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QUALITY OF LIFE AMONG PATIENTS WITH A BRAIN TUMOR AND THEIR CARERS

MONIKA JANDA, PHD, SUZANNE STEGINGA, PHD, DANETTE LANGBECKER, BPHEALTH, JEFF DUNN, PHD, DAVID WALKER, MD, ELIZABETH EAKIN, PHD

School of Public Health and Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia
Viertel Centre for Research in Cancer Control, Cancer Council Queensland, Brisbane, Queensland, Australia
Department of Neurosurgery, Royal Women's and Brisbane Hospital, Brisbane, Queensland, Australia
Cancer Prevention Research Centre, School of Population Health, University Queensland, Brisbane, Queensland, Australia

CORRESPONDING AUTHOR
Monika Janda, PhD
QUT School of Public Health and Institute of Health and Biomedical Innovation
Victoria Park Rd
Kelvin Grove 4059
Australia
Phone: ++ 61 7 3138 9674
Fax: ++61 7 3138 3130
E-mail: M.Janda@qut.edu.au

SHORT RUNNING HEAD: Brain tumours and quality of life

ABSTRACT

Objective: To assess the quality of life and psychosocial well-being of brain tumour patients and their carers.

Methods: A cross-sectional postal survey was completed by 75 patients and 70 carers (response rate 29.8%) who were listed on a community-based brain tumour support group database. Measures were the Functional Assessment of Cancer Therapy (FACT-G) and the Hospital Anxiety and Depression Scale (HADS). Queensland population-based norms for the FACT-G were used for comparison.

Results: On average compared to population norms, FACT-G summary scores of patients (mean = 74.6, SD =18.6) and carers (mean = 76.7, SD = 17.7) were between one half and one standard deviation lower, representing a clinically significant reduction in quality of life. Among patients and carers, 30% and 40% reported anxious mood and 17% and 10% depressed mood on the HADS, respectively. Significant correlations were observed between FACT-G and HADS subscales, in particular emotional well-being and anxiety, as well a physical and functional well-being and depression, and between patients' and their carers' quality of life. Among patients, predictors of lower quality of life were older age and female gender, whereas for carers there was a trend for lower quality of life among those looking after a patient with high-grade disease.

Conclusions: The degree of detriment to quality of life by a brain tumour for both patients and their carers is similar and clinically significant. The association between the FACT-G subscales and the HADS indicate that improvements could be achieved by alleviating emotional distress and improving functional well-being.

KEY WORDS: anxiety, brain tumours, carers, depression, patients, quality of life

Introduction

The last 20 years have seen advances in the treatment and outcomes for patients with a brain tumour. These include refinements of surgical techniques, introduction of new chemo- and radio-therapeutic regimens such as temozolomide for glioma and trials of novel biologic therapies [1, 2]. However, due to their anatomical location, most brain tumours increase the intracranial pressure and displace healthy brain tissue, thus resulting in temporary or permanent disruptions to the associated executive functions, and overall survival is till poor [1] and some centres did not observe a beneficial trend in prognosis among patients with high- or low-grade gliomas [3] .

Due to the severity of disease and subsequent focus on improving survival, quality of life and psychosocial well-being of survivors of brain tumours have only more recently received attention [4]. Frequently, self-reported quality of life does not correlate well with measures of physical or neurological functioning such as the Karnofsky Performance Scale [5, 6], leading to the development of brain tumours specific quality of life scales [5, 7]. For example, the Functional Assessment of Cancer Therapy- General (FACT-G) is one of the most widely used quality of life assessment instruments in cancer research [8, 9] and recently general population based norms have also become available [10]. A brain tumour specific quality of life subscale to accompany the FACT-G was developed in 1995 [7]. Using this brain tumour specific instrument, comparatively good quality of life among samples of brain tumour patients has been reported in some studies [7], while other studies noted significant reductions in quality of life among patients treated for a brain tumour [5, 11]. Up to 90% of brain tumour patients self-report morbidity in one and 70% in two or more health attributes such as cognition, mobility, vision, hearing, speech or pain, with more severe reductions in quality of life found to be associated with early mortality from a brain tumour [12]. This is in line with several other studies, which demonstrated diminished survival prospective among brain tumour patients with depressed mood or changes in mental status – in particular among patients with low grade disease [13-16], and consistently, higher scores of depression were associated with lower quality of life [17-19]. However, to date, most research on the quality of life of patients with a brain tumour was conducted using clinic derived samples, thus little is known about the quality of life and mood among community dwelling patients with a brain tumour.

While some patients with a brain tumour will make a complete recovery after treatment, most will require at least some support and care in subsequent years [20, 21]. Care is primarily provided by relatives and friends and few cancer patients rely solely on formal care [22, 23]. Stress associated with caregiving can be considerable, and this has been shown to impact on quality of life in various carer populations, including carers of patients with Alzheimer's disease, cancer in general and brain tumours in particular [22-26]. Patients and carers quality of life has been shown to be closely associated among breast and colorectal cancer survivors [27-29]. Earlier, we identified a number of unmet supportive care needs which may result in reductions in quality of life of patients with a brain tumour and their and carers [30].

To extend the knowledge about how patients living in the community and their carers fare in the medium to long term, the present study aimed to describe the quality of life and psychosocial well-being of patients with a brain tumour and their carers who subscribed to a dedicated brain tumour support network. A further aim was to compare the quality of life of patients with a brain tumour and their carers to population norms and to assess factors associated with low quality of life.

Methods

Approval for this study was obtained from the Behavioral and Social Sciences Research Ethical Review Committee of the University of Queensland, Australia. The Queensland Cancer Fund is a community-based not-for-profit organisation serving the Queensland population with cancer related information and support services. One of these services is a Brain Tumour Support Service which provides information about brain tumours, treatment, support agencies, rehabilitation services and practical assistance. The service holds regular meetings for patients, carers and health professionals interested in brain tumours at which a specific topic is presented and discussed by a health professional; provides opportunities for peer support through discussions with other people who have been affected by a brain tumour; and distributes quarterly newsletters.

Overall, 363 survey packages (containing a study information sheet, and patient and carer questionnaires) were mailed to current members of the Brain Tumour Support Service. Overall, of 363 survey packages mailed, 48 were returned to sender or returned with a note that the patient was deceased. After two written reminders, at

least one completed questionnaire was received from 94 households resulting in an overall response rate of 29.8%. Among the 94 households, 75 patients and 73 carers returned completed questionnaires. Of those, 53 patients-carer pairs from the same household responded, while within 23 households only the patient and within 20 households only the carer responded.

Measures

Patients and carers were asked to report on their own demographic details, quality of life and psychosocial well-being. The only exception from this was the questions about details of the brain tumour diagnosis and treatment where carers were asked to report on the patient's medical details.

Demographic and health characteristics: Patients and carers were asked to give their age, sex, education, work status, marital status, the number of children in the household, income and number of people dependent on that income. Patients and carers self-reported on the date of diagnosis of brain tumour, if the tumour was benign or malignant, type of tumour, and treatment received, as well as date of last treatment.

Quality of life: The Functional Assessment of Cancer Therapy was used to assess patients' and carers' own quality of life [8, 9]. Patients also completed a brain tumour specific subscale, which together with the FACT-General forms the FACT-Brain (FACT-BR) [7]. Carers completed the general population version of the FACT, (FACT-GP), which can be prorated to result in scores equivalent to the FACT-G. All questions are answered on a 5-point Likert-scale ranging from "not at all" to "very much". The FACT-G allows generation of 4 subscales indicating participants' physical well-being (range 0-28), social well-being (range 0-28), emotional well-being (range 0-24), and functional well-being (range 0-28), as well as the FACT-G summary score (0-108). Adding the brain tumour specific subscale for patients results in the FACT-Br score (range 0-160). Higher scores indicate better quality of life. Test-retest reliability for the FACT-Br was reported to be 0.78, and good convergent validity has also been reported for the FACT-Br [7]. Within the present sample, Chronbach alpha for the FACT-G among the patient group was 0.92, and 0.88 for carers.

Psychological Well-being: The Hospital Anxiety and Depression scale (HADS) was used to measure psychological distress in patients and carers. The HADS is a well validated questionnaire suitable for cancer populations as it contains only non-physical symptoms of both anxiety and depression, and has also been used extensively in non-clinical populations [31-34]. Participants indicate their agreement with each item on 4-point Likert scales with various anchors. According to scoring instructions, seven items are recoded and summarised to form the depression scale (range 0-21) and seven items form the anxiety scale (range 0-21). Participants who score 8-10 on either sub-scale are considered doubtful cases and those who score 11 or higher are considered cases with regards to anxiety or depression [32].

Statistical analysis

Descriptive analysis was undertaken to summarise patients' and carers' demographics and patients' health characteristics. It was expected that among members of the support service, patients with low-grade tumours would be overrepresented. To allow adjustment for this, all patient data were weighted using the 20-year prevalence of brain tumours by morphological subgroups in Queensland. Comparison with normative FACT-G quality of life data for the Queensland population was undertaken and patient and carers scores plotted against t-distributed normative scores. As recommended previously [10, 35], a diversion of ½ a standard deviation or more was regarded as a clinically significant difference from the normative score. Pearson correlations were used to assess correlation of quality of life, anxiety and depression reported among the 53 patient-carer pairs. Associations between quality of life and the HADS among patients and carers separately were also investigated utilising Pearson correlations. Patients' and carers' quality of life scores were then dichotomised where a clinical significant deviation from the population norms was observed (in other words, patients and carers were divided into 2 groups each, characterised by quality of life similar to the population and quality of life clinically significantly below the general population). Variables that were associated with quality of life in bivariate logistic regression were entered into a multivariate logistic regression analysis; non-significant variables were removed to achieve the most parsimonious model while retaining the best fit.

Results

Overall, of 363 survey packages mailed, 48 were returned to sender or returned with a note that the patient was deceased. After two written reminders, at least one completed questionnaire was received from 94 households resulting in an overall response rate of 29.8%. Among the 94 households, 75 patients and 70 carers returned completed questionnaires. Of those, 53 patients-carer pairs from the same household responded. Patients and carers reported on their own demographic characteristics, quality of life and mood. Carers were asked to report on the medical details of the patient with a brain tumour they were caring for.

The majority of participants in both groups were women (54.1% of patients and 64.3% of carers), and 53.5% of patients and 43.1% of carers were younger than 50 years. Other demographic details are listed in Table 1. The most common tumour morphologies reported by patients and carers were meningioma, glioblastoma and astrocytoma, and 58.7% of patients and 71.0% of carers self-reported the brain tumour to be malignant. Most patients had received a combination of two or more treatments, most commonly surgery followed by radiotherapy. More than 70% of patients had received their last treatment within the past year and a similar percentage of treatment within the past year was reported by the carers (Table 1).

FACT-G subscale and overall scores as well as HADS scores for patients and carers are reported in Table 2. Among the 53 patient-carer pairs living in the same household, significant correlations were found between patients' and carers' emotional and social well-being as well as overall quality of life but not between patients' and carers' physical or functional well-being. Reductions in several aspects of quality of life by ½ a standard deviation or more compared to the Queensland population were observed (Figure 1). Patients' overall quality of life as measured by the FACT-G was clinically significantly lower compared to the general population driven by low scores within the physical, emotional and function well-being subscales. Carers' overall quality of life, although 3 points higher than that of patients on average, was also clinically significantly lower than the quality of life among the general Queensland population, again driven mainly by reductions in the physical, emotional and function well-being subscales. Among the quality of life subscales in patients, low emotional well-being was most closely associated with anxiety, while

low physical and functional well-being was associated with depression. Similarly, in carers highest correlation coefficients were observed between low emotional well-being and anxiety as well as low functional well-being and depression (Table 3).

In bivariate analysis among patients, female gender (OR 5.8, 95% CI 1.8-18.1), age 50 years or older (OR = 2.6, 95% CI 0.94-7.4) were associated with lower quality of life, while no difference was found by education, current employment status, marital status, income, time since diagnosis, self-reported malignancy of the tumour, tumour morphology, or time since treatment. In multivariate logistic regression analysis, female gender and age 50 years and over remained significant predictors of low quality of life in patients when adjusting for tumour type (Table 4).

For carers, responsibility for a patient with a glioblastoma was associated with low quality of life in univariate analysis (OR= 6.7; 95% CI 1.8-25.2). In the adjusted analysis, there was some indication of better quality of life among older carers. There was a trend for carers who looked after a patient with glioblastoma to report low quality of life compared to carers looking after patients with other tumours (Table 4).

Discussion

This study suggests that on average, both patients with a brain tumour and their carers live with a clinically significant reduction in their overall quality of life compared to the general population. This finding holds true irrespective of the time since diagnosis or the time since last treatment. Among patients, women and older patients appear to be more susceptible to reductions in quality of life, while among carers, the burden of looking after a patient with glioblastoma has the greatest impact on quality of life. Preoperatively, quality of life has been reported to be worse in patients with highly malignant tumours as well as those with tumours located in the right hemisphere or in the anterior cortex compared with left hemisphere or posterior tumours [36, 37]. Also among a group of newly diagnosed high-grade glioma patients, quality of life scores (measured by the FACT-Br and a linear analogue scale) were found to be predictive of survival [38]. Klein et al. assessed quality of life using the SF-36 health survey to compare the quality of life among 68 newly diagnosed patients with glioma to general population norms and reported significant reductions of quality of life within all domains [39].

Similar to other studies within the present investigation, few predictors of reduced quality of life among patients were found [7, 38]. Apart from depression and anxiety strongly correlated with quality of life in this and others studies [14, 15, 18, 40], female gender was the only predictor of low quality of life in our study also reported by others [41, 42]. There was no apparent difference in quality of life depending on self-reported tumour histology, time since diagnosis or last treatment, again similar to results reported by others [43]. This indicates that living with a diagnosis of a brain tumour can be difficult for patients and their carers irrespective of the malignancy of the disease. This is further supported by the magnitude of detriment in quality of life observed among the patients and carers in our study when compared to the general population of Queensland. On the other hand, within the present study we did not measure other factors such as dispositional optimism, coping approaches or social support which could potentially explain some of the variance in patients' and carers' quality of life observed.

The finding that carers looking after a patient with high grade malignancies such as glioblastoma were somewhat more likely to report lower quality of life is likely to reflect the high burden associated with caring for family members with frequent and complex care needs. A significant number of these patients will be affected by neuro-psychological deficits, fatigue and pain which often parallel advancing disease [6, 43]. During focus groups and qualitative interviews carers of patients with a brain tumour reported that caring had a significant impact of on their own well-being [30]. This is reflected in the significant correlation between patients and carers overall quality of life in this study with patients and carers in the same household reporting similar reductions especially in their emotional and social well-being. Similar associations between patients and carers well-being have been reported previously among breast and colorectal cancer samples [27-29], indicating that supportive care programs need to be directed at both the patients and their carers to effectively alleviate distress.

While levels of anxiety and depression measured by the Hospital Anxiety and Depression Scale were high, with at least 30% of patients and carers identified as likely cases with elevated anxious mood, and at least 17% of patients and 10% of carers identified as likely cases with elevated depressed mood, they are comparable to those observed among other cancer populations [31, 33, 34]. In a previous study

among patients with a brain tumour, using a health utility instrument, up to 50% of patients reported emotional morbidity through anxiety [12]. Further research is needed to understand the physical and psychological factors associated with high levels of anxiety and depression in brain tumour patients and their carers as well as strategies for their reduction.

Limitations

Several limitations of this study must be noted. Prospective studies have highlighted the difficulty of collecting and interpreting data from patients with a brain tumour, due to a high prevalence of neurological morbidity and disease progression [38, 44]. It is likely that patients with more severe reductions in quality of life, as well as those with neuropsychological deficits will have decided not to participate in this survey. Also the patients and carers attending the Brain Tumour Support Service are likely to represent a selected group of active support seekers. Such a group may have a higher prevalence of people with better quality of life and thus the resources to attend support groups or alternative of those with poorer quality of life who search more than others for support to improve their situation. Similar to other studies conducted among populations affected by a brain tumour, the response rate amongst the potential participants was low [45]. However, the calculated response rate of 29.8% may be a low estimate, as some of the addresses on the mailing list will have contained persons interested in brain tumour support in general who wished to receive the Brain Tumour Support Group's correspondence, but were not necessarily a patient or carer. The fact that tumour morphologies reported by patients were roughly similar to the 20-year prevalence of brain tumours in Queensland leaves us confident that the bias through the low response rate should be minimal. However, another caveat when interpreting the results of the study is related to the brain tumour morphology and malignancy of the tumour, which was derived from patient and carer self-reports only and was not checked against medical records.

A major strength of the present investigation is the comparison with population-based normative data for the FACT-G, which have only very recently become available in the USA [10] and Queensland, Australia [46] allowing comparison of patient and carer findings with age-matched norms. Patients' and carers' quality of life could therefore be described in the magnitude and direction in which it deviates from

population norms making the interpretation of this cross-sectional data much more meaningful. In addition, access to the 20-year prevalence data of brain tumours in Queensland through the Queensland Cancer Registry allowed weighting the patient data to the expected number of patients within each subgroup living in Queensland.

In summary, the clinically significantly lower levels of quality of life observed among patients with a brain tumour and their carers compared to the general population and the association between patients' and carers' quality of life suggest that supportive care services need to be further improved to alleviate the burden this diagnosis takes on patients and carers.

Table 1 Patient (n = 75) and carer (n=70) characteristics *****

	Patients		Carers	
	n	%	n	%
Sex				
Women	40	54.1	45	67.2
Men	34	45.9	22	32.8
Age				
Less than 50 years	38	53.5	28	43.1
50 years and over	33	46.5	37	56.9
Education				
University degree	20	27.0	12	17.6
Trade/technical certificate or diploma	32	43.2	21	30.9
Senior high school or less schooling	22	29.7	35	51.5
Current Employment Status				
Not currently employed	46	62.2	30	44.1
Employed part-time	9	12.2	17	25.0
Employed full-time	19	25.7	21	30.9
Reason for Not Working				
Looking for work	7	13.2	7	17.5
Unable to work due to illness	25	47.2	0	0.0
Retired/ Student	15	28.3	17	42.5
Home carer	6	11.3	16	40.0
Marital Status				
Married	46	62.2	55	80.9
Living together	4	5.4	4	5.9
Divorced/ Separated/ Widowed	12	16.2	9	13.2
Never married	12	16.2	0	0.0
Income				
<$20,000	22	29.3	11	16.2
$20-40,000	15	20.0	18	26.5
$40-60,000	12	16.0	9	13.2
$60-80,000	10	13.3	16	23.5
$80-100,000	3	4.0	4	5.9
>$100,000	3	4.0	4	5.9
Don't know/refuse to answer	10	13.3	6	8.8

Table 1 continued

	Patients		Carers	
	n	%	n	%
Time since BT diagnosis				
5 years or less	29	46.0	38	55.1
>5 to 10 years	20	31.7	17	24.6
>10 years	14	22.2	14	20.3
Tumour malignancy				
Malignant	44	58.7	49	71.0
Benign	31	41.3	20	29.0
Type of tumour				
Meningioma	16	21.6	9	13.2
Glioblastoma	10	13.5	14	20.6
Astrocytoma	11	14.9	11	16.2
Pituitary adenoma	8	10.8	5	7.4
Oligodendroglioma	7	9.7	8	11.8
Other	21	10.9	18	26.5
Don't know	1	1.4	3	4.4
Treatments undertaken**				
Chemotherapy	16	23.5	31	44.3
Radiotherapy	44	64.7	57	81.4
Surgery	53	77.9	55	78.6
Other treatment	2	2.9	4	5.7
No treatment	2	2.9	0	0.0
Time since last treatment				
5 years or less	53	73.6	48	75.0
>5 to 10 years	10	13.9	8	12.5
>10 years	9	12.5	8	12.5

*Tumour and treatment characteristics reported by patients and carers do not correspond one to one as within some households only the patients or only the carers participated in the survey. Numbers within categories vary slightly due to missing responses.
** Multiple responses possible

Table 2 Quality of life, HADS anxiety and depression scores amongst 75 patients and 70 carers

	Mean (sd) scores		Correlation coefficient**; p-value
	Patients*	Carers	
Domain			
Physical Well-Being	18.5 (6.4)	23.3 (3.8)	r = 0.19, p = 0.18
Social/Family Well-Being	20.1 (6.3)	18.3 (7.3)	r = 0.38, p = 0.007
Emotional Well-Being	16.7 (5.1)	17.5 (5.9)	r = 0.31, p = 0.03
Functional Well-Being	17.9 (6.7)	17.8 (6.9)	r = 0.21, p = 0.15
Overall score			
Brain tumour specific subscale	61.7 (17.3)	NA	NA
FACT-G	74.6 (18.6)	76.7 (17.7)	r = 0.32, p = 0.03
FACT-Br	136.0 (32.9)	NA	NA
Other indicators			
Anxiety	8.1 (4.2)	9.2 (4.6)	r = 0.28; 0.04
% 11+ points	29.8	39.7	
Depression	5.7 (4.9)	5.4 (4.0)	r = -0.32; 0.02
% 11+ points	17.2	10.3	

Abbreviations: HADS: Hospital Anxiety and Depression Scale, FACT: Functional Assessment of Cancer Therapy

* Patient scores are weighted to the 20-year prevalence of brain tumours in Queensland

** Pearson correlation of patient and carer pairs from 53 households

Table 3 Correlation between quality of life and anxiety and depression for 75 patients with a brain tumour and for 70 carers of patients with a brain tumour (carers results marked in bold)

	PWB	SWB	EWB	FWB	FACT-G	Anxiety	Depression
PWB		0.34	0.59	0.73	0.85	-0.64	-0.78
SWB	**0.28**		0.27	0.48	0.68	-0.34	-0.33
EWB	**0.58**	**0.13**		0.52	0.73	-0.72	-0.54
FBW	**0.49**	**0.47**	**0.46**		0.88	-0.58	-0.81
FACT-G	**0.71**	**0.69**	**0.69**	**0.84**		-0.72	-0.79
Anxiety	**-0.64**	**-0.22**	**-0.77**	**-0.52**	**-0.70**		0.51
Depression	**-0.67**	**-0.27**	**-0.54**	**-0.71**	**-0.71**	**0.66**	

Note: Bold figures represent scores derived from carers
Need Abbreviations PWB = Physical Well-being, SWB = Social Well-being, EWB = Emotional Well-being, FWB = Functional Well-being, FACT-G = Functional Assessment of Cancer Therapy, Anxiety = Anxiety Subscale from the Hospital Anxiety and Depression Scale, Depression = Depression Subscale from the Hospital Anxiety and Depression Scale.

Table 4 Adjusted multivariate logistic regression analysis of factors predicting low quality of life* in patients with a brain tumour and their carers

	PATIENTS	CARERS
	Adjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Gender		
Men	1.00	1.00
Women	7.76 (2.14-28.1)	1.09 (0.31-3.82)
Age		
18-49	1.00	1.00
50+	4.90 (4.89-134.9)	0.72 (0.21-2.45)
Diagnosis		
Oligodendroglioma	1.00	1.00
Glioblastoma	1.41 (0.19-10.4)	3.94 (0.60-25.6)
Astrocytoma	1.36 (0.22-8.37)	0.31 (0.04-2.44)
Other benign	0.19 (0.10-3.59)	0.70 (0.11-4.31)
Other malignant	2.44 (0.43-13.9)	0.78 (0.13-4.75)

Abbreviations: CI = Confidence Interval.
The variables in the model are adjusted for all other factors.
* Low quality of life was defined as a score one standard deviation or more below the mean normative score derived from the Queensland General Population
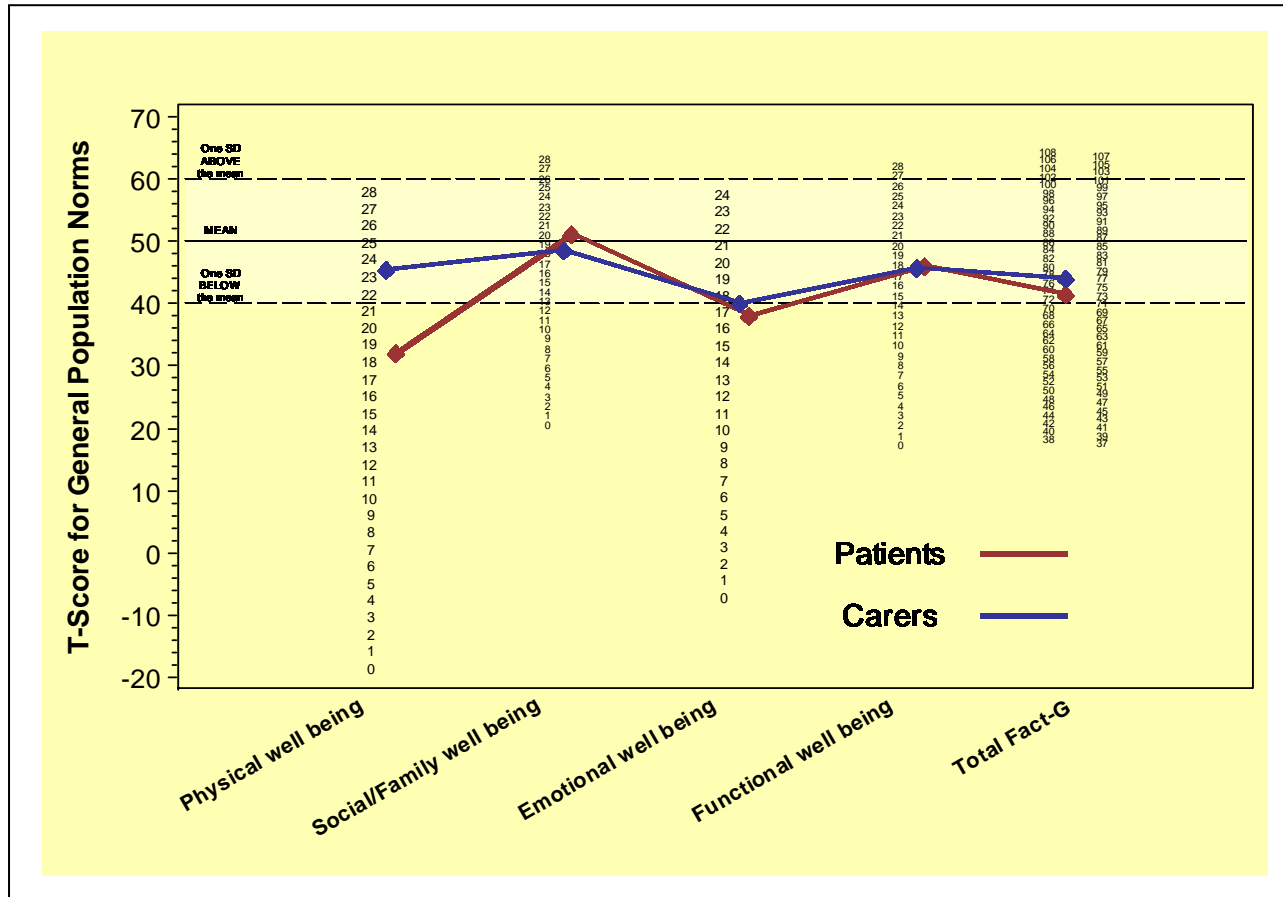
Figure 1 FACT-G subscale and total score of patients and carers plotted against Queensland population normative scores

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