

This is a repository copy of Discussing factors associated with quality of life in cancer follow-up appointments: a preliminary test of a pragmatic model for clinical practice.

White Rose Research Online URL for this paper: http://eprints.whiterose.ac.uk/140661/

Version: Accepted Version

## Article:

Lindner, OC orcid.org/0000-0001-5442-8393, McCabe, MG, Boele, F orcid.org/0000-0003-0409-7949 et al. (4 more authors) (2019) Discussing factors associated with quality of life in cancer follow-up appointments: a preliminary test of a pragmatic model for clinical practice. Clinical Rehabilitation, 33 (4). pp. 762-772. ISSN 0269-2155

https://doi.org/10.1177/0269215518820093

© 2018, The Author(s). This is an author produced version of a paper published in Clinical Rehabilitation. Reprinted by permission of SAGE Publications.

#### Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

#### Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk https://eprints.whiterose.ac.uk/ **Clinical Rehabilitation** 

# **Clinical Rehabilitation**

## Discussing factors associated with quality of life in cancer follow-up appointments: A preliminary test of a pragmatic model for clinical practice.

Journal:	Clinical Rehabilitation
Manuscript ID	CRE-2018-7261.R2
Manuscript Type:	Original Article
Date Submitted by the Author:	27-Nov-2018
Complete List of Authors:	Lindner, Oana; University of Leeds, Leeds Institute of Health Sciences McCabe, Martin; University of Manchester, Faculty of Biology, Medicine and Health, Division of Molecular and Clinical Cancer Sciences Boele, Florien; University of Leeds, Leeds Institute of Cancer Sciences, Patient-Centered Research Group Mayes, Andrew; University of Manchester, School of Biological Sciences, Division of Neuroscience and Experimental Psychology Talmi, Deborah; University of Manchester, School of Biological Sciences, Division of Neuroscience and Experimental Psychology Radford, John; University of Manchester, Faculty of Biology, Medicine and Health, Division of Molecular and Clinical Cancer Sciences Wearden, Alison; University of Manchester, School of Biological Sciences, Division of Neuroscience and Experimental Psychology
Keywords:	Quality of life, Follow-up care, Illness perceptions, cancer, Survivors

# SCHOLARONE<sup>™</sup> Manuscripts

## Abstract

Objective: To perform a preliminary test of a practical, evidence-based model to enable discussions around quality of life-related concerns during cancer follow-up appointments.Design: Cross-sectional study measuring quality of life, illness perceptions, emotional distress, fatigue, and subjective cognitive complaints.

Setting: Cancer outpatient follow-up clinics in four National Health Services in the United Kingdom.

**Participants:** Working age post-treatment cancer patients, treated with curative intent. **Interventions:** Not applicable.

**Main measures:** European Organisation for the Research and Treatment of Cancer - Quality of Life Questionnaire-Core 30, Illness Perceptions Questionnaire-Revised, Hospital Anxiety and Depression Scale, Chalder Fatigue Scale, Cognitive Failures Questionnaire.

**Results:** Fifty seven cancer patients, with a mean age of 36 and on average 2.75 years posttreatment, returned the completed questionnaires. Anxiety partially mediated the association between subjective cognitive complaints and illness identity (60%) and timeline (25%). Cognitive complaints mediated the relationships between quality of life and anxiety (45%), depression (30%), and fatigue (62%). Depression mediated the relationships between quality of life and illness identity (48%) and timeline (40%).

**Conclusions:** Our study provides a preliminary test of an evidence-based model to help elicit quality of life-related concerns during cancer follow-up appointments. Illness perceptions are associated with quality of life through the mediation of other cancer-relevant factors.

Discussing the type, origin, and expected duration of symptoms may elicit other concerns, such as emotional distress, fatigue, or cognitive complaints, which explained a significant amount of the relationship between illness perceptions and quality of life.

Keywords: Quality of life, Follow-up care, Illness perceptions, Cancer, Survivors.

Discussing factors associated with quality of life in cancer follow-up appointments: A preliminary test of a pragmatic model for clinical practice.

Running head: Quality of life in cancer

Oana C. Lindner<sup>a,b\*</sup>, PhD, Martin G. McCabe<sup>c</sup>, PhD, Florien Boele<sup>d</sup>, PhD, Andrew Mayes<sup>a</sup>, PhD, Deborah Talmi<sup>a</sup>, PhD, John Radford<sup>b</sup>, PhD, Alison Wearden<sup>a</sup>, PhD Author affiliations:

<sup>a</sup>Division of Neuroscience and Experimental Psychology, School of Biological Sciences, University of Manchester, Manchester, UK.

<sup>b</sup>Division of Psychological and Social Medicine, Leeds Institute of Health Sciences, School of Medicine, University of Leeds, Leeds, UK.

<sup>c</sup>Division of Molecular and Clinical Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK.

<sup>d</sup>Patient-Centred Research Group, Leeds Institute for Medical Research at St. James's University Hospital, University of Leeds, Leeds, UK.

\*Corresponding author: Oana C. Lindner, Division of Psychological and Social Medicine, Leeds Institute of Health Sciences. Room 10.90, Level 10, Worsley Building, Clarendon Way, Leeds, LS2 9NL; Tel: +44(0)113.343.2722; Email: o.c.lindner@leeds.ac.uk.

## Abstract

Objective: To perform a preliminary test of a practical, evidence-based model to enable discussions around quality of life-related concerns during cancer follow-up appointments.Design: Cross-sectional study measuring quality of life, illness perceptions, emotional distress, fatigue, and subjective cognitive complaints.

Setting: Cancer outpatient follow-up clinics in four National Health Services in the United Kingdom.

Participants: Working age post-treatment cancer patients, treated with curative intent.Interventions: Not applicable.

**Main measures:** European Organisation for the Research and Treatment of Cancer - Quality of Life Questionnaire-Core 30, Illness Perceptions Questionnaire-Revised, Hospital Anxiety and Depression Scale, Chalder Fatigue Scale, Cognitive Failures Questionnaire.

**Results:** Fifty seven cancer patients, with a mean age of 36 and on average 2.75 years posttreatment, returned the completed questionnaires. Anxiety partially mediated the association between subjective cognitive complaints and illness identity (60%) and timeline (25%). Cognitive complaints mediated the relationships between quality of life and anxiety (45%), depression (30%), and fatigue (62%). Depression mediated the relationships between quality of life and illness identity (48%) and timeline (40%).

**Conclusions:** Our study provides a preliminary test of an evidence-based model to help elicit quality of life-related concerns during cancer follow-up appointments. Illness perceptions are associated with quality of life through the mediation of other cancer-relevant factors.

Discussing the type, origin, and expected duration of symptoms may elicit other concerns, such as emotional distress, fatigue, or cognitive complaints, which explained a significant amount of the relationship between illness perceptions and quality of life.

Keywords: Quality of life, Follow-up care, Illness perceptions, Cancer, Survivors.

## Introduction

Two million people are currently living with and beyond cancer in the United Kingdom. Sixty-six percent are estimated to be education- and working-age adults, namely teenagers, young, and middle-aged adults (1,2). After treatment, they undergo many years of follow-up monitoring, which involves regular scheduled appointments. These appointments have two roles – to identify any signs of recurrence or secondary cancers (through clinical examinations, blood, and radiological reports), ensuring quick access to treatment, and to identify and manage treatment-related physical and psychosocial effects (3,4).

To provide the greatest benefit for patients, the follow-up process should hence appropriately elicit patients' concerns to enable clinicians to provide tailored support (5). Several recommendations have been put forward to improve follow-up care (5), both in terms of content (i.e. clinical examination/symptom monitoring) and structure of the follow-up process (i.e. when/where it takes place) (3,6). In recent years there has been a strong movement towards the inclusion of psychosocial and patient-reported symptoms/concerns in the follow-up process, in addition to the monitoring and management of clinician-observed physical effects (4,7). This has motivated national initiatives and guidelines promoting the use of quality of life as a metric for the provision of care that can enhance patients' well-being (8). However, quality of life is a highly multifaceted construct, associated with a plethora of clinical and psychological factors (9). The psychological factors most frequently cited as involved in cancer patients' quality of life are emotional distress (10), fatigue (11), subjective cognitive complaints (12), and illness perceptions (13). While we have evidence that cancer patients' quality of life suffers, and we

#### **Clinical Rehabilitation**

3
4
5
6
7
2 2
0
9 10
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
27 28
20
29
50 21
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
50
51
52 52
53
54 57
55
56
57
58
59

60

have assessments available to measure potential factors (14), the applied value of this knowledge is yet to be fully realised, to the detriment of patients and healthcare providers alike (15–17). This may stem from a knowledge gap regarding the key factors to be monitored and addressed in the time-limited and overloaded healthcare context. We suggest that a validated theoretical model, such as the Common Sense Model of Illness (18), could bridge the gap between what we know from research are patients' concerns and actually addressing them in practice. To our knowledge, there are no other models that have been tested that could comprehensively help elicit specific psychological concerns that may be relevant to each persons' quality of life. Here we take a first step in testing such a model. On the basis of the Common Sense Model of Illness, we assume that it is not only the event itself (i.e. diagnosis, treatment, transition to follow-up), but the core personal beliefs about the illness and related events (i.e. illness perceptions) that will predict other outcomes such as quality of life. We hypothesise that illness perceptions will be associated with quality of life either directly or through the mediation of other highly cited factors - emotional distress, fatigue (11), and subjective cognitive complaints (12). This theoretical model could provide a simplified and pragmatic method to promote and improve consistency in monitoring and addressing, in a

personalised manner, the psychological factors relevant to each patients' quality of life during follow-up.

# **U**

# Methods

Design

This cross-sectional observational study was approved by the National Research Ethics Service Committee North West – Greater Manchester North (11/NW/0185).

# Participants

Patients were invited to the study by their clinical teams in four National Health Service Trusts in the United Kingdom, between 2011 and 2013. They were offered the opportunity to participate if aged 16 to 50 and between 6 months and 6 years post-treatment. Time limits ensured patients were well enough after treatment, but that participation was early enough for researchers to measure short to medium term influences of the cancer-related psychological factors on quality of life. Patients were included if they were diagnosed with a type of cancer highly prevalent in this age group (lymphoma, breast cancer, germ cell tumour, or sarcoma); were treated with curative intent; were in complete remission. Patients were excluded if: the malignancy was a relapse or secondary cancer; if they had a history of central nervous system disease, cranial irradiation, mental health problems, substance abuse; if they were not proficient in English.

## Procedure

Consecutive patients were identified by their treatment team during their regular follow-up appointments. Upon confirmation of eligibility, the clinical team referred the patient to the study. Patients were offered a participant information sheet detailing the study and were given time to ask questions and consider participation. After obtaining written informed

#### **Clinical Rehabilitation**

consent patients were offered an envelope containing the questionnaires described below, to complete at home and mail back to the research team. Where participants did not return the questionnaires, mail reminders were sent six months following the initial contact and at the end of the project.

#### Instruments

Questionnaires were chosen based on their brevity, sensitivity, and recommendations of use in current clinical research and practice (16). Quality of life was evaluated with the European Organisation for the Research and Treatment of Cancer - Quality of Life Questionnaire-C30 (19). The general version was used due to the mixed diagnoses in the patient group. It contains several subscales, of which we focused on the two items of the global quality of life scale. The minimum score is 0 and maximum 100, higher scores representing a higher quality of life. Emotional distress was measured with the Hospital Anxiety and Depression Scale, designed to identify anxiety and depression symptoms in clinical groups. It consists of two 7-item subscales (anxiety and depression), each item being rated between 0 (not at all) to 3 (very often). The minimum score is 0 and maximum is 21, with a possible case cutoff score of 8+ for each scale (20). Fatigue was evaluated with the 11-item Chalder Fatigue Scale (21), providing a continuous measure of fatigue ranging from 0-33, whereby higher scores represent more fatigue. Subjective cognitive complaints were evaluated with the 25-item Cognitive Failures Questionnaire (22), measuring self-reported failures in memory, attention, perception, and motor functioning. Items can be rated from 0 (never) to 4 (very often). The total score is obtained by summing items and ranges between 0 and 100, with higher scores representing more self-reported cognitive complaints. Illness perceptions were measured with the Illness Perception Questionnaire-Revised (23). The questionnaire evaluates eight

http://mc.manuscriptcentral.com/clinrehab

dimensions of illness perceptions: illness identity (number of symptoms the patients

Page 8 of 41

perceives as part of the illness), timeline (how long the patient believes the illness will last), consequences (expected effects of the illness), personal control (the expectation that the illness/symptoms can be controlled through one's behaviour), treatment control (expectation that the illness/symptoms can be controlled by treatment), illness coherence (whether patients believe they understand the diagnosis and treatment), timeline-cyclical (belief regarding the predictability and stability of symptoms), and emotional representation (emotions elicited by thinking about the illness). Apart from the identity symptom checklist, all questions are rated on a 5-point Likert scale, high scores being associated with a higher level of the illness perception defined by each scale. Patients were asked to describe their illness perceptions during their post-treatment phase of their cancer pathway.

#### Statistical analyses

Following descriptive analyses we evaluated the relationship between illness perceptions, quality of life, and other factors (emotional distress, fatigue, subjective cognitive complaints) in the patient sample. Bootstrapped correlations were initially explored between the factors. Following this, we pursued the preliminary examination of our hypothesized model (Figure 1), using the factors most highly correlated with quality of life, namely: anxiety, depression, fatigue, illness identity and timeline. We explored the model through bootstrapped mediation analyses using the SPSS PROCESS macro (24). Bootstrapping calculates the level of

explained variances in a distribution-independent manner, by inferring properties about the
population based on the re-sampling of the observed data.
[Insert Figure 1 around here]
In two of the analyses the predictors were the dimensions of illness
perceptions most highly correlated with quality of life (identity and timeline), while the
outcomes were either quality of life or cognitive complaints, potentially mediated by
depression, anxiety, or fatigue. In the third analysis the predictors were, in turn,
depression, anxiety, or fatigue, the outcome was quality of life, potentially mediated by
cognitive complaints. Consistent with the steps suggested in classic mediation
analyses, we evaluated each model through three steps (25). In the first two steps we
explored whether the predictors correlated with the outcomes (direct effect or path c')
and the mediators (path a), and whether the mediators correlated with the outcomes
(path b). In the third step, we tested for the indirect effect and we evaluated whether
the direct effect (path c') is smaller than the indirect/mediated effect (path a*b). Finally,
we calculated the percentage of total effect (path c) accounted for by the indirect effect
(i.e. $P_m$ = a*b/(a*b+c')). We present the coefficients, associated 95% confidence
intervals (95% CI) of each path, the effect size associated with the mediation (small ${\rm if}$

<.20, moderate if .21-.79, and large if >.80), and the percentage of total effect accounted

for by the mediator  $(P_m)$ .

## Results

 Patient recruitment and characteristics

Figure 2 details the three year recruitment process that lead to the inclusion of 57 patients in the present study.

# [Insert Figure 2 around here]

Participants were on average 35.3 years old (sd = 9.79), 31 were female (54.4%), 43 (75.4%) had a university degree, 13 (22.8%) college education, and one had finalised secondary school, reflecting national trends for this age group (26). On average, patients were 2.7 years post-treatment and their quality of life was on average 64 (sd=20.76), out of a total possible of 100 (Table 1). Figure 3 in the Electronic Supplementary Material depicts the spread of individual patient quality of life scores.

[Insert Table 1 around here]

# Relationships between factors

Almost all variables correlated with quality of life (Table 2). The strongest (>.50) negative correlations were found between quality of life, emotional distress, and cognitive

complaints. Quality of life correlated moderately (.30-.49) with fatigue, illness identity,

timeline, and consequences, but no other dimensions of illness perceptions. This suggests that patients who are fatigued, distressed, attribute more of their ongoing post-treatment symptoms to their diagnosis, and perceive that their illness is chronic with multiple consequences also have a reduced quality of life. Only identity and timeline also had moderate to strong

#### **Clinical Rehabilitation**

correlations with the other factors. Consequently, these two dimensions of illness perceptions were included in further analyses. **Cognitive complaints** were strongly and significantly correlated with distress and fatigue and showed a moderate relationship with timeline. Depression was moderately and positively correlated with illness identity and moderately with the perceived timeline.

[Insert Table 2 around here]

#### Mediation analyses

Before evaluating the relationship between quality of life and other factors, we first tested whether emotional distress and fatigue mediated the relationship between illness perceptions and cognitive complaints (Figure 1, Model 1). This was examined because patients' beliefs of their illness may include both expected physical and cognitive symptoms. There was a significant indirect effect of the identity dimension on cognitive complaints, mediated by anxiety (.97, .19 to 2.31), while the direct effect was not significant. Anxiety accounted for 60% of the total effect of identity on cognitive complaints, suggesting anxiety partially mediates the relationship between illness identity and cognitive complaints (Table 3). Similarly, there was a significant indirect effect of timeline on cognitive complaints via the mediation of anxiety (.42, .04 to 1.12), which accounted for 25% of the total effect. This suggests that a stronger attribution of any ongoing symptoms to the cancer diagnosis/treatment and a longer perceived

illness timeline are related to cognitive complaints when patients report higher levels of anxiety (Figure 4, Supplementary Material).

Second, we explored whether the relationship of distress and fatigue with quality of life was mediated by cognitive complaints (Figure 1, Model 2). Both aspects of emotional distress had a significant direct effect on quality of life. Otherwise said, higher levels of anxiety (-1.64, -2.86 to -.42) or depression (-2.56, -3.66 to -1.46) were related to a poorer quality of life. However, there was also an indirect effect of cognitive complaints, accounting for 45% and 30%, respectively, of the total effect of these factors on quality of life. Fatigue was related to quality of life through the mediation of cognitive complaints (-1.89, -3.22 to -.88), in the absence of a direct effect. Cognitive complaints explained 62% of the total effect of fatigue on quality of life. This indicated that both emotional distress and especially fatigue related to guality of life when cognitive complaints were also reported (Figure 5, Supplementary Material).

[Insert Table 3 around here]

Finally, the last part of the model explored whether the identity and timeline dimensions of illness perceptions were related to quality of life via distress and fatigue. This step explored whether our hypothesized model (Figure 1, Model 3), which suggested that the interpretation of an event may lead to higher levels of emotional distress, is also related to cancer survivors' quality of life. There was a significant indirect effect of identity on quality of life through the mediation of depression (-1.42, -2.54 to -.61), accounting for 48% of the total effect. Depression also mediated the relationship between timeline and quality of life (-.76, -1.51 to -.27), accounting for 40% of the total effect. In other words, working-age cancer survivors who attributed ongoing symptoms to their cancer diagnosis and treatment had a poor quality of life when also reporting depression symptoms (Figure 6, Supplementary Material). To sum up, in working-age cancer survivors, guality of life is related to illness perceptions, particularly the attribution of ongoing symptoms to their cancer and the perceived timeline of the illness. However, this relationship is mediated by depression.

Emotional distress and fatigue are also related to quality of life when cognitive

complaints are reported. Furthermore, cognitive complaints mediate the relationship

between illness perceptions and quality of life. Hence, quality of life receives a double influence, via depression and cognitive complaints.

### Discussion

The aim of the present study was to conduct a preliminary analysis of a model inspired by the validated Common Sense Model of Illness (18). We suggested that such a model would help healthcare professionals elicit discussions around factors that are of most relevance to individual cancer patients' quality of life during follow-up. We focused on working-age patients as this group is under-researched despite their increased survival rates (2,27,28) and the known role of frequently cited unmet needs in patients' poor quality of life and recovery (16,29). The model incorporated the factors which have been most frequently cited as key in patients' recovery following their diagnosis and treatment - illness perceptions, emotional distress, fatigue, and subjective cognitive complaints.

Consistent with the literature in cancer patients of all ages, diagnoses, and in a similar fashion to patients with chronic health conditions, the quality of life of our follow-up participants was only just above average. Not all frequently cited psychological factors that we included in our model had the same strong relationship to quality of life. Different aspects of illness perceptions have been shown to be associated with patients' distress, including consequences and emotional representations (13,23). In our sample, consistent with prior literature, dimensions of illness perceptions that correlated with emotional distress were identity, timeline, consequences, the timeline-cyclical dimension, and emotional representations (13). However, only the first two also correlated with all other factors and especially quality of life, therefore only identity and timeline were included in the model. These two aspects were associated with cognitive complaints through the mediation of anxiety. In other words, attribution of a higher number of symptoms to cancer and a belief that these may

#### **Clinical Rehabilitation**

last a long time, was related to increased subjective cognitive complaints when patients also reported anxiety. This could be a result of an expected, perceived, or an actual poorer performance in daily activities due to a lower level of concentration or memory (30,31). Future studies could explore this further.

We continued by investigating whether the relationship between emotional distress/fatigue and quality of life changed with the inclusion of cognitive complaints. Increased levels of distress and fatigue were significantly associated with a lower quality of life when patients also perceived their cognitive abilities to be poorer, potentially adding to the cluster of symptoms on which patients are focusing (31). Finally, the same dimensions of illness perceptions were related to quality of life, mediated by depression. Patients who perceived their illness to have a strong identity (i.e. multiple ongoing symptoms) or a longer timeline might focus more on their physical symptoms and attribute them to the illness and treatment, irrespective of whether they are related (31). The symptoms may be interpreted as an ongoing chronic illness, being associated with a low mood and poorer quality of life.

This study has several limitations. Given its cross-sectional design we cannot draw any causal inferences. However, our aim was to explore a novel preliminary integration of evidence-based relevant factors into a simple, practical model. Following its definition here, our preliminary study now motivates the exploration of this model in more complex longitudinal studies. We chose to use the Common Sense Model of Illness framework while relating it to the factors that are most commonly cited to be of concern for cancer patients' quality of life and which are also recommended by current patient care guidelines (8,32). We acknowledge, however, that other factors could be tested, such as those included in the Chronic Care Model (33), or models including social determinants of health (34). Hence, while our chosen psychological mediators explained a significant amount of the associations, other sociodemographic (i.e. deprivation level (29)), clinical (i.e. treatment types, co-morbidities (7)), or

*'*)),

service delivery factors (i.e. self-management support (3,4)) may still play a role. Additional research is warranted to determine which other type of factors within such other categories, may be most relevant to be discussed and addressed in clinical practice. Lastly, our study is based on a relatively small and clinically heterogeneous sample, potentially limiting the generalisability of findings. However, depending on local, national, and international guidelines, the structure of follow-up services (especially for people aged 16 to 39) tends to be multidisciplinary as they cater for heterogeneous clinical groups (27,28). Recruitment difficulties, highly prevalent in this age group (35), resulted in a lower recruitment rate than expected. We did achieve a complete questionnaire return rate, close to similar studies (36). However, we acknowledge that this model would now need to be further validated in larger samples.

It is paramount to ensure patients receive the care they need to enable them to return to normal activity following curative treatment. This is not only the case for cancer patients, but applies to all patients with chronic illnesses who are under the management of a healthcare service or multidisciplinary team. Patients diagnosed and undergoing management for other chronic illnesses, such as diabetes (37) or spinal cord injuries (38) also have a poor quality of life. But as for the case of cancer, depicted here, for other such illnesses there is still a large gap between the evidence of factors influencing quality of life and the means to tackle them in clinical practice. Illness perceptions have been shown to be predictive of coping and adjustment in most patients long-term illnesses (23), while emotional distress is an important predictor of well-being of in patients with cardiovascular disease (39). These needs will not be addressed comprehensively by clinical services without a simplified model of what could influence patients' quality of life. The model described here suggests that instead of simply discussing quality of life in a general sense, or inquiring about a multitude of factors, future studies could

test whether a clear communication around expected symptoms and their duration may be closely related to the quality of life of patients who attend outpatient appointments for routine illness management.

## **Clinical Message**

- A pragmatic model to discuss quality of life in time-strained clinical appointments is needed
- Illness perceptions such as the identity and duration of the illness are closely related to quality of life
- This relationship is mediated by patients' emotional distress, fatigue, and subjective cognitive complaints.

## Acknowledgements:

The authors thank all participants and National Health Service Trusts who contributed to this study, the research assistants, student volunteers, nurses, and oncologists who provided support during the data collection and Dr. Sebastian E. Bartos (University of Northampton) for advice during statistical analyses.

## Author Contributions:

Study initiation: OCL, MGM, AM, DT; Study design: OCL, MGM, AM, DT, AW; Progress monitoring: MGM, AM, DT, JR, AW; Analysis and interpretation of data: OCL, FB, AW; Manuscript preparation: OCL, MGM, FB, AM, DT, JR, AW; Guarantor: OCL.

Conflicts of interest:

None declared

Funding:

This work was funded by the Medical Research Council (grant number G1000399).

erien

Office of National Statistics. Cancer Survival Rates, Cancer Survival in England,

http://webarchive.nationalarchives.gov.uk/20160129224133/http://www.ons.go

2010/stb-cancer-survival--2005-09-and-followed-up-to-2010.html. Accessibility

Jacobs LA, Shulman LN. Follow-up care of cancer survivors: challenges and solutions.

Heathcote LC, Goldberg DS, Eccleston C, Spunt SL, Simons LE, Sharpe L, et al.

NHS Improvement. Innovation to implementation: Stratified pathways of care for

https://www.england.nhs.uk/wp-content/uploads/2016/04/stratified-pathways-

Howell D, Hack TF, Oliver TK, Chulak T, Mayo S, Aubin M, et al. Models of care for

post-treatment follow-up of adult cancer survivors: A systematic review and quality

appraisal of the evidence. Journal of Cancer Survivorship. 2012; 6(4):359-71.

Advancing shared decision making for symptom monitoring in people living beyond

v.uk/on s/rel/cancer-unit/cancer-survival-rates/2005-2009--followed-up-to-

Maddams J, Utley M, Møller H. Projections of cancer prevalence in the United

Kingdom, 2010-2040. Br J Cancer. 2012;107(7):1195–202.

The Lancet Oncology. 2017; 18(1):e19-e29.

cancer. Lancet Oncol. 2018;19(10):e556-63.

people living with and beyond cancer. Available from:

update.pdf. Accesibility verified January 24th, 2018.

Patients Diagnosed 2005-2009 and Followed up to 2010. Available at

verified January 24th, 2018.

1		
2		
3		
4		
5	Refe	erences
0		
/	1	Offic
8	1.	Onic
9		
10		Patie
11		
12		
13		
14		nttp:/
15		
16		
17		v uk/
18		
19		
20		
21		2010
22		
23		
24		verifi
25		
26		
27	2	Made
28		muu
29		Vina
30		Killg
31 22	-	
2∠ 22	3.	Jacob
34		
35		The I
36		
37	4	Heatl
38		
39		A due
40		Auva
41		
42		cance
43		
44	5.	NHS
45		
46		peop
47		P · · P
48		https://
49		nups
50		1
51		updat
52		
53	6.	How
54		
55		post-
56		r
57		annra
58		appro
59		
60		

7.	Thanarajasingam G, Minasian LM, Baron F, Cavalli F, De Claro RA, Dueck AC, et al.
	Beyond maximum grade: modernising the assessment and reporting of adverse events
	in haematological malignancies. Lancet Haematol. 2018;5(11):e563-98.
8.	Independent Cancer Taskforce. Achieving World-Class Cancer Outcomes - A Strategy
	for England - Executive Summary. Available at
	https://cancerresearchuk.org/sites/default/files/achieving_worldclass_cancer_o
	utcomes_a_strategy_for_england_2015-2020.pdf. Accessibility verified January
	24th, 2018.
9.	World Health Organisation. WHOQOL Measuring Quality of Life. Available from:
	http://www.who.int/mental_health/media/68.pdf. Accesibility verified January 24th,
	2018.
10.	Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, et al. Prevalence of
	depression, anxiety, and adjustment disorder in oncological, haematological, and
	palliative-care settings: a meta-analysis of 94 interview-based studies. Lancet Oncol.
	2011;12(2):160–74.
11.	Brown LF, Kroenke K. Cancer-related fatigue and its associations with depression and
	anxiety: A systematic review. Psychosomatics. 2009;50(5):440-7.
12.	Hutchinson AD, Hosking JR, Kichenadasse G, Mattiske JK, Wilson C. Objective and
	subjective cognitive impairment following chemotherapy for cancer: a systematic
	review. Cancer Treat Rev. 2012;38(7):926–34.
13.	Kaptein AA, Schoones JW, Fischer MJ, Thong MSY, Kroep JR, van der Hoeven KJM.
	Illness Perceptions in Women with Breast Cancer—a Systematic Literature Review.
	Curr Breast Cancer Rep. 2015;7(3):117–26.
	19

2		
3	14.	Velikova G, Coens C, Efficace F, Greimel E, Groenvold M, Johnson C, et al. Health-
5 6		Related Quality of Life in EORTC clinical trials - 30 years of progress from
7 8		methodological developments to making a real impact on oncology practice. Eur J
9 10		Cancer, Suppl. 2012;10(1):141–9.
11 12	15.	Watson E, Rose P, Neal R, Hulbert-Williams N, Donnelly P, Hubbard G, et al.
13 14 15		Personalised cancer follow-up: risk stratification needs assessment or both? Br I
16 17		Concer Concer Reg. 2012: 106(1):1.5
18		Cancer Cancer Res. $2012$ , $106(1)$ :1–5.
19 20	16.	Jarrett N, Scott I, Addington-Hall J, Amir Z, Brearley S, Hodges L, et al. Informing
21 22		future research priorities into the psychological and social problems faced by cancer
23 24		survivors: a rapid review and synthesis of the literature. Eur J Oncol Nurs.
25 26 27		2013;17(5):510–20.
28 29	17.	Greenhalgh J. Long AF, Flynn R. The use of patient reported outcomes measures in
30 31		routine clinical practice: lack of impact or lack of theiry? SocSciMed. 2005; 60
32 33		(4):833-43.
34 35	18.	Hagger MS. Koch S. Chatzisarantis NLD. Orbell S. The common sense model of self-
36 37		regulation: Meta-analysis and test of a process model. Psychol Bull
38 39		regulation. Weta-analysis and test of a process model. I sychol Dun.
40 41		2017;143(11):1117–54.
42 43	19.	Fayers P, Aaronson N, Bjordal K. EORTC QLQ-C30 scoring manual [Internet].
44 45 46		EORTC. 2001. Available at http://www.eortc.be/qol/files/SCManualQLQ-
47 48 49		C30.pdf. Accessibility verified January 24th, 2018.
50		
51 52	20.	Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety
55 55		and Depression Scale. An updated literature review. J Psychosom Res. 2002;
56 57		52(2):69–77.
58 59	21.	Taylor RR, Jason LA, Torres A. Fatigue rating scales: an empirical comparison.
60		20

Psychol Med. 2000; 30(4):849-56.

- 22. Broadbent DE, Cooper PF, FitzGerald P, Parkes KR. The Cognitive Failures Questionnaire (CFQ) and its correlates. Br J Clin Psychol. 1982;21 (Pt 1):1–16.
- 23. Moss-Morris R, Weinman J, Petrie K, Horne R, Cameron L, Buick D. The RevisedIllness Perception Questionnaire (IPQ-R). Psychol Health. 2002;17(1):1–16.
- Hayes AF, Rockwood NJ. Regression-based statistical mediation and moderation analysis in clinical research: Observations, recommendations, and implementation. Behav Res Ther. 2017;98:39–57.
- Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol. 1986;51(6):1173–82.
- 26. Statistical Bulletin. Youth Cohort Study & Longitudinal Study of Young People in England : The Activities and Experiences of 18 year olds : England 2010. Available at https://www.gov.uk/government/statistics/youth-cohort-study-and-longitudinal-

study- of-young-people-in-england-the-activities-and-experiences-of-19-year-

olds-2010. Accessibility verified January 24th, 2018.

- O'Hara C, Moran A, Whelan JS, Hough RE, Stiller CA, Stevens MCG, et al. Trends in survival for teenagers and young adults with cancer in the UK 1992-2006. Eur J Cancer. 2015;51(14):2039–48.
- 28. Stark D, Bowen D, Dunwoodie E, Feltbower R, Johnson R, Moran A, et al. Survival patterns in teenagers and young adults with cancer in the United Kingdom:
  Comparisons with younger and older age groups. Eur J Cancer. 2015;51:2643–54.
- 29. Garg A, Boynton-Jarrett R, Dworkin PH. Avoiding the Unintended Consequences of

2		
2 3 4		Screening for Social Determinants of Health. JAMA. 2016;316(8):813.
5 6	30.	Jorm AF, Christensen H, Korten AE, Jacomb PA, Henderson AS. Memory complaints
7 8		as a precursor of memory impairment in older people: a longitudinal analysis over 7-8
9 10		years. Psychol Med. 2001;31(3):441–9.
12 13	31.	Eysenck MW, Derakshan N, Santos R, Calvo MG. Anxiety and cognitive
14 15		performance: Attentional control theory. Emotion. 2007;7(2):336-53.
16 17	32.	Macmillan Cancer Support. Holistic Needs Assessment. Care and Support Planning.
18 19 20		Available from:
20 21 22		http://be.macmillan.org.uk/Downloads/CancerInformation/ResourcesForHSCP/Inform
22		
24 25		ationResources/MAC16266HNAHowtoguide2016A4DIGITALAW.pdf. Accessibility
26 27		verified January 24 <sup>th</sup> , 2018.
28 29	33.	Wagner EH, Glasgow RE, Davis C, Bonomi AE, Provost L, McCulloch D, et al.
30 31		Quality improvement in chronic illness care: a collaborative approach. Jt Comm J Qual
32 33		Improv. 2001;27(2):63-80.
35 36	34.	Wilkinson R, Marmot M. Social Determinants of Health: the Solid Facts. World Heal
37 38		Organ. 2003;2(2):1–33.
39 40	35.	Taylor RM, Aslam N, Lea S, Whelan JS, Fern LA. Optimizing a Retention Strategy
41 42		with Young People for BRIGHTLIGHT, a Longitudinal Cohort Study Examining the
43 44		Value of Specialist Cancer Care for Young People. J Adolesc Young Adult Oncol
45 46		
47 48		2017; 6(3):459-469.
49 50	36.	Ashley L, Marti J, Jones H, Velikova G, Wright P. Illness perceptions within 6 months
51 52		of cancer diagnosis are an independent prospective predictor of health-related quality
53 54		of life 15 months post-diagnosis. Psychooncology. 2015;24(11):1463-70.
55 56 57	37.	Trikkalinou A, Papazafiropoulou AK, Melidonis A. Type 2 diabetes and quality of life.
58 59		World J Diabetes. 2017;8(4):120–9.
60		22

- Dijkers MPJM. Quality of life of individuals with spinal cord injury: a review of conceptualization, measurement, and research findings. J Rehabil Res Dev. 2005; 42(3 Suppl 1):87–110.
  - 39. Palacios JE, Khondoker M, Achilla E, Tylee A, Hotopf M. A Single, One-Off Measure of Depression and Anxiety Predicts Future Symptoms, Higher Healthcare Costs, and Lower Quality of Life in Coronary Heart Disease Patients: Analysis from a Multi-Wave, Primary Care Cohort Study. PLoS One. 2016;11(7):e0158163.

# Illustrations

## Tables

		Mean (SD)	Observed range	Possible range
Patient	Age	36.7 (9.01)	19-50	-
characteristics	Sex	Female=31	-	-
		Male=26		
	Education	Secondary =1	-	-
		College = 13		
		University = 43		
	Years since treatment	2.75 (1.87)	-	-
IPQ-R	Identity	6.18 (3.33)	0-12	0-14
	Timeline (Acute/Chronic)	17.41 (4.29)	5-28	0-30
	Consequences	31.09 (5.28)	8-30	0-30
	Personal control	19.18 (4.81)	8-30	0-30
	Treatment control	18.47 (3.59)	6-25	0-25
	Coherence	19.27 (3.83)	9-25	0-25
	Timeline cyclical	11.99 (3.67)	4-21	0-30
	Emotional representation	18.9 (5.62)	6-30	0-30

2
3
4
5
6
7
, 8
a
10
10
11
12
13
14
15
10
1/
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
<u>1</u> 2
-1-J ///
-1-1 1 E
40

1

EORTC – QLQ-C30	Quality of life	64.26 (20.76)	16-100	0-100
	(Global health status)			
CFQ	Cognitive complaints	46.78 (18.21)	7-87	0-100
CFS	Fatigue	16.35 (3.35)	8-26	0-33
HADS	Anxiety	8.62 (3.85)	0-21	0-21
	Depression	4.84 (4.01)	0-20	0-21

 Table 1. Descriptive data for all sociodemographic patient characteristics, and variables included in analyses. Abbreviations: IPQ – Illness

 Perceptions Questionnaire – Revised; EORTC – QLQ-C30 – European Organisation for the Research and Treatment of Cancer – Quality of Life

 Questionnaire – Core 30; CFQ- Cognitive Failures Questionnaire; CFS – Chalder Fatigue Scale; HADS – Hospital Anxiety and Depression

 Scale; SD – standard deviation.

CFS – Cin.

	SCC	Fatigue	Anxiety	Depression	ID	Time	Conseq	Personal	Treat	Coherence	Cycle	Emotion
								Ctrl	Ctrl			
QoL	66**	49**	61**	71**	45**	39*	32*	.09	.16	.22	26	30
SCC		.56**	.62**	.56**	.29*	.38**	.24	20	23	05	.18	.22
Fatigue			.53**	.58**	.33*	.36**	.15	.04	03	002	.15	.30*
Anxiety				.67**	.44**	.26	.29*	26*	22	19	.44**	.58**
Depression					.49**	.32**	.32*	19	16	10	.26*	.39*
ID						.34*	.07	28*	27*	33*	.08	.11
Time				Ur.			.28*	03	.02	.004	.09	.23
Conseq					P			30*	.02	03	.67**	.59**
Personal Ctrl					0				.51**	.25	13	19
Treat Ctrl					C	1				.44*	03	.07
Coherence						1	0,				22	15
Cycle								6				.69**

 Table 2. Bootstrapped correlations between quality of life (QoL, EORTC Quality of Life Questionnaire, global health status score), emotional distress (anxiety and depression, Hospital Anxiety and Depression Scale), fatigue (Chalder Fatigue Scale), subjective cognitive complaints (SCC, Cognitive Failures Questionnaire) and dimensions of illness perceptions (Illness Perceptions Questionnaire-Revised) – identity (ID), timeline of illness (Time), consequences of illness (Conseq), Personal control over illness (Personal Ctrl), Treatment control (Treat Ctrl),

 Coherence, Timeline Cyclical (Cycle), and Emotional representation of illness (Emotion). **Bold:** moderate (.30-.49) and large (>.50) correlations between factors. Light grey: factors included in mediation analyses. \*p<.05, \*\*p<.01, \*\*\*p<.001.

For peer Peview

Relationship	a (p)	b (p)	Direct pathway	Total effect c (p)	Indirect pathway	Effect size [95%	P <sub>m</sub> (%
	[95%CI]	[95%CI]	c' (p) [95%CI]	[95%CI]	a*b [95%CI]	CIJ	
	Model/Mediation	1: IPs (Identity/Tim	eline) - Emotional	distress (Anxiety/D	epression)/Fatigue-S	SCC	
Identity-Anxiety-	0.57 (.0004) [.27 to	1.69 (.008) [.46 to					
SCC	.88]	2.92]			.97 [.19 to 2.31]	.18 [.04 to .42]	6
Identity - Depression	.59 (.0001)[.31 to	.78 (.26) [59 to	34 (.60) [-1.62	1.60 (0.03) [.19 to			
- SCC	.88]	2.17]	to .95]	3.01]	.47 [21 to 1.13]	.08 [04 to .21]	2
		1.46 (.04) [.07 to		$\sim$			
dentity-Fatigue-SCC	.34 (.009) [.08 to .59]	2.84]		101.	.49 [009 to 1.20]	.09 [002 to .21]	3
Timeline-Anxiety-	.26 (.05) [003 to	1.64 (.008) [.44 to					
SCC	.52]	2.84]			.42 [.04 to 1.12]	.09 [.009 to .24]	2
Timeline-Depression-		.57 (.39) [76 to	.71 (.13) [22 to	1.65 (.003) [.58 to			
SCC	.30 (.01) [.06 to .55]	1.89]	1.65]	2.72]	.17 [18 to .51]	.04 [04 to .11]	1
Timeline-Fatigue-		1.21 (.09) [19 to					
SCC	28 (.005) [.09 to .49]	2.62]			.35 [05 to .80]	.08 [01 to .20]	2

**Clinical Rehabilitation** 

Page	30	of 41	
------	----	-------	--

	Model/Mo	ediation 2: Emotion	al distress (Anxiety	//Depression)/Fatigi	ue - SCC - QoL		
Anxiety - SCC - QoL	2.7 (<.0001) [1.79 to	50 (.0008) [79	0 (.0008) [79   1.64 (.009) [-2.86   -3.00 (<.0001) [-				
	3.6]	to22]	to42]	4.05 to -1.95]	.57]	27 [46 to12]	45%
Depression - SCC -	2.58 (<.0001) [1.57	42 (.0009) [66	-2.56 (<.0001) [-	-3.65 (<.0001) [-	-1.09 [-1.96 to -		
QoL	to 3.59]	to18]	3.66 to -1.46]	4.64 to -2.66]	.46]	21 [35 to09]	30%
	3.05 (<.0001) [1.83	62 (<.0001) [89	-1.18 (.12) [-2.69	-3.07 (.0001) [-	-1.89 [-3.22 to -		
Fatigue - SCC - QoL	to 4.26]	to34]	to .32]	4.53 to -1.62]	.88]	30 [51 to14]	62%
	Model/Mediation 3	3: IPs (Identity/Time	eline) - Emotional o	distress (Anxiety/De	epression)/Fatigue -	QoL	1
Identity - Anxiety -	.57 (.0004) [.27 to	97 (.14) [-2.28 to		2			
QoL	.88]	.323]		CV:	56 [-1.42 to .22]	09 [22 to .04]	19%
dentity - Depression	.59 (.0001) [.31 to	-2.38 (.002) [-3.84	83 (.22) [-2.19	-2.97 (.0002) [-	-1.42 [-2.54 to -		
- QoL	.88/	to92]	to .53]	4.44 to -1.49]	.61]	23 [39 to10]	48%
Identity - Fatigue -		46 (.53) [-1.93 to	-				
QoL	.34 (.009) [.09 to .59]	1.01]			15 [73 to .26]	02 [11 to .04]	5%
Timeline - Anxiety -	26 ( 05) [- 003 to	-1.06(09)[-2.30	81 (.09) [-1.77	-1.88 (.002) [-3.07	- 27 [- 77 to 09]	- 05 [- 15 to 02]	14%

QoL	.52]	to .18]	to .14]	to69]			
Timeline -	20 ( 01) [ 0( +- 54]	-2.49 (.0006) [-			7([1514, 27]	161 20 4- 061	400/
Depression- QoL	.30 (.01) [.06 to .54]	3.86 to -1.12]			/0 [-1.51 to2/]	16 [29 to06]	40%
Timeline - Fatigue -	28(005)[00 to 10]	12 (.87) [-1.58 to			02 [ 50 to 42]	0.07 [ 11 to 0.0]	10/
QoL	20 (.00 <i>3)</i> [.09 10 .49]	1.33]			03 [30 t0 .43]	007 [11 10 .09]	1 / 0

**Table 3.** Preliminary analysis of a practical model that includes three mediation analyses describing the relationships between illness perceptions, quality of life and four potential mediators – anxiety, depression, fatigue, and subjective cognitive complaints. Abbreviations and measures: QoL – quality of life, EORTC Quality of Life Questionnaire; Fatigue – Chalder Fatigue Scale; Anxiety and Depression – Hospital Anxiety and Depression Scale; SCC – subjective cognitive complaints, Cognitive Failures Questionnaire; IPs – illness perceptions (Illness Perceptions Questionnaire – Revised). **In bold:** statistically significant pathways suggesting mediation. *In italics:* statistically significant pathways *not* associated with mediation.

# Figures



**Figure 1.** Hypothesized model for the relationship between illness perceptions, emotional distress, fatigue, subjective cognitive complaints, and quality of life. The model was tested through three mediation analyses focusing on the relationship between illness perceptions and subjective cognitive complaints (blue); distress/fatigue and quality of life (orange), and illness perceptions and quality of life (red).



**Figure 2.** Recruitment process leading to the inclusion of 57 post-treatment cancer patients in the study

**Clinical Rehabilitation** 



 **Clinical Rehabilitation** 

Figure 3. Scatterplot depicting individual quality of life scores for the participants included in the study.

For peer Perieu

**Clinical Rehabilitation** 



Figure 4. Graphical depiction of one of the relationships in Model/Mediation 1 - Identity, Anxiety, and Subjective cognitive

complaints. The scatterplot depicts patient-level relationships between each 2 factors. As the identity of the illness increases,

http://mc.manuscriptcentral.com/clinrehab

 cognitive complaints (grey) as anxiety increases. In our model anxiety accounted for 60% of the relationship between illness identity

and cognitive complaints.

For per Per Periew



Model 2: Fatigue - Cognitive complaints - Quality of life



quality of life. The scatterplot depicts patient-level relationships between each 2 factors. As fatigue increases, quality of life

decreases (blue). As subjective cognitive complaints increase, fatigue increases (orange); quality of life decreases as cognitive

complaints increase (grey). In our model subjective cognitive complaints accounted for 62% of the relationship between fatigue and

quality of life.

For peer Review



Figure 6. Graphical depiction of one of the factor relationships in Model/Mediation 3 - Identity, Depression, Quality of life. The

scatterplot depicts patient-level relationships between each 2 factors. As the illness identity increases, quality of life decreases

http://mc.manuscriptcentral.com/clinrehab

 Clinical Rehabilitation

In our model anxiety accounted for 48% of the relationship between identity and quality of life.

For per per perieu