structure of a standard medical interview was affected very little by the patient reported outcome intervention. The clinicians are trained to encourage patients to report their problems/concerns through open questions. These would usually be followed by more specific or closed questions from the clinicians to delineate the problem in order to formulate differential diagnoses and management plan for the problems reported. However, it appears that patients reporting poor functioning on their questionnaires were not enough to prompt the oncologists to make further enquiries of these issues with their patients.

In order to investigate how doctors use the patient reported HRQoL information in the consultation and to examine the effective use of this patient reported data, conversation analysis of previously recorded and transcribed consultations has been carried out. This project was guided by a theoretical framework which attempts to explain mechanisms underlying the impact of HRQoL intervention on patient well-being (Greenhalgh et al., 2013) Findings indicate that

- The way clinicians referred to the HRQoL data had implications for further discussion about symptoms.
- The data appeared to play an important role in orienting the patient to a discussion about symptoms and providing structure to the consultation.
- The HRQoL data were most commonly used to identify patient problems.
- Patients participated most in the consultation when doctors referred to the HRQoL data to not only allow patients to confirm or contradict the presence of the problem, but also to enable patients to explain the problem further to the doctor.

- Establishing patient burden, offering treatment, advice or referral and exploring patient views on management options were identified as key behaviours in responding to the HRQoL issues.

This work has provided helpful information on how patient-reported data can be effectively integrated into routine clinical practice.

These analyses have highlighted and reconfirmed that cancer and cancer therapy have impact on many aspects of patients' health related quality of life. There is high prevalence of unmet psychological, supportive and information needs among cancer patients (Cella and Cherin, 1988) and there is increasing recognition and expectations that communications during oncology consultations should encompass patients' psychosocial functioning in addition to cancer and treatment issues (Fayers, 2007, Department of Health, 2007). Asking patients to report their HRQoL concerns through questionnaires can be a way of drawing attention to any needs they may have. However, the above analysis indicates that simply asking the patients to complete HRQoL questionnaires alone is not enough to help address their psychosocial problems or meet their needs.

The previous interview study with the oncologists has indicated their concerns about use of HRQoL questionnaires routinely in clinics in this way. Their concerns were mainly around what they should do if patients report problems they feel they are ill equipped in managing or they had little advice to offer to the patients, indicating that not all oncologists are comfortable in discussing psychosocial issues. Clearly, oncologists have varied levels experience in managing and discussing such topics with their patients. The interview study also raised their concerns about the impact of launching into discussions about such issues in busy clinics where they are constantly faced with time constraints. In addition, some oncologists felt that there were inevitable consequences of cancer and cancer treatment for which there were no obvious solutions and that repeatedly asking about such issues may have a negative impact on patients' well being. It was clear that oncologists were naturally keen to offer some kind of a solution or treatment where a problem is identified. This is undoubtedly more complex for psychosocial issues compared to managing treatment side effects where they are able to provide patients with a prescription for a supportive medication. These are clear barriers which may be preventing important psychosocial issues being raised in clinic consultations. These are reasons/barriers recognized by other investigators preventing psychosocial issues being discussed in clinic consultations (Frost et al., 2007) and it is quite possible that they were some of the reasons/barriers

for the limited discussion of patients' functions in the consultations in the above analyses.

These analyses support the need for additional training and support for the oncologists, if the patient reported outcome intervention is to become more effective in addressing patients' psychosocial problems. The training and support will require several facets including better understanding and familiarisation of the questionnaires; guidelines for managing some of the psychosocial issues such as emotional distress; linking with supportive services (Clinical Nurse Specialist where available or Psycho-Oncology Service, Social Services) so that oncologists are able to provide information and sign posts for patients to seek further advice. Assisting oncologists in this way may increase their confidence in discussing psychosocial issues with their patients to help to prevent important issues for patients being missed or ignored. Training process may also help engage with the oncologists who may perhaps be more sceptical about using patient reported outcome measures in this manner.

There are a number of limitations to these analyses. The trial was conducted in a single centre with study population predominantly of women. They were relatively young and with good performance status. Therefore, the true impact of cancer and its treatment on patients' HRQoL among wider patient population may be underestimated. In addition, the unit of randomization within the trial was patients. Therefore, oncologists taking part in the study will have encountered patients in all three study arms which may have cause contamination. Furthermore, the study population did not include patients with colorectal cancer, which is my population of interest. This is because colorectal cancer patients received their treatment in another hospital in Leeds at the time when this trial was conducted. Nevertheless, the analyses have been performed on a relatively large sample of real life oncology consultations of patients, many of whom were receiving palliative treatment for advanced incurable cancer. It has helped to highlight the differences in the communication of symptoms and psychosocial functioning during oncology clinic consultations and the findings appear to echo the concerns raised by the oncologists regarding the use of patient reported outcome measures.

However, another limitation to the study is the way the consultations were analysed. The content analysis does not allow any assessment on the quality of the communication between the oncologists and the patients. The content analysis noted whether a particular issue was raised during the consultation. This is clearly an important initial step for any problems/concerns to be addressed. However, it is not an

assessment of how the problems raised have been dealt with. This is an important consideration for future analyses of clinic consultations. The analyses of clinic consultations will need be able to evaluate whether any problems highlighted has been addressed and be able to make an assessment of how the patient reported outcome feedback may have contributed to the consultation. This would be of particular importance in evaluating the impact of any training for oncologists that may be implemented.

## 5.12 Conclusions

These analyses have highlighted that communication of patients' psychosocial functioning is less prevalent compared to that of symptoms, despite patient reported outcome feedback, indicating the presence of barriers restricting discussion of such issues.

These barriers may be explained by some of the concerns raised by the oncologists during the interview study. These barriers need to be overcome in order to facilitate discussions of patients' psychosocial functioning.

Consideration needs to be given to how clinic consultations may be analysed in the future in order to better capture the impact of patient reported outcome intervention and to evaluate how problems reported by patients are being addressed.

# Chapter 6 Training programme for integration of patient reported HRQoL in routine consultations

## 6.1 Introduction

Training has been identified as one of the ways which may help to overcome some of the healthcare professional related barriers to successful integration of HRQoL assessment in routine clinical practice (Luckett et al., 2009). These barriers include:

1. Healthcare professionals' lack of familiarity or experience with routine HRQoL assessments (Morris et al., 1998b)

2. Healthcare professionals' ability to interpret the patient reported data and use the information to assist decision making about patient care/management in the way they use laboratory and radiological investigation results (Sutherland and Till, 1993, Giesler, 2000).

3. Healthcare professionals' concerns that HRQoL assessment would unearth multiple problems and impact on the duration of consultation (Luckett et al., 2009).

4. Healthcare professionals' concerns about HRQoL assessments revealing problems for which there are no straight forward solutions to be offered to the patient (Donaldson, 2004)

In order for the assessment of patient's HRQoL to become integrated in clinical practice, these barriers need to be addressed.

Descriptions about training for the recipients of patient reported HRQoL data within published studies have been brief, where this has been provided (Greenhalgh and Meadows, 1999). They seem to focus on the HRQoL instruments used in the study and how they are scored (Detmar et al., 2002, Velikova et al., 2004). There was no indication about specific guidance as to how the healthcare professionals should manage patients in relation to the scores derived from the questionnaires.

For example, Detmar et al (Detmar et al., 2002) described training provided to physicians as half an hour meeting with the individual oncologist specifically about the instruments they used in their study (EORTC QLQ-C30 (Aaronson et al., 1993)) but no further guidance as to how the data may be used in the consultation was provided. Similarly, in the study by Velikova et al (Velikova et al., 2004), the training given to

oncologists included face to face meeting with each of the participating oncologists about the instruments used (EORTC QLQ-C30 (Aaronson et al., 1993) and Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983)), descriptions of items within the questionnaires which formed some of the functional scales and how they were scored. The oncologists were provided with a manual about the questionnaires which were available in the consultation rooms during the study period. The oncologists were asked to use the data obtained from the patients but again, no further specific instructions were provided as to how the oncologists may use the data during their consultations.

Interpretation of instruments used is clearly an important component of the training as it is essential for the recipient of the patient reported data to be able to make sense of the information derived from questionnaires. However, these scores need to have a meaning on which the healthcare professional can act upon, just as the laboratory tests have a meaning to them in terms of what's normal and what is abnormal and whether anything needs to be done about any of the abnormal results.

The training therefore needs to expand in facilitating the patient reported HRQoL data to be incorporated into the management of patients along with laboratory and radiological investigations to assist in clinical decision making. Training also needs to provide opportunities to engage with the healthcare professionals and present evidence of how patient reported data can help make consultations more efficient by focusing and prioritizing the discussions on areas which are concerning for the patients (Luckett et al., 2009).

Patient reported HRQoL information has been shown to influence communication between patients and physicians during clinic consultations but the impact this has on distal patient outcomes such as improved patient outcomes and satisfaction have not been shown consistently. Longitudinal analysis of the data of the previous randomized controlled study (Velikova et al., 2004) conducted by the Leeds POCPRG have shown that oncologists readily discussed some of the symptom issues reported by the patients. However, despite patients' data indicating significant problems with some of their function domains, these issues were often not discussed during the consultations (Chapter 5), suggesting that perhaps they felt unequipped or uncomfortable in discussing these issues. The training therefore needs to address this barrier by provision of management guidelines to enable healthcare professionals to raise such problems reported by the patients. Such guidelines may help healthcare professionals

to make decisions about referring patients to appropriate supportive care services (Frost et al., 2007).

Training, therefore, needs to function in many ways to influence the mindset and attitudes of the health professionals so that the value of routine assessment of HRQoL can be realised. This in turn may assist patient reported HRQoL being incorporated into the clinical practice and decision making process between patients and doctors, thus leading to the intervention having impact on the more distal patient outcomes.

This chapter describes the ground work in the development of a training programme to facilitate the use of patient reported data in clinical practice.

## 6.2 Theories of knowledge acquisition and learning styles

Training is a form of education that helps develop a person's abilities to gain new knowledge, acquire new skills and employ creative methods of problem-solving (Patrick, 1992). In order to develop an effective training programme, it is helpful to understand how adults learn.

Many adult learning theories have been described; however, most of these are based on the work by Malcolm Knowles who attempted to develop a conceptual basis for adult education and learning through the notion of andragogy. He defined andragogy as "art and science of helping adults learn" (Knowles, 1980), in an attempt to differentiate learning in childhood from learning in adulthood.

Knowles' concept of andragogy is built on two major attributes; first is the idea that adult learners are self-directed and autonomous; and second idea that the role of the teacher as facilitators of learning rather than deliverer of content (Pratt, 1998). Knowles proposed a number of assumptions about the characteristics of adult learners and how these assumptions may impact on the process elements of adult education.

The characteristics of adult learners proposed by Knowles are:

1. Self-concept: As people mature they become internally motivated and self-directed
2. Experience: As people mature, they bring their life experiences and knowledge to their learning experiences.

3. Readiness to learn: As people mature, they are more interested in learning subjects that have immediate relevance to their work or their personal lives.
4. Orientation to learning: As people mature, their time perspective changes from acquiring knowledge for future use to immediate application of knowledge. Therefore, adult learners become more problem-centered rather than focusing on the actual subject.
5. Motivation to learn: As people mature, they become more motivated by internal incentives such as desire to achieve and satisfaction of accomplishment.
6. Relevance: As people mature, they need to know why they need to learn something.

Knowles proposed to adult educators to employ a seven step process in the delivery of teaching in order to implement and to make the most of the assumptions made of the adult learners. These steps include:

1. Creating a co-operative learning environment
2. Planning goals of learning mutually
3. Indentify the needs and interests of the adult learner
4. Help them formulate learning objectives based on their needs and interests
5. Design sequential activities in order to achieve these objectives
6. Carry out the design to meet the objectives with selected methods, materials and resources
7. Evaluate the quality of the learning experience for the learner that included reassessing the needs for continued learning.

Another learning theory often referred in medical education is Kolb's Learning Cycle (Kolb, 1984). It is based on experiential learning theory, which has been defined as "the process whereby knowledge is created through the transformation of experience. Knowledge results from the combination of grasping and transforming experience" (Kolb, 1984).

Kolb was influential in describing how learning takes place and helping to understand the learning process. His learning cycle as shown in Fig 6.1 below, illustrates the idea of learning as experiential (learning by doing or learning by observation). Experiential learning is relevant in medical education, particularly in clinical teaching which often involves seeking out opportunities for learners to practice clinical skills ranging from simple procedures to much more complex skills such as breaking bad news or carrying out an operation.

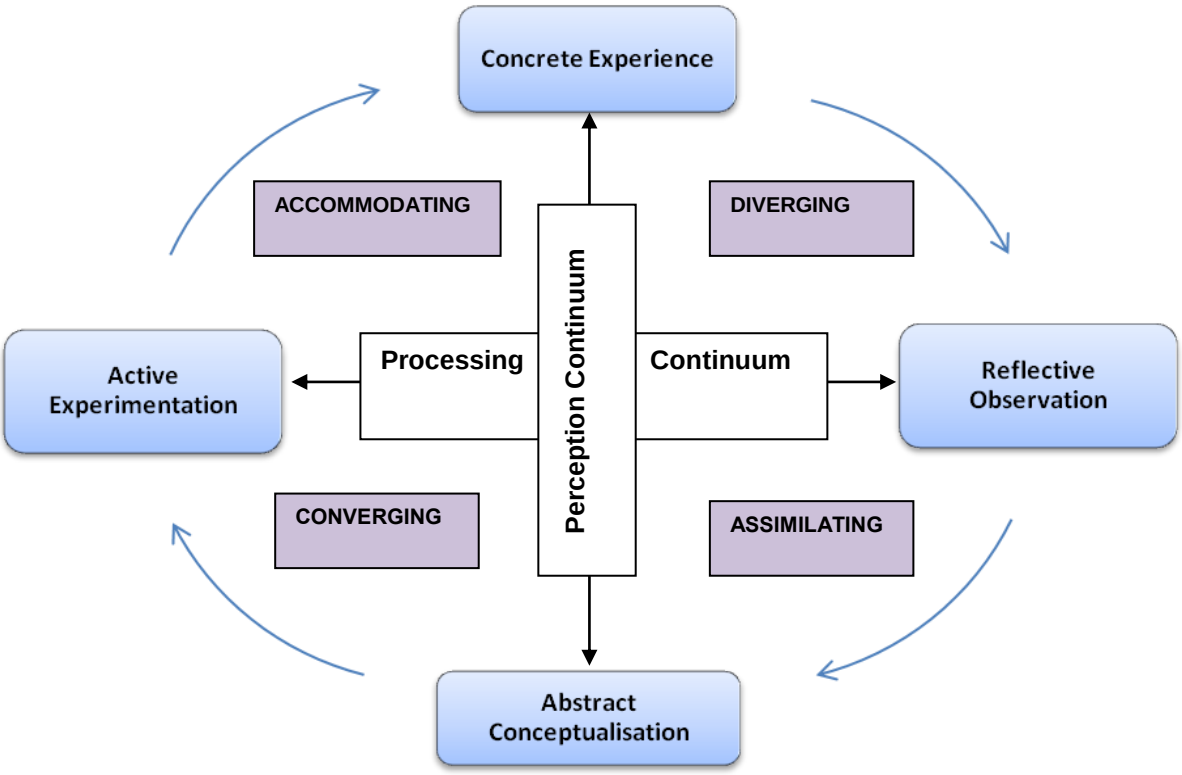



**Figure 6-1 Kolb's learning cycle**

The Kolb's learning cycle consists of 4 stages of learning from experience. These stages are

1. Concrete experience – learners becomes actively involved in new experiences. This may be reading, attending a course, trying out a skill.

2. Reflective observation – learners review and reflect on the experience from different perspectives. Reflections may be through discussions with mentors and talking to peers.

3. Abstract conceptualization – learners form and process ideas and integrate them into logical theories. This may involve reading new ideas and information, reflecting on actions and considering how things may be done differently.

4. Active experimentation – learner use the skills and knowledge again but with the benefit of prior experience and reflection along with new and revised ideas and input.

Kolb suggests that learning is an integrated process with each stage being mutually supportive of and feeding into the next. He therefore suggested that effective learning occurs when a learner is able to complete all four stages of the model.

Kolb's learning theory sets out four distinct learning styles or preferences based on his four stage learning cycle (Kolb and Fry, 1974). Kolb suggests that different people naturally have preference for a certain type of learning style, which may be influenced by the learner's social environment, educational background and their ability to process information. Kolb posited that there were two continuums involved in the learning cycle (Fig 6.1). In the vertical perception dimension, people will have preference along the continuum between Concrete Experience and Abstract Conceptualisation. In the horizontal processing dimension, people will, take the results of their perception and process it in preferred ways along the continuum between Active Experimentation and Reflective Observation. The two axis forms a quadrant, which provides characteristics of the learning styles or preferences which Kolb described as Diverging, Assimilating, Converging and Accommodating (Kolb and Kolb, 2005). Descriptions of each learning style are given in Table 6.1.

**Table 6.1 Kolb's learning styles**

| Learning Style | Dominant Learning Abilities | Characteristics |
|---|---|---|
| Diverging | CE/RO | Views situation from different points of view.<br>Good at generating ideas<br>Imaginative and emotional<br>Prefers collaborative work<br>Likes personalised feedback |
| Assimilating | AC/RO | Good at understanding broad-ranging information and translating into concise, logical form<br>Less interested in people<br>Needs time to consider things |
| Converging | AC/AE | Good at finding practical uses for ideas and theories<br>Good at problem solving<br>Learns through experimentation, simulation and practical work |
| Accommodating | CE/AE | Learn from "hand-on" experience.<br>Enjoy carrying out plans and new experiences<br>Act on "gut feeling" over logic<br>Rely on people for information for problem solving |
| CE: Concrete experience<br>RO: Reflective observation<br>AC: Abstract conceptualisation<br>AE: Active experimentation<br><br>Based on Kolb, AY and Kolb, D. Learning Styles and Learning Spaces (Kolb and Kolb, 2005) | | |

Learning is a highly individualised process. However, these conceptual models of knowledge acquisition and learning styles can provide practical applications when designing learning activities as they can be transferred into concrete teaching actions. They help teachers realise that learners have different ways and approaches in how

they acquire new knowledge and skills. Therefore, application of multiple teaching methods is necessary to enhance effectiveness of both teaching and learning.

## 6.3 Types of teaching formats

Many teaching situations involve a group of one size or another. Elton proposed a model in classifying teaching and learning into three broad categories based on the side of the group of learners (Elton, 1993):

- Mass instruction
- Individual Instruction
- Group learning

Elton's classification has been used to describe the types of instructional materials that may be useful, and the role of the teacher in each of the categories. Table 6.2 illustrates examples for each of the types of Elton's teaching categories.

**Table 6.2 Elton's teaching categories**

| Type of Techniques | Examples | Role of teacher/trainer |
|---|---|---|
| Mass instruction | Conventional lecture<br>Expository lessons<br>Film presentations<br>Educational broadcasts | Expository role |
| Individualised instruction | Directed study of materials in textbooks<br>Computer/web based learning<br>Individual assignments<br>One to one teaching | Producer of learning resources<br>Tutor |
| Group learning | Tutorials<br>Seminars<br>Group exercises/projects<br>Simulations<br>Discussions | Organiser and facilitator |

Mass instruction techniques, such as lectures, are effective in the transmission of information for recall as knowledge. However, group learning and small group work can facilitate development of higher level skills. Effective teaching strategies can be created considering strength of each type of teaching methods.

Small group teaching is considered to be highly relevant in adult learners and to clinical situations, as learning in a small group facilitates learning through discussion, active participation, feedback and reflection. Small group environment also allows opportunities co-operative behavior such as group problem solving (Fisher and Ellis, 1990). For this reason, there has been a gradual shift towards group based learning strategies being increasingly adopted in medical education.

## 6.4 Communication skills training in oncology

As the intervention of colleting patient reported HRQoL data in routine oncology practice aims to impact on doctor – patient communication in the way that it changes the behavior of healthcare professionals and patients, reviewing the training methods used in advanced communication skills training for oncologists was considered useful.

The efficacy of Communication Skills Training (CST) in improving communication skills of healthcare professionals involved in cancer patients have been demonstrated through a number of randomized controlled studies (Fallowfield et al., 2002, Delvaux et al., 2005, Wilkinson et al., 2008, Lienard et al., 2010). CST has been shown to increase more patient-centred communication with healthcare professionals demonstrating empathic responses to patient cues (Delvaux et al., 2005, Fallowfield et al., 2002). In addition, CST has also been shown to increase confidence in healthcare professionals communicating with their patients by providing them with necessary skills to achieve this (Wilkinson et al., 2008, Butow et al., 2008). The aims of the CST include provision of support for the healthcare professionals in structuring the medical consultation, exchanging information effectively, building a working relationship with the patient and responding their emotions. These attributes are all relevant to the use of patient reported data in clinical practice as the intervention aims to highlight any problems patients may be experiencing and for the healthcare professionals to be able to communicate effectively in managing these issues.

### 6.4.1 Types of teaching interventions used during CST

Most of the studies that evaluated the CST specified use of learner–centred, experiential, adult learning methods grounded on the conceptual models for adult learning, with training facilitated by experienced facilitators (Moore et al., 2013). Studies generally utilized multi-faceted approach with different components within the training. In many of the CST, participants were provided with written material describing key studies and articles from the communication skills literature to provide evidence base for the CST with short didactic lectures (Moore et al., 2013). Actual skills training took place in small groups with experiential learning opportunities provided through role–play, which were either with peers or with simulated/standardised patients. The scenarios for the role-play (for example, breaking bad news, communicating transfer of care from active treatment to best supportive care and handling difficult emotions) were often learner generated to make the training relevant to their own learning needs (Fallowfield et al., 2002, Delvaux et al., 2005, Finset et al., 2003). The small group teaching environment allowed discussions among the peers and verbal feedback to be given immediately from the facilitators, peers and from simulated patients in many of the CST evaluated (Moore et al., 2013). Fallowfield emphasized that provision of constructive feedback, both positive and negative, played a key role in the effectiveness of the CST (Fallowfield, 2005). Delvaux et al (Delvaux et al., 2005) found use of learner generated peer role – plays with immediate feedback showed increased use of eliciting and clarifying psychological concerns directed towards patients, with an increase in patients' global satisfaction with the interview.

### 6.4.2 Evaluation of training

Most of the studies evaluated outcomes before and after the CST (or no CST). Changes in the behavior of the healthcare professionals were measured through interviews either with real patients or standardised patients which were audio-recorded or videoed (Moore et al., 2013). What was actually measured differed from one study to another with different scales being used to evaluate healthcare professionals' communication skills such as information gathering, clarifying or summarising, eliciting concerns, appropriate information giving and negotiating (Moore et al., 2013).

Other outcomes relating to the healthcare professionals included their health status and their perception of their attitude change. Outcomes relating to patients included their health status and their perception of or satisfaction with the interview.

In summary, communication skills training employ a variety of teaching methods which provides diverse stimulus for learners with different learning styles. Many of the training described included experiential component within the training in the form of role-play, with participants often enacting scenarios chosen by them so that teaching was directly relevant to their own learning needs. The teaching was often conducted in the small group environment to facilitate discussion, active participation and reflection.

Having reviewed the theories of adult learning and how they can be applied to teaching communication skill in oncology, I decided to consider the following key aspects when developing the oncologist training. Different types of teaching materials are needed to cater for individuals who have different learning needs and styles. The training needs to contain some evidence behind the intervention or skill that needs to be taught and why the learners might need those skills. Experiential learning is a key component in clinical skills teaching and the doctor training programme would need to consider how best to achieve this. In addition, I have attended one of the Cancer Action Advanced Communication Skills Training which was facilitated by Professor Fallowfield. I was fortunate enough to attend the course with her to try and gain the necessary facilitation skills in such a training programme.

## 6.5 Development of the training programme to facilitate integration of patient reported HRQoL in clinical practice

The purpose of the training programme within the Cancer Research UK funded project undertaken by the Leeds POCPRG was to address how the patient reported HRQoL data may be integrated into the clinic consultation effectively in order to influence the behavior of the healthcare professionals and the patients. The training had to serve a specific role in relation to the patient reported data and illustrate how this information can help assist healthcare professionals in managing their patients, rather than providing training on generic communication skills. However, the training strategies used in the communication skills training provided useful framework to build on the training for integrating patient reported data.

Use of various teaching methods (didactic lectures, written references, small group discussions, role–play with feedback and reflection) to stimulate learners with different learning styles and to create simultaneous rather than sequential skills development and to stimulate knowledge acquisition are all highly relevant to this training. However, the training needed to focus and tailored on a very specific aspect of patient-doctor communication.

The length of communication skills training varied widely; from 1 day course to 3 day courses with various follow up training (Moore et al., 2013). It was necessary to consider the time required for this training focused on the use of patient reported data. I took a practical approach in suggesting the length first, rather than driven by content of the training, as organising several oncologists with busy clinical commitments to meet at the same time was going to be difficult. Half day session was considered to be the most feasible duration for the training at this stage, with a view to reviewing this later if necessary.

Once the time frame for the training was decided, the content and the structure of the training could be explored. Clear objectives of the training needed to be established, which were mainly around addressing healthcare professional related barriers to routine collection of patient reported HRQoL described earlier. The training needed to illustrate the potential benefits of the intervention and by doing so, engaging with the oncologists in the process. As with CST, different types of teaching methods were needed to address these objectives.

Experiential learning is highly valued in skills training and role-play featured heavily in many of the CST described (Moore et al., 2013). Role-plays are resource intensive and time consuming therefore considered to be unfeasible in a short half day training session. However, some form of training material which provided experiential learning component was considered necessary.

Jenkins et al (Jenkins et al., 2005) devised a training programme for oncologists and research nurses, specifically concerning communication around randomized controlled trials in cancer. In their study, they used a variety of training methods, including didactic lectures/presentations, interactive exercises and discussions around videotaped scenarios of oncologists conducting interviews with simulated patients discussing various types of randomized controlled trials in cancer. They also produced other video based materials for their modules, each module describing a specific challenge/ situation healthcare professionals may be faced with when communicating randomized controlled trials with their patients. These “trigger” films or tapes were utilized to

stimulate constructive discussions among the group. Their main positive outcomes of the training were participants reporting increased confidence about recruiting patients into trials and behavioural changes in the style and content of the participants' discussions about randomized trials. This training has now been adopted by the National Institute for Health Research Clinical Research Network and is widely accessible throughout the network. I considered that "trigger" tapes used in a similar manner could provide valuable teaching material within the training programme for patient reported HRQoL intervention.

The training also needed a way to evaluate its' impact. The primary outcomes would be how the training changed the way oncologists used the patient reported HRQoL data, before and after the training, through evaluation of clinic consultations using a pilot study. It was anticipated that the pilot study would utilize the cancer site specific questionnaires which were being developed simultaneously with the development of this training programme. Secondary outcomes would include changes in oncologists' views and attitudes towards patient reported HRQoL intervention, before and after the training.

In summary, teaching strategies and structures of CST can be transferred to the training programme for patient reported HRQoL intervention but the content needed to be focused on this specific aspect. Trigger tapes were considered to provide different but valuable experiential learning strategy compared to role-play, and serve an important role in facilitating small group discussions.

## 6.6 Development of trigger tapes

Trigger tapes, or trigger videos are brief clips that are used to provoke reflection, stimulate discussion and help learners confront their feelings (Fisch, 1972). In the context of healthcare, the trigger tape can be a short scene depicting a typical clinical situation with a patient and a doctor, which can be used to trigger discussions of the issues and circumstances raised in the film (Ber and Alroy, 2001). Trigger tapes have been used successfully as facilitation tool in education in a variety of settings for many years, including in communication skills training in cancer (Fallowfield et al., 1998, Fleissig et al., 2001, Jenkins et al., 2005). Trigger tapes can provide enduring teaching material particularly when the films are based on "real life" situations, (for example, interactions between a patient and a doctor), although the discussion points may

change over time (Ber and Alroy, 2001). The film provides an experiential learning opportunity to learn through observations (Kolb, 1984).

I considered trigger tapes to be useful training material for the training programme. Trigger tapes can illustrate how the patient reported HRQoL information may be integrated and used during the consultations and help to stimulate discussions within the group. These discussions may provide ideas for the participants about how they might use the patient reported data. In addition, these trigger tapes provide opportunities to learn and acquire skills through observing their peers.

### 6.6.1 Scenario development

#### 6.6.1.1 Methods

Clinical scenarios were necessary to enact the consultations to be made into trigger tapes. The scenarios needed to illustrate examples of patients or situations where patient reported HRQoL information can be expected to play a significant role in the management of the patient or contribute to the decision making. The scenarios also needed to depict patients whose HRQoL scores may present challenges for the oncologists receiving the information so that discussions may take place as to how best manage these patients.

In order to identify these patient characteristics and situations, transcripts from the interviews with oncologists (Chapter 3) were reviewed for comments made by the oncologists about the kind of patients (as depicted by their HRQoL scores) who they expressed concerns, in terms of how they might manage the patient or the situation. In addition, I explored the literature for other situations where utility of patient reported data may be demonstrated.

Once these patient characteristics for the scenarios were determined, data from the previous randomized study (Velikova et al., 2004) conducted by the Leeds POCPRG were reviewed to identify real patients on which the scenarios may be based on, as determined by their HRQoL scores. Using data from this study was considered helpful in making the cases more realistic and relevant as they came from real patients.

The scores from the HRQoL instruments obtained from patients who were randomized to the intervention arm of this trial were examined to identify patients with HRQoL scores that reflected relevant cases for the scenarios. Once the candidate patients

were identified, their clinic consultation audio-recordings were examined to see what actually happened when oncologists were presented with their HRQoL scores during the study. Those clinic consultations where oncologists actually referred to the questionnaire data were selected and examined to see how they used the information and whether this patient reported data had an impact on the consultation in reality.

## 6.6.2 Results

### 6.6.2.1 Review of the interviews with oncologists and literature

There were two aspects of the patient reported HRQoL intervention which the clinical scenarios needed to illustrate. One aspect was for the scenarios to portray patients, characteristics of whom the oncologists had concerns. The other aspect was the positive utility of the intervention and how healthcare professionals' anxieties about the intervention may be alleviated through the scenario.

Oncologists were generally comfortable in discussing most of the symptoms and treatment side effects. Their concerns were around patients who may report multiple problems and what they should do when there are time constraints in busy clinics (Chapter 3). However, there is evidence to suggest that this intervention does not necessarily increase the duration of consultations (McLachlan et al., 2001, Detmar et al., 2002, Velikova et al., 2004) and that HRQoL data actually can help to focus on the patient problem and make the consultation more efficient (Newell et al., 1997).

Oncologists' other concerns included patient reported HRQoL raising issues which they felt poorly equipped in dealing with themselves, such as emotional distress, and welcomed guidelines in how to manage such issues and providing a prompt for when action was actually needed (Chapter 3). These concerns are echoed by other healthcare professionals in the literature (Donaldson, 2004).

One of the utility of patient reported HRQoL often described is to help unearth patients' problems which may otherwise go undetected (Higginson and Carr, 2001) and to provide means of monitoring patients over time through patients' own assessment of their HRQoL (Asay et al.). One of the oncologists stated that patient reported HRQoL would support in making decisions about treatment, particularly when other standard investigations show results that are not clear cut (Chapter 3).

6.6.2.2 Generating ideas for scenario cases

From the above results, I came up with ideas for the characteristics of patients for the scenarios. These are listed below:

1. Patient with HRQoL scores indicating poor emotional functioning: This scenario could raise discussions about how such results may be brought into the consultation and how the patient may be managed. This scenario would also provide opportunity to integrate locally developed guidelines for managing emotional distress.

2. Patient whose HRQoL indicating they are coping well with minimal issues reported on their HRQoL: This scenario could help to demonstrate how consultations may be made efficient.

3. Patient with multiple problems reported on their HRQoL questionnaires: This scenario could illustrate how such situation may be managed and to discuss how the HRQoL data may help to structure the consultation by helping the doctor and the patient to prioritise issues.

4. Patient indicating some functional issues on their HRQoL: This scenario could illustrate how a doctor may explore these issues with the patient to investigate what may be accounting for their poor functioning.

5. Patient whose HRQoL scores have shown steady improvement over the course of treatment period: This scenario could highlight use of HRQoL in monitoring patients over time.

6.6.2.3 Data from the randomized controlled trial

144 patients were assigned to the intervention arm of this trial. Patients in this arm of the study completed the EORTC QLQ-C30 and Hospital Anxiety and Depression Scale with feedback of the results to the oncologists at each study visit. 113 patients completed the planned 3 study consultations. HRQoL outcomes were available from 97 of these patients (Velikova et al., 2004). HRQoL scores from these 97 patients were visually scanned to identify patients whose scores represented characteristics of patients for the scenarios as described above.

Two or three possible patients were identified for each scenario cases to narrow the search. Audio-recording from these patients' consultations were then examined to see whether and how the patient reported HRQoL data was used in these consultations. Following this, one patient for each scenario was chosen.

The randomized controlled trial did not include patients with colorectal cancer as all colorectal cancer patients were treated in another hospital within Leeds which was not a study site for the trial. As I was developing colorectal cancer specific questionnaire for my thesis and the pilot study to examine the impact of the doctor training was planned to involve patients with colorectal cancer, one of the scenario was changed to represent a case of colorectal cancer patient, although the nature of the case remained as the original patient.

#### 6.6.2.4 Operationalisation of the cases into scenarios

Once the patients were selected, clinical scenarios for the patients were written, building on the basic information already collected as part of the study (primary cancer diagnosis, demographic information and type of treatment they were receiving for their cancer).

Each scenario needed two versions; one for the oncologist and the other for the patient. The scenarios were supplemented by additional hypothetical information in order to provide the patient with necessary background information which may be useful when it came to enacting these scenarios. The versions for the oncologists had to contain relevant clinical information concerning the case including any information about radiological or laboratory investigation results to mirror real life situations. The scenarios for patients contained some background information in order to provide some social context for the patient, such as their marital status, family circumstances and employment details. The versions for the patients were also supplemented with explanation about the disease process and details about the cancer treatment the patient would have been receiving so that the person enacting the role would have better understanding about the diagnosis and side effects of treatment.

6.6.2.5 Questionnaire Output

The result from HRQoL instruments (EORTC QLQ-C30 (Aaronson et al., 1993) and Hospital Anxiety Depression Scale (Zigmond and Snaith, 1983)), obtained from the patients on whom the scenario cases were based on, were presented in a graphical format, similar to how the results were presented to the oncologists within the original randomized study (Velikova et al., 2004). In order to assist the oncologists to use the patient reported data, traffic light coding was applied to the graphs to highlight scores from the HRQoL instruments indicating presence of significant symptom issues or poor functioning.

6.6.2.6 Medical Education Department at University of Leeds

In order to produce the trigger tapes, access to audio-visual equipment was necessary. In addition, people to enact the patient roles were needed. Leeds POCPRG had established a collaborative working with the Medical Education Department at University of Leeds. They have facilities for video-recording of the consultations and access to a group of standardised patients or simulated patients who regularly took part in communication skills teaching and in Objective Structured Clinical Examination (OSCE) for medical examinations.

Standardised patient (SP) is an umbrella term used to describe both a simulated patient (a well person trained to simulate a patient's illness in a standardised way) and an actual patient (who is trained to present his or her own illness in a standardized way) (Barrows, 1993). They have been used in medical education and clinical skills assessment and evaluation for many years.

The standardised patient is trained using a scenario based on a real patient case. Well-prepared SPs are virtually indistinguishable from the real patients. SPs can realistically convey an illness to a student and perform in a consistent and measurable way. There are a number of advantages in using standardised patients. They are generally well people who are not necessarily worried about their medical care. Therefore they can focus on the teaching and evaluation of the task in question. They can provide a “safe” environment for the learner to practice their skills without worries over potentially upsetting a “real” patient. Standardised patients are also trained in providing feedback

to the learners in terms of their professional manner, attitudes and interpersonal skills (Good, 2003).

### 6.6.2.7 Matching the scenario with suitable standardised patient

The scenarios were presented to the team within the Medical Education Department (Dr Robert Lane and Miss Jools Symons) who facilitated in selecting the most appropriate standardised patient for each scenario. Individual meetings took place with the relevant standardised patient so that the scenarios would be reviewed with them. Some modifications were implemented according to suggestions made by the standardised patient and by the education facilitators from the Medical Education Department.

Final versions of the scenarios, together with respective questionnaire output can be found in Appendix 8. Brief synopses of the cases are shown in Table 6.3 below.

**Table 6.3 Synopsis of clinical scenarios**

| Scenario | Brief synopsis | Issues highlighted |
|---|---|---|
| A | A 51 year old woman with advanced breast cancer on palliative chemotherapy.<br>She is tolerating treatment well with signs of response but developing depressive symptoms (insomnia, anorexia and high depression score on HADS) | Screening for emotional distress/depression |
| B | A 63 year old man with metastatic leiomyosarcoma on palliative chemotherapy. He is tolerating treatment well. This is reflected in the questionnaire scores showing very few problems. | Questionnaire may help to make consultation more efficient |
| C | A 70 year old lady with advanced ovarian cancer. She has undergone bowel surgery which has resulted in a formation of a stoma. She has multiple symptoms and problems and this is manifested in the questionnaire scores. | Questionnaire may help to structure the consultations by prioritising important issues. |
| D | A 45 year old woman with advanced breast cancer who has recently started on third line chemotherapy. She has symptoms which limit her physically. She is unable to work resulting in financial concerns, poor social and role functioning. | Questionnaire to help detect problems |
| E | A 68 year old woman with advanced bowel cancer. She has completed a 3 months of palliative chemotherapy during which she has had significant improvement in her symptoms. Her restaging CT scan has shown that the appearance of her cancer has not changed very much (stable disease). | Monitoring and assessing treatment effect |

6.6.2.8 Matching the scenarios with the oncologists

The scenarios consisted of patients with different primary cancer sites. Therefore, five oncologists with expertise in relevant cancer site were invited to take part in this trigger tape production. In order to simulate a real clinic situation, the clinical scenario was presented to the relevant consultant immediately prior to filming. They were presented with "mock" case notes of the patient with relevant clinical details and investigation results filed within them. Oncologists were also presented with the questionnaire output from the HRQoL instruments together with copies of the instruments so that they were aware of the questions behind the functional scales.

6.6.2.9 Filming of the scenarios

The filming for all the scenarios took place in a studio within the Medical Education Department at University of Leeds. There were three stages in the filming of all the consultation scenarios. Initially, the doctor was presented with the mock case notes of the simulated patient they were about meet. This included results of relevant investigations and clinical correspondence normally found in real case notes. The doctor was asked to read through the notes and describe what kind of a patient he or she might meet and any particular topic they might raise depending on the content of the previous consultation records. The doctors were then presented with the graphical output of the patient reported outcome information derived from the questionnaires. They were then asked how this information impacted on their expectation about the patient and how this might influence their consultation they were about to have. The second stage was the filming of the consultation with the simulated patient. The third and final stage was the feedback session; both the doctor and the simulated patient(s) were able to provide comments about the consultation they have just had. The focus of the discussion particularly centred on the role of the patient reported information during the consultation. Discussion sessions were facilitated by Dr Robert Lane and Miss Jools Symons from the Medical Education Department.

6.6.2.10 Production of trigger tapes

All the recordings of the simulated consultations, including the pre and post consultation discussions, were transcribed verbatim. The transcripts were then studied alongside the video recordings to examine how doctors interpreted and used the patient reported data and the role this information played during the consultations. The different ways by which doctors introduced the information during their consultations were also examined. The transcripts were scrutinized for any sections where patient reported information played an important role during the consultations.

Sections of videos were subsequently edited from the original recordings in order to create the "trigger tapes" which were short clips of video with specific relevance to the utility of the patient reported data. Editing of the video clips was performed by Mr Richard Garry, a member of the Leeds POCPRG.

Transcripts of selected "trigger tapes" are shown in Table 6.4.

**Table 6.4 Selection of transcripts from "trigger tapes"**

| **Example of pre-consultation discussion** | |
|---|---|
| *Fac:* | *Having been through the questionnaire results, do you think that'll help you approach the consultation in any way different to usual?* |
| *Doc:* | *Okay. I think the results are interesting, actually. I think I was already mentally prepared for somebody who might not be so well from the story that I'd heard already but I was quite struck by these scores. The physical functioning and the emotional functioning and indeed role and social functioning which are extremely low. So clearly this woman is you know, not operating in anything like her normal capacity or how she might describe herself as a normal person or her normal self. So those are quite striking I think, really. And you know, significant level of impairment and physically not functioning well at all and although I would have asked about that I'm really quite struck by how apparent degree of that. And also some of these aspects seem to have got worse with the chemotherapy whereas I would have been hoping and actually statistically slightly expecting her to be getting better. But perhaps she isn't. And that's what I would say from the functional impairment scores. …..*<br><br>*The symptom scores which I realise is the reverse she's got some very significant symptoms, she's short of breath which wasn't something which came out of the history so she would have had to have volunteered that to me unless I'd noticed it myself…... Poor sleep, which we don't often ask about I must say, err and then she's clearly got very bad diarrhoea which I'm sure we would have covered but that is a very striking problem and then there's this enormous score, you know, on financial concerns which I have to say I wouldn't routinely ask about ……..if there was time I would try to avoid ignoring that because that's clearly a key issue.* |
| *Fac:* | *Do you think that would change how you structure the consultation?* |
| *Doc:* | *It might somewhat. I think the cognitive function is interesting because sometimes you're establishing a rapport with a patient; you're assessing how much they understand about things, you're quite quickly working out if they know what's happening. And you tailor what you do according to that. But this suggests that she is thinking very straight and all these things are major problem for her. So I might …. I might say to her that "Look, I can see from the scores and what I know already from the letters that you know, you're having a very rough time at the* |

*moment and these things are very difficult". And you know shall we go through these things……*

*Fac:* *Perhaps a quicker way into….*

*Doc:* *… a quicker way into some of these issues, exactly. Whereas you might have looked for a longer rapport building for permission to raise them so I think it might be quicker….*

**Example of how the patient reported data is introduced during the consultation**

*Doc:* *Are there other things that the disease and the treatment are interfering with? Your job and your money and ….*
*SP:* *Well, I just don't … I'm just not quite the same. I sort of…I don't go out as much. Don't see people as much. Don't get as much fresh air as …well, you know? I can't just go for a walk. Well, walking is free isn't it?*
*Doc:* *True*
*SP:* *It clears your mind.*
*Doc:* *umm. Ok.*
*SP:* *I can't…. it just hurts a bit. I mean it's "uncomfy"*
*Doc:* *Is that getting you down?*
*SP:* *Umm……. Yeah.*
*Doc:* *OK. There seems to be a kind of…. a number of related issues here. There're issues about your money and your finance. You're not sleeping very well. Cos you're obviously anxious about the situation that you're in. And you're quite …. Well, not very depressed but it looks as though you are a bit depressed from the scores that are coming out on ….. (pointing at the questionnaire output)*
*SP:* *Yeah, yeah. I didn't know quite what to say with that thing because people sort of use depression as a word don't they?*
*Doc:* *They do.*
*SP:* *You know? But I suppose I am a bit, yeah. I mean you'd have to be wouldn't you ….*
*Doc:* *Well, I mean some of this….some of this of course is completely natural reaction to the situation that you're in.*
*SP:* *Yeah. That's what I mean.*
*Doc:* *And the issue really is how we best support you through that. Make you feel as though you've got some help and support. That people are listening to you.*
*SP:* *Umm*
*Doc:* *Um and try and get you through it as best we can.*

**Example of post-consultation discussion**

*Fac:* *What do you feel went well in that consultation?*

*Doc:* *It feels as though we've covered quite a lot of ground. I mean I ….as presented, you were coming to me for a discussion about your next course of chemotherapy and it would have been very easy just to focus on what the side effects of the your last treatment, what do we need to change, you're coming in next week and you're coming back in 3 weeks….. I could have done that in 20 seconds or so. I think having the information on these sheets it kind of immediately gave me a red alert to a number of issues. Financial issue I think was a very obvious a trigger in that scenario that I wouldn't have gone into I don't think without the information on the sheet. But actually that was a way into to a whole load of other things, wasn't it?.... in fact.*
*Um, I think we did explore quite a lot of …quite a lot of issues. I wondered whether it might be about your job but actually it was more about your family and your daughter and ur … your uncertainties for the future. So I was pleased to be able to explore some of those issues, which I don't think I would have done …otherwise.*

Fac: Faciliator

Doc: Doctor

SP: Simulated patient

## 6.7 Doctor Training Programme

The objectives of the training were to highlight the utility of patient reported HRQoL information in clinic consultations and to illustrate different ways in which this information may be used to aid/support clinical decision making.

The length of the training was decided to be half day session to fit in with clinicians' busy schedules. The training needed to incorporate different components to accommodate different learning styles people may have.

The training consisted of a didactic component detailing the available evidence base for patient reported HRQoL assessment with feedback to oncologists and the role of such intervention within clinical practice. The training also highlighted the findings from the longitudinal analysis of the previous randomized controlled study (Chapter 5), indicating that psychosocial issues are often ignored even when the patients have reported problems.

The interactive or experiential component of the training was provided by the trigger tapes produced; illustrating how different doctors have used the patient reported information in different clinical situations. These trigger tapes were used to promote small group discussions amongst the participants.

The training programme also incorporated guidelines developed by the Leeds POCPRG for managing emotional distress and fatigue, which mapped onto existing supportive services available locally in Leeds. These guidelines were produced in such a way that it can be used as a template which can easily be adapted according to locally available resources in any hospital, so that the doctor training can be tested in other institutions in the future.

Participating doctors were asked to complete a questionnaire before and after the training session, concerning use of patient reported HRQoL information in clinical practice as part of the evaluation process. The components of the training programme were brought together with Dr Absolom and Prof Velikova. The trainers' manual developed for the training programme is shown in Appendix 9.

## 6.8 Summary

This chapter has described the processes undertaken to formulate the framework for the doctor training programme aimed at increasing the utility and integration of patient reported HRQoL information in clinic consultations.

As the patient reported HRQoL aims to influence communication between patients and healthcare professionals, training methods used in advance communication skills training were reviewed to inform the structure for the training programme for patient reported HRQoL intervention. Conceptual models of adult learning and learning styles have helped to better understand how adults learn and provided better appreciation of the strategies used in the communication skills training; these strategies were considered relevant to training doctors in using patient reported HRQoL data.

I have developed trigger tapes which illustrates different ways patient reported data can be used. These video clips offer learners opportunities for experiential learning through peer observation and provide ideas for how they may use the patient reported data. Trigger tapes can also help to make the training more stimulating for the learners and hopefully help generate small group discussions about utility of patient reported HRQoL data.

The final half day doctor training programme included a didactic component to provide evidence base for the use of patient reported HRQoL information in clinical practice. The programme also offered a platform to integrate clinical guidelines for the management of emotional distress and fatigue to help doctors discuss these issues more readily with their patients.

The next stage was to test the impact of the training programme in pre and post test pilot study to examine the impact of the training on how doctors use the patient reported data in their consultation. This pilot study also provided the opportunity to test the tumour site specific questionnaires (Chapters 3 and 4). The design and set up of the study is described in Chapter 7.

# Chapter 7 Doctor training pilot study

## 7.1 Introduction

This chapter describes the methodology of a pilot study designed to assess the impact of the doctor training programme described in chapter 6.

The study aimed to provide an estimate of the impact of the doctor training on utilising patient reported outcome data on patient-doctor communication in routine chemotherapy review consultation. The results could then be used to contribute to the preparation and sample size calculation for future studies planned as part of the wider programme of research by the Leeds POCPRG.

The study protocol was written and submitted to the Local NHS Ethics committee for ethical approval by myself. The training session was led by Prof Velikova and Dr Absolom but I attended and took part in facilitating the training session. The recruitment and analysis of the study took place outside the timeframe of my doctorate degree.

## 7.2 Measure of impact of doctor training

It was necessary to consider how the physician training programme and the patient reported outcome intervention as a whole would be evaluated.

Leeds POCPRG have collected and analysed a large number of oncology clinic consultations (over 1500 consultations from over 400 patients) as part of their studies. The consultations were analysed using content analysis as previously described in Chapter 2.

It was necessary to expand this content analysis to provide a better measure of the impact of doctors' training programme. This developmental work was based on the theoretical framework of "patient centred communication". Definition of patient centred communication includes 1) eliciting and understanding the patient's perspective, 2) understanding the patient within his or her psychosocial context, 3) finding common ground and 4) assist patients to share control and allow involvement in decision making to the degree they wish (Epstein et al., 2005). These concepts fit well with the aims of

the patient reported outcomes intervention research, and provide the theoretical framework for the development and evaluation of the training programme.

A review of coding systems used to analyse doctor-patient communication in oncology has revealed the majority of these systems to be based on interaction process analysis with focus on coding “utterances” and evaluating general communication skills (Fallowfield et al., 2002, Razavi et al., 2003, Roter et al., 2004) (e.g. breaking bad news, empathic communication). These skills are undoubtedly important and necessary and advanced communication skills training is now an essential component of training for all oncologists. However, it was felt that these systems were not wholly suitable for evaluating a training programme specifically on the utility of patient reported HRQoL information.

Several instruments have been developed with the aim of measuring patient centred communication (Mead and Bower, 2000, Elwyn et al., 2000, Shields et al., 2005, Brown et al., 2001a). Of these, the Measure of Patient Centred Communication (MPCC) (Brown et al., 2001a) was considered to be the most appropriate as it is the only instrument which focuses on clinician response to patient issues and incorporates assessment of shared decision making. The MPCC was developed with the Patient Perception of Patient Centredness (PPPC) questionnaire (Stewart et al., 2004). This questionnaire aims to capture patients’ views on how patient centred their consultations are. Although this framework was developed specifically for consultations within the primary care setting, its’ fundamental principals are applicable to any clinical consultations, including oncology clinic consultations in hospitals.

In anticipation of this pilot study and for future studies investigating the impact of patient reported outcomes intervention, Leeds POCPRG are evaluating the feasibility of applying MPCC consultation coding to oncology consultations.

## 7.3 Method

### 7.3.1 Study design

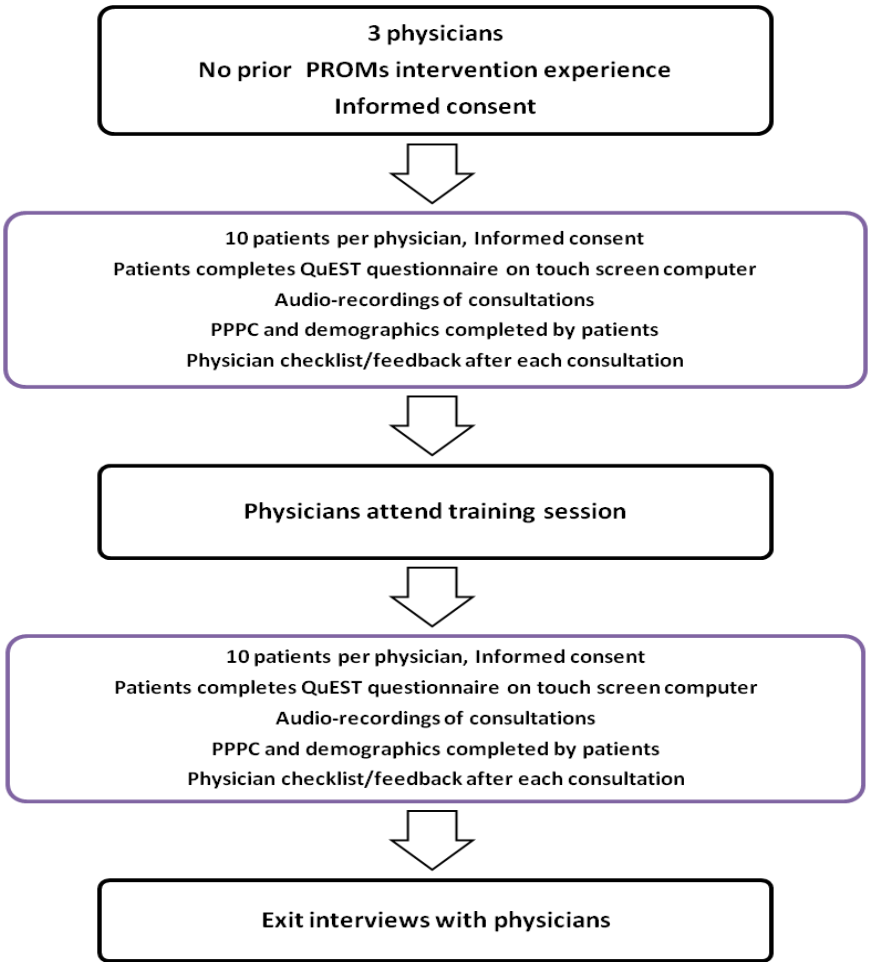
This was a quasi experimental (before and after) study. The study schema is shown in Fig 7.1. The participating oncologists attended the training programme half way through the study. Individual meetings were arranged with the participating oncologists

prior to study commencement in order to provide them with basic information about the HRQoL instrument (QuEST questionnaires) used in the pilot study.

The impact of this training will be assessed by comparing study measures obtained from both patients and physicians, along with content of clinic consultations before and after the training.

Informed consent was obtained from both patients and oncologists taking part in the study.

**Figure 7-1 Study schema for pilot study of doctor training**



### 7.3.2 Study sample

#### 7.3.2.1 Oncologists

Three oncologists involved in the management of patients with breast, colorectal and gynaecological cancer respectively, who had no prior experience of patient reported outcome intervention, were invited to take part in the study. Consultants and specialist registrars/clinical fellows were invited to take part in this pilot study as the training will be delivered to doctors with varied oncology experiences in future studies.

#### 7.3.2.2 Patients

Patients undergoing anti-cancer chemotherapy for advanced breast, colorectal and gynaecological cancers, who were attending the oncology out-patient clinics for review at the Leeds Cancer Centre, were invited to take part. Patients needed to be over the age of 18 years and be able to read and understand English. Patients exhibiting psychopathology or those with significant cognitive impairment which would prevent them from being able to provide informed consent were excluded. In addition, those patients who were considered too ill by the clinic staff were excluded from the study.

#### 7.3.2.3 Sample size

Analysis of previous studies conducted by Leeds POCPRG showed that non-specific symptoms and functional issues were discussed on average in 30% of outpatient consultations. The observed increase in discussion of symptoms or functioning when patient reported HRQoL data was measured and fed back to the oncologists was of the order of 10-15%. Therefore, for a comparison of proportions in before-after design, based on wanting to detect an improvement from 30% to 45%, 3 oncologists with 10 patients before training and 10 patients after training were planned to be recruited into the study. This assumed the common variability in percentage before and after could be up to 12%.

### 7.3.2.4 Study measures

Both patients and physicians were participants in this study. Consenting patients were asked to complete the relevant cancer site specific QuEST questionnaire on touch screen computer immediately prior to their planned clinic consultation. The results of these questionnaires were automatically scored and presented in a graphical format within the patient's electronic notes in real time so that they were available for their oncologists to review and use during the consultation. The scores were given colour coding ("traffic light system") depending on the severity of the symptom or functional concerns. The colour coding was performed in reference to the cut off points derived from distribution and anchor based methods (Chapter 4).

Patient characteristics

Clinical information including the site of primary cancer, stage of disease and the chemotherapy regimen patient was receiving were recorded from medical notes at study entry. In addition, patients' age, gender, marital status, level education and employment status were obtained through a demographic survey.

Oncologist characteristics

Oncologists' age, gender, qualification level, number of years practicing in medicine and in oncology was recorded from demographic survey completed by the oncologists.

### 7.3.2.5 Outcome measures and analysis

The Patient Perception of Patient-Centredness questionnaire (PPPC)

The Patient Perception of Patient-Centredness questionnaire (PPPC) (Stewart et al., 2004) has 9 items and the score ranges from 1-4, with a higher score indicating more positive patient perceptions (Appendix 10). The internal consistency of the questionnaire (Cronbach's alpha) is 0.80 (n=85). Validity of the questionnaire was

based on the origin of the items, Measure of Patient Centred Communication (MPCC), with all items being significantly related to the MPCC (Stewart et al., 2004).

Descriptive statistics (mean and standard deviation) will be calculated for the PPPC questionnaire scores. The scores will be correlated with the analysis of the audio-recording of consultations (see below).

## Patient doctor communication

### *Content analysis of consultation*

A study specific checklist will be used to note whether HRQoL issues included in the QuEST questionnaires are discussed and who (doctor or patient) initiates the discussion. Symptoms and functions mentioned during the consultation will be recorded, along with any other problems or concerns reported by patients.

Medical decision and non-medical actions taken in response to patients' problems will also be recorded. Medical decisions are defined as decisions on cancer treatment, symptomatic/supportive treatment, investigations and referrals. Non-medical actions include advice on lifestyle, coping, and reassurance.

The content of communication will be presented as a list of binary variables (topics discussed or not) and descriptive statistics will be calculated showing the proportion of consultations when symptoms or functional issues are discussed. Medical and non-medical actions taken in response to patient problems will also be analysed descriptively.

## Measure of Patient-Centred Communication (MPCC)

All audio-recordings of the clinic consultation will be subjected to an analysis, using the coding framework outlined in the MPCC (Brown et al., 2001a). There are three components to the coding framework. These are:

Component 1: Exploring both the disease and the illness experience,

Component 2: Understanding of the whole person

Component 3: Finding common ground

Descriptive statistics will be calculated for scores from each component (mean and standard deviation). The scores derived from this analysis will also be correlated with the PPPC scores.

Comparative analysis will be performed on outcome measures obtained before and after the training to examine its' impact.

Oncologist questionnaires

*Oncologist checklist*

Following every consultation with a patient participating in the study, the oncologist were asked to complete a brief checklist regarding the use of patient reported HRQoL in the consultation and its' impact. Oncologists' perception of the usefulness of patient reported symptoms and HRQoL and their impact on the consultation will be analysed descriptively from the checklist.

*Oncologist self assessment questionnaire*

Oncologists were also asked to complete a self assessment/feedback questionnaire relating to patient-doctor communication after each study consultation. This is the physicians' version of the PPPC questionnaire; results from this questionnaire will be correlated with the results from PPPC questionnaire.

*Exit interviews with physicians*

Interviews were held with the participating physicians at the end of the study to explore their views on their experience of patient reported HRQoL intervention before and after the training programme. Oncologists were asked to provide their opinions on the training programme, having used the patient reported information during the study. The interviews were audio-recorded, transcribed and will be analysed using framework analysis (Ritchie et al., 1994). The result from this analysis will assist in tailoring the content of the training programme for future studies.

## 7.4 Preliminary results

The study was conducted by the Leeds POCPRG between August 2011 and January 2013.

3 oncologists (one Consultant Clinical Oncologist, one Clinical Fellow and one Specialist Registrar in Medical Oncology specialising in the treatment of breast, colorectal and gynaecological cancer respectively) were invited and consented to take part in the study.

When the study began, there was another specialist registrar working with the gynaecological cancer team who initially took part in the study and had consultations with six patients. However, he had to rotate to another team during the study period and therefore these six patients were excluded from the analysis as this doctor did not attend the training session.

Total of 251 patients were approached to take part in the study. 73 patients (29%) consented, of which 69 patients completed the study. 4 patients could not complete the study due to mainly timing issues. 178 patients declined or did not enter the study. For those patients who gave a reason for non participation, many stated that they would prefer to see another member of the team (59 patients). There were also patients who became ineligible due to their treatment being stopped or changed to something other than chemotherapy after the initial contact with the patient to introduce the study. Patients were initially approached by the clinic nurses before the researcher could discuss the study in detail. This multi-stage patient approach may have had some impact on the recruitment figures.

6 patients' consultations were excluded from analysis for reasons given above regarding the doctor rotating to another team during the study period. This left 21 patients from each disease group who took part in the study and completed the measures as described above for analysis. There were 10 patients in the pre-training phase and 11 patients in post training phase in the breast group; 11 patients in the pre-training phase and 10 patients in the post training phase in the colorectal and gynaecological cancer groups. There were 50 female and 13 male participants, with mean age of 63 years (range 33 – 84 years, SD 9.6). 81% of patients were receiving cytotoxic chemotherapy, 9.5% were on biological/antibody therapy and 9.5% were on endocrine therapy. Majority of patients were receiving palliative treatment for metastatic

disease (95% of breast cancer patients, 50% of gynaecological cancer patients and 100% of colorectal cancer patients).

The oncologists attended the doctor training after the pre-training phase recruitment had completed for each disease group. The training was arranged so that all three oncologists within the study could attend at the same time, in order to create a small group teaching environment. I took part in the training session as a facilitator, along with Dr Absolom and Prof Velikova. Once the training had taken place, post training phase of the study resumed.

The analysis of the pilot study is being undertaken by the Leeds POCPRG, in order to gain an estimate of the impact of the doctor training. 61 patients' consultation audio recordings were available for analysis (31 pre-training and 30 post-training) due to two audio-files being partially complete.

The preliminary findings suggest interactive training sessions appear to be associated with some improvements on discussion/communication between patients and doctors. The study analysis indicated that patient reported HRQoL data were explicitly referred to in significantly more consultations in the post training phase (48.4 % vs 76.7 %, $p<0.05$). Although the mean number of common cancer symptoms being raised in the consultation did not differ pre and post training phase (3.81 vs 4.27, $p = 0.24$), the mean number of functions discussed were significantly higher post training (2.23 vs 2.90, $p<0.05$). In particular, physical functioning was raised more frequently in the post-training consultations (61.3 % vs 86.7 %, $p<0.05$) as was pain (51.6 % vs 86.7 %, $p<0.05$) (Absolom et al., 2014).

# Chapter 8 Discussion

The overarching hypothesis of this thesis is that patient self reported HRQoL instruments specifically developed for colorectal cancer patients to be used in routine clinical practice would play several important functions; improving patient-doctor communication, highlighting areas of unmet needs and providing a method of monitoring patients' symptoms and side effects over time. An instrument with such specific purpose may be built on existing questionnaires, by adapting them through processes involving both patients and healthcare professionals to ensure its' clinical utility and relevance to the specific group of patients. In addition, training healthcare professionals on how to respond to and integrate patient reported HRQoL data during consultations would further enhance the intervention by assisting them to incorporate patient data in clinical decision making process.

My expectations were that a questionnaire developed for patients with colorectal cancer specifically for use in clinical practice, together with training for the healthcare professionals would serve the following functions:

1. Enhance patient-doctor communication, by allowing patients' views to be actively presented and facilitate collaborative working relationship between the two parties.
2. Provide a reliable assessment of colorectal cancer specific physical symptoms and treatment toxicities and thus provide a way of monitoring treatment response and symptoms over time and help support clinical decision making.
3. Screen for and identify problems which are not always addressed, such as emotional distress, impact of disease and treatment on daily activities and physical function, and impact on family/personal relationships. Doctors can raise and encourage patients to discuss these issues and, where necessary, refer for supportive care services.

Patient reported outcome intervention is a complex intervention. It requires multiple components to come together and ultimately change the behaviour of both patients and healthcare providers. Evaluating the role of PROMs in clinical practice is equally challenging. Medical Research Council (MRC) has given a guidance on developing and evaluating complex interventions (Craig et al., 2008). Emphasis is given on indentifying active components of the intervention and developing/piloting each component to assess its' impact on the outcomes before definitive evaluation of the

intervention as a whole. This framework fits well with the development and evaluation of PROMs intervention.

The objectives of the thesis outlined in Chapter 1 can broadly be divided under two main themes. Below I summarise my key results and achievements in each theme:

1. Enhancing the clinical practice through the development of colorectal cancer specific HRQoL questionnaire

I have reviewed discussion topics from routine oncology consultations among colorectal cancer patients and reviewed the relevant literature to identify relevant HRQoL topics concerning patients with colorectal cancer. I have successfully conducted semi-structured interviews with 7 oncologists and 10 patients to explore and highlight these issues further to ensure the topics relevant in routine clinical practice were selected. The questionnaire was validated in a sample of 155 colorectal cancer patients but also by 448 patients overall as part of the wider research being undertaken by the Leeds POCPRG.

2. Exploring the ways in which patient reported information may be incorporated into the routine practice, thus overcoming some of barriers for its successful implementation.

I have performed secondary analyses of communication and use of HRQoL data during oncology consultations, using the rich dataset from the randomized controlled study previously conducted by POCPRG. These analyses highlighted that repeated patient reported outcomes intervention can have an impact on patient-doctor communication over time but this finding was only limited to discussion of physical symptoms. Patients' psychosocial issues remained largely unaddressed, despite patients reporting significant problems. Doctors may not necessarily have the tacit knowledge of what the HRQoL scores indicate. Within clinical practice, doctors rely on normal parameters on laboratory tests gage their clinical decisions as to whether they need to act on the results. The cut off score analysis of the QuEST-Cr questionnaire will help provide clinicians an idea of a parameter which may in turn help them use the information to make clinical decisions where indicated. These findings have informed the content of the doctor training programme.

Using theory of adult learning and the model of communication skills training, and through collaborative working with University of Leeds Medical Education Unit and

oncology colleagues, I developed and recorded scenarios for trigger tapes which can be used as part of the doctor training to provide a valuable experiential learning opportunity. I designed and implemented these components within a training programme for oncologists, with the aim of enabling them to use patient reported HRQoL data more effectively during clinic consultations. This training programme has been tested within a pilot study, to examine its' impact of the utility of patient reported HRQoL information.

## 8.1 Enhancing the clinical practice through the development of colorectal cancer specific HRQoL questionnaire

QuEST-Cr is a 55 item questionnaire which has been developed specifically for colorectal cancer patients for use in routine clinical practice. As colorectal cancer can affect both men and women, there are gender specific questions concerning sexual function. It also includes items specific to patients with a stoma.

The processes undertaken for the development of QuEST-Cr have incorporated both clinimetric (Feinstein, 1983) and psychometric approach. The combination of EORTC QLQ-C30 (Aaronson et al., 1993) and EORTC QLQ-CR29 (Whistance et al., 2009) was found to provide best coverage of topics raised in routine colorectal cancer patients' clinic consultations and was used as the basis for adaptation. It is noteworthy that the adaptation process has not increased the number of items contained in the questionnaire as brevity of instruments is an important factor for use in clinical practice to ensure patients are able to complete the questionnaire and for the healthcare professional to be able to interpret the data efficiently.

QuEST-Cr provides assessment of commonly reported symptoms and side effects of colorectal cancer treatments, which are essential to oncologist supervising their patients' treatment course. QuEST-Cr provides a way of monitoring these symptoms over time. QuEST-Cr includes a more detailed assessment of physical activity compared to the EORTC instruments; a function considered important by the oncologists. Similarly, there are more items addressing fatigue as this was one of the commonly reported symptom by patients but often poorly managed within the oncology practice in general (Borneman et al., 2007); improved assessment may play a role in increased recognition and treatment of the condition. Variety of questions was explored for the assessment of emotional distress. Both patients and oncologists

expressed concerns for the word “depressed” within the question. MHI-5 (Berwick et al., 1991) was considered the most appropriate as the items contained both positive and negatively worded questions but also used language which patients could relate to. In addition, based on the work by Cull et al (Cull et al., 2001), MHI-5 can be used as part of a step-wise screening process in conjunction with the HADS (Zigmond and Snaith, 1983), providing a method of identifying patients who may warrant referral to supportive care services .

I felt it was important to include questions concerning stoma within this questionnaire as having a stoma has an enormous impact on patients, both physically and psychologically (Brown and Randle, 2005). Many of the existing questionnaires asks patients predominantly about their bowel function when addressing issues relating to their stoma, which often overlaps with other bowel related questions. Therefore, items were chosen which would address practical issues relating to the stoma and the psychosocial impact patients may experience because of the stoma.

There were mixed views about inclusion of questions concerning body image and sexual function from both patients and oncologists. However, these are issues relevant to patients with colorectal cancer (Bullen et al., 2012, Traa et al., 2012) and as one of the aims of the questionnaire is to help raise issues which are often ignored, it was considered necessary to include items addressing these issues within the questionnaire, but provide patients with options to skip the items if they did not wish to answer.

The questionnaire has undergone psychometric testing in a sample of 155 colorectal cancer patients plus amongst nearly 450 wider cancer patient patients to test the reliability of the subscales which have been identified through exploratory factor analysis.

In summary, the QuEST-Cr provides a comprehensive assessment of colorectal cancer patients with particular focus on those undergoing chemotherapy treatments; the questionnaire addresses disease and treatment related symptoms but also general HRQoL issues which may affect these patients. The questionnaire allows patients to report problems which they may find otherwise difficult to raise during the consultation (such as sexual issues). It may also assist in detection of important issues which may be amenable to further treatment, such as emotional distress.

## 8.2 Exploring the ways in which patient reported information may be incorporated into the routine clinical practice

Exploratory work around the development of doctor training programme has indicated that psychosocial and other functional issues are rarely discussed in routine oncology consultations. Although many consultation models have been developed over the last four decades, highlighting the importance of holistic approach to patient management, the clinic consultations were often doctor led with discussion topics centred on physical symptoms. Even when patients reported significant problems with their psychosocial functioning, doctors often failed to raise these issues with their patients. I have published this observation identified through the exploratory analysis of longitudinal data from the previous randomized controlled study, conducted by the Leeds POCPRG in Journal of Clinical Oncology (Takeuchi et al., 2011). This was the first attempt being made linking the questionnaire scores and content of patient-doctor communication.

It is necessary for doctors to be able to respond to patient reported information so that patients' problems are not left unaddressed (Velikova et al., 2004, Detmar et al., 2002); analysis described above indicates the need to identify ways to assist doctors in how to respond to patient reported HRQoL information.

Details about training given to healthcare professionals receiving patient reported information have been sparse, even where there was indication of such training being provided. They generally focused on the HRQoL instruments used but not *how* the healthcare professionals might use the information.

Interviews with oncologists, as part of the questionnaire development, highlighted many of the recognised barriers (Deyo and Patrick, 1989) to the implementation of patient reported HRQoL assessments. These were time constraints, lack of familiarity with HRQoL instruments in general, and their ability to deal with a wide range of problems which patients may report. However, involving the healthcare professionals in the development of QuEST-Cr has helped to gain their interest in the intervention and their engagement with the process, which is one of the key factors needed for patient reported HRQoL to be adopted in clinical practice (Locklear et al., 2014).

Although training clinicians has been suggested as a way of overcoming these barriers, there was no specific guidance on how such training may look like. It was helpful to look at the conceptual models of adult learning and learning styles together with teaching methodologies in identifying the components necessary in the training

programme. I used the teaching strategies used in advanced communication skills training as the model for the training programme for patient reported HRQoL intervention as the content of the communication skills training incorporate key elements of the adult learning theory.

I identified that there needs to be a didactic component to highlight the evidence for the utility of patient reported HRQoL information, how such information may assist them during clinic consultations and alleviate their fears and concerns about patient reported data. Experiential learning is an important strategy in clinical skills training, including communication skills, where role-play feature heavily as a method to acquire new skills. As the training programme for patient reported HRQoL intervention had to be relatively short in order to fit in with doctors' demanding clinical schedules, it was necessary to consider options on how experiential learning can be included in the training. Trigger tapes have been used successfully in clinical skills training for many years, including communication skills training. I felt this was the most appropriate tool to illustrate how patient reported data can be used, facilitate discussions among the participants and provide them with ideas on how they might use the patient reported data and act on it.

The specific content and components of the training programme has been brought together with Dr Absolom and Prof Velikova. The training programme has also incorporated locally produced guidelines on the management of emotional distress and fatigue, in order to facilitate oncologists to discuss these issues with the patients where indicated. The approach taken for the development of this training programme contributes to the description and practical ideas on how to design and implement a training programme of this kind.

This study highlights the need for the training to be specifically tailored to the specific nature of the patient reported outcome instruments being used in the intervention, as well as having an understanding of the training needs among the healthcare professionals. Different training methodologies may be necessary to cater for the specific situation in which the patient reported outcome intervention is being carried out. The importance of this tailored approach is highlighted in a study by Santana and her colleagues (Santana et al., 2015). Although the training may take different formats and may utilize different resources, the need for an experiential learning opportunity is emphasized in order to facilitate clinicians to acquire new skills.

## 8.3 Methodological issues

### 8.3.1 Strengths

#### 8.3.1.1 Questionnaire development/adaptation

The questionnaire development used mixed methods approach, using both qualitative and quantitative methodologies. The processes undertaken for the development of QuEST-Cr are comparable to published guidelines on the development of HRQoL instruments (Johnson et al., 2011), which included interviews with both patients and healthcare professionals and review of literature. However, rather than using the interviews with patients and healthcare professionals to generate a list of topics to be included in the questionnaire, I used the consultation data from real oncology clinics involving colorectal cancer patients to ensure relevant topics were included.

The questionnaire items were refined using both psychometric and clinimetric approach. Psychometric approaches used in the study were well established traditional questionnaire development methodologies. The clinimetric approach was used to ensure clinical utility of the questionnaire. This has lead to the creation of QuEST-Cr, an instrument for use in clinical practice specifically for patients with colorectal cancer.

#### 8.3.1.2 Doctor training

The longitudinal analysis of the previous randomized controlled study allowed exploration of a very rich longitudinal database of real life oncology consultations, where patient reported HRQoL information was used. The analysis indicated that the intervention of collecting patient reported HRQoL with feedback to the oncologists helps to maintain discussions over time, albeit mainly about physical symptoms. This study highlighted the need to improve discussions about patients' psychosocial concerns.

There was no guidance available on how to construct a training programme to assist oncologists in how to use patient reported HRQoL information. I examined the conceptual models of adult learning and learning styles to inform the type of teaching

interventions that were required and used the communication skills training methodology as a guide to developing the training. I felt communication skills training was particularly relevant, as patient reported HRQoL intervention ultimately aims to impact on doctor-patient communication as a first step in changing the behaviour of doctors and patients.

The development of trigger tapes was guided by existing literature. The strength of my trigger tapes is that they are based on real patient consultations and their HRQoL scores, ensuring clinical relevance.

#### 8.3.1.3 Limitations

There are a number of limitations in the methodologies applied in this thesis.

The consultation data from colorectal cancer patients used in the initial phase of the questionnaire development came from a randomized controlled study, called the Attention Control Study (Velikova et al., 2008), which looked at the impact of patients completing the HRQoL questionnaires without feedback to the oncologists. Completion of HRQoL alone may have had an impact on the discussion topics raised by the patients during these recorded consultations.

In addition, there are concerns about the sample size for each of the elements of this thesis. The colorectal cancer patient sample in the Attention Control Study was only 17, providing 68 consultations between them from four consecutive clinic visits. Some of the issues raised during these consultations may have been recurring issues for the sample population, thus giving an overestimate of the frequency at which these topics were raised.

During the interview stages of the questionnaire development, only 7 oncologists and 10 patients were interviewed. The colorectal cancer practice in Leeds Cancer Centre does not have a clinical nurse specialist within their team, who would routinely attend oncology clinics to review patients. They are mainly based with the surgical teams but are able to provide support if patients are having problems such as stoma related issues. I therefore interviewed all oncologists, who routinely prescribed chemotherapy treatment for colorectal cancer patients, who were based at the Leeds Cancer Centre. The number of patients interviewed is in keeping with the EORTC questionnaire

development guidelines. At the end of both sets of interviews, similar issues and problems were emerging.

The sample size for the questionnaire validation study was calculated for all three disease groups for which the questionnaire was being developed as part of the CRUK funded programme of research by the Leeds POCPRG (i.e. colorectal, breast and gynaecological cancers) rather than for the colorectal cancer questionnaire alone. Therefore, the sample size used may be considered suboptimal, particularly for items which are only included in the colorectal cancer questionnaire. As stoma related items were branching items, only relevant to a small proportion of patients, these items and the sexual function items were excluded from the factor analysis. Further research is necessary to test the QuEST-Cr for its reliability and validity. As there is currently no standard HRQoL instrument for measuring HRQoL in clinical practice, it may be difficult to make a comparison with other HRQoL instruments.

## 8.4 Future Directions

### 8.4.1 QuEST-Cr

#### 8.4.1.1 Further validation of QuEST-Cr

QuEST-Cr was validated in a relatively small sample of colorectal cancer patients from single institution. In addition, the questionnaire was only administered to patients once; hence test-retest data was not available to assess the stability of scoring among the study population and how the questionnaire performs over time. Therefore, QuEST-Cr may be improved further by testing its psychometric properties in a larger group of patients and to administer the questionnaire repeatedly. The most efficient way of collecting this data would be to administer the questionnaire in routine clinical practice.

Validating a questionnaire intended to make an assessment of individual patients also require careful consideration as to how it may be validated, not just at group level but also at individual level. As there is no gold standard questionnaire available which can be used to compare against the QuEST-Cr, other strategies may need to be explored. Kocks et al (Kocks et al., 2010) used in-depth semi-structured interviews with individual patients to assess the individual validity of a health status questionnaire used among patients with chronic obstructive airways disease (COPD) called Clinical COPD

Questionnaire (CCQ). They found that the outcomes from CCQ from individual patients showed good agreement from that obtained through the interviews. However, such a method is time consuming and can only realistically be applied for short questionnaires addressing a specific topic within a defined clinical setting. Alternatively, patients may be asked to undergo several different assessments to evaluate various domains included in the QuEST-Cr (for example, physical function and psychosocial needs); however, this will again require large patient sample and may increase patient burden.

#### 8.4.1.2 Further refinement of QuEST-Cr

Item response theory is concerned with accurate test scoring and development of test items. Item response theory models, such as the Rasch model, may allow reduction in the number of items within a scale without compromising the measurement accuracy. This may help reduce patient burden in completing the questionnaire.

One of the limitations of QuEST-Cr approach is that the questionnaire aims to capture most of the experiences of patients with colorectal cancer. However, patients differ in their symptom experience and level of health. Therefore, the questionnaire may contain items which may be irrelevant for a particular patient.

Item response theory provides basis for the computer adaptive testing (CAT) (Gershon, 2005), which is a form of computer based test that adapts to the ability of the person taking the test. CAT is particularly appealing within the clinical context (Walker et al., 2010), as the questionnaire is tailored to the individual patients. However, CAT requires a large item bank to test each domain (such as physical function) and large sample size for validation. As one of the utilities of QuEST-Cr is to function as a screening tool for a number of domains of HRQoL, CAT may not be the most suitable approach.

## 8.5 Implementing QuEST-Cr into clinical practice

### 8.5.1 Doctor training

8.5.1.1 Pilot study

The doctor training programme has been tested in a pilot study as described in Chapter 7. The study was carried out by the Leeds POCPRG and patients were recruited between August 2011 and January 2013. The aim of the pilot study was to provide an estimate of the impact of the training on patient-doctor communication. This will inform requirements of future studies to evaluate the complex intervention of using the cancer site specific questionnaires together with doctor training programme.

The pilot study utilized a quasi-experimental design (before and after); 3 oncologists and 73 of their patients from colorectal, breast and gynaecological cancer practices respectively consented to take part. Of these 73 patients, 69 patients completed the study. Consultation data from 61 patients (31 from pre-training and 30 from post-training) were available for analysis. Preliminary results have shown that the training has had an impact on patient doctor communication with more oncologists specifically referring to the patient reported data and increase in discussion of symptoms. These findings will inform future study plans to evaluate the training and also the QuEST questionnaires.

8.5.1.2 Provision of management guidelines

Interviews with the oncologists have highlighted the need for information provision and management guidelines for issues which may be reported by patients through the HRQoL instrument, such as emotional distress, body image and sexual function issues.

Managing emotional distress was a particular priority and Leeds Psychosocial Oncology Group have developed guidelines in association with the Psycho-Oncology and Liaison Psychiatry teams, based around services which are available locally, using the recommendations set out by National Institute for Health and Clinical Excellence (NICE) guidance (National Institute for Clinical Excellence, 2004). This guideline will be incorporated into the training.

Issues about body image and sexual functions raised concerns from the oncologists in terms of how they might help their patients if they reported problems in this area. Oncologists suggested that guidelines and specific referral pathway would help them in raising these issues with their patients. However, the prevalence of these issues among patients with advanced colorectal cancer is largely unknown and warrant further investigation. This would help inform development of supportive services to meet the needs.

#### 8.5.1.3 Measure of impact of doctor training

It is necessary to consider how the doctor training programme and the patient reported HRQoL intervention as a whole will be evaluated. Leeds POCPRG have collected and analysed a large number of oncology clinic consultations. These consultations were analysed using basic content analysis using a study specific checklist to note whether issues covered in the HRQoL questionnaires were discussed during the consultation, who (doctor or patient/relative) initiated the discussion and the actions that followed. Any other concerns or issues raised by the patients were also noted.

As the training aims to incorporate patient views actively into the consultation discussions, the measure of the impact of training should also aim to assess how well the communication between doctors and patients have centred around patient reported issues. In order to capture whether the consultation have been “patient centred”, it is necessary to expand the content analysis to provide a better measure of the impact of doctor training. There are plans for the consultations from the pilot study to be analysed using the Measure of Patient Centred Communication framework (MPCC) (Brown et al., 2001a). This work was outside the scope of the thesis, however, MPCC consultation analysis tool will be used alongside the content analysis to evaluate the impact of doctor training. .

## 8.6 Implementing QuEST-Cr and doctor training

I have developed a colorectal cancer specific HRQoL questionnaire for clinical practice to allow patients to report relevant symptoms, side effects of treatment and psychosocial issues. I have also developed a training programme for oncologists to assist them in using the patient reported information as part of their decision making

process, with the aim of improving patient outcomes such as patient well-being and satisfaction with their care.

It is therefore necessary to bring the two elements together to test the impact of these interventions within the clinical practice. The pilot study using before-after study design was aiming to provide the initial experience with the doctor training and early estimates of potential impact and its effect size. The effectiveness of this intervention should be tested prospectively in a randomized controlled trial.

The design of the randomized study will require careful consideration to minimize contamination effect, which may obscure the true impact of the intervention. This is particularly relevant in studies where traditional two arm study design was used in which doctors saw patients in both the intervention and control arms. Alternative study designs may be more favourable, such as cluster randomized studies where the doctor, a particular clinic or hospital is the unit of randomization. However, this approach will require large numbers of clusters and likely to need multi-centre involvement.

Employing traditional experimental study designs to evaluate such intervention is resource intensive. The studies require time, skilled investigators and their research team (consisting of research assistants, data managers and statisticians among others) and adequate funding.

Alternative evaluation methods which may be considered include quasi-experimental or continuous quality improvement designs and methods. Such evaluation methods can provide evidence of effectiveness of the intervention, may be cheaper to conduct and it can be built on quality improvement programmes which may already exist within the health institutions (Snyder et al., 2012). For example, continuous quality improvement design aims to make small changes incrementally with regular evaluation and modifications, such as in the plan-do-study-act (PDSA) cycles (Langley et al., 2009). PDSA cycle provides a framework for developing, testing and implementing changes leading to improvement.

Disadvantage of such an approach includes risk for bias and low internal validity due to lack of experimental control. However, these methods allow qualitative assessment of the mechanism of patient reported HRQoL intervention (how the data is used by the patients and clinicians and how it is integrated into the routine workflow) and describe the local conditions that have influenced the outcome of the intervention (Berwick,

2008). Such analyses can help to identify aspects of the intervention that may be generalisable to other contexts and inform how effective changes can be implemented.

## 8.7 Future directions

We now have sophisticated electronic patient health records, which are increasingly being adopted within the NHS. This move towards increased use of technology has been associated with move towards patient portals allowing patients to access their own health records. Patient reported outcomes can be integrated in electronic notes system, as already demonstrated in the work described in this thesis and in wider literature.

With the development of reliable mobile technology and availability/wider use of internet can allow online and mobile patient reporting to be feasible. Patient reported data can be incorporated in to their electronic records in real time. This approach of collecting patient reported outcomes can permit remote monitoring of symptoms and follow up.

However, the key issues of choosing an instrument best suited to fulfill the necessary function and training of healthcare professionals remain critical in the successful application of such an intervention. My work in this thesis informs these current developments being made.

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# Appendices

## Appendix 1 Healthcare professional interview questions (Chapter 3)

Table 1 Physical Functions (Healthcare professionals were asked to comment about the three physical function assessments below)

| EORTC QLQ-C30 | Rotterdam Symptom Check List | WHO PS |
|---|---|---|
| • Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?<br>• Do you have any trouble taking a long walk?<br>• Do you have any trouble taking a short walk outside of the house?<br>• Do you need to stay in bed or a chair during the day?<br>• Do you need help with eating, dressing, washing yourself or using the toilet?<br><br><u>Responses:</u><br>not at all<br>a little<br>quite a bit<br>very much | A number of activities are listed below. We do not want to know whether you actually do these, but only whether you are able to perform them presently. Would you please mark the answer that applies most to your condition of the past week?<br><br>Care for myself<br>Walk about the house<br>Light housework/household jobs<br>Climb stairs<br>Heavy housework/household jobs<br>Walk out of doors<br>Go shopping<br>Go to work<br><br><u>Responses:</u><br>unable<br>only with help<br>without help with difficulty<br>without help | Please select one of the following items that best describes your current level of physical ability<br><br>0 - I am fully active and more or less as I was before my illness<br>1 – I cannot carry out heavy physical work, but can do anything else<br>2 – I am up and about more than half the day; I can look after myself, but not well enough to work<br>3 – I am in bed or sitting in a chair for more than half the day; I need some help in self care<br>4 – I am in bed or a chair all the time and need a lot of looking after<br><br>Modified from Cancer Research UK Cancer Help website |

Table 2A List of symptoms and toxicities

| Questions | Useful | Somewhat Useful | Not useful |
|---|---|---|---|
| **Instructions for patients:**<br>Please answer the following questions by telling us how you have felt since your last cycle of chemotherapy<br>**Response options:** not at all, a little, quite a bit, very much | | | |
| | | | |
| ***Infection*** | | | |
| 1. Have you had any infection since your last cycle of chemotherapy? | | | |
| 2. Have you been bothered by fevers or chills? | | | |
| ***Gastrointestinal symptoms*** | | | |
| 3. Have you had sore mouth or tongue? | | | |
| 4. Have you had dry mouth? | | | |
| 5. Have you had problems with sense of taste? | | | |
| 6. Did food and drink taste different from usual? | | | |
| 7. Have you lacked appetite? | | | |
| 8. Have you had trouble with eating? | | | |
| 9. Have you felt full up too quickly after beginning to eat? | | | |
| 10. Have you worried about losing weight? | | | |
| 11. Have you had indigestion or heartburn? | | | |
| 12. Have you felt nauseated? | | | |
| 13. Have you vomited? | | | |
| 14. Have you been constipated? | | | |
| 15. Did you have bloated feeling in your abdomen? | | | |
| 16. Were you troubled by passing wind/gas/flatulence? | | | |
| 17. Have you had diarrhoea? | | | |
| 18. Have you blood in your stools? | | | |
| 19. Have you had mucus in your stools? | | | |
| 20. Have your skin or eyes been yellow (jaundiced)? | | | |
| ***Skin*** | | | |
| 21. Have you had soreness or redness of your hands or feet? | | | |
| 22. Have you had any other skin problems (e.g. itching, dryness, sensitivity to sun)? | | | |
| ***Sensory Neuropathy*** | | | |
| 23. Have you had tingling or numbness in your hands or feet? | | | |
| 24. Are you concerned by any changes in your hearing? | | | |
| ***Alopecia*** | | | |
| 25. Have you lost your hair as a result of your treatment? | | | |
| 26. Have you been upset by hair loss? | | | |
| ***Fatigue*** | | | |
| 27. Have you had trouble sleeping? | | | |
| 28. Did you need to rest? | | | |
| 29. Have you felt weak? | | | |
| 30. Were you tired? | | | |
| 31. Have you been less active than you would like to be? | | | |
| 32. Have you felt slowed down? | | | |
| 33. Have you felt lacking in energy? | | | |

| Questions | Useful | Somewhat Useful | Not useful |
|---|---|---|---|
| ***Pain*** | | | |
| 34. Have you had pain? | | | |
| 35. Did pain interfere with your daily activities? | | | |
| 36. Did you have abdominal pain? | | | |
| 37. Have you had pain in your stomach area? | | | |
| 38. Have you had discomfort in your stomach area? | | | |
| 39. Did you have pain in your buttocks/anal area/rectum? | | | |
| 40. Have you had pain in your back? | | | |
| ***Urinary symptoms*** | | | |
| 41. Did you urinate frequently during the day? | | | |
| 42. Did you urinate frequently during the night? | | | |
| 43. Have you had any unintentional release (leakage) of urine? | | | |
| 44. Did you have pain when you urinated? | | | |
| ***Other symptoms*** | | | |
| 45. Were you short of breath? | | | |
| 46. Were your eyes painful, irritated or watery? | | | |
| 47. Did you feel ill or unwell? | | | |
| ***Emotional /Cognitive Functioning*** | | | |
| 48. Have you had difficulty in concentrating on things, like reading the newspaper or watching television? | | | |
| 49. Did you feel tense? | | | |
| 50. Did you worry? | | | |
| 51. Did you feel irritable? | | | |
| 52. Did you feel depressed? | | | |
| 53. Have you had difficulty remembering things? | | | |
| 54. Have you had trouble talking about your feelings to your family and friends? | | | |
| 55. Have you felt stressed? | | | |
| 56. Have you felt less able to enjoy yourself? | | | |
| ***Body image*** | | | |
| 57. Have you felt physically less attractive as a result of your disease or your treatment? | | | |
| 58. Have you been feeling less feminine/masculine as a result of your disease or your treatment? | | | |
| 59. Have you been dissatisfied with your body? | | | |
| ***Sexual Functioning*** | | | |
| 60. Has the disease or treatment affected your sex life (for the worse)? | | | |
| For men only | | | |
| 61. To what extent were you interested in sex? | | | |
| 62. Did you have difficulty getting or maintaining an erection? | | | |
| For women only | | | |
| 63. To what extent were you interested in sex? | | | |
| 64. Did you have pain or discomfort during intercourse? | | | |

| Questions | Useful | Somewhat Useful | Not useful |
|---|---|---|---|
| ***Coping during treatment*** | | | |
| 65. How much has your disease been a burden to you? | | | |
| 66. How much has your treatment been a burden to you? | | | |
| 67. How much has your chemotherapy treatment interfered with your normal daily activities? | | | |
| 68. Have you worried about your health in the future? | | | |
| 69. Were your worried about your family in the future? | | | |
| 70. Did you feel uncertain about the future? | | | |
| 71. Were the side effects of treatment worse than you expected? | | | |
| 72. Were you concerned about disruption of family life? | | | |
| ***Role and Social Functioning*** | | | |
| 73. Were you limited in doing either your work or other daily activities? | | | |
| 74. Were you limited in pursuing your hobbies or other leisure time activities? | | | |
| 75. Has your physical condition or medical treatment interfered with your family life? | | | |
| 76. Has your physical condition or medical treatment interfered with your social life? | | | |
| 77. Has your physical condition or medical treatment caused you financial difficulties? | | | |
| 78. Have you had trouble having social contact with friends? | | | |
| ***Treatment worth*** | | | |
| 79. Since you started chemotherapy, how worthwhile do you think your treatment has been? | | | |

Table 2B Stoma function (Healthcare professionals were asked to comment about the four stoma function assessments below)

| **FOCUS 2** | **EORTC QLQ-CR38** | **EORTC QLQ-CR29** | **FACT-C** |
|---|---|---|---|
| Do you have a stoma?<br>☐ Yes ☐ No<br><br>If yes, have you had any problems with it (for example soreness of skin, increased frequency, leakage)? | Do you have a stoma?<br>☐ Yes ☐ No<br><br><u>Only for patients WITHOUT a stoma</u><br>Did you have frequent bowel movements during the day?<br>Did you have frequent bowel movements during the night?<br>Did you feel the urge to move your bowel movements without actually producing any stools?<br>Have you had any unintentional release of stools?<br>Have you had any blood in your stools?<br>Have you had any difficulty in moving your stools?<br>Have your bowel movements been painful?<br><br><u>Only for patients WITH a stoma</u><br>Were you afraid that other people would be able to hear your stoma?<br>Were you afraid that other people would be able to smell your stoma?<br>Were you worried about possible leakage from the stoma?<br>Did you have problems caring for your stoma?<br>Was your skin around the stoma irritated?<br>Did you feel embarrassed because of your stoma?<br>Did you feel less complete because of your stoma? | Do you have a stoma bag (colostomy/ ileostomy)?<br>Please circle the correct answer.<br>☐ Yes ☐ No<br><br>Answer these questions ONLY IF YOU HAVE A STOMA BAG<br>Have you had unintentional release of gas/flatulence from your stoma bag?<br>Have you had leakage of stools from your stoma bag?<br>Have you had sore skin around your stoma?<br>Did frequent bag change occur during the day?<br>Did frequent bag change occur during the night?<br>Did you feel embarrassed because of your stoma?<br>Did you have problems caring for your stoma?<br><br>Answer these questions ONLY IF YOU DO NOT HAVE A STOMA BAG<br>Have you had unintentional release of gas/flatulence from your back passage?<br>Have you had leakage of stools from your back passage?<br>Have you had sore skin around your anal area?<br>Did frequent bowel movements occur during the day?<br>Did frequent bowel movements occur during the night?<br>Did you feel embarrassed because of your bowel movement? | Do you have an ostomy appliance?<br>☐ Yes ☐ No<br><br>If yes, please answer the next two items:<br>I am embarrassed by my ostomy appliance<br><br>Caring for my ostomy appliance is difficult |
| Not at all<br>A little<br>Quite a bit<br>Very much | Not at all<br>A little<br>Quite a bit<br>Very much | Not at all<br>A little<br>Quite a bit<br>Very much | Not at all<br>A little<br>Somewhat<br>Quite a bit<br>Very much |

## Appendix 2 QuEST-Cr item origin and references

| Abbreviated name | Full name and reference |
|---|---|
| FACT-C | Functional Assessment of Cancer Therapy-Colorectal (Ward et al., 1999) |
| FOCUS2 | Item from FOCUS2 trial (Seymour et al., 2011) |
| QLQ-BN20 | EORTC QLQ-BN20, Brain cancer module (Taphoorn et al., 2010) |
| QLQ-Br23 | EORTC QLQ-Br23, Breast cancer module (Sprangers et al., 1996) |
| QLQ-C30 | EORTC QLQ-C30, Core quality of life questionnaire (Aaronson et al., 1993) |
| QLQ-CR29 | EORTC QLQ-CR29, Colorectal cancer module 29 items (Whistance et al., 2009) |
| QLQ-CR38 | EORTC QLQ-CR38, Colorectal cancer module 38 items (Sprangers et al., 1999) |
| QLQ-HDC29 | EORTC QLQ-HDC29, High dose chemotherapy module (Velikova et al., 2007b) |
| QLQ-LMC21 | EORTC QLQ-LMC21, Colorectal liver metastasis module (Blazeby et al., 2009) |
| QLQ-OV28 | EORTC QLQ-OV28, Ovarian cancer module (Greimel et al., 2003) |
| RSCL | Rotterdam Symptom Checklist (de Haes et al., 1990) |
| WHO PS | WHO performance status (World Health Organization, 1979) |
| QLQ-HDC45 | under development |


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# Appendix 3 Longitudinal impact analysis – Mixed effects model (Chapter 5)

## Method

A summated score was calculated for the total number of symptoms (0-7) and functions (0-5) discussed at each consultation. Mixed effects models were employed to assess whether number of symptoms/functions discussed differed between study arms over time. Potential covariates (age, gender, diagnosis, response at 3 months, performance status, extent of disease, time in study, months since diagnosis and a measure of extent to which patients have seen the same oncologist) were identified by univariate regression (the number of issues discussed at first consultation as the outcome variable and each covariate as the predictor, controlling for baseline). Covariates meeting the inclusion criterion ($p<0.1$) were entered in multivariate mixed effects models.

p values following univariate regressions

(Significant covariates have been highlighted by **bold text**)

| | **Symptoms** | **Functions** |
|---|---|---|
| Age | .815 | .451 |
| Gender | **.046** | .766 |
| Diagnosis | **.006** | **.047** |
| Response at 3 months | **.080** | .674 |
| Performance status | .262 | .660 |
| Extent of disease | .213 | **.076** |
| Time in study | .848 | **.051** |
| Months since diagnosis | .843 | **.045** |
| K Index | .991 | .338 |

# Appendix 4 Dynamic of communication analysis (Chapter 5)

## Method

Multivariate logistic regression was employed to explore predictors for who initiated discussions of symptoms/functions (oncologist vs patient/relatives). To identify covariates for inclusion, univariate regression models for each symptom/function at each visit were fitted with the person initiating discussion as the outcome and the potential covariate (gender, age, diagnosis, performance status, extent of disease, oncologist gender and grade [consultant or specialist registrar]) as single explanatory variable. In the multivariate regression model, outcome variable was person initiating discussion at each visit and independent variables were study arm and significant covariates ($p<0.1$). This was repeated for all symptoms and functions. A significance level was set at $p<0.01$ for the multivariate analysis to adjust for multiple tests.

p values following univariate regression

(Variables which were significant at minimum of two time points were planned to be included in the multivariate model. No variable fulfilled this criterion for this model.)

| **Fatigue** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.474 | 0.387 | 0.551 |
| Patient gender | 0.528 | 0.686 | 0.151 |
| Age | 0.123 | 0.051 | 0.461 |
| Diagnosis | 0.185 | 0.639 | 0.451 |
| Performance Status | 0.056 | 0.138 | 0.584 |
| Extent of disease | 0.526 | 0.27 | 0.458 |
| Oncologist gender | 0.429 | 0.755 | 0.169 |
| Oncologist grade | 0.528 | 0.094 | 0.647 |

| **Dyspnoea** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.468 | 0.315 | 0.444 |
| Patient gender | 0.12 | 0.372 | 0.169 |
| Age | 0.54 | 0.64 | 0.355 |
| Diagnosis | 0.991 | 0.964 | 0.814 |
| Performance Status | 0.677 | 0.443 | 0.182 |
| Extent of disease | 0.655 | 0.722 | 0.859 |
| Oncologist gender | 0.771 | 0.549 | 0.388 |
| Oncologist grade | 0.355 | 0.744 | 0.077 |

| **Insomnia** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.354 | 0.43 | 0.395 |
| Patient gender | 0.327 | 0.656 | 0.557 |
| Age | 0.482 | 0.524 | 0.689 |
| Diagnosis | 0.968 | 0.853 | 0.967 |
| Performance Status | 0.427 | 0.252 | 0.546 |
| Extent of disease | 0.139 | 0.371 | 0.766 |
| Oncologist gender | 0.295 | 0.149 | 0.099 |
| Oncologist grade | 0.635 | 0.212 | 0.134 |

| **Pain** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.654 | 0.437 | 0.29 |
| Patient gender | 0.729 | 0.178 | 0.064 |
| Age | 0.924 | 0.294 | 0.34 |
| Diagnosis | 0.963 | 0.256 | 0.635 |
| Performance Status | 0.143 | 0.271 | 0.94 |
| Extent of disease | 0.583 | 0.91 | 0.743 |
| Oncologist gender | 0.501 | 0.403 | 0.507 |
| Oncologist grade | 0.652 | 0.198 | 0.741 |

| **Nausea + Vomiting** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.416 | 0.003 | 0.136 |
| Patient gender | 0.789 | 0.206 | 0.873 |
| Age | 0.334 | 0.767 | 0.403 |
| Diagnosis | 0.675 | 0.521 | 0.413 |
| Performance Status | 0.492 | 0.81 | 0.537 |
| Extent of disease | 0.99 | 0.957 | 0.72 |
| Oncologist gender | 0.113 | 0.758 | 0.224 |
| Oncologist grade | 0.007 | 0.187 | 0.195 |

| **Bowels** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.605 | 0.912 | 0.605 |
| Patient gender | 0.49 | 0.531 | 0.036 |
| Age | 0.655 | 0.86 | 0.812 |
| Diagnosis | 0.745 | 0.457 | 0.839 |
| Performance Status | 0.541 | 0.386 | 0.319 |
| Extent of disease | 0.281 | 0.043 | 0.349 |
| Oncologist gender | 0.986 | 0.227 | 0.662 |
| Oncologist grade | 0.054 | 0.115 | 0.154 |

| **Anorexia** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.9 | 0.566 | 0.282 |
| Patient gender | 0.98 | 0.632 | 0.052 |
| Age | 0.785 | 0.144 | 0.921 |
| Diagnosis | 0.900 | 0.802 | 0.991 |
| Performance Status | 0.476 | 0.145 | 0.582 |
| Extent of disease | 0.382 | 0.405 | 0.828 |
| Oncologist gender | 0.212 | 0.173 | 0.772 |
| Oncologist grade | 0.055 | 0.943 | 0.564 |

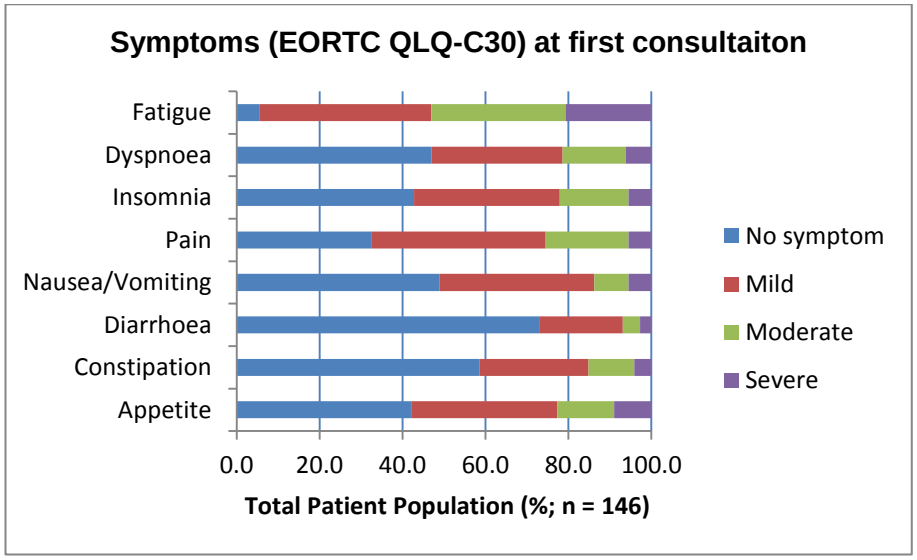
| **Physical Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.234 | 0.599 | 0.893 |
| Patient gender | 0.846 | 0.611 | 0.828 |
| Age | 0.154 | 0.443 | 0.057 |
| Diagnosis | 0.421 | 0.755 | 0.982 |
| Performance Status | 0.711 | 0.424 | 0.583 |
| Extent of disease | 0.239 | 0.045 | 0.124 |
| Oncologist gender | 0.483 | 0.844 | 0.615 |
| Oncologist grade | 0.081 | 0.694 | 0.460 |

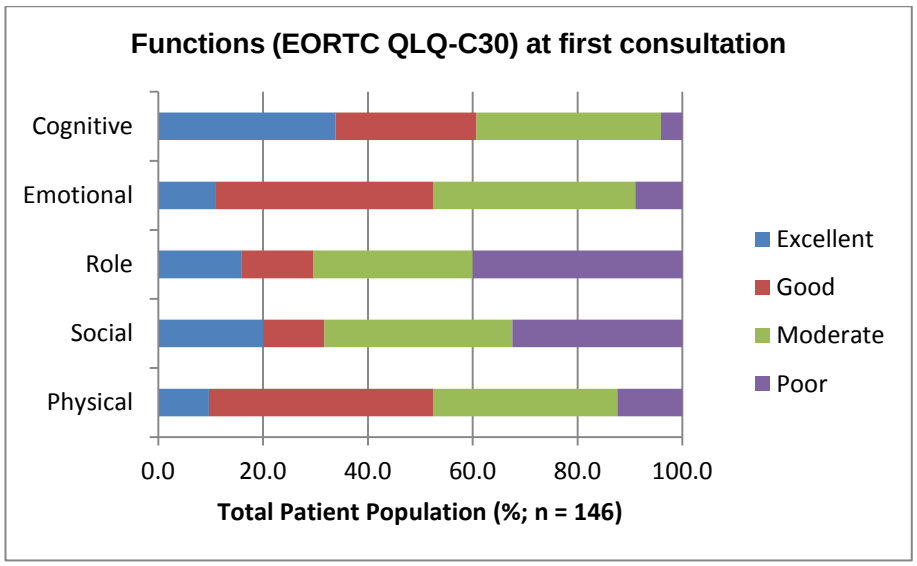
| **Social Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.519 | 0.571 | 0.768 |
| Patient gender | 0.167 | 0.868 | 0.905 |
| Age | 0.209 | 0.479 | 0.253 |
| Diagnosis | 0.478 | 0.665 | 0.903 |
| Performance Status | 0.771 | 0.828 | 0.685 |
| Extent of disease | 0.261 | 0.279 | 0.596 |
| Oncologist gender | 0.454 | 0.421 | 0.840 |
| Oncologist grade | 0.657 | 0.888 | 0.489 |

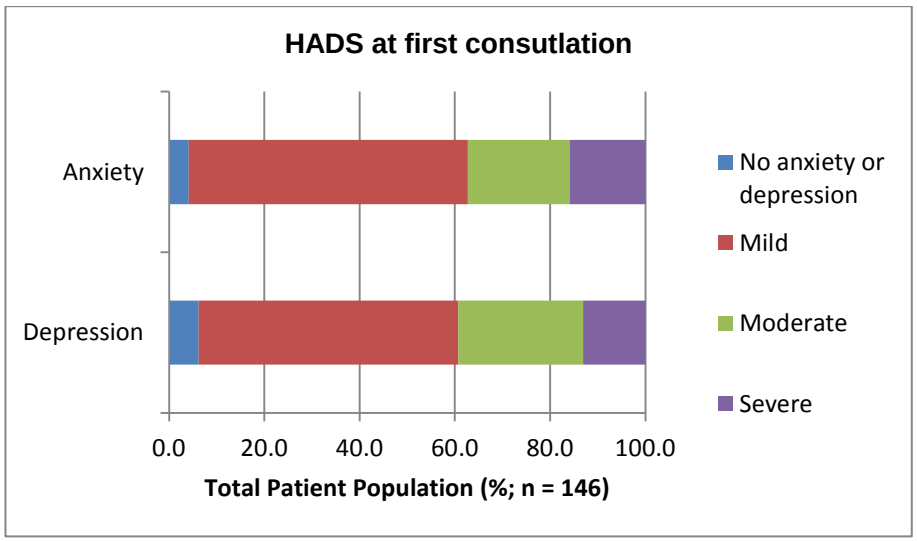
| **Role Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.769 | 0.269 | 0.348 |
| Patient gender | 0.087 | 0.452 | 0.974 |
| Age | 0.073 | 0.648 | 0.649 |
| Diagnosis | 0.984 | 0.838 | 0.987 |
| Performance Status | 0.45 | 0.369 | 0.105 |
| Extent of disease | 0.452 | 0.565 | 0.188 |
| Oncologist gender | 0.870 | 0.879 | 0.468 |
| Oncologist grade | 0.081 | 0.694 | 0.460 |

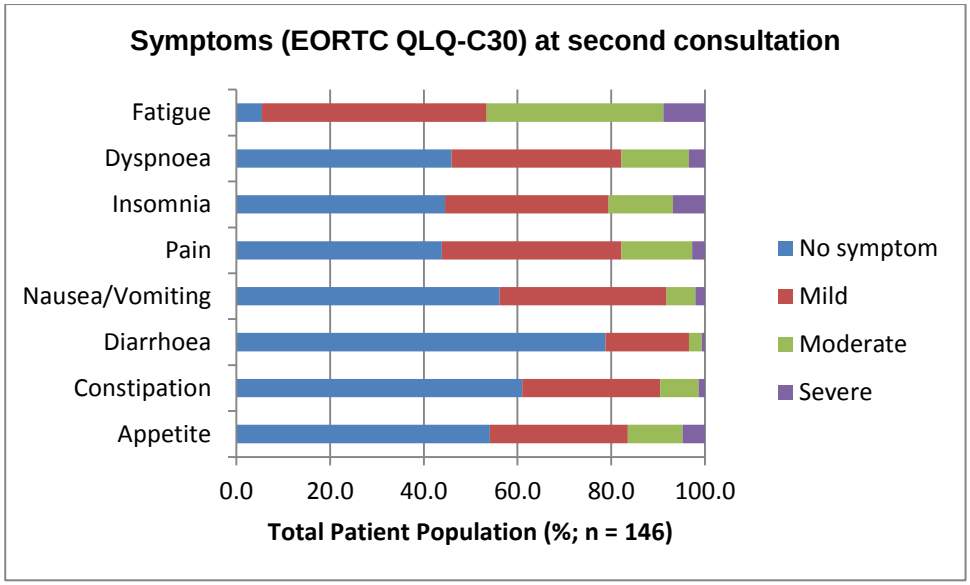
| **Emotional Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study Arm | 0.219 | 0.35 | 0.982 |
| Patient gender | 0.53 | 0.629 | 0.178 |
| Age | 0.192 | 0.152 | 0.799 |
| Diagnosis | 0.737 | 0.407 | 0.696 |
| Performance Status | 0.911 | 0.424 | 0.202 |
| Extent of disease | 0.552 | 0.471 | 0.089 |
| Oncologist gender | 0.043 | 0.485 | 0.111 |
| Oncologist grade | 0.570 | 0.159 | 0.190 |

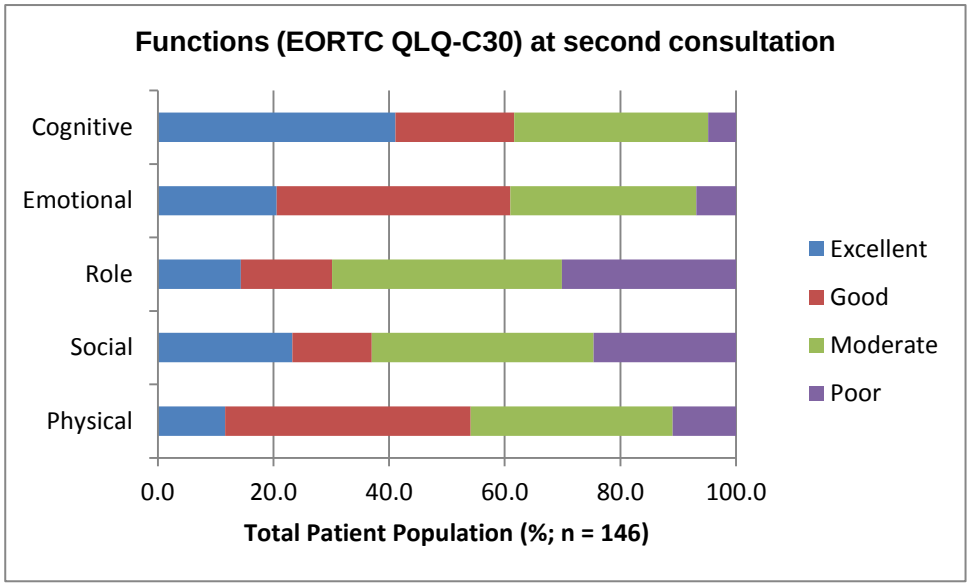
# Appendix 5 Prevalence and Severity of Symptoms and Functions Reported by Patients

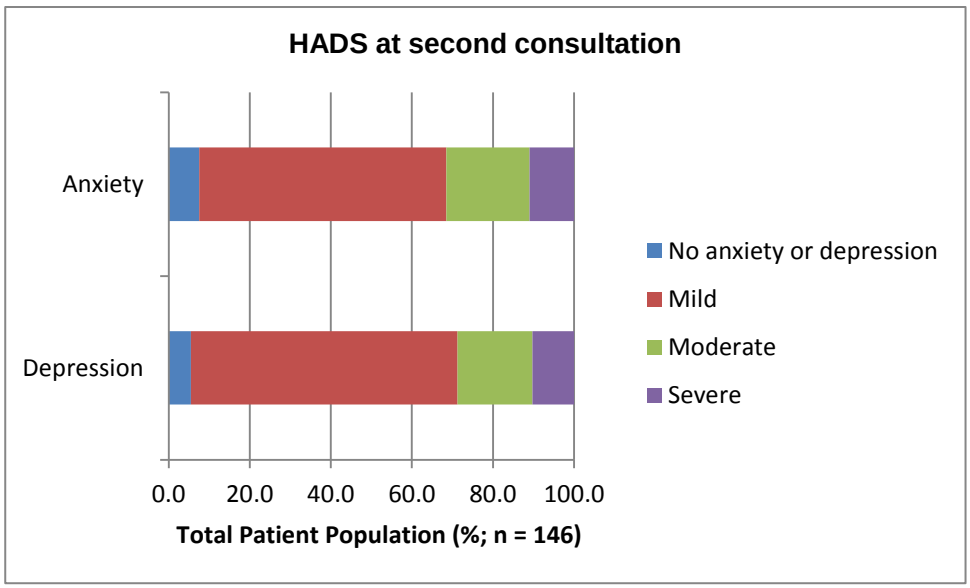


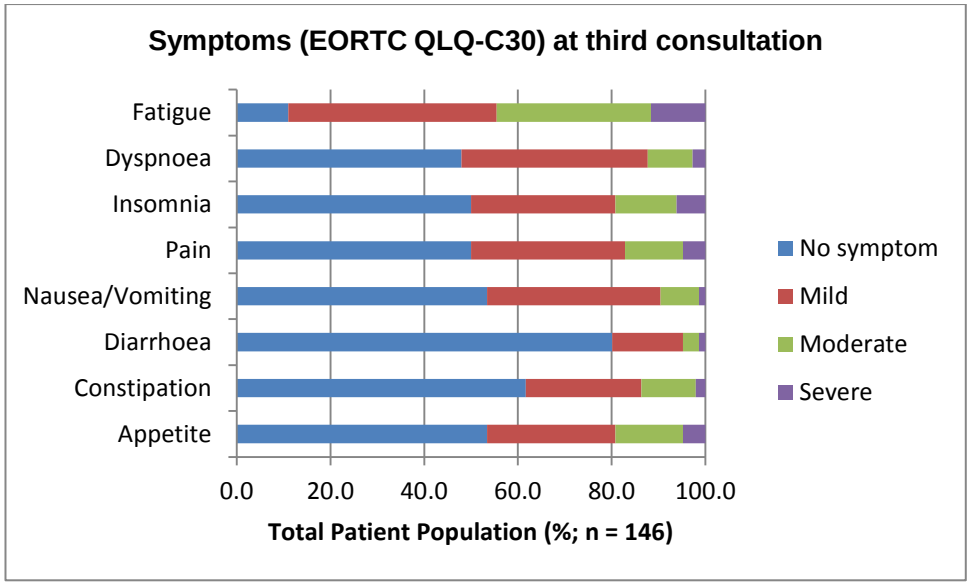



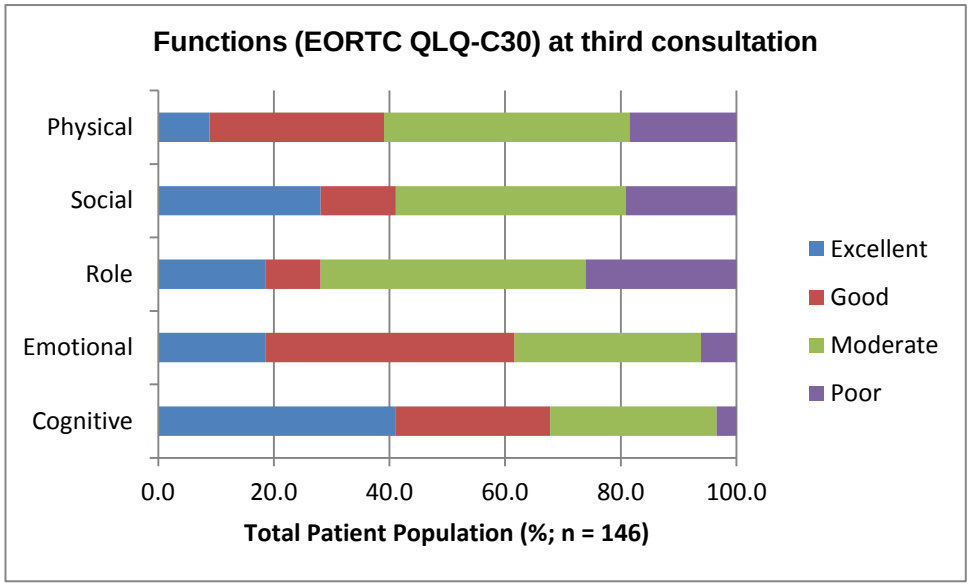



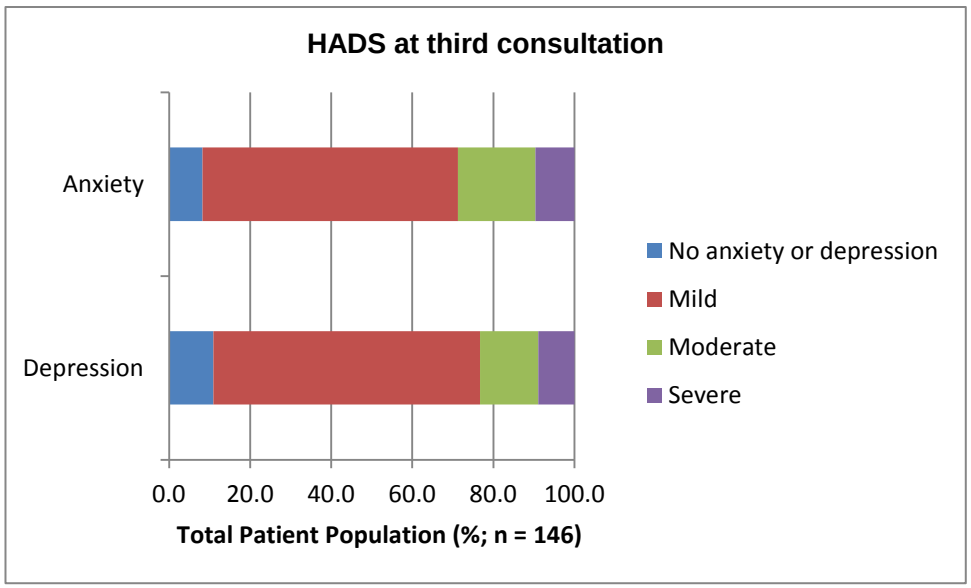

Symptoms (EORTC QLQ-C30) at second consultation
Fatigue
Dyspnoea
Insomnia
Pain
Nausea/Vomiting
Diarrhoea
Constipation
Appetite
0.0
20.0
40.0
60.0
80.0
100.0
Total Patient Population (%; n = 146)
No symptom
Mild
Moderate
Severe


Functions (EORTC QLQ-C30) at second consultation
Cognitive
Emotional
Role
Social
Physical
0.0
20.0
40.0
60.0
80.0
100.0
Total Patient Population (%; n = 146)
Excellent
Good
Moderate
Poor


HADS at second consultation
Anxiety
Depression
0.0
20.0
40.0
60.0
80.0
100.0
Total Patient Population (%; n = 146)
No anxiety or depression
Mild
Moderate
Severe


Symptoms (EORTC QLQ-C30) at third consultation
Fatigue
Dyspnoea
Insomnia
Pain
Nausea/Vomiting
Diarrhoea
Constipation
Appetite
0.0
20.0
40.0
60.0
80.0
100.0
Total Patient Population (%; n = 146)
No symptom
Mild
Moderate
Severe


Functions (EORTC QLQ-C30) at third consultation
Physical
Social
Role
Emotional
Cognitive
0.0
20.0
40.0
60.0
80.0
100.0
Total Patient Population (%; n = 146)
Excellent
Good
Moderate
Poor


HADS at third consultation
Anxiety
Depression
0.0
20.0
40.0
60.0
80.0
100.0
Total Patient Population (%; n = 146)
No anxiety or depression
Mild
Moderate
Severe

# Appendix 6 Association between severity of patient reported symptoms/functions and clinic discussion

## Method

Subgroup analyses were performed on patients in Intervention and Attention-Control arms (n=146). Multivariate logistic regression was used to investigate the association between severity of problems and the clinic discussion content. Potential covariates (age, gender, diagnosis, performance status, extent of disease, discussion of respective symptom/function at baseline, oncologist gender and grade) were identified by univariate regression, with particular symptom/function discussed or not as the outcome variable.

In the multivariate regression model, outcome variable was whether a symptom/function was discussed or not and the independent variables were questionnaire score for relevant symptom/function, study arm and significant covariates ($p<0.1$). Variables which were significant at minimum of two time points were planned to be included in the multivariate model. These variables have been highlighted by **bold text**. Analysis was repeated for all symptoms and functions at each consultation.

A significance level of $p<0.01$ was used in the multivariate analysis to adjust for multiple tests. Variables which were significant at minimum of two time points have again been highlighted by **bold text** in the multivariate models.

Univariate analysis

| **Fatigue** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| **Gender** | **0.1** | **0.037** | **0.067** |
| Age | 0.347 | 0.430 | 0.606 |
| Diagnosis | 0.477 | 0.934 | 0.331 |
| Performance status | 0.924 | 0.958 | 0.787 |
| Extent of disease | 0.08 | 0.921 | 0.717 |
| **Baseline fatigue discussed** | **0.002** | **0.041** | **0.029** |
| **Oncologist gender** | **0.079** | **0.010** | 0.228 |
| Oncologist grade | 0.200 | 0.107 | 0.949 |

Results of multivariate analysis

| **Fatigue** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.466 | 0.781 | 0.051 |
| **Fatigue score** | 0.239 | **0.002** | **0.003** |
| Gender | 0.343 | 0.125 | 0.272 |
| Baseline fatigue discussed | 0.008 | 0.062 | 0.092 |
| Oncologist gender | 0.111 | 0.003 | 0.816 |

Univariate analysis

| **Dyspnoea** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.228 | 0.898 | 0.668 |
| Age | 0.550 | 0.048 | 0.530 |
| Diagnosis | 0.826 | 0.410 | 0.800 |
| Performance status | 0.040 | 0.111 | 0.174 |
| Extent of disease | 0.661 | 0.485 | 0.136 |
| **Baseline dyspnoea discussed** | **0.003** | **0.024** | 0.153 |
| Oncologist gender | 0.008 | 0.246 | 0.962 |
| Oncologist grade | 0.747 | 0.050 | 0.946 |

Results of multivariate analysis

| **Dyspnoea** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.008 | 0.753 | 0.413 |
| **Dyspnoea score** | **0.01** | **0.001** | **0.001** |
| Baseline dyspnoea discussed | 0.011 | 0.092 | 0.434 |

Univariate analysis

| **Insomnia** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.078 | 0.110 | 0.561 |
| Age | 0.939 | 0.047 | 0.877 |
| Diagnosis | 0.649 | 0.894 | 0.364 |
| Performance status | 0.753 | 0.737 | 0.169 |
| Extent of disease | 0.565 | 0.910 | 0.183 |
| **Emotional function score** | **0.055** | **0.037** | 0.242 |
| Anxiety score | 0.153 | 0.004 | 0.461 |
| **Depression score** | **0.01** | **0.013** | 0.643 |
| **Baseline insomnia discussed** | **0.051** | **0.002** | **0.014** |
| Oncologist gender | 0.839 | 0.357 | 0.961 |
| Oncologist grade | 0.041 | 0.475 | 0.270 |

Results of multivariate analysis

| **Insomnia** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.642 | 0.560 | 0.002 |
| **Insomnia score** | **0.002** | **0.002** | 0.512 |
| Emotional function score | 0.410 | 0.825 | 0.207 |
| Depression score | 0.136 | 0.431 | 0.624 |
| **Baseline insomnia discussed** | 0.171 | **0.007** | **0.004** |

Univariate analysis

| **Pain** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.304 | 0.878 | 0.432 |
| Age | 0.994 | 0.270 | 0.807 |
| Diagnosis | 0.641 | 0.173 | 0.108 |
| Performance status | 0.527 | 0.878 | 0.062 |
| **Extent of disease** | **0.087** | **0.093** | **0.068** |
| BL pain m/d | 0.639 | 0.009 | 0.521 |
| Oncologist gender | 0.703 | 0.522 | 0.151 |
| Oncologist grade | 0.622 | 0.063 | 0.192 |

Results of multivariate analysis

| **Pain** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.901 | 0.626 | 0.836 |
| **Pain score** | **<0.0001** | **0.001** | **<0.0001** |
| Extent of disease | 0.125 | 0.152 | 0.137 |

Univariate analysis

| **Nausea + Vomiting** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.420 | 0.160 | 0.097 |
| Age | 0.828 | 0.383 | 0.814 |
| Diagnosis | 0.086 | 0.762 | 0.644 |
| Performance status | 0.864 | 0.490 | 0.747 |
| Ext of disease | 0.556 | 0.689 | 0.591 |
| **Baseline nausea discussed** | **0.0005** | **0.0005** | **0.035** |
| Oncologist gender | 0.906 | 0.246 | 0.024 |
| Oncologist grade | 0.447 | 0.534 | 0.368 |

Results of multivariate analysis

| **Nausea + Vomiting** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.142 | 0.519 | 0.578 |
| **Nausea + vomiting score** | 0.056 | **0.006** | **0.004** |
| **Baseline nausea discussed** | **0.004** | **<0.0001** | 0.074 |

Univariate analysis

| **Bowels** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.274 | 0.367 | 0.166 |
| Age | 0.285 | 0.321 | 0.381 |
| Diagnosis | 0.472 | 0.132 | 0.226 |
| Performance status | 0.110 | 0.153 | 0.537 |
| Ext of disease | 0.477 | 0.598 | 0.121 |
| **Baseline bowels discussed** | **0.003** | **0.007** | **0.001** |
| Oncologist gender | 0.624 | 0.115 | 0.635 |
| Oncologist grade | 0.614 | 0.128 | 0.949 |

Results of multivariate analysis

| **Bowels** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.885 | 0.752 | 0.137 |
| Diarrhoea score | 0.055 | 0.044 | 0.076 |
| Constipation score | 0.001 | 0.015 | 0.030 |
| Baseline bowels discussed | 0.023 | 0.023 | 0.006 |

Univariate analysis

| **Anorexia** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.075 | 0.946 | 0.946 |
| **Age** | 0.161 | **0.005** | **0.061** |
| Diagnosis | 0.519 | 0.732 | 0.155 |
| Performance status | 0.020 | 0.748 | 0.705 |
| Extent of disease | 0.660 | 0.331 | 0.331 |
| **Baseline anorexia discussed** | **0.011** | **0.013** | **0.070** |
| Oncologist gender | 0.895 | 0.392 | 0.518 |
| Oncologist grade | 0.883 | 0.895 | 0.176 |

Results of multivariate analysis

| **Anorexia** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.619 | 0.687 | 0.171 |
| **Anorexia score** | **<0.0001** | 0.753 | **0.01** |
| Age | 0.228 | 0.015 | 0.141 |
| Baseline anorexia discussed | 0.394 | 0.069 | 0.187 |

Univariate analysis

| **Physical Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Patient gender | 0.619 | 0.414 | 0.777 |
| Age | 0.416 | 0.848 | 0.015 |
| Diagnosis | 0.938 | 0.677 | 0.682 |
| Performance status | 0.153 | 0.864 | 0.390 |
| Extent of disease | 0.086 | 0.538 | 0.423 |
| **Baseline physical function discussed** | 0.459 | **0.025** | **0.055** |
| Oncologist gender | 0.665 | 0.125 | 0.166 |
| Oncologist grade | 1.0 | 0.206 | 0.848 |

Results of multivariate analysis

| **Physical Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.704 | 0.684 | 0.704 |
| Physical function score | 0.085 | 0.622 | 0.003 |
| Baseline physical function discussed | 0.734 | 0.037 | 0.223 |

Univariate analysis

| **Social Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.495 | 0.155 | 0.598 |
| Age | 0.498 | 0.013 | 0.266 |
| Diagnosis | 0.167 | 0.499 | 0.875 |
| Performance status | 0.370 | 0.159 | 0.965 |
| Extent of disease | 0.912 | 0.704 | 0.502 |
| **Baseline social function discussed** | **0.008** | **0.032** | **0.012** |
| Oncologist gender | 0.382 | 0.754 | 0.274 |
| Oncologist grade | 0.653 | 0.906 | 0.008 |

Results of multivariate analysis

| **Social Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.971 | 0.208 | 0.808 |
| Social function score | 0.91 | 0.306 | 0.644 |
| Baseline social function discussed | 0.01 | 0.05 | 0.013 |

Univariate analysis

| **Role Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.751 | 0.818 | 0.997 |
| Age | 0.036 | 0.102 | 0.772 |
| Diagnosis | 0.092 | 0.129 | 0.533 |
| Performance status | 0.034 | 0.211 | 0.182 |
| Extent of disease | 0.652 | 0.581 | 0.714 |
| Baseline role function discussed | 0.055 | 0.764 | 0.883 |
| Oncologist gender | 0.051 | 0.614 | 0.932 |
| Oncologist grade | 0.104 | 0.075 | 0.281 |

Results of multivariate analysis

| **Role Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.022 | 0.578 | 0.799 |
| Role function score | 0.224 | 0.756 | 0.672 |

Univariate analysis

| **Emotional Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Gender | 0.377 | 0.345 | 0.032 |
| Age | 0.210 | 0.738 | 0.490 |
| Diagnosis | 0.997 | 0.689 | 0.874 |
| Performance status | 0.705 | 0.302 | 0.239 |
| Extent of disease | 0.077 | 0.502 | 0.906 |
| **Baseline emotional function discussed** | **0.002** | **0.08** | 0.685 |
| Oncologist gender | 0.339 | 0.037 | 0.484 |
| Oncologist grade | 0.650 | 0.644 | 0.630 |

Discussion of Emotional functioning was linked to the EORTC QLQ-C30 emotional functioning score, HADS anxiety and HADS depression scores. As these are expected to be highly correlated, we examined three multivariate models with each variable as predictor.

Results of multivariate analysis (EORTC QLQ-C30 Emotional Function score)

| **Emotional Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.658 | 0.199 | 0.643 |
| Emotional function score | 0.023 | 0.394 | 0.410 |
| Baseline emotional function discussed | 0.011 | 0.095 | 0.778 |

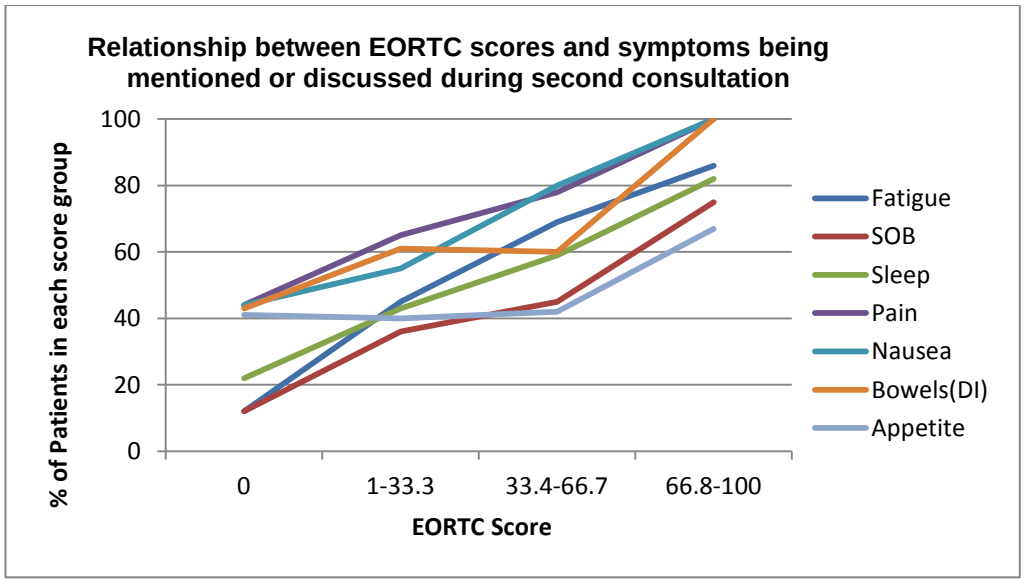
Results of multivariate analysis (HADS Anxiety score)

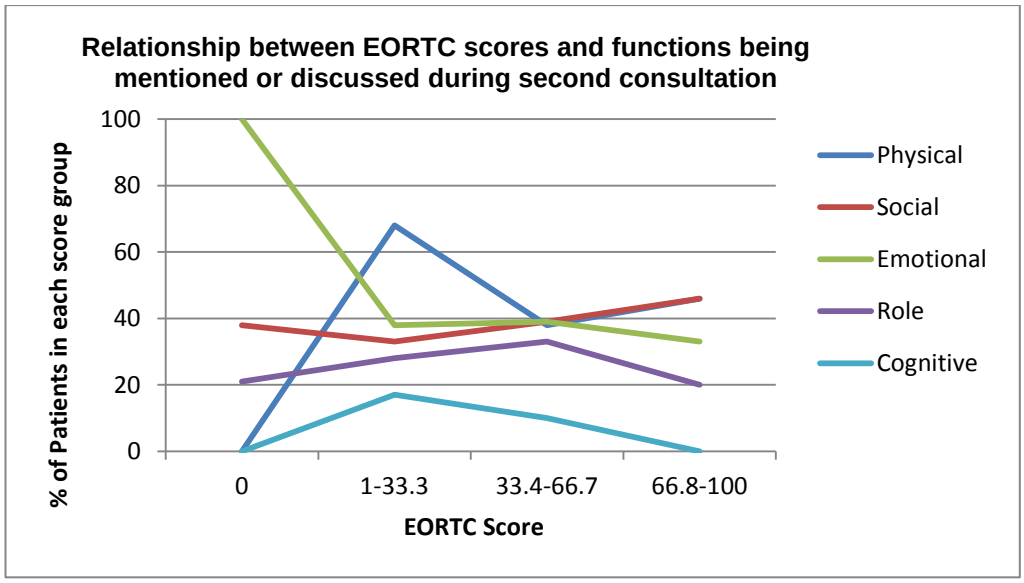
| **Emotional Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.425 | 0.140 | 0.597 |
| Anxiety score | 0.003 | 0.053 | 0.273 |
| Baseline emotional function discussed | 0.009 | 0.141 | 0.818 |

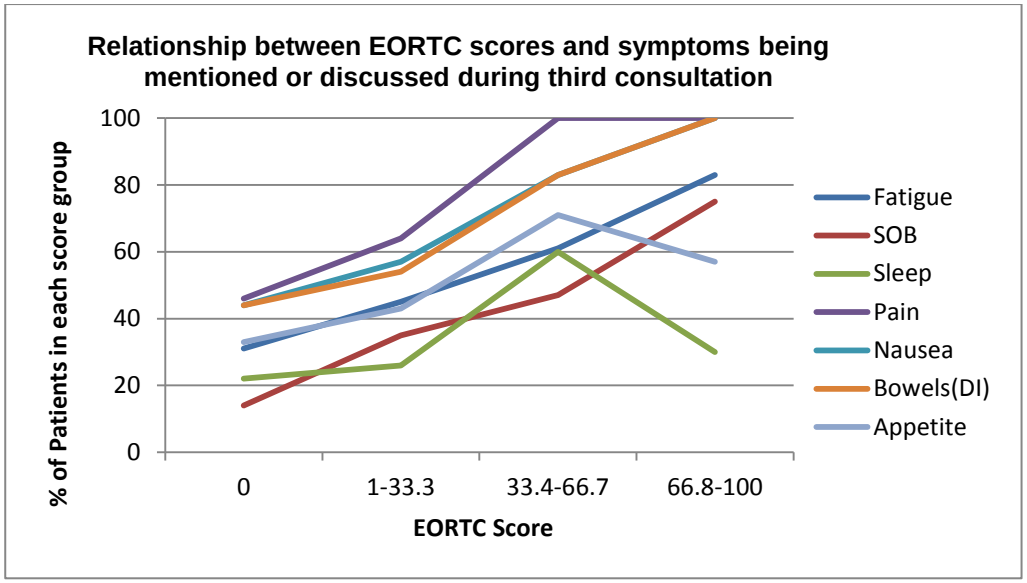
Results of multivariate analysis (HADS Depression score)

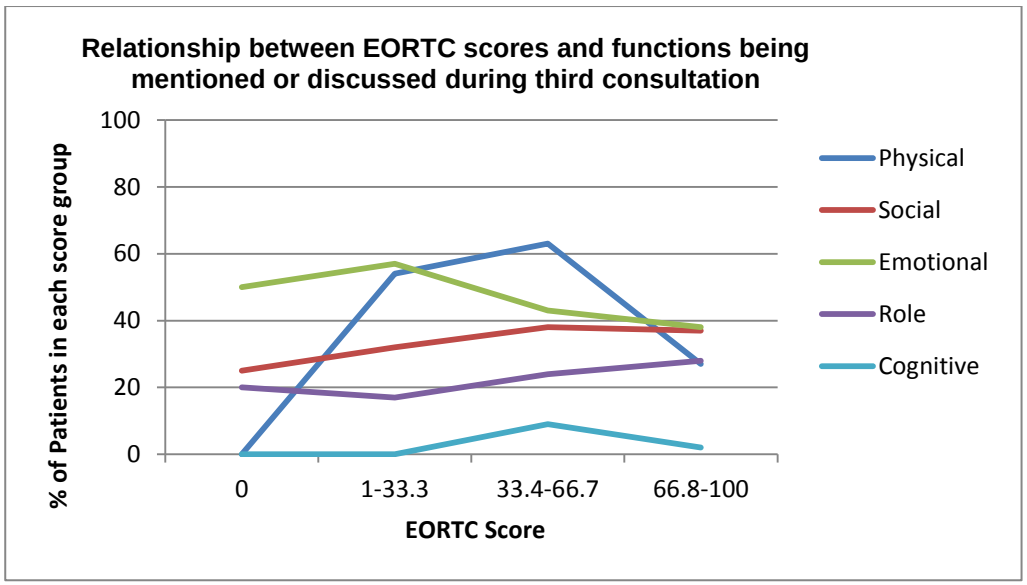
| **Emotional Function** | | | |
|---|---|---|---|
| | Consultation 1 | Consultation 2 | Consultation 3 |
| | *p* | *p* | *p* |
| Study arm | 0.475 | 0.160 | 0.682 |
| Depression score | 0.023 | 0.526 | 0.602 |
| Baseline emotional function discussed | 0.01 | 0.077 | 0.646 |

## Appendix 7 Graphical representation of the relationship between severity of symptoms and clinic discussions at second and third consultations




Relationship between EORTC scores and symptoms being mentioned or discussed during third consultation
% of Patients in each score group
100
80
60
40
20
0
0
1-33.3
33.4-66.7
66.8-100
EORTC Score
Fatigue
SOB
Sleep
Pain
Nausea
Bowels(DI)
Appetite


Relationship between EORTC scores and functions being mentioned or discussed during third consultation
% of Patients in each score group
100
80
60
40
20
0
0
1-33.3
33.4-66.7
66.8-100
EORTC Score
Physical
Social
Emotional
Role
Cognitive

# Appendix 8 Clinical scenarios for trigger DVDs

## Scenario A

### Mary Taylor 51 year old lady with metastatic breast cancer

Information given to doctor:

Breast Cancer History

1. Diagnosed at the age of 45 with ductal carcinoma of left breast.
T1 (19mm) G3 N2 (4/16) ER Positive HER2 Negative.

2. Underwent left mastectomy with immediate reconstruction.

3. Adjuvant chemotherapy with FEC x 6 cycles

4. Adjuvant hormone therapy with Tamoxifen for 5 years.

5. Metastatic disease diagnosed 12 months ago – Developed left sided SCF nodes which were biopsy positive. Restaging CT and bone scan revealed lung mets. No other visceral or bone disease.

6. Started on Arimidex with initial response which was clinically assessable with the left SCF nodes and with regular CXR.

7. Clinical disease progression was evident after 9 months. Restaging CT scan did not reveal new sites of disease. She had shortness of breath and cough which was thought to be due to the lung mets.

8. Started on Docetaxel 6 weeks ago. Attends for review prior to cycle 3.

Social Background

Used to work as a practice nurse in a GP surgery
Never married. No children. Next of kin is an aunt living in Scotland.
Socially quite isolated

Information given to simulated patient:

You are Miss Mary Taylor, a 51 year old lady with advanced breast cancer. You work part time as a practice nurse at a GP surgery. Recently you have been on sick leave.

Your breast cancer was originally diagnosed 6 and half years ago, when you noticed a lump in your left breast whilst in the shower. After the biopsy, confirming the cancer diagnosis, you had your left breast surgically removed (mastectomy) and had reconstruction at the same time.

After the operation, you were told the cancer had spread to the lymph nodes in your arm pit (axilla) with 4 of the 16 lymph nodes removed being positive for cancer cells and you were recommended to have chemotherapy to try and reduce the risk of the cancer coming back.

You received 6 cycles of chemotherapy with 3 agents (5FU, Epirubicin and Cyclophosphamide) abbreviated to FEC. These were given as injections into the vein every 3 weeks. You recall that chemotherapy made you slightly sickly and tired but you got through the treatment without any other major problems. You were then given a hormone tablet called Tamoxifen, which you took every day for 5 years.

You were very relieved when you completed your treatment. You were discharged from routine follow up thereafter.

About a year ago, you noticed a hard pea sized lump on the left side of your neck, just behind your collar bone, which grew in size over a period of few weeks. Your GP sent you to an ENT (Ear Nose and Throat) surgeon urgently and he arranged for you to have a biopsy of this lump. This was actually an enlarged lymph node and the result came back showing that the breast cancer had come back.

You were then referred back to the cancer specialist, who had discharged you after you completed the Tamoxifen. He organised a CT scan and bone scan and this came back showing that there was cancer recurrence within your chest (lungs) also. You had some cough at the time and this was the likely cause for your symptoms.

You were told by the doctor that they cannot cure you but they can give you treatment which can control the cancer.

The news of cancer recurrence left you feeling anxious and overwhelmed, you had many concerns about how you would cope both physically and emotionally but felt that you could not verbalise them with the doctors or nurses.

You started on a hormone treatment called “Arimidex”, a tablet form of treatment which you had to take once a day. This worked well for about 9 months with obvious shrinkage of the lymph node but you noticed that your lymph node was getting bigger again. Around the same time, you were starting to feel more breathless and you started to have trouble with dry cough. This was reflected on your chest x ray which showed that your lung disease was deteriorating. You found this very frightening and at first tried to tell yourself that it wasn’t really happening and that the lymph node had not increased in size however eventually you had to admit to yourself that it was getting bigger and that you were less well.

You had a CT scan to confirm the above finding. You could not sleep during the week leading up to the CT scan dreading that it would confirm bad news. This did not show any new sites of disease but confirmed your worst fears that things were deteriorating.

You were recommended to have some chemotherapy and were started on a drug called “Taxotere”. This was decided after you had a long discussion with the cancer specialist who thought that chemotherapy was likely to work quicker and hopefully alleviate some of your symptoms quicker compared to trying a different hormone tablet.

You have now had 2 cycles of this treatment and tolerated it reasonably well. You have had some minor discomfort in your joints for a few days after the chemotherapy but this has now subsided. You have sometimes had a throbbing sensation in your lymph node in your neck but you have noticed that the node is shrinking in size; you look at this as a good sign but you cannot get the doctors statement that your disease is not curable out of your mind.

You used to work as a practice nurse at a GP surgery. You have been working part time after your breast cancer recurrence was diagnosed whilst you were on your Arimidex tablets but have been on sick leave since you have started on chemotherapy. During your professional life you have seen a number of patients die from cancer and keep thinking that this is your fate. You recall patients who have died with severe pain.

You were never married and live alone in a flat. You have no children and your closest relative is an aunt living in Scotland, she is in her 70s and you feel it would be wrong to burden her with your problems.

You are somewhat socially isolated, and this has worsened since you have stopped working and started chemotherapy.

Your mood is low; you are getting very little enjoyment from anything, including television programmes you always enjoyed (e.g. soaps). You find that you cannot look forward to things any more (e.g. visits from work colleagues which you have actually discouraged). Previously you took pride in your appearance but recently making the effort has all been too much and you have not worn makeup for several weeks. Your sleep has deteriorated; you get off to sleep but wake in the early hours and cannot get back to sleep again. You find your thoughts frightening being unable to take your mind off memories of patients you have known with cancer who died and all the problems they faced. You keep returning to things in your life where you feel you have failed – you blame yourself for all the failed relationships in your life and don't believe you are worth knowing. You have thought about your own death and found this very frightening – both in terms of how you might die but also what being dead actually means. Part of you thinks it might be better to get it all over with and die soon but you have not had any thoughts about harming yourself.

Current List of Medications

- Paracetamol 500mg tablets 2 tablets as required up to 4 times/day
(Pain killer)

- Ibuprofen 200mg tablets 2 tablets as required up to 3 times/day
(Pain killer for joint pains)

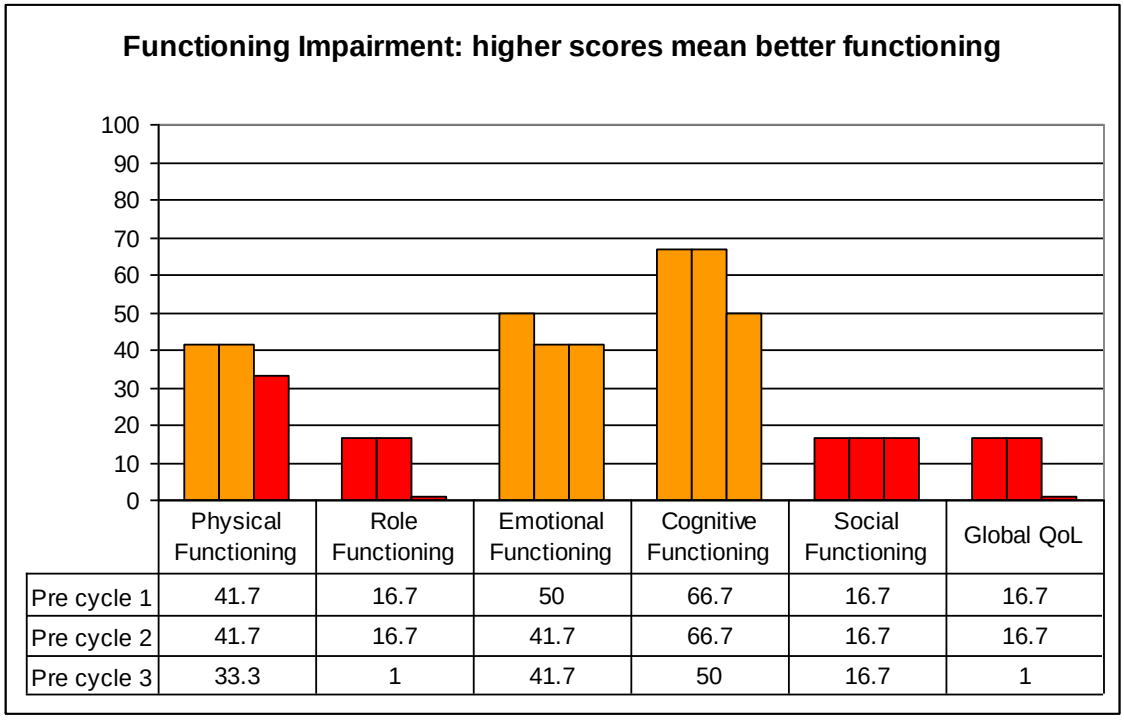
- Domperidone 10mg tablets 1 tablet as required up to 4 times/day
(Anti-sickness - You have not needed to take this very often)

- Mouth wash 1 capful 4 times/day

- Dexamethasone 2mg tablets 4 tablets twice a day for 3 days

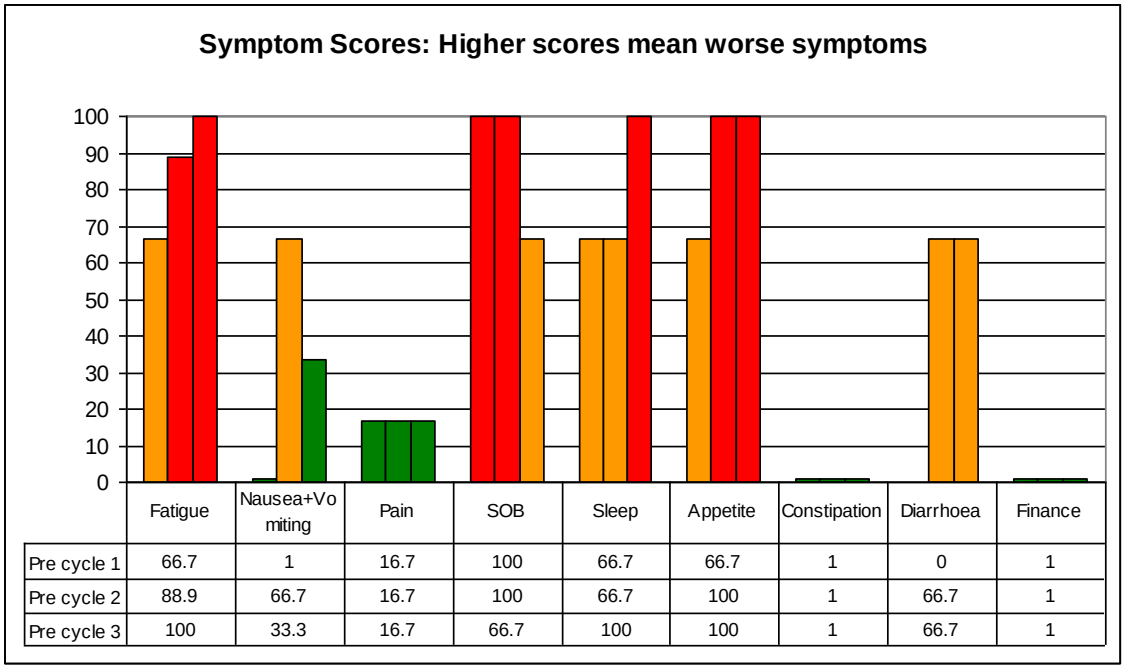
(Steroid tablets as part of the chemotherapy treatment - Taken twice a day starting the day before the chemotherapy for 3 days)

***Scenario A Questionnaire Output***



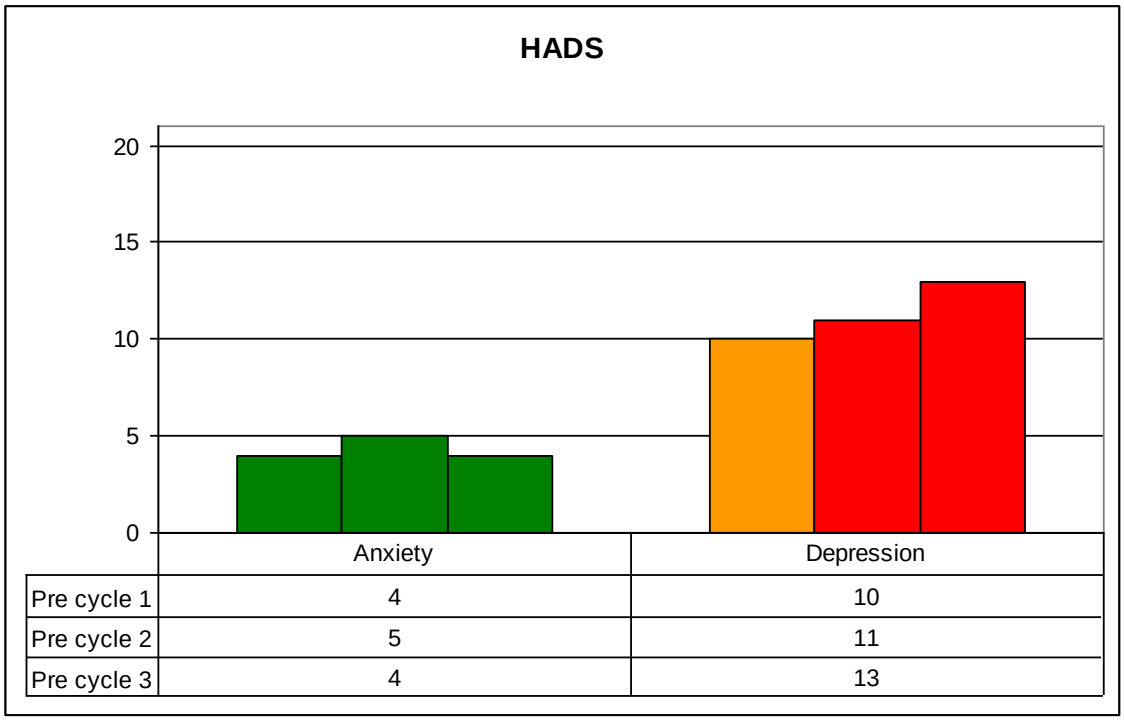

| | Physical Functioning | Role Functioning | Emotional Functioning | Cognitive Functioning | Social Functioning | Global QoL |
|---|---|---|---|---|---|---|
| Pre cycle 1 | 41.7 | 16.7 | 50 | 66.7 | 16.7 | 16.7 |
| Pre cycle 2 | 41.7 | 16.7 | 41.7 | 66.7 | 16.7 | 16.7 |
| Pre cycle 3 | 33.3 | 1 | 41.7 | 50 | 16.7 | 1 |

Mild 66.8 - 100 Moderate 33.4 – 66.7 Severe 0 – 33.3




| | Fatigue | Nausea+Vomiting | Pain | SOB | Sleep | Appetite | Constipation | Diarrhoea | Finance |
|---|---|---|---|---|---|---|---|---|---|
| Pre cycle 1 | 66.7 | 1 | 16.7 | 100 | 66.7 | 66.7 | 1 | 0 | 1 |
| Pre cycle 2 | 88.9 | 66.7 | 16.7 | 100 | 66.7 | 100 | 1 | 66.7 | 1 |
| Pre cycle 3 | 100 | 33.3 | 16.7 | 66.7 | 100 | 100 | 1 | 66.7 | 1 |

Mild 0 – 33.3 Moderate 33.4 – 66.7 Severe 66.8 – 100


HADS
20
15
10
5
0
Anxiety
Depression
Pre cycle 1
4
10
Pre cycle 2
5
11
Pre cycle 3
4
13
Mild0 – 7
Moderate
8 – 10
Severe
>11

**Scenario B**

**James Kitching 63 year old man with metastatic leiomyosarcoma**

Information given to the doctor:

Sarcoma History

1. Diagnosed with T1b (40mm) G3 (stage II) leiomyosarcoma arising from left thigh 18 months ago.

2. Underwent excision followed by adjuvant radiotherapy.

3. Asymptomatic lung mets diagnosed through routine CXR about 2 months ago, which was arranged by the GP as the patient has developed sinus symptoms

4. Restaging CT scan shows no disease outside of the lungs.

5. He has been commenced on palliative chemotherapy with single agent Doxorubicin 3 weeks ago.

6. Attends for review prior to 2$^{nd}$ cycle of chemotherapy

Social background

Very fit man who enjoyed many sports throughout his life.
Took early retirement after diagnosis of cancer
Married and lives with his wife.
He has 3 children all living in Yorkshire.

Information given to simulated patient number 1 (Mr Kitching):

You are Mr. James Kitching, a 63 year old retired postman. You noticed a lump on your inner left thigh about 18 months ago. You went to see your GP straight away as it was rubbing on your bicycle seat when you were doing your post delivery and it caused you discomfort.

The doctor looked rather worried when he saw the lump as it was very hard and you were referred to an orthopaedic surgeon fairly promptly.

After you saw the surgeon, he organised for you to have a scan called a Magnetic Resonance Scan. This was a very noisy scan in which you had to lie still for about 30 minutes. You then went onto have a biopsy of the lump, which confirmed that it was cancerous.

You then went on to have a big operation to remove the lump, which was about a size of a golf ball by the time you had it removed. You were told that the cancer had arisen from your muscle in your thigh and it was called Leiomyosarcoma.

After the operation, you had radiotherapy to try and reduce the risk of the cancer coming back in the same place.

You recovered from this operation well and tolerated the radiotherapy afterwards but you decided to take early retirement thereafter.

You developed some symptoms of sinus irritation associated with a bit of a cough and went to see your GP about 6 weeks ago. Your GP was quite thorough and suggested that you have a routine chest x ray.

Unfortunately, this revealed that the cancer had come back in your lungs and your follow up appointment with the cancer specialist was brought forward. You underwent a CT scan and this did not show any disease outside of your lungs.

You were rather baffled as you felt very well. Antibiotics soon sorted out the sinus problems and the cough also stopped.

You have been started on chemotherapy with a drug called Doxorubicin and you have completed your first cycle. Doxorubicin is given as an injection into the vein by the chemotherapy nurse over about 10 minutes and is administered as an out-patient. The drug is red in colour and can sometimes stain your body fluid (for example, urine). You are due to attend for a review prior to your 2nd cycle.

You had read the information about this drug, telling you all sorts of possible side effects but you have actually had no major problems at all. You did have some sickly feeling for a few days but you were not sick. You have felt a little off food and noticed some changes in the way it tasted. You are slightly bothered by the fact that your hair is thinning. You had a moustache which you were quite proud of but you decided to shave it off when you started the treatment as you were told that chemotherapy would affect your facial hair.

You have always been a very fit man, who enjoyed many sports throughout your life. You were able to play football with your grandchildren every week but you have felt a little more tired since the chemotherapy and have not been as active.

You are married and have 3 children (2 sons, Daniel and Andrew and a daughter Ruth) all living close by.

You had been worried about how chemotherapy may affect you but having had the first cycle and managed it reasonably well you are feeling quite relieved. However, at the same time, the enormity of your current situation (recurrence of cancer) is beginning to sink in.

At the time of recurrence you remember being told that the cancer could not be cured but did not wish, at that time, to know more.

Your daughter is getting married in 9 months time and you have been wondering as to how you might be physically then. You feel that you need to concentrate on the treatment at the moment but this is something that you have on the back of your mind.

Now you feel that a more in-depth discussion would be helpful as there are decisions to be made about your will, a family holiday and how you no longer being around will impact on others, particularly your children.

Current Medication

- Domperidone 10mg (Anti-sickness tablets)1 tablet to be taken when required up to 4 times a day

(You were advised to take these tablets for the first 24 hours after the chemotherapy but you have not needed to take them regularly thereafter)

Information given to simulated patient number 2 (Mrs Kitching):

You are Elaine Kitching, wife of James Kitching.

Your husband, James, was diagnosed with a type of cancer called Leiomyosarcoma about 18 months ago.

You remember him complaining of a lump on the inner left thigh which was rubbing on his bicycle seat when he was doing the post delivery round.

James had arranged to see a doctor straight away, who quickly referred him to an orthopaedic surgeon. He underwent various tests which confirmed that this lump in his thigh was a cancerous lump.

The diagnosis came as a shock to both James and yourself. However, it seemed as though James' cancer was caught at relatively early stage and the doctors seemed optimistic that James will do well.

You were shocked when you heard that James was diagnosed with recurrence of his sarcoma, particularly because he had been very well with no warning signs whatsoever. You were devastated when you were told by the doctor that his condition was not curable and that treatment was mainly to try and control the behaviour of the cancer and hopefully buy James "some time".

You are still coming to terms with the fact that James has incurable cancer but you find this very hard to believe as James remains very well. You were naturally very pleased to see how well James has tolerated the first cycle of chemotherapy, having read all the possible things that could happen to him. You had been anxious as to how you might cope yourself if he had become poorly after the chemotherapy.

You were very upset when he shaved off his moustache as this was his characteristic feature and this reminded you that he was on chemotherapy.

Your daughter, Ruth is getting married in 9 months time. Although you try and remain optimistic and strong, you are anxious as to how James might be then. You have had

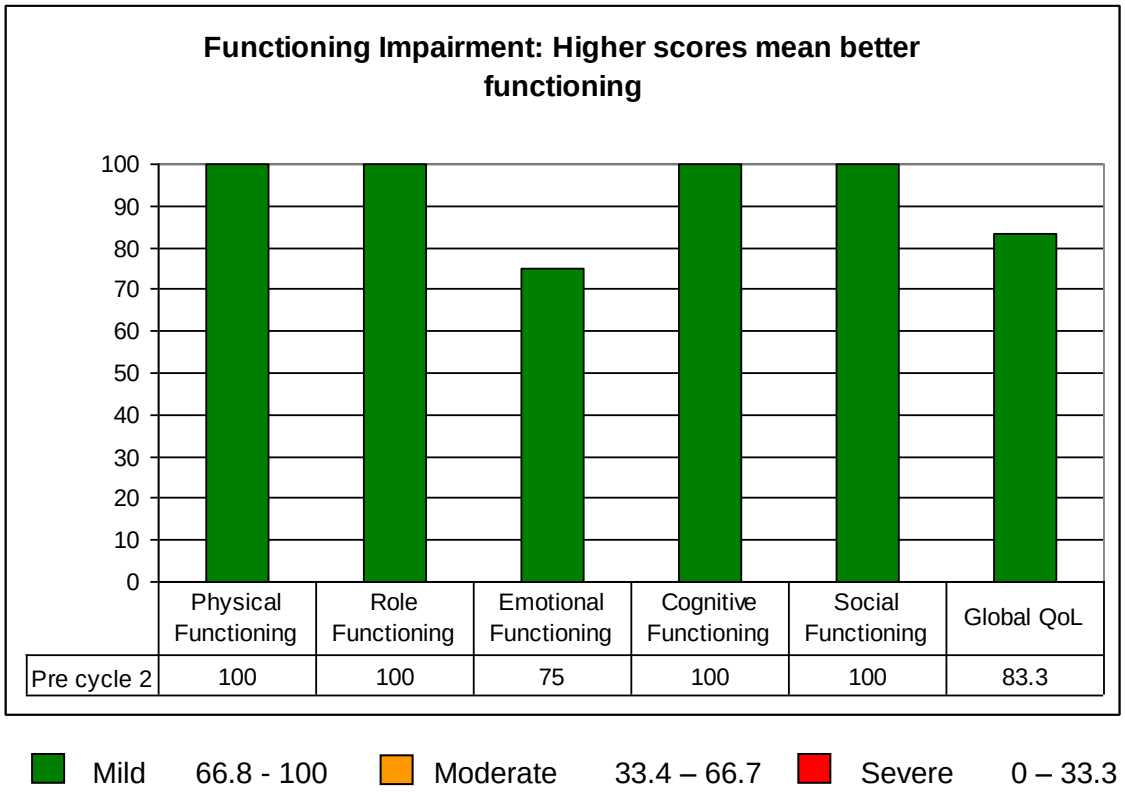
awful thoughts cross your mind that James might not be alive to see Ruth get married. You are also scared of losing him.

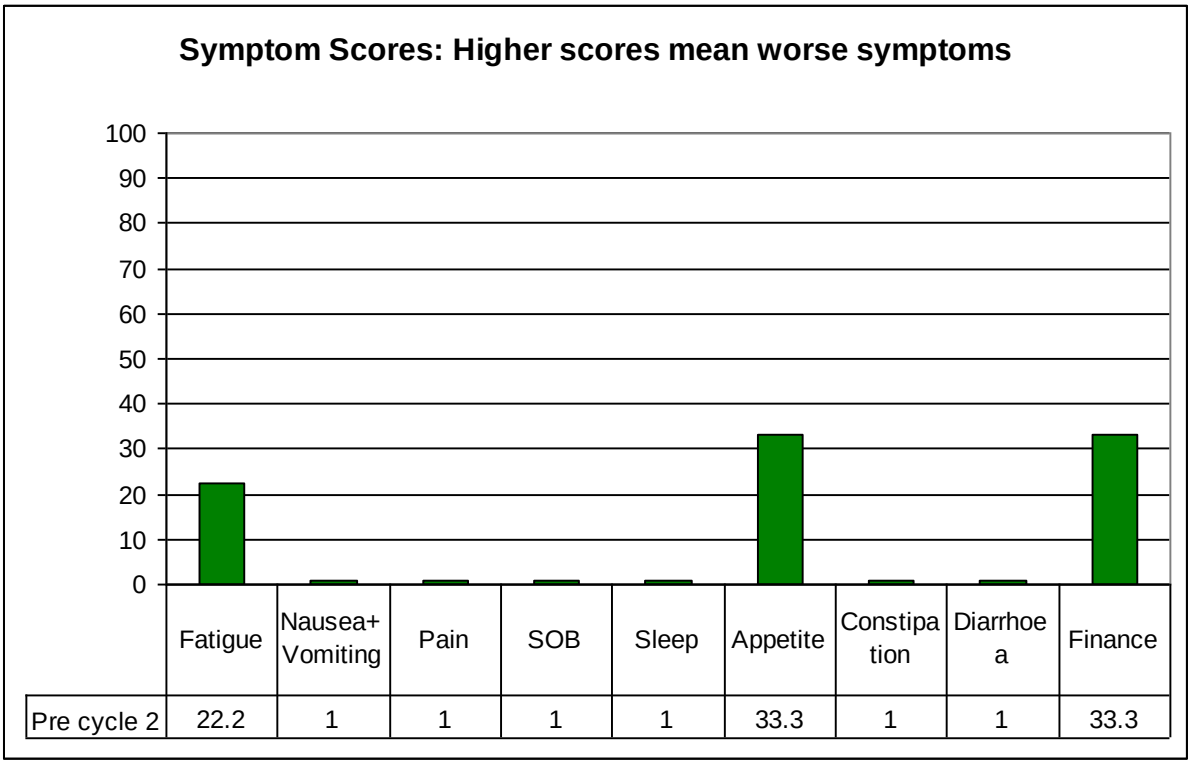
James's Current Medication

- Domperidone 10 mgs (Anti-sickness tablets) 1 tablet to be taken when required up to 4 times a day

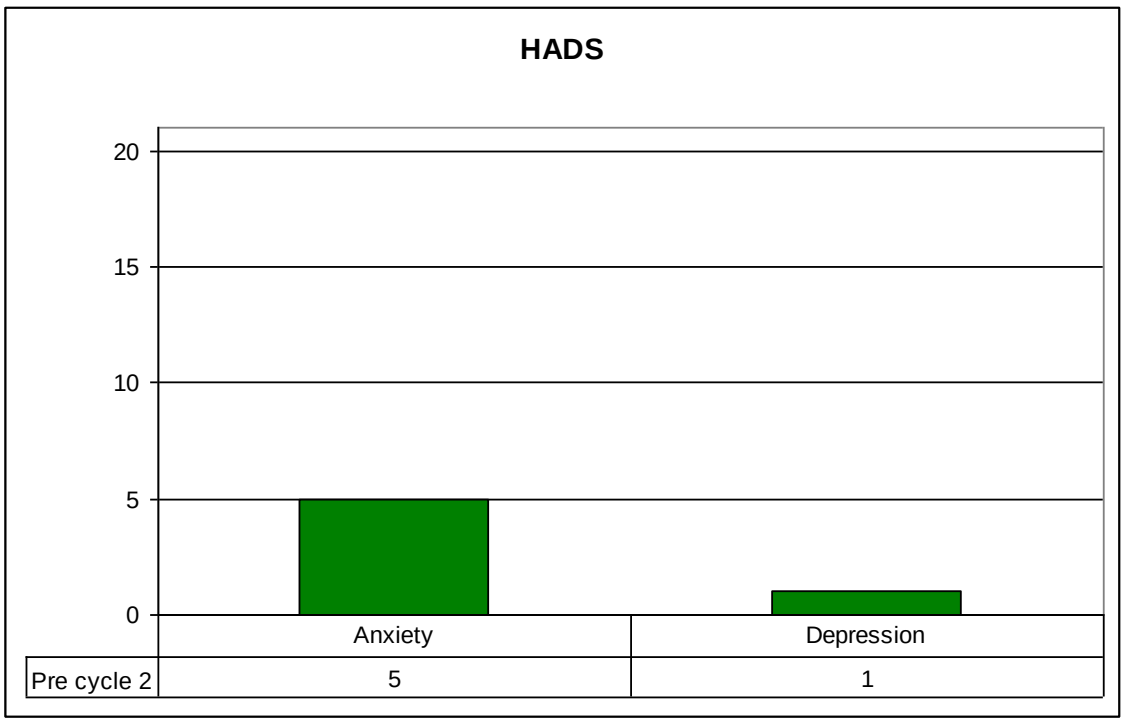
(He was advised to take these tablets for the first 24 hours after the chemotherapy but he has not needed to take them regularly thereafter)

***Scenario B Questionnaire Output***






Mild 0 – 33.3 Moderate 33.4 – 66.7 Severe 66.8 – 100




Mild0 – 7 Moderate 8 – 10 Severe >11

**Scenario C**

**Pauline Barker 70 year old lady with advanced ovarian cancer**

Information given to doctor:

Ovarian cancer history

1. Admitted via A+E with subacute bowel obstruction. Found to have pelvic mass with omental disease. CA125 >3000

2. Primary surgery unsuccessful due to tumour causing frozen pelvis – defunctioning ileostomy formation

3. Problems with high output stoma

4. Started on single agent Carboplatin

5. Attends for review prior to cycle 3

Social Background

Lives with elderly husband, who is also recovering from recent abdominal surgery. Mrs. Barker was his main carer.

3 children all living outside of Yorkshire – one lives in Manchester

Information given to simulated patient:

You are a 70 year old lady called Mrs Pauline Barker who has been diagnosed with advanced stage ovarian cancer.

You were initially admitted via the accident and emergency department 10 weeks ago, when you developed pain in your tummy area with vomiting for 3 days.

You had several tests after you were admitted under the General Surgical doctors, including a CT scan. This revealed that you had a tumour in your right ovary with evidence of spread within your abdomen. You were told at this stage that this was likely to be advanced ovarian cancer and you were subsequently referred to the gynaecology surgeons.

You were very shocked to hear this news. In hindsight, you have had vague tummy discomfort for 6 months or so but you thought this was due to the fact that you had been going through stressful time with your husband also being unwell and requiring surgery. He has history of gall stones, which caused pancreatitis (significant inflammation of the pancreas) and he was in a lot of pain. He was on various drips in the hospital. He developed complication from his pancreatitis which required surgery. All this had made your husband very weak and dependent on your help.

You had a discussion with the gynaecology surgeon and it was suggested that the best approach would be an operation because the bowel had become twisted and this was causing your pain and vomiting. He painted a reasonably optimistic picture that the operation will help with your symptoms and that they will probably be able to take most of the cancer away.

Although you were warned of the possibility of a stoma (bag attached through your skin directly to your bowel to collect its contents, which is worn under your clothes, you were devastated to see the stoma when you woke up from the anaesthetic after the operation. To make the situation worse, you were told by the surgeon that the cancer had caused everything to stick together and that they actually could not remove any of the cancer. So you were left with a stoma, which was producing very watery green stools, and none of the cancer being removed from your body.

After the operation, you struggled to come to terms with your stoma. It was producing large volume of watery stools and you needed to change the bag almost every hour. You were seen by the stoma nurse regularly to try and deal with this but you became naturally very distressed when the stoma leaked. Even by the time you were discharged from hospital, you were not really confident about dealing with the stoma yourself. You feel that people will know you have a stoma and be able to smell it; this makes you reluctant to socialise. You also found it very difficult to look at your body in a mirror.

You were referred to one of the cancer specialists (oncologist) who talked about giving chemotherapy to try and shrink the cancer. You were told that the cancer was not curable. Although you knew this, it was nevertheless painful to hear it again.

You were told that you had a reasonable chance of response to the chemotherapy and that if you respond well then there might be a possibility that the stoma could be reversed and joined up.

You were given information about a drug called Carboplatin, which is a drug given via the drip over 30 minutes. You were told that the side effects from this chemotherapy were reasonably manageable and that you weren't going to lose your hair.

You were also told that the dose of this drug depended on your kidney function and because the doctors were worried about the volume of fluid you were passing through the stoma each day and the possible impact it may have on your kidney function, they decided to do a special kidney function test which required you to come into the hospital for a day and have 3 blood tests.

You were also asked to go to your doctors' surgery 10 days after each cycle of chemotherapy to check your kidney function and your blood counts to make sure that your body was handling the chemotherapy drug ok.

You have now had 2 cycles of chemotherapy. You have tolerated the chemotherapy reasonably well with little in the way of side effects but you are struggling with the watery stools from your stoma.

The bags fill up quite quickly over night and you are up couple times during the night to change the bag. This is making you feel very tired. You have started to sleep in a

separate bedroom from your husband as you are concerned that you would disturb his sleep also.

You have also noticed that you are becoming breathless, especially on walking, even after short distance in the house.

You feel embarrassed and afraid that people could smell your stools when you are out. You had had problems with it leaking few times. You have now become quite withdrawn and fears whenever you need to go out. You are becoming increasingly dependent on your husband, who is also recovering from surgery himself.

Your son, who lives in Manchester, has been arranging your grocery shopping on the internet, which has helped to some extent.

You have stopped seeing your friends.

You have been told by the doctors that you must try and drink plenty but you find this quite difficult because you feel the more you drink, the more watery stool you will pass.

You are clinging on the hope that this stoma can be reversed and desperate that the chemotherapy is working.

<u>Current Medication</u>

- Codeine Phosphate 30 mg tablets 2 tablets four times/day

(These are pain killers but one of their side effects is constipation. You have been given these to try and slow down your bowel movement)

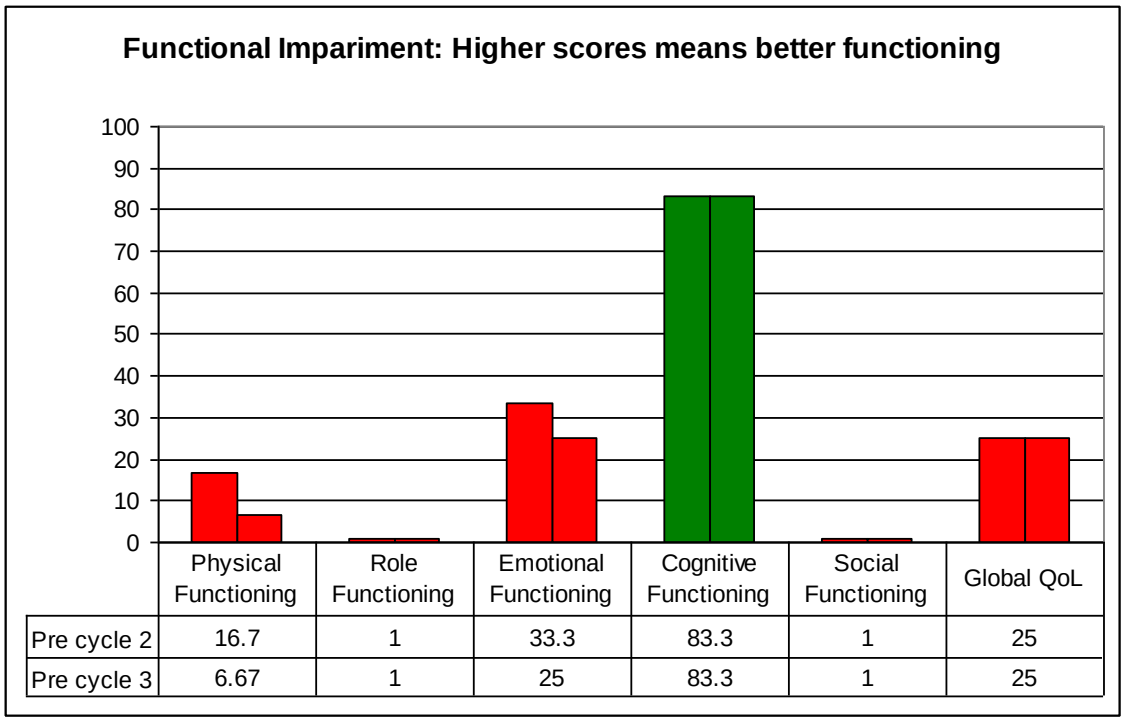
- Imodium 2mg tablets 1 tablet 4 times/day

(These are tablets for diarrhoea. You have been given these to slow down your bowel movement)

- Cyclizine 50 mg tablets 1 tablet up to 3 times/day when needed

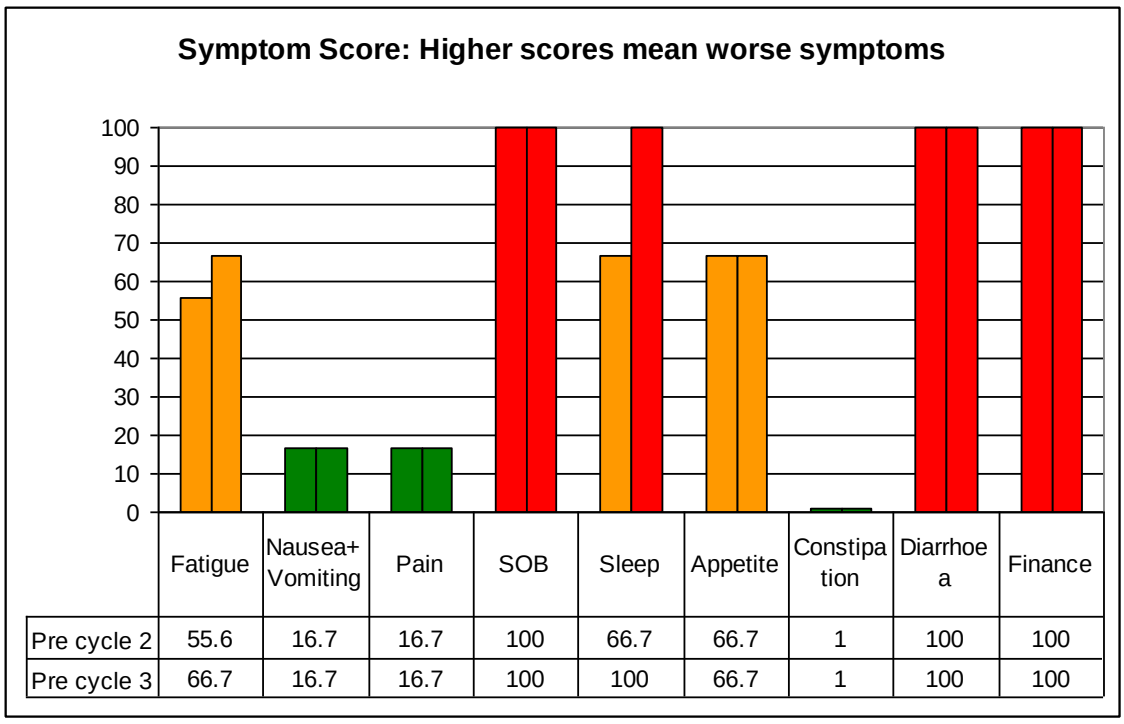
(These are anti-sickness tablets given with your chemotherapy. You have not needed to take many of these tablets)

***Scenario C Questionnaire Output***



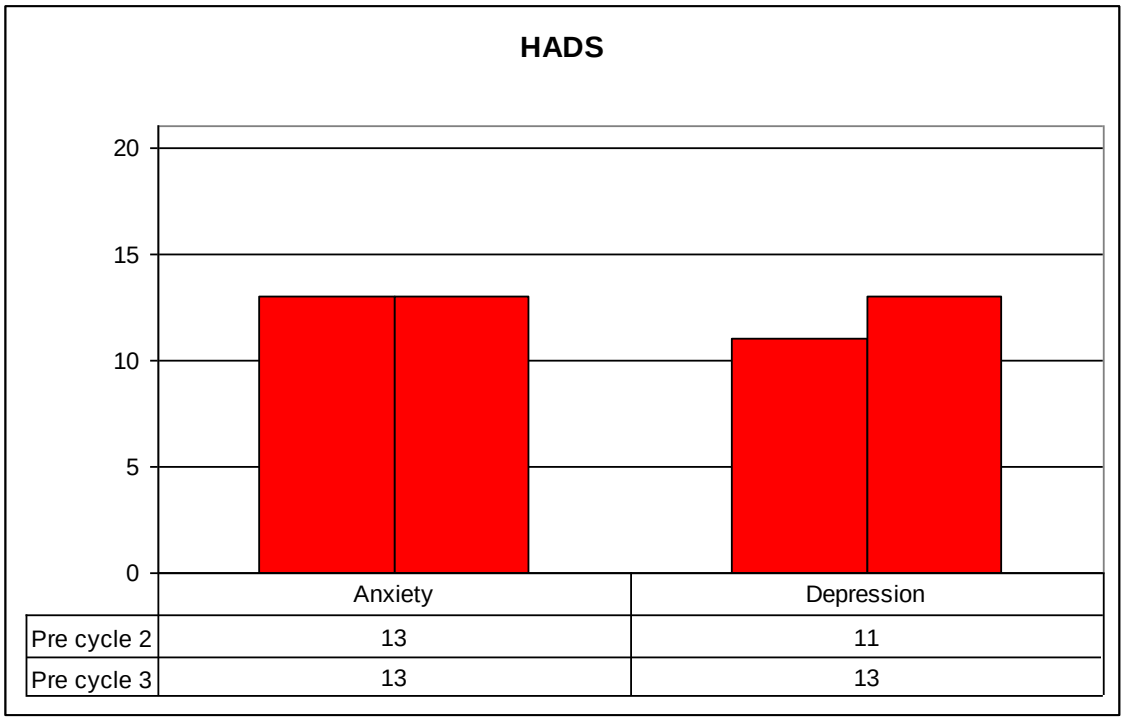

| | Physical Functioning | Role Functioning | Emotional Functioning | Cognitive Functioning | Social Functioning | Global QoL |
|---|---|---|---|---|---|---|
| Pre cycle 2 | 16.7 | 1 | 33.3 | 83.3 | 1 | 25 |
| Pre cycle 3 | 6.67 | 1 | 25 | 83.3 | 1 | 25 |

Mild 66.8 - 100 Moderate 33.4 – 66.7 Severe 0 – 33.3




| | Fatigue | Nausea+ Vomiting | Pain | SOB | Sleep | Appetite | Constipation | Diarrhoea | Finance |
|---|---|---|---|---|---|---|---|---|---|
| Pre cycle 2 | 55.6 | 16.7 | 16.7 | 100 | 66.7 | 66.7 | 1 | 100 | 100 |
| Pre cycle 3 | 66.7 | 16.7 | 16.7 | 100 | 100 | 66.7 | 1 | 100 | 100 |

Mild 0 – 33.3 Moderate 33.4 – 66.7 Severe 66.8 – 100




Mild 0 – 7 Moderate 8 – 10 Severe >11

**Scenario D**

**Janet Roberts, 45 year old lady with metastatic breast cancer**

Information given to doctor:

Breast cancer history

1. Diagnosed with metastatic breast cancer 2 years ago. Triple receptor negative disease.

2. Has received 2 lines of palliative chemotherapy so far.

3. Presented with discomfort in right hip. Restaging revealed progressive bone disease. Started on further palliative chemotherapy with ECF.

4. Attends for review prior to second cycle of chemotherapy

Social Background

Single parent. Has a daughter currently studying for A-levels.

Had been working as a part time dinner lady in a primary school

On sick leave since starting ECF chemotherapy.

Information given to simulated patient:

You are Miss Janet Roberts. You are 45 years of age and a single parent with a teenage daughter, Anne, who is currently studying for her A-Levels.

You were diagnosed just over 2 years ago (October 2007) with advanced breast cancer which had spread to your liver and bones.

You developed some right sided tummy/stomach pains and your GP organised for you to have an ultra sound scan (like what the pregnant ladies have) which showed that there were secondary cancers within the liver. You were referred to a specialist who examined you and found a lump in your left breast. A biopsy from this showed that you had breast cancer. You had other investigations (scans) which showed that the cancer had also spread to the bones.

You were told at that your cancer was treatable but not curable.

You have previously had 2 courses of chemotherapy in the past. First was a combination of 2 drugs called Epirubicin and Cyclophosphamide and the second course was with a drug called Taxotere.

Rough dates

Nov 07 – Mar 08: Epirubicin and Cyclophosphamide

Jan 09 – Apr 09: Taxotere

You have been reasonably well up until 6 weeks ago when you started to have increasing discomfort in your right hip. This has led to further tests (CT scan and bone scan) which have shown that your cancer in the bones has got worse particularly in the right pelvis, which was thought to be the cause of your discomfort. The disease in your liver had not changed.

You were not surprised about the result of the scan but was very disappointed as it has only been about 5 months since you had completed previous course of chemotherapy. You had hoped that the cancer would be controlled for longer.

You have been started on a combination of chemotherapy with Epirubicin, Cisplatin and 5-FU. You were told that this was going to be more complicated than your previous chemotherapy treatments.

You were told you needed a heart scan before the treatment was started. This showed that your heart was completely normal.

In order to start this chemotherapy, you also had to have a special tube inserted through your chest into one of the big veins near your heart called a Hickman Line. You have to be admitted to hospital for the first 2 days of the 3 weekly cycle and you are connected to a 5FU pump which needed changing every week, which meant that you needed to visit the hospital every week.

You have tolerated the chemotherapy reasonably well, although you did have some sickness for few days after the chemotherapy. You have not been sick. Your hair is starting to come out.

The main problem you have at present is the “ache” in your right hip. This is limiting your mobility and hence affecting many aspects of your activities of daily living. The discomfort sometimes makes you feel nauseous and is generally making you feel miserable.

You perceive this as an “ache” rather than “pain” and therefore have not been reaching out for pain killers (as you don’t really like taking tablets anyway). You feel that there will come a time when you will have “pain” and you don’t want to take the pain killers until such time for fear that they will become less effective later on, although this “discomfort” is actually causing quite a lot of problems.

Your daughter Anne is 17 and she is studying for her A-levels. Her father is not on the scene but provides a small maintenance. She is reasonably self sufficient but you have good friends who can see to her if needed.

You have been working at a primary school as a dinner lady 3 days a week. Since starting this ECF chemotherapy you have been unable to work and had to go on sick leave. This has led to some financial difficulties. (Food costs, bus fares to hospital, Anne’s Geography field trip etc)

You are generally anxious about the future; about what the future holds for you and the welfare of your daughter. You want to live for as long as possible and would like to see your daughter go to university and even get married and have children. You are able to hold these positive thoughts most of the time (often telling yourself that it is possible to live for many years with breast cancer – look at Jane Tomlinson) but sometimes at night doubts creep in and you worry that your daughter will have to find her own way in life and that it is extremely unlikely that you will see your grandchildren.

Current Medication

- Domperidone 10 mg Tablets 1 tablet when needed up to 4 times a day

(These are anti-sickness tablets, which you have taken occasionally when you felt sick with the discomfort in your hip)

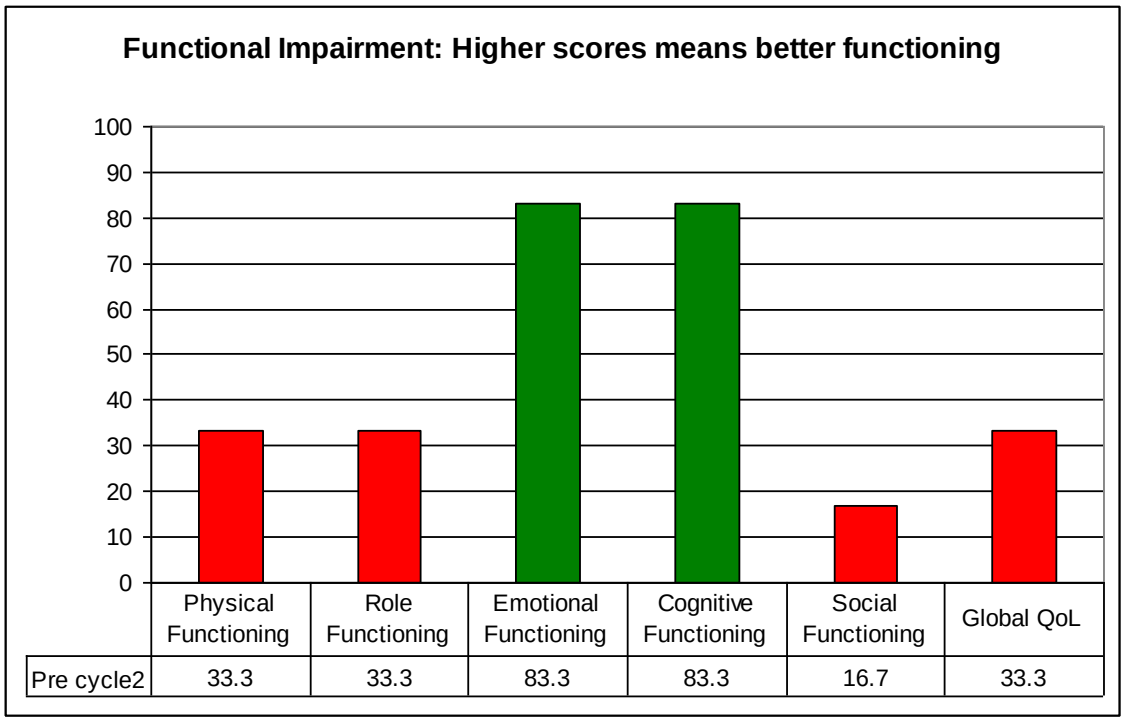
- Paracetamol 500 mg Tablets 2 tablets when needed up to 4 times a day

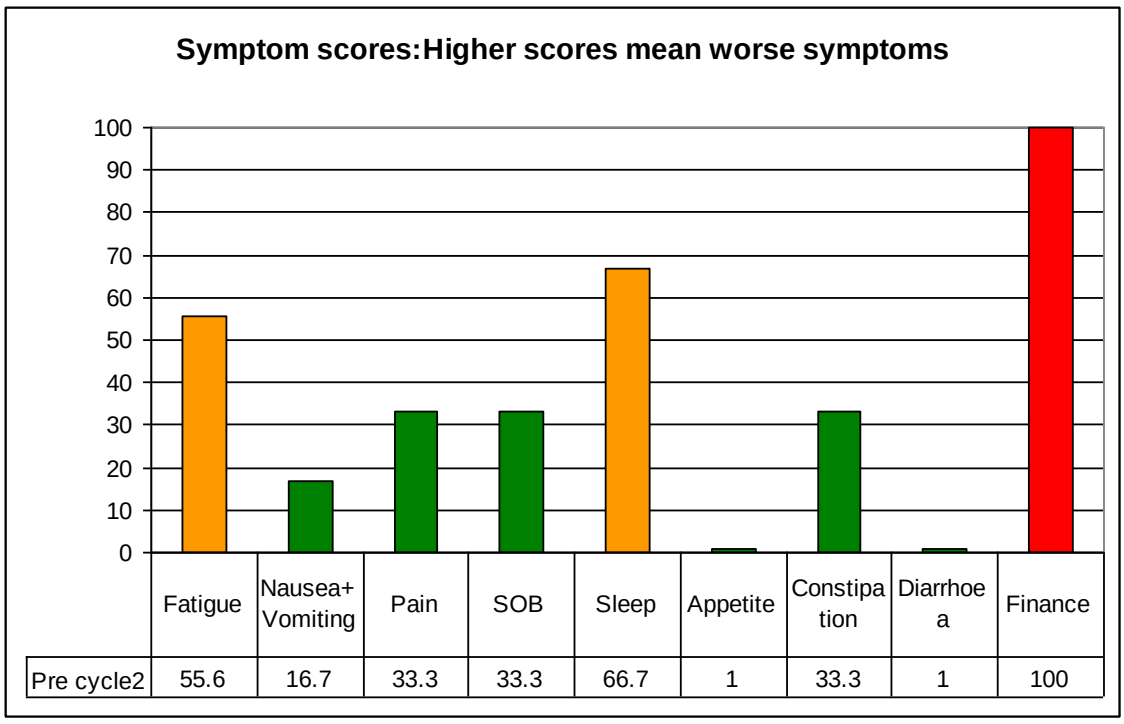
(These are pain killers. You have not taken these as you have “discomfort” rather than “pain”. You feel that there will come a time when you will need to take pain killers in the future and want to try without them as long as possible)

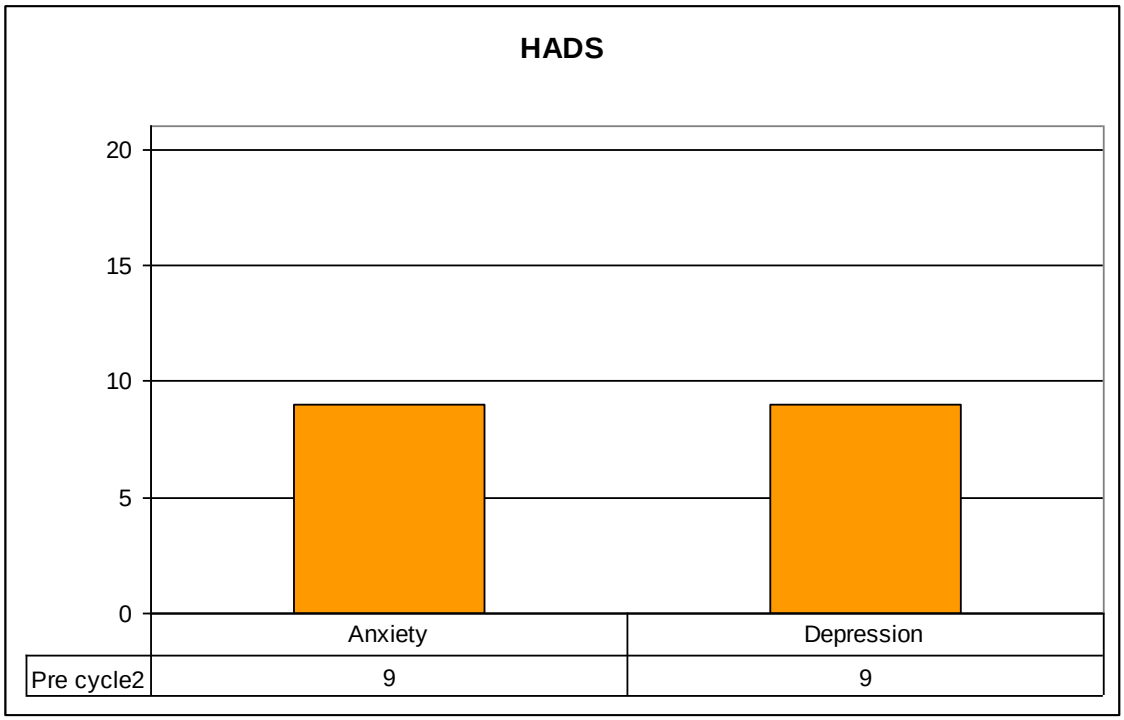
- Chlorhexidine mouthwash capful up to 4 times a day as required

(This is mouthwash for when your mouth gets sore during chemotherapy)

***Scenario D Questionnaire Output***






Mild0 – 7 Moderate 8 – 10 Severe >11

**Scenario E**

**Mrs Sheila Parker, 68 year old lady with advanced bowel cancer**

Information given to the doctor:

Bowel cancer history

1. Presented to GP in July with weight loss and upper abdominal discomfort. Found to have hepatomegaly. Referred to GI surgeon.

2. CT scan showed thickening of Sigmoid colon with evidence of multiple liver and peritoneal metastases

3. Referred to Medical Oncology for palliative chemotherapy

4. Completed 6 cycles of chemotherapy with OxaliCap

5. Attends for review with CT scan report.

Social Background

Widow. Husband died following CVA 12 months ago. Daughter (Mary Robinson) lives about 10 minutes away.

Information given to simulated patient number 1 (Mrs Sheila Parker):

You are Mrs. Sheila Parker, a 68 year old woman with advanced bowel cancer.

You initially visited your GP approximately 5 months ago, as your daughter was concerned that your appetite was diminishing and you were losing weight. You also started to get some discomfort in your upper abdomen with indigestion, which were all new symptoms for you. In hind sight, you probably also had a change in your bowel habits for about 6 months prior to this, with intermittent episodes of diarrhoea and constipation for no apparent reason. You thought this was related to the bereavement after your husband Peter passed away, rather unexpectedly, after suffering a stroke.

When you were seen by your GP, she was very worried as she was able to feel your enlarged liver.

Your GP sent you to see a surgeon, Mr. Jayne, who arranged various tests, which included a CT scan and a colonoscopy (camera in the back passage), following which you were told you had advanced bowel cancer, which had spread to the liver and to the lining of the bowel called peritoneum.

You were advised to see a cancer specialist (oncologist) who talked to you about chemotherapy. You were told that your condition was not curable. The aim of the treatment would be to try and control the cancer, shrink the disease and hopefully this will translate to better outcome overall, i.e. better symptom control and may be prolong your life.

You found the diagnosis very hard to take on board, particularly without your husband, Peter, by your side. Although you were scared about having chemotherapy, you wanted the best possible treatment to try and prolong your life, so that you might have the chance to see your grand children grow up.

You were recommended combination chemotherapy with Oxaliplatin and Capecitabine. Oxaliplatin was given via a drip every 2 weeks and Capecitabine, a tablet form of chemotherapy you took twice a day by mouth every day.

After starting the chemotherapy, you felt very tired, partly because you were not sleeping very well. You were very anxious about all the possible side effects you had been warned about.

Starting chemotherapy has impacted significantly on your daily routine as you have had to visit the hospital twice every 2 weeks. First visit to have a blood test to make sure you could have the chemotherapy and to see the doctor and the second visit to actually receive the treatment.

Chemotherapy was not all that pleasant. It made you feel rather sickly and gave you worsening of the indigestion and diarrhoea. You got into the routine of taking the Imodium tablets as soon as your tummy started to grumble and you seemed to get on top of things. You also had trouble with tingling sensation affecting your fingers and toes, especially in the first week after Oxaliplatin. This made things like doing up buttons more difficult. Your skin on the palms of your hands was becoming quite dry and sore at times.

Despite all the side effects of the treatment, you started to feel better in yourself. This was particularly noticeable after the first 3 cycles of chemotherapy. Over time, you were feeling stronger and your appetite started to return. Your weight also seemed to level out and you were starting to regain the weight you had lost.

You felt you had a little more energy to do things you used enjoy, like going out for a walk.

You are anxious about getting the results of the CT scan you had last week to assess how well the chemotherapy has worked. However, you have little doubt that the chemotherapy has helped you because you feel much better in yourself.

You were told at the start that you will be given chemotherapy for 3 months, which you have now completed and stop thereafter. You are worried as to what's going to happen now. What the future holds and whether you would be able to have more treatment in the future.

Your daughter Mary has invited you on a trip to Northumberland with her family in few months time and you are hopeful that you will be well enough to go with them.

Current Medication

- Bendrofluazide 2.5 mg tablets 1 tablet once a day

(This medication is for high blood pressure which you have been taking for many years)

- Domperidone 10 mg tablets1 tablet up to 4 times a day

(This is anti-sickness medication, given with chemotherapy but you have not needed to take them very often)

- Pyridoxine 50mg tablets 1 tablet taken three times a day

(These are Vitamin tablets, given to you when you started having some soreness in your fingers, which you were told was due to the Capecitabine chemotherapy tablets. You have been on them for about 4 weeks)

Information given to simulated patient number 2 (Mrs Mary Robinson)

You are Mrs. Mary Robinson, daughter of Mrs. Sheila Parker. You live about 10 minutes drive away from your mother. You are married to John and have 2 children, aged 12 and 10.

Your mother was diagnosed with advanced bowel cancer about 5 months ago but you recall that she had not been quite right for few months before she was diagnosed (going off food, losing weight and complaining of discomfort in his tummy). You encouraged her to seek medical attention after these symptoms persisted for few months.

You had general concerns over her health particularly after your father, Peter, passed away rather unexpectedly after suffering a stroke. Your father's death had impacted on the whole family but particularly on your mother. They had been married for over 45 years. You felt that some of the symptoms might be due to bereavement process but you had become more concerned when her weight loss became more apparent and she started to complain of tummy pains.

You were devastated when your mother was diagnosed with advanced bowel cancer and was told by the doctor that her condition was not curable. You bitterly regretted

about not encouraging her to seek medical attention sooner. The news was also extremely upsetting, particularly so soon after the death of your father.

Your mother rarely talked about her illness at home and you could see that she was trying to carry on with her usual routine as much as possible. You know this was partly not to make you worry and partly because she was trying to maintain some form of normality.

Starting chemotherapy made a significant impact on your lives, however, with 2 visits to the hospital every 2 weeks. One visit for blood tests and a consultation with the doctor, and the another visit for the treatment. These visits have been physically challenging for your mother and for you in terms of adjusting your working hours so that you were able to accompany her to the hospital. Your husband John has been very supportive.

Although the chemotherapy made your mother rather tired, you started to notice that she was eating more and looking a little brighter after 2-3 cycles of chemotherapy. You have noticed ongoing improvement particularly over the course of last 3 weeks.

You are hopeful that the CT scan your mother had last week will show good results. You and your husband are keen to take her on a short trip to Northumberland during your children's school holidays in couple of month's time and you are hoping that the doctor will say it would not be a problem for your mother to go.

<u>Current Medication Mrs. Sheila Parker is taking</u>

- Bendrofluazide 2.5 mg tablets 1 tablet once a day

(This medication is for high blood pressure which you have been taking for many years)

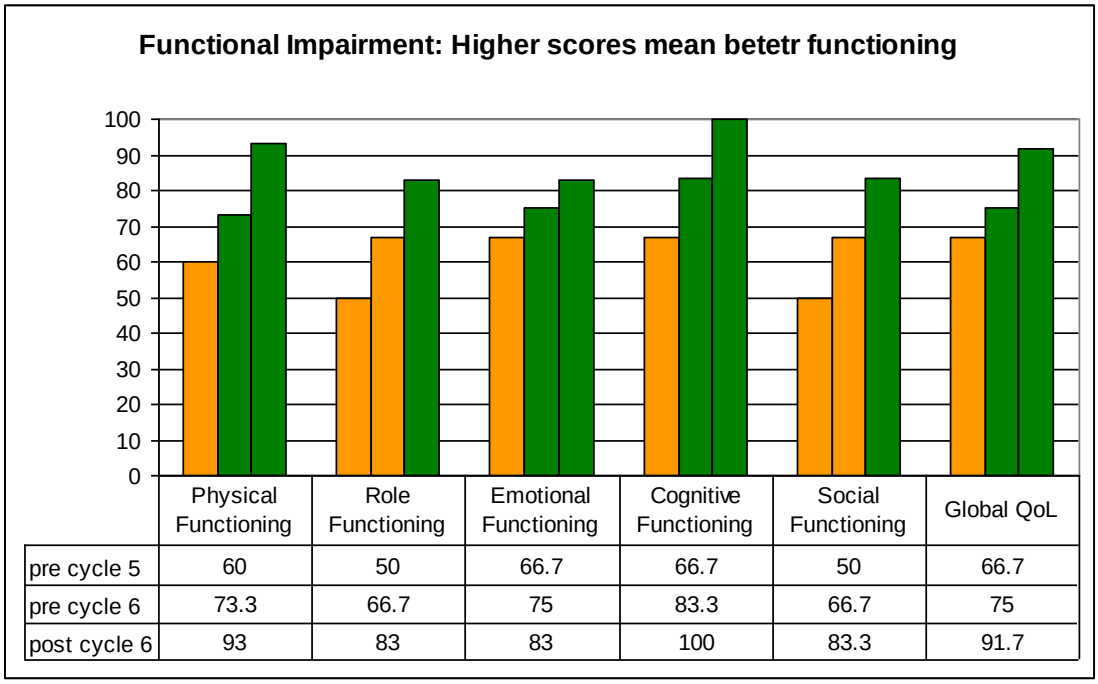
- Domperidone 10 mg tablets1 tablet up to 4 times a day

(This is anti-sickness medication, given with chemotherapy but you have not needed to take them very often)

- Pyridoxine 50mg tablets 1 tablet taken three times a day

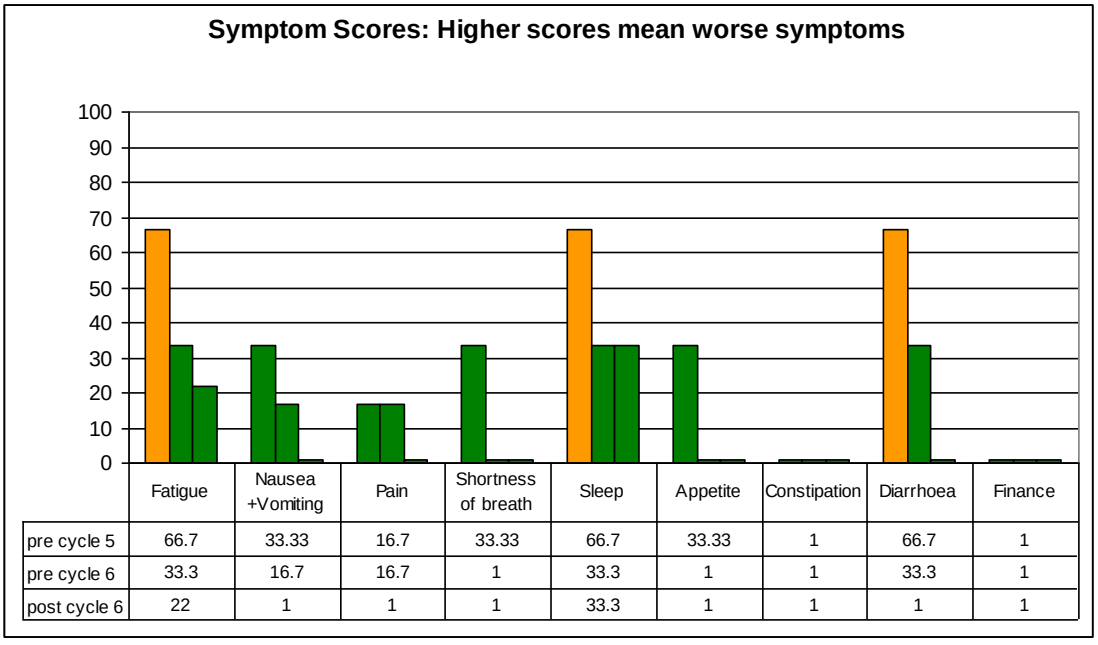
(These are Vitamin tablets, given to you when you started having some soreness in your fingers, which you were told was due to the Capecitabine chemotherapy tablets. You have been on them for about 4 weeks)

***Scenario E Questionnaire Output***



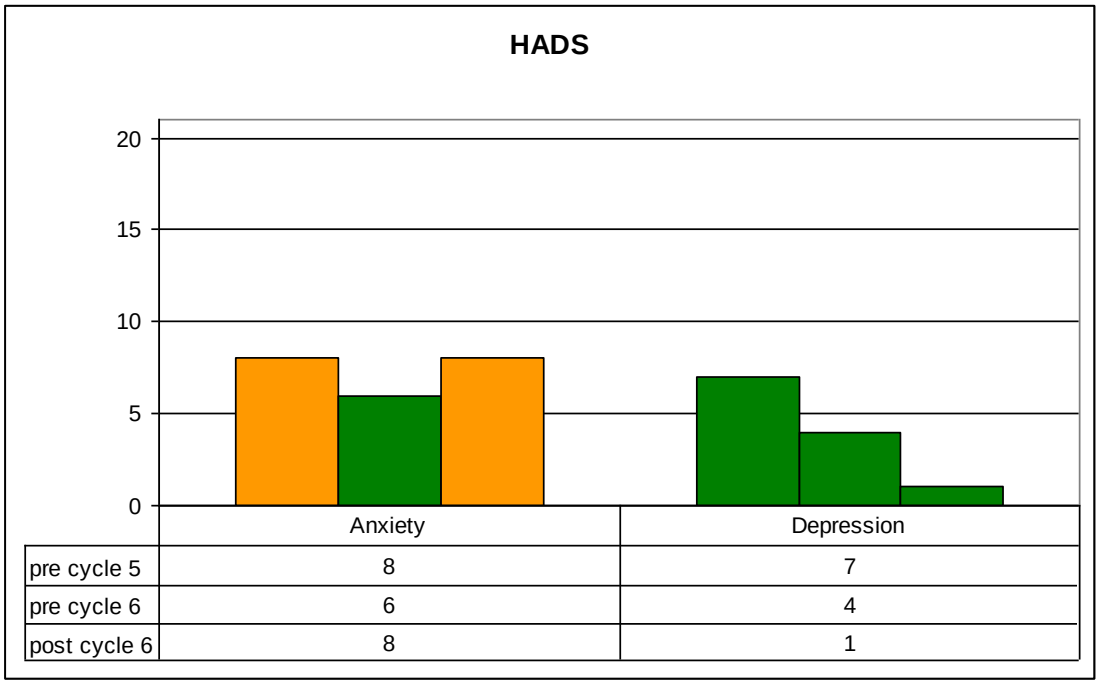

| | Physical Functioning | Role Functioning | Emotional Functioning | Cognitive Functioning | Social Functioning | Global QoL |
|---|---|---|---|---|---|---|
| pre cycle 5 | 60 | 50 | 66.7 | 66.7 | 50 | 66.7 |
| pre cycle 6 | 73.3 | 66.7 | 75 | 83.3 | 66.7 | 75 |
| post cycle 6 | 93 | 83 | 83 | 100 | 83.3 | 91.7 |

Mild 66.8 - 100 Moderate 33.4 – 66.7 Severe 0 – 33.3




| | Fatigue | Nausea +Vomiting | Pain | Shortness of breath | Sleep | Appetite | Constipation | Diarrhoea | Finance |
|---|---|---|---|---|---|---|---|---|---|
| pre cycle 5 | 66.7 | 33.33 | 16.7 | 33.33 | 66.7 | 33.33 | 1 | 66.7 | 1 |
| pre cycle 6 | 33.3 | 16.7 | 16.7 | 1 | 33.3 | 1 | 1 | 33.3 | 1 |
| post cycle 6 | 22 | 1 | 1 | 1 | 33.3 | 1 | 1 | 1 | 1 |

Mild 0 – 33.3 Moderate 33.4 – 66.7 Severe 66.8 – 100




| | Anxiety | Depression |
|---|---|---|
| pre cycle 5 | 8 | 7 |
| pre cycle 6 | 6 | 4 |
| post cycle 6 | 8 | 1 |

Mild 0 - 7 Moderate 8 - 10 Severe >11

## Appendix 9 Doctor Training Programme Manual

Psychosocial Oncology and Clinical Practice Research Group

# Utilising patient reported data in clinical practice

Doctor training manual
June 2012

CANCER RESEARCH UK

The Leeds Teaching Hospitals NHS
NHS Trust

UNIVERSITY OF LEEDS

2

## Utilising patient reported data in clinical practice

pog Psychosocial Oncology and Clinical Practice Research Group

## Overview of session

- Background to using patient reported outcome (PRO) data in clinical practice
- Findings from previous POG research
- Development of PRO measures
- Watch and discuss DVD scenarios of simulated scenarios using PRO

2

## Some requests

- In order to make the most of this session, we would be grateful if you would:
  - Contribute to the discussions
  - Turn off any bleeps/mobile phones

3

## Background to using PRO: Challenges in cancer care


4

## Routine measurement of symptoms and functioning in oncology practice

Clinical method-Medical Interview
Gathering of subjective information
Diagnostic aim
Not good for monitoring change or assessment of outcomes

Patient Reported Outcomes Measures
Quantitative information on symptoms and functioning
See changes overtime

Benefits
- Detect and monitor physical and emotional problems
- Impact on patient-doctor communication
- Facilitate patient involvement in decision making

## PROMs intervention = Complex Intervention


5

## Previous findings from POG research

Velikova et al. Journal of Clinical Oncology 2004;22, 714-724

Measuring Quality of Life in Routine Oncology Practice Improves Communication and Patient Well-Being: A Randomized Controlled Trial

ABSTRACT

Purpose
To examine the effects on process of care and patient well-being, of the regular collection and use of health-related quality-of-life (HRQL) data in oncology practice.

Patients and Methods
In a prospective study with repeated measures involving 39 oncologists, 266 cancer patients were randomly assigned to either the intervention group (regular completion of European Organization for Research and Treatment of Cancer-Core Quality of Life Questionnaire version 3.0 and Hospital Anxiety

## Study design

Patients starting chemo/biological therapy

- **Intervention 50%** EORTC QLQ-C30 HADS on touch screen and feedback
- **Attention-control 25%** EORTC QLQ-C30 HADS,no feedback
- **Control 25%** No PRO in clinic

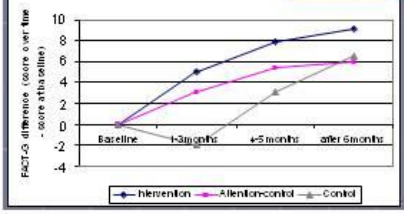
Process outcomes: Communication
Tape-recording of consultations and Physician checklists

**Patient outcomes**
FACT-G (QOL Questionnaire)

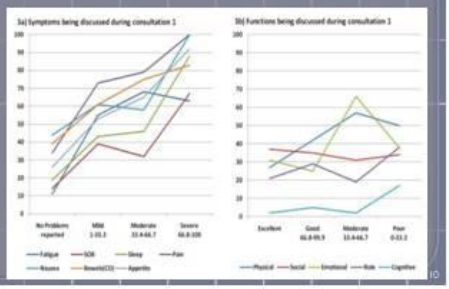
→ @ baseline
after 3 interventions
@ 4 months
@ 6 months

## Results

FACT-G changes overtime




## Results (Velikova et al., 2011, JCO)




## Results

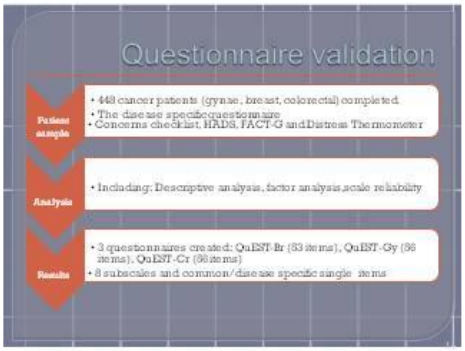
- Providing QOL data lead to more consistent discussion of
  - Insomnia (p=0.003)
  - Dyspnoea (p=0.03)
- Regular feedback of patient reported symptoms= positive impact on the range of symptoms discussed
- PRO feedback of functions had no impact on discussion
  - Low discussion of role and social function

## Our studies suggest…

- Some positive findings for the value of PRO data in clinical practice
- Important for doctors to respond to PRO information
- Doctors have requested:
  - More training in interpreting data
  - Tumour group specific questionnaires
    - Many questionnaires developed for clinical trials

4


Breast, Gynaecological, Colorectal
Literature search of existing questionnaires
Review of issues discussed in 664 oncology outpatient consultations
Semi-structured interviews
Healthcare professionals (n = 25)
Patients (n = 30)
3 disease specific item banks created
Breast (83 items)
Cervix (84 items)
Colorectal (82 items)
13


Questionnaire validation
Patient sample
• 448 cancer patients (gynae, breast, colorectal) completed:
• The disease specific questionnaire
• Concerns checklist, HADS, FACT-G and Distress Thermometer
Analysis
• Including: Descriptive analysis, factor analysis, scale reliability
Results
• 3 questionnaires created: QuEST-Br (83 items), QuEST-Gy (86 items), QuEST-Cr (90 items)
• 8 subscales and common/disease specific single items


Aims of current study
Test the new questionnaires in practice
Pilot testing the impact of a doctor training session on using patient reported data
Watch some scenarios of PRO data in use
Guidance for managing challenging problems- emotional distress

# DVD Scenarios

## Scenario 1 – Pauline Barker
## Patient with multiple problems

**70 year old woman with stage 3C ovarian cancer (papillary serous histology).**

Presented with subacute bowel obstruction. Scan showed bulky pelvic disease and omental cake. Surgery attempted but frozen pelvis and not amenable to debulking surgery. She underwent defunctioning ileostomy formation and multiple biopsies, which confirmed histological type.

Post operative problems with high output stoma,

She has been commenced on palliative chemotherapy with single agent carboplatin.

She has been treated on AUC5 for the first 2 cycles with careful monitoring of her renal function and nadir FBC on day 10 of the chemotherapy.

She has come for review prior to 3rd cycle of chemotherapy.

Her CA125 which was initially >3000 is improving. The last result was 2640 after cycle 1. She has not had any problems with neutropenia or thrombocytopenia so far but she is becoming anaemic. Hb was 9.1 g/dl last week at nadir on day 10 following 2nd cycle of chemotherapy. Results from today are still awaited.

Social background

- Married. Lives with elderly husband who is 77 years of age, who has had major abdominal surgery 6 months ago and has not quite recovered from it. She is his main carer.
- Has a district nurse that visit regularly.
- 3 children all living outside of Yorkshire. One son lives in Manchester with his family.

6

**Pauline Barker: Clinic letter**

**Annotation**
**Team: Dr. B. Crosse, Calderdale Royal Hospital**

| | | | |
|---|---|---|---|
| Patient Name | Pauline Barker | DOB (Age) | (70) |
| Address | | NHS No. | |
| | | Unit. No | |
| | | GP | Dr. AN Other |
| Tel | 0113 2067500 | | |

**Clinical Summary**

**Diagnosis**
Stage 3C G2 papillary serous ovarian cancer

**Treatment History**
1. Presented to A+E with subacute bowl obstruction. Pre-op CT showed right sided pelvic mass with bulky omental disease. CA 125 >3000 at presentation
2. Underwent laparotomy – found to have frozen pelvis. Defunctioning ileostomy formation plus biopsies
3. Started palliative chemotherapy with single agent carboplatin

**Treatment Plan**
To have 3 cycles of chemotherapy with Carboplatin and then reassess. If good response then may consider second attempt at debulking surgery plus reversal to stoma

| | | | |
|---|---|---|---|
| Author: | Specialist Registrar | | |
| Entered By: | Secretary | | |
| Subject: | Review prior to 2nd cycle of chemotherapy with single agent carboplatin | | |
| Addressed to: | GP | Copy to: | Gynae Surgeon<br>Stoma nurses |

I reviewed Mrs. Barker in clinic today after her first cycle of chemotherapy with single agent carboplatin. I was pleased to see that she has tolerated her first cycle reasonably well. She had grade 1 nausea but no vomiting. No other significant toxicity of note. Her nadir bloods were fairly respectable and her renal function has stayed stable. It was also encouraging to see that her CA125 has dropped slightly.

Her main problem continues to be her stoma which is draining liquid stools. She does not feel that the addition of codeine has helped particularly. I sense that she is very conscious of her stoma, which is continuing to interfere with her activities of daily living. I don't think that things are any worse since starting chemotherapy. She tells me that she is up couple of times at night to empty her bag. Clearly this is not helping with her sleep and she is very tired.

Perhaps the stoma nurse may be able to give Mrs. Barker some further practical advice. No doubt they know her well and are fully aware of her current situation.

On examination today, she appeared comfortable at rest but looks tired. Heart rate 92b/min. Oral mucosa slightly dry. Chest clear. Abdominal examination revealed palpable right pelvic mass and omental disease. I don't think there has been any obvious change from 3 weeks ago. Some ascites as before. Tumour markers repeated today and results awaited.

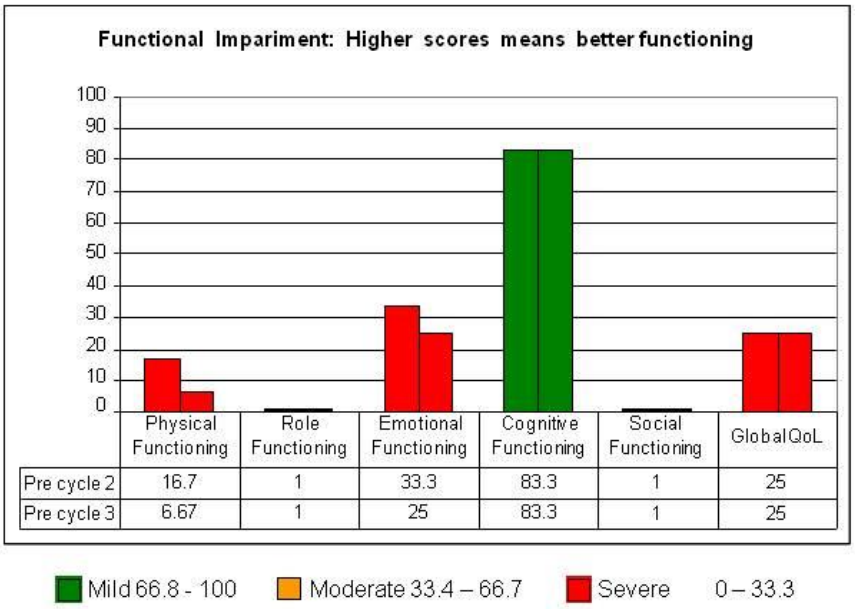
I think we will go ahead with the second cycle of chemotherapy, pending blood results. If her renal function remains stable then we will give her the same dose as cycle 1, calculated based on measured GFR which was 31mls/min on 16th July 2009. I have asked her to repeat the blood test again on day 10 like last time.

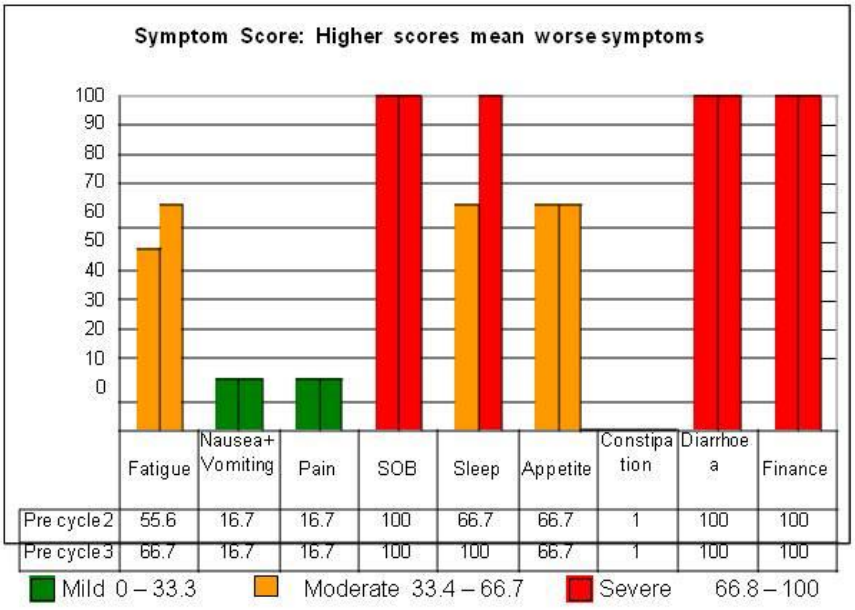
Assuming that we will proceed with the treatment as planned on 7th August, I will request a restaging CT scan for the week commencing 7th September and book her into for MDT discussion on the 16th September so that we'll know whether she would be a candidate for surgery after cycle 3.

Kind regards,

8

**Pauline Barker 1: Patient reported data (2 visits)**



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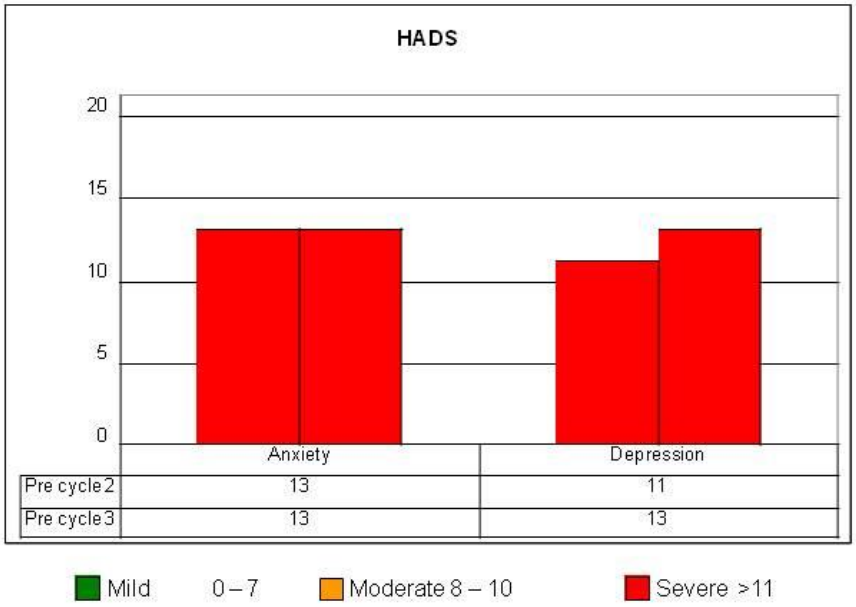
**Pauline Barker: Patient reported data (2 visits)**



## Scenario 2 – Mary Taylor
## Managing emotional distress

**51 year old woman with metastatic breast cancer**

Her original cancer diagnosis was made over 6 years ago. She had left ductal carcinoma. T1 (19mm), G3, N1 (4/16), ER positive, HER2 negative. Left mastectomy with immediate reconstruction followed by adjuvant chemotherapy with FEC x 6 and 5 years of Tamoxifen.

Diagnosed with lung and nodal recurrence 12 months ago. Started on Anastrozole which controlled her disease for 9 months but disease in the lungs started to deteriorate and she has been commenced on palliative chemotherapy with Docetaxel.

Attending for review prior to 3rd cycle of chemotherapy.

She has evaluable disease on CXR and serial examination shows that she is responding and her palpable left SCF nodes are getting smaller.

Social background

- Used to work as a practice nurse in a GP surgery
- Never married. No children. Closest family is an aunt living in Scotland
- Socially rather isolated

11

## Mary Taylor: Clinic letter

**Annotation**
**Team: Dr. J. Dent, Huddersfield Royal Infirmary**

| | | | |
|---|---|---|---|
| Patient Name | Mary Taylor | DOB (Age) | (51) |
| Address | | NHS No. | |
| | | Unit. No | |
| | | GP | Dr. A.N. Other<br>Beckett Street Surgery |
| Tel | 0113 2067500 | | |

Clinical Summary
**Diagnosis**
Ductal carcinoma of the left breast. T1 (19mm) G3 N1 (4/16) ER positive HER2 negative

**Treatment History**
1. Left mastectomy and immediate reconstruction + ANC
2. Followed by adjuvant chemotherapy with FEC x 6 cycles and Tamoxifen for 5 years
3. 2011: Recurrence in left SCF nodes and lung. Started on Arimidex
4. Progressive disease with increase in size of SCF nodes and lung mets after 9 months
5. Started on Docetaxel

| | |
|---|---|
| Author: | Specialist Registar |
| Entered By: | Secretary |
| Subject: | Review prior to 2nd cycle of chemotherapy with Docetaxel |
| Addressed to: | GP |

I reviewed Miss Taylor in the Oncology Clinic today.

She has now received her first cycle of chemotherapy with Docetaxel. She appears to have tolerated the chemotherapy reasonably well although she has had some nausea, diarrhoea and some arthralgia. She has not noticed any change in the size of her lymph nodes but it is still early days. She has not noticed any changes to her breathing either.

Miss Taylor admits to feeling quite tired. Lethargy was a problem before she started chemotherapy, possibly due to the fact that she has been quite breathless due to her lung metastases. This has caused some limitations in what she can do around the house and I note that she has gone on sick leave from her work as a practice nurse.

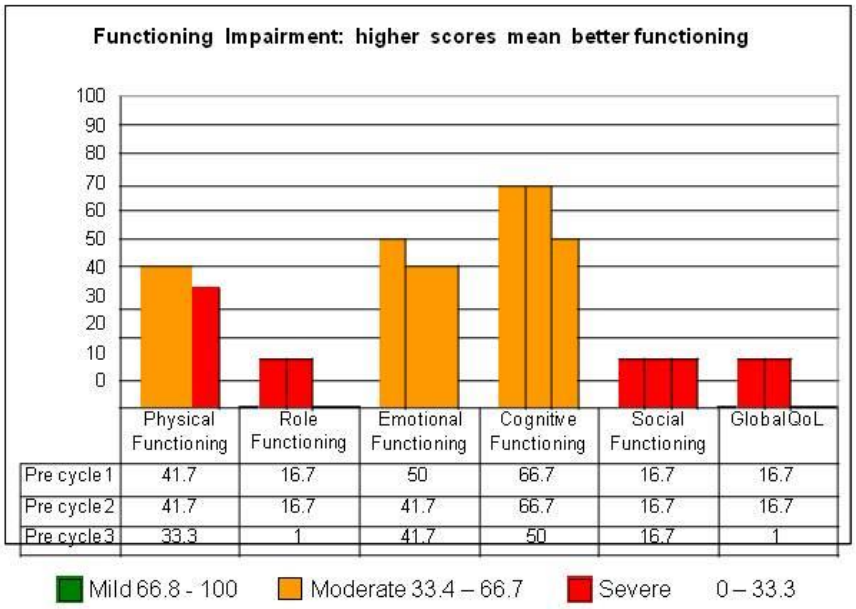
It was quite difficult to engage with her about how she is coping with it all at the moment. She appeared rather withdrawn. I think we'll need to monitor her quite carefully.

We will go ahead with her chemotherapy tomorrow pending blood results. We will see her again in clinic in 3 weeks time.

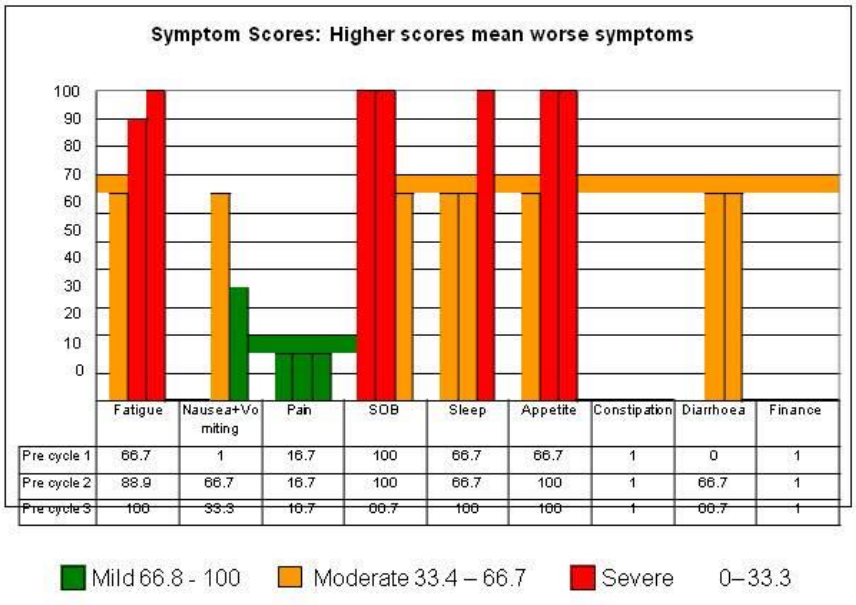
Kind regards,

12

**Mary Taylor: Patient reported data (3 visits)**




| | Physical Functioning | Role Functioning | Emotional Functioning | Cognitive Functioning | Social Functioning | Global QoL |
|---|---|---|---|---|---|---|
| Pre cycle 1 | 41.7 | 16.7 | 50 | 66.7 | 16.7 | 16.7 |
| Pre cycle 2 | 41.7 | 16.7 | 41.7 | 66.7 | 16.7 | 16.7 |
| Pre cycle 3 | 33.3 | 1 | 41.7 | 50 | 16.7 | 1 |




| | Fatigue | Nausea+Vomiting | Pain | SOB | Sleep | Appetite | Constipation | Diarrhoea | Finance |
|---|---|---|---|---|---|---|---|---|---|
| Pre cycle 1 | 66.7 | 1 | 16.7 | 100 | 66.7 | 66.7 | 1 | 0 | 1 |
| Pre cycle 2 | 88.9 | 66.7 | 16.7 | 100 | 66.7 | 100 | 1 | 66.7 | 1 |
| Pre cycle 3 | 100 | 33.3 | 16.7 | 66.7 | 100 | 100 | 1 | 66.7 | 1 |

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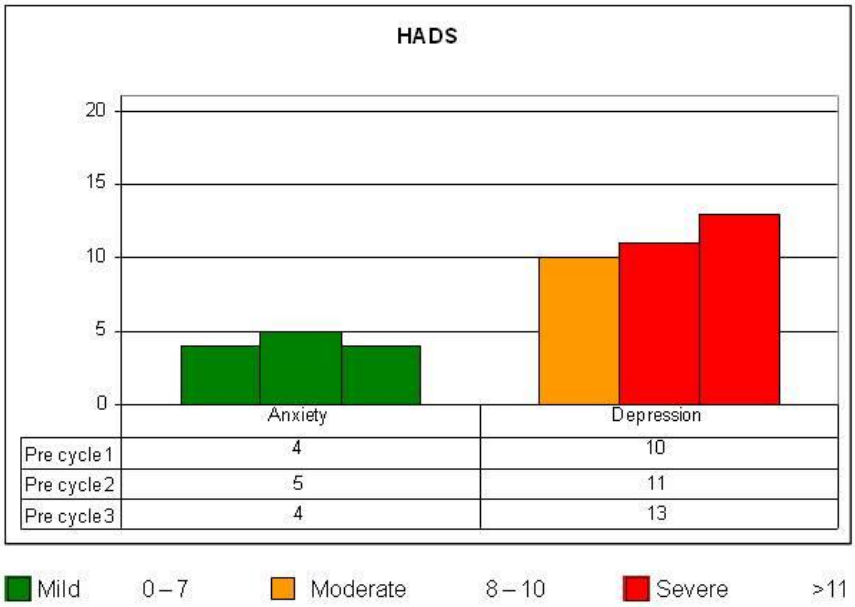
**Mary Taylor: Patient reported data (3 visits)**



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## Scenario 3 – Ms Jane Roberts

**Jane Roberts: 45 year old woman with metastatic breast cancer**

Breast cancer history

1. Diagnosed with metastatic breast cancer 2 years ago. Triple receptor negative disease.
2. Has received 2 lines of palliative chemotherapy
3. Presented with discomfort in right hip. Restaging with a CT scan and bone scan revealed progressive bone disease. Started on further palliative chemotherapy with ECF
4. Attends for review prior to second cycle of chemotherapy

Social Background

- Single parent. Has a daughter currently studying for A-levels
- Had been working as a part time dinner lady in a primary school
- On sick leave since starting ECF chemotherapy

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**Jane Roberts: Clinic letter**

**Annotation**
**Team: Dr. TJ Perren, St. James's University Hospital**

| | | | |
|---|---|---|---|
| Patient Name | Janet Roberts | DOB (Age) | (45) |
| Address | | NHS No. | |
| | | Unit. No | |
| | | GP | Dr. AN Other |
| Tel | 0113 2067500 | | |

Clinical Summary
**Diagnosis**
Invasive ductal carcinoma of the left breast. Presented with metastatic disease with secondaries in liver and bones. Grade 3, ER/PR/HER2 NEGATIVE

**Treatment History**
1.Presented with right sided abdo pain – USS showed multiple liver metastases. Subsequent investigations revealed left sided breast cancer.
2. Palliative chemotherapy with EC achieving good radiological and clinical response
3. Progressive disease after 9 months
4. Chemotherapy with Docetaxel – good response in liver and stable disease in bones
5.Worsening discomfort in right hip 5 months after Docetaxel – Bone scan shows progressive bone disease. CT shows stable appearance of liver
6. Oct 09: To commence further chemotherapy with ECF

| | |
|---|---|
| Author: | Specialist Registrar |
| Entered By: | Secretary |
| Subject: | Review with MUGA scan, starting ECF chemotherapy |
| Addressed to: | GP |

I reviewed Ms. Roberts in the Oncology Clinic today. She remains well in herself with no change in her symptoms since her last review a week ago. She underwent a MUGA scan which showed a normal LVEF of 63%.

She has had the opportunity to go through the information sheet about the proposed ECF chemotherapy and also regarding the insertion of a Hickman line. She is happy to go ahead and has been formally consented today.

I had provisionally booked an admission for Hickman line insertion and for initiation of chemotherapy so we can go ahead with the treatment early next week.

I have reiterated the possible side effects of the treatment to her again. I have also stressed the importance of getting in touch should she become unwell, particularly with a fever. She already has our chemotherapy blue book with all the key contact details.

She will be attending chemotherapy outpatients on a weekly basis anyway as she will require a pump change for the 5-FU chemotherapy so we will be able to monitor her reasonably closely.

I have arranged to see her again in clinic in 3 weeks time just before her 2$^{nd}$ cycle of chemotherapy is due.

We will keep you informed of her progress.

Yours sincerely,

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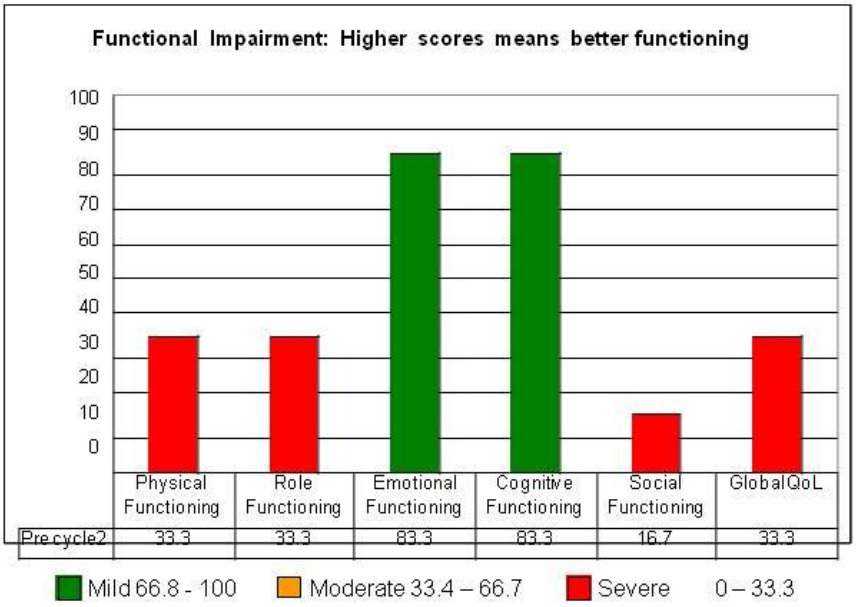
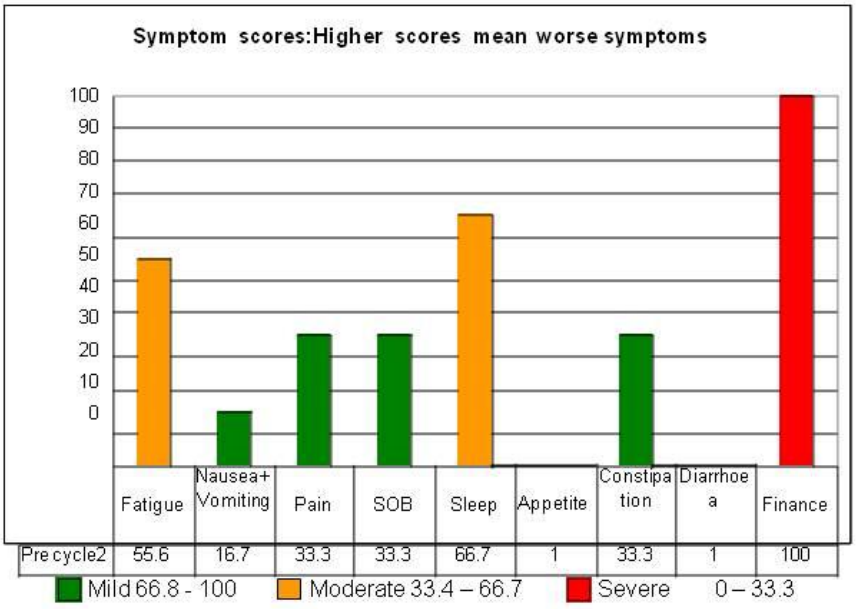
**Jane Roberts: Patient reported data**



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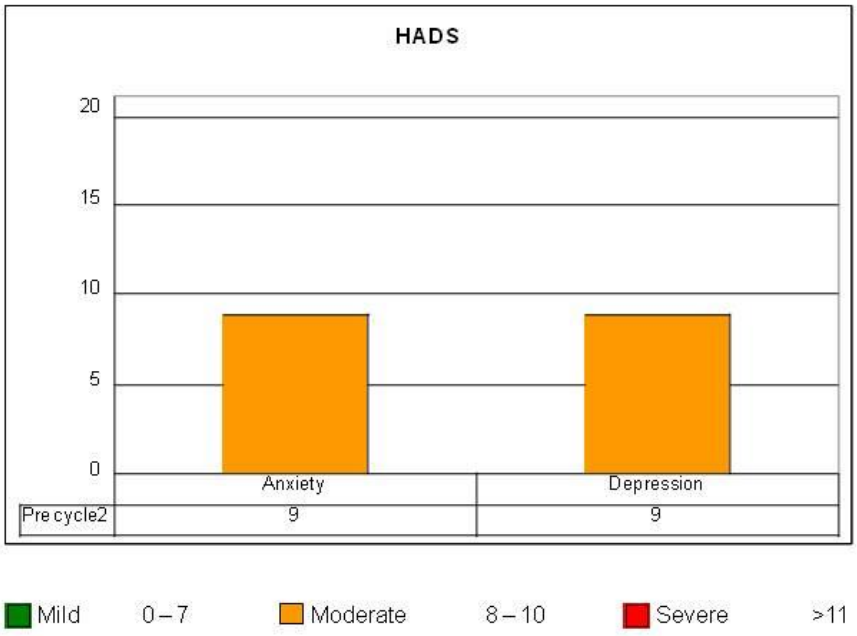
**Jane Roberts: Patient reported data**



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## Scenario 4 – Mrs Sheila Parker

**60 year old woman with advanced bowel cancer**

History

1. Presented to GP in July with weight loss and upper abdominal discomfort. Found to have hepatomegaly. Referred to GI surgeon.
2. CT scan showed thickening of Sigmoid colon with evidence of multiple liver and peritoneal metastases
3. Referred to Medical Oncology for palliative chemotherapy
4. Completed 6 cycles of chemotherapy with OxaliCap
5. Attends for review with CT scan report.

Social Background

- Mrs Parker is a widow, her husband died following CVA 12 months ago.
- Her daughter (Mary Robinson) lives about 10 minutes away.

**Shelia Parker: CT scan report (post chemo)**

Name: Sheila Parker Unit Number: AN1234
Address : 123 Worsley Street, Leeds LS1
DOB: 01/03/1949
Consultant: Prof. Seymour

Clinical History: Known metastatic bowel cancer. Post 6 cycles of chemotherapy. Restaging.

CT Thorax & abdo\pelvis with contrast:

This examination has been compared to the CT scan of 10/08/2009. Within the thorax the two previously noted pulmonary nodules in the left upper lobe remain unchanged. There is no mediastinal, supraclavicular or axillary lymphadenopathy.

Below the diaphragm, there are multiple low attenuation lesions within the liver. The sizes of some of the lesions look subjectively smaller however, overall the appearance is considered stable. The hepatic duct dilatation has improved.

Wispy peritoneal thickening persists but this appears less extensive than previously. The primary tumour on sigmoid colon is visible. The surrounding mesenteric stranding has resolved.

Normal appearances to the remaining small and large bowel, with no evidence of obstruction. Apart from a simple cyst in the left kidney, normal appearances of both kidneys, spleen, uterus and gallbladder.

No destructive bony lesion identified.

Conclusion:
There appears to be some improvement in the liver and the peritoneal disease but this investigation shows stable disease overall.

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## Sheila Parker: Clinic letter (new patient consultation)

**Annotation**
**Team: Prof. MT Seymour, St. James's University Hospital**

| | | | |
|---|---|---|---|
| Patient Name | Sheila Parker | DOB (Age) | (60) |
| Address | | NHS No. | |
| | | Unit. No | AN1234 |
| | | GP | Dr. AN Other |
| Tel | 0113 2067500 | | |

Clinical Summary
**Diagnosis**
Metastatic adenocarcinoma of sigmoid colon with liver and peritoneal metastases

**Treatment History**
1. Commenced on palliative chemotherapy with Oxaliplatin and capecitabine

| | |
|---|---|
| Author: | Registrar |
| Entered By: | |
| Subject: | New patient consultation |
| Addressed to: | GI Surgeon |

Mrs. Parker presented to her GP early July with several month history of poor appetite and weight loss. She had developed vague discomfort in her upper abdomen and indigestion which eventually led her to seek medical attention. When her GP examined her, she was found to have very obvious hepatomegaly and an urgent referral was made.

She underwent a CT scan on 10th August which revealed thickening of sigmoid colon with evidence of liver and peritoneal metastases. She then had colonoscopy on the 13th August which confirmed the presence of a circumferential tumour (scope was traversable) in mid sigmoid colon and the biopsy from this investigation has shown moderate to poorly differentiated adenocarcinoma.

I have gone through the diagnosis with Mrs. Parker today in the presence of her daughter. I have explained to Mrs Parker that her condition is treatable but not curable.

Social History
Widow. Husband died approx 12months ago after a stroke. Lives alone in a house. Independent with all daily activities. Daughter lives 10minutes away.

Family History
No relevant family history of note

System Enquiry
Appetite remains poor. Lacking in energy. Some vague discomfort in the right hypochondrium due to hepatomegaly. Has lost approx 2 stones in weight over the last 6 months. Bowels can be erratic at times. No vomiting.

Examination

Comfortable at rest. PS 1/2. Rather frail looking. HR 88b/min. HS normal. Chest clinically clear. Abdominal examination revealed hepatomegaly with palpable liver edge 4 cm below the costal margin at mid-clavicular line. Some tenderness overlying the liver. Vague fullness in the left iliac fossa. BS active. PR not performed.

Impression and Plan of Action:
Mrs. Parker is a 60 year old with metastatic bowel cancer. I have spoken to Mrs Parker about the standard palliative chemotherapy options for metastatic bowel cancer in terms of Oxaliplatin and 5 Fluorouracil and Folinic Acid through a Hickman line or Oxaliplatin and Capecitabine. She has decided to go for the option of Oxaliplatin in combination with Capecitabine which would not require a Hickman Line insertion. I have gone into some details of the side effects of the proposed treatment and have given Mrs Parker a written information sheet. We proposed that we give her 6 cycles of chemotherapy and reassess.

Mrs Parker has been consented to start this chemotherapy next week.

We will keep you informed of her progress

Kind regards,

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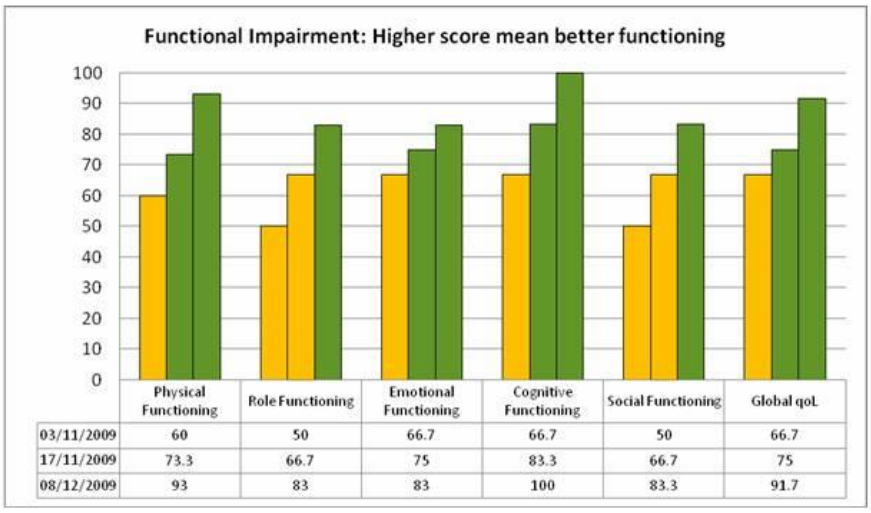
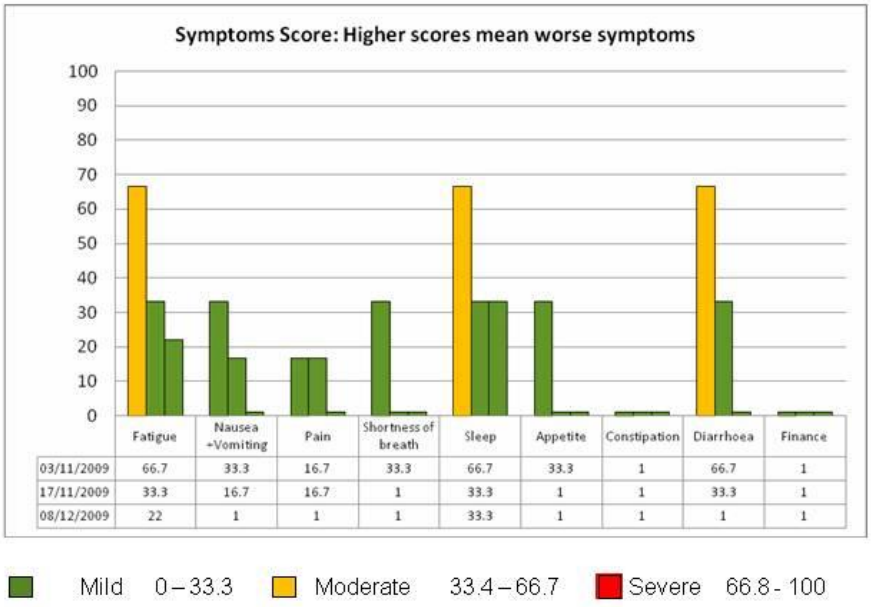
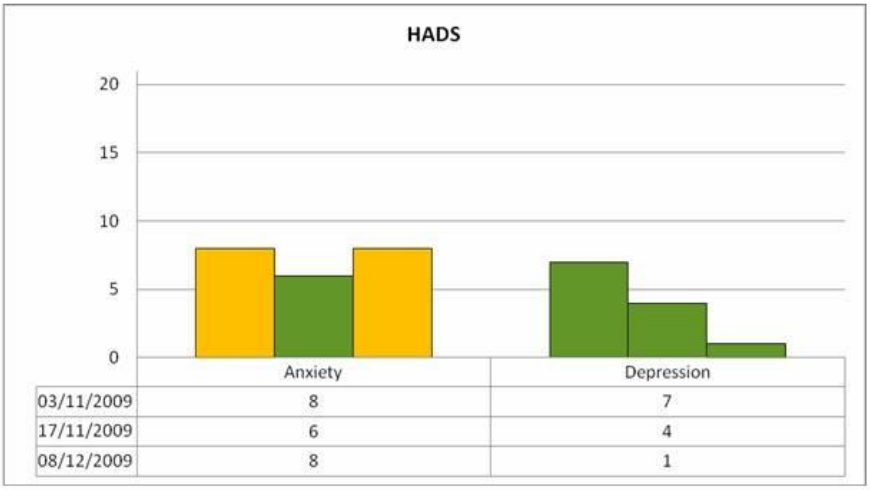
**Sheila Parker: Patient reported data (3 visits)**



**Sheila Parker: Patient reported data (3 visits)**



## Appendix 10 Patient Perception of Patient Centredness Questionnaire

**Patient-Perception of Patient-Centredness Questionnaire**

1. To what extent was your main problem(s) discussed today?
   *Completely* □ *Mostly* □ *A little* □ *Not at all* □

2. How satisfied were you with the discussion of your problem (s)?
   *Very satisfied* □ *Satisfied* □ *Somewhat satisfied* □ *Not satisfied* □

3. To what extent did the doctor listen to what you had to say?
   *Completely* □ *Mostly* □ *A little* □ *Not at all* □

4. To what extent did the doctor explain things to you?
   *Completely* □ *Mostly* □ *A little* □ *Not at all* □

5. To what extent did you and the doctor discuss your respective roles? (Who is responsible for making decisions and who is responsible for what aspects of your care?)
   *Completely* □ *Mostly* □ *A little* □ *Not discussed* □

6. To what extent did the doctor explain treatment?
   *Very well* □ *Well* □ *Somewhat* □ *Not at all* □

7. To what extent did the doctor explore how manageable this (treatment) would be for you? He/she explored this
   *Completely* □ *Mostly* □ *A little* □ *Not at all* □

8. How well do you think your doctor understood you today?
   *Very well* □ *Well* □ *Somewhat* □ *Not at all* □

9. To what extent did the doctor discuss personal or family issues that might affect your health?
   *Completely* □ *Mostly* □ *A little* □ *Not at all* □

Centre for Studies in Family Medicine, 1997