

ORIGINAL ARTICLE

Quality of life in patients with prostate cancer: development and application of a hybrid assessment method

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Investigator-derived quality of life (QoL) instruments such as the Functional Assessment of Cancer Therapy—Prostate (FACT-P) questionnaire do not allow participants to weight the relative importance of QoL domains. We investigated the effect of allowing patients the ability to weight the relative importance of the five areas included in the FACT-P (Physical, Social, Emotional and Functional well-being, and Additional concerns). Patients ($n = 150$) completed the FACT-P and gauged the relative importance of each QoL domain using a direct-weighting approach. This was then used to provide an adjusted Hybrid QoL score. Patients also completed a Visual Analogue Scale. Patients considered Social well-being to be the most important domain and Additional concerns to be the least important. When patient weightings were taken into account overall QoL scores increased. The validity of the Hybrid score was supported by its ability to distinguish between patients with metastatic and locoregional disease and its ability to detect expected decreases in global QoL over time. Application of the direct-weighting approach to the FACT-P allows assessments to more accurately reflect individual QoL. Unadjusted QoL scores may lead researchers to incorrectly estimate the true QoL of respondents.

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Introduction

Quality of life (QoL) assessment instruments are widely used in cancer clinical trials and have an established place in measuring the impact of cancer and its treatment on patients' well-being.^{1,2} The Functional Assessment of Cancer Therapy—General (FACT-G) questionnaire is one of the most widely used Health-Related Quality of Life (HRQoL) instruments.³ It measures HRQoL in four different domains (Physical well-being, Functional well-being, Emotional well-being and Social/Family well-being). To this core questionnaire can be added various cancer-site specific modules for use in particular cancer populations. Thus, the Functional Assessment of Cancer Therapy—Prostate (FACT-P) questionnaire contains an additional series of questions specific to prostate cancer⁴ and the FACT-B some specific questions about breast cancer.⁵ QoL data can be reported with respect to the specific QoL domains, or as a global QoL score obtained from summing the various subscales.

The FACT system has a number of advantages as a method of measuring QoL. The questionnaires have been

developed to reflect patients' concerns, they are reliable, reproducible and have been validated in numerous studies.^{3–7} One drawback with the FACT system (and with other investigator-derived QoL questionnaires) is the inability of individual patients to express a view about how important they consider the various QoL domains to be to their particular circumstances. Thus, if a subject has a very 'poor' functional well-being but does not consider this to be a particularly important contributor to his/her overall QoL, then this will not be suitably reflected in his/her FACT score.

Individualized Quality of Life (IQoL) assessment methods do not rely on the use of specific questionnaires, but allow respondents the opportunity to describe QoL in their own terms.^{8,9} The Schedule for the Evaluation of Individualized Quality of Life—Direct Weighting (SEIQoL-DW) interview¹⁰ allows subjects to nominate the five areas of their life that they consider to be the most important, to score how well they are performing in each area and to rate the relative importance of each area. One of the drawbacks with the SEIQoL-DW approach is that it is not possible to make direct comparisons between participants in a study with respect to particular QoL domains. Thus, it would not be possible to judge the effect of an intervention on 'anorexia' using SEIQoL-DW unless all of the subjects in the study nominated this as one of their five most important QoL domains.

One way to obtain both the systematic coverage of key QoL domains afforded by the FACT system and the

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individuality afforded by the SEIQoL-DW interview would be to administer both instruments to all participants in a clinical study.¹¹ However, this approach is time-consuming (adding approximately 20 min to data collection per subject) and resource intensive. The purpose of this study was to explore an alternative approach to measuring QoL that relies on a combination of the FACT questionnaire with the 'direct-weighting' method of gauging QoL domains employed in the SEIQoL-DW. It was hypothesized that this 'hybrid' approach would be feasible to use and would provide a more nuanced characterization of QoL than use of the FACT questionnaire in isolation.

Patients and methods

This was a prospective, observational study. The study protocol was approved by the Wandsworth Local Research Ethics Committee and received Research and Development approval from St George's Healthcare NHS Trust.

Population

As part of a larger study¹¹ patients with prostate cancer were recruited from the uro-oncology outpatient department and from among hospice inpatients. To be eligible for the study, patients had to have a proven diagnosis of prostate cancer, sufficient English language skills to participate in a semi-structured interview and be able to give written informed consent.

Patients who re-attended clinic at least 1 month later were invited to participate in a second interview and to complete a second questionnaire. Every effort was made to recruit all eligible patients at each clinic, however, in the absence of the research assistant (due to sickness or annual leave) recruitment was suspended.

Assessments

Subjects were asked to complete a number of questionnaires. A more detailed description of the FACT-P and the SEIQoL-DW is provided in the accompanying paper.¹¹

The FACT-P questionnaire version 4⁴ is a 39-item questionnaire consisting of five domains; 'Physical well-being', 'Social/Family well-being', 'Emotional well-being', 'Functional well-being' and 'Additional concerns' (consisting of items relating specifically to prostate cancer and/or its treatment).

Subjects were asked to perform a direct weighting of the FACT-P domains. The direct-weighting procedure is a method of quantifying the relative importance (or weight) that each subject attaches to QoL domains. The direct-weighting procedure was originally developed to replace 'judgement analysis' as a means of allocating weights to QoL domains identified during the SEIQoL interview.¹² It has subsequently been successfully used in numerous studies of QoL as part of the SEIQoL-DW interview.^{10,13-16} In this study the direct-weighting procedure was applied to the five domains of QoL included in the FACT-P interview. Subjects were asked to weight the relative importance of each of these domains using a pie chart. The domains were listed on each of five

overlapping rotating discs. Subjects were then asked to adjust the position of the discs such that the relative size of each 'slice' represented the relative importance that the individual accorded to each QoL 'domain'. The domains were summarized to the subject in the following terms; the 'Physical well-being' subscale was described as 'Physical Health', the 'Social/Family well-being' subscale was described as 'Family and Social life', the 'Emotional well-being' subscale was described as 'Mental Health', the 'Functional well-being' subscale was described as 'My ability to function and 'get on' with life' and the 'Additional concerns' subscale was described as 'The side-effects of my cancer and/or its treatment'.

QoL was also assessed using a Visual Analogue Scale (VAS). Subjects were asked to mark the point on a 100 mm horizontal line that best represented their global QoL. The anchor descriptors were 'worst possible' at 0 mm and 'best possible' at 100 mm.

Subjects completed the SEIQoL-DW method.¹⁰ Details of the administration of the SEIQoL-DW and a description of the commonly reported concerns of patients with prostate cancer have been reported in the accompanying paper.¹¹

Patients' Eastern Cooperative Oncology Group (ECOG) performance status and the time taken to complete each instrument were recorded. At the second assessment patients were asked whether they felt that their QoL was 'better', 'the same' or 'worse' than at the first assessment.

Statistical methods

Data were summarized using means and standard deviations. Comparisons between patients were made using unpaired *t*-tests, within-group comparisons were analysed using paired *t*-tests. For comparison of proportions χ^2 -tests were used. Sensitivity to change was evaluated by calculating effect sizes.¹⁷

The total FACT-P score was calculated by addition of the five subscale scores. The 'Physical', 'Social' and 'Functional' subscales consist of seven items, the 'Emotional' subscale consists of six items and the 'Additional concerns' subscale has twelve items. This distribution of items in the FACT-P means that in effect the relative weighting of the five subscales is 7 of 39 (17.9%) for the 'Physical', 'Social' and 'Functional' subscales', 6 of 39 (15.4%) for the 'Emotional' subscale and 12 of 39 (30.8%) for the 'Additional concerns' subscale.

Thus a patient who scored 72, 65, 75, 42 and 90 on the physical, social, emotional, functional and additional concerns subscales respectively would have an 'unadjusted' FACT-P score of

$$\begin{aligned} & (72 \times 17.9) / 100 + (65 \times 17.9) / 100 + (75 \times 15.4) / 100 \\ & + (42 \times 17.9) / 100 + (90 \times 30.8) / 100 \\ & = 71.3 \end{aligned}$$

If the same subject had allocated weights of 25, 17, 10, 40 and 8% to the physical, social, emotional, functional and additional concerns subscales using the direct-weighting procedure, then the total 'Hybrid' score would have been

$$\begin{aligned} & (72 \times 25) / 100 + (65 \times 17) / 100 + (75 \times 10) / 100 \\ & + (42 \times 40) / 100 + (90 \times 8) / 100 \\ & = 46.2 \end{aligned}$$

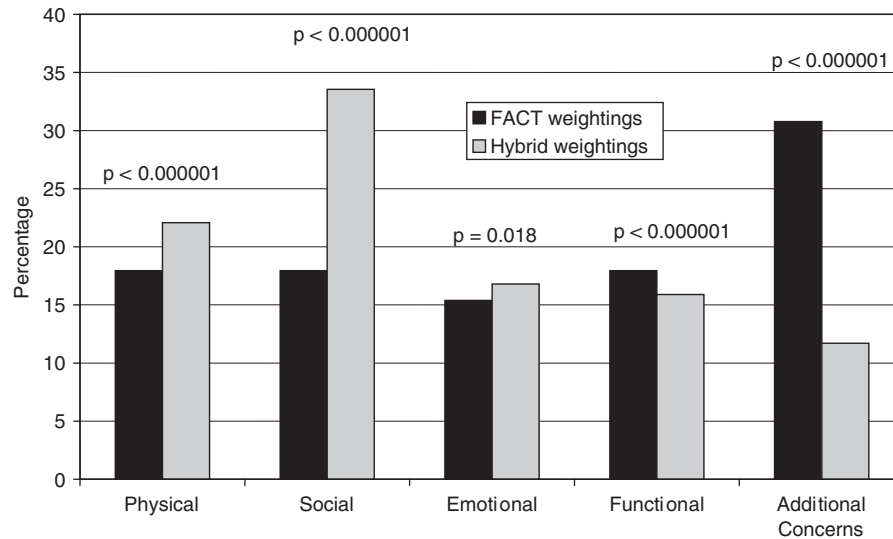


Figure 1 Comparative weightings.

Thus although in both cases the subject rated his performance the same on each of the subscales the overall QoL score would be markedly different on the two instruments (because the respondent gave a much higher weighting to functional items and a much lower weighting to the 'additional concerns' items).

Results

From the 194 subjects included in the original study,¹¹ 155 patients were invited to participate in an assessment of the direct-weighting procedure of FACT-P domains. Five subjects were subsequently excluded from the analysis (one man failed to understand the direct-weighting procedure and four men did not complete a sufficient number of the FACT items to provide useable data). The mean age of the remaining 150 subjects was 70 (s.d. 8.1) years. Patients had suffered from prostate cancer for a mean of 197 (s.d. 140) weeks prior to study entry. The mean prostate-specific antigen of study entrants was 263.0 ng ml^{-1} (s.d. 667.1, $n = 78$), 72 of 150 (48%) patients had metastatic disease. Most patients had a good ECOG performance status (PS 0, $n = 67$, 45%; PS 1, $n = 53$, 35%; PS 2, $n = 22$, 15%; PS 3, $n = 5$, 3%; PS 4, $n = 3$, 2%). Of the 150 patients who underwent a first assessment, 78 proceeded to a second assessment a mean of 21 (s.d. 9.2) weeks later. Among them 8 subjects had to be excluded from the analysis because of incomplete data, leaving 70 subjects with analysable data at both time points. The mean time taken to complete the FACT-P was 13.5 min (s.d. 4.6) and the mean time taken to complete the direct-weighting procedure was 5.4 min (s.d. 2.7).

Weighting of QoL domains

The FACT-P questionnaire consists of 39-items in five subscales. The total FACT-P score is simply the total of the five subscale scores. However, because some subscales contain more items than others, they make a

disproportionate contribution to the total FACT-P score. Figure 1 illustrates the weightings that participants attributed to the different QoL domains when they were given the opportunity to do so, compared to the inherent weightings of the questionnaire itself (determined by the relative number of items in each domain). The FACT-P gives greatest weighting to the 'additional concerns' subscale (12 of 39 items) and least weighting to the 'Emotional well-being' subscale (6 of 39 items). However, patients considered the most important subscale to be 'Social well-being' and the least important domain to be 'Additional concerns'. The differences between the inherent weightings of the FACT-P and the direct weightings of the Hybrid were statistically significant.

Global QoL scores on FACT-P and Hybrid

Global FACT-P scores were re-calculated using the individual direct weightings obtained from each patient. The differences between the 'unadjusted' total FACT-P scores and the 'Hybrid' scores for each of the 150 subjects are shown in Figure 2. The Hybrid instrument rated global QoL as better than the unadjusted FACT-P on 107 of 150 (71%) occasions. The Hybrid instrument scores were significantly ($P < 0.000001$) better than the unadjusted FACT-P scores, with a mean difference between the two instruments of 2.1.

Difference between instrument scores for patients with locoregional or metastatic disease

To assess the effectiveness of the different instruments at detecting expected differences in QoL between known groups of patients, global QoL scores were calculated for patients with locoregional and metastatic disease. All three instruments recorded statistically significant differences in QoL between these two groups (Table 1).

Difference between first and second assessments

To assess the sensitivity of the different instruments to changes in QoL over time, subjects who completed two

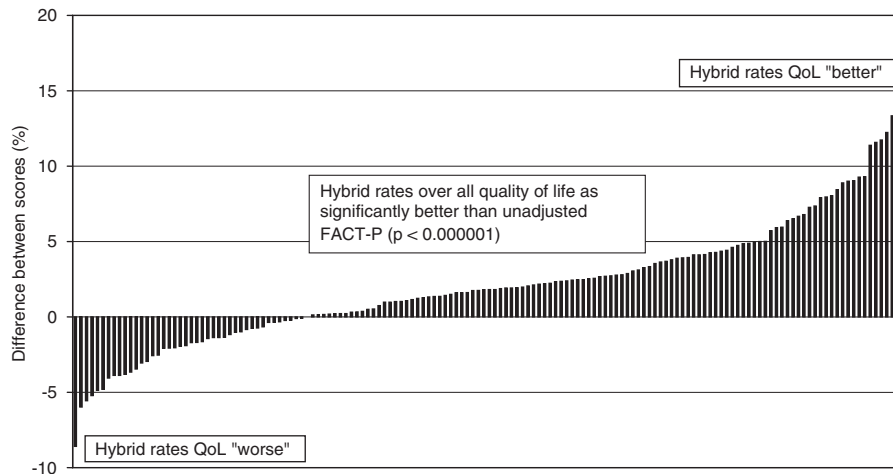


Figure 2 Difference between Hybrid measure and unadjusted Functional Assessment of Cancer Therapy—Prostate (FACT-P) questionnaire scores.

Table 1 Comparison between patients with locoregional and metastatic diseases

	Locoregional disease, mean (s.d.)	Metastatic disease, mean (s.d.)	P-value for difference
Unadjusted FACT-P	76.2 (12.4)	67.4 (15.2)	0.0002
Hybrid VAS	77.6 (12.8)	70.3 (14.4)	0.002
VAS	72.2 (20.7)	60.2 (24.9)	0.002

Abbreviations: FACT-P, Functional Assessment of Cancer Therapy—Prostate; VAS, Visual Analogue Scale.
n = 146, because four men did not complete VAS.

assessments were asked whether they felt that their overall QoL was ‘better’, ‘the same’ or ‘worse’ than at the first assessment (Figure 3). Most patients reported that their overall QoL had stayed the same (*n* = 35) or got worse (*n* = 28), with only seven patients reporting an improvement in QoL. Both FACT-P and the Hybrid measure showed statistically significant changes (in the expected direction) in QoL, in patients in whom self-reported global QoL decreased. None of the instruments showed statistically significant changes in QoL scores in the small number of subjects who reported an improvement in global QoL, although the observed changes were in the expected direction.

Discussion

In this paper we have described the application of a ‘direct-weighting’ procedure to the five QoL domains included in the FACT-P. We have demonstrated that this new Hybrid instrument is quick to complete, is able to distinguish between patients with localized or advanced disease and is able to detect expected changes in QoL over time. Although the scores on the FACT-P and the Hybrid measure are closely correlated (*r* = 0.96), the two measures are not interchangeable. The Hybrid instrument tends to score global QoL better than the FACT-P. This is because when subjects are allowed to weight the

domains according to how important they perceive them to be, they tend to give greatest weight to the ‘Social well-being’ items and least weight to the ‘Additional concerns’ items. In contrast, the FACT-P inherently gives the greatest weight to ‘Additional concerns’ and the least weight to ‘Emotional well-being’. This means that adjusting QoL scores in the light of patients’ individual priorities is not a trivial exercise—it results in real and substantial changes in global QoL scores. If the results of this study are verified in subsequent research then currently used investigator-derived QoL instruments are likely to be underestimating the QoL of respondents.

The FACT QoL measurement system includes a generic QoL core (the FACT-G) with additional disease- or symptom-specific modules that can be included for use in particular populations. The items are investigator determined (although partially derived from the concerns articulated by patients themselves). The clear advantage of using an investigator-derived questionnaire is that all participants in a clinical trial are able to provide core information about specific QoL domains. The drawback is that respondents are not given the opportunity to describe their own individual QoL concerns. Individualized assessment methods such as SEIQoL-DW allow respondents more flexibility, but at the expense of comparable data about specific QoL domains that may be of interest to the study designers. In an accompanying paper¹¹ we have described the different sorts of information that investigators can obtain from trial participants by using a combination of SEIQoL-DW and FACT-P. Although providing a rich data source, the SEIQoL-DW is somewhat time consuming to complete (mean 20.5 min) and is even more time consuming to analyse. The Hybrid approach only adds 5 min to data collection, and analysis is relatively easy (there is no free text to interpret or categorize). Incorporating the Hybrid approach into clinical trials would retain all of the benefits of using the FACT-P (validity, reproducibility, coverage of key domains and so on) with the added benefit of being more reflective of individual patients’ own priorities.

Although this study describes the use of the Hybrid method as applied to the FACT-P, the direct-weighting

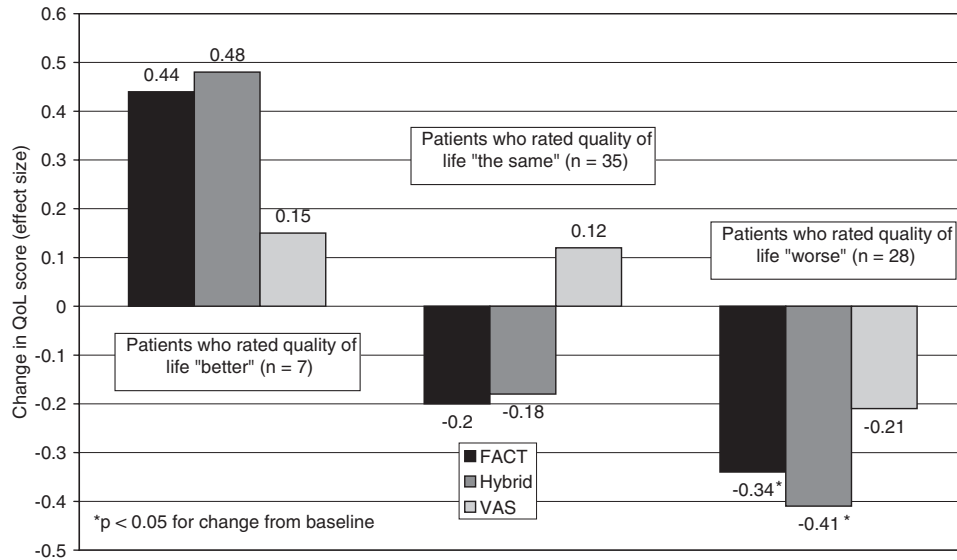


Figure 3 Change in quality of life (QoL) scores (effect size) related to change in global QoL.

process could in theory be applied to any investigator-derived questionnaire. The FACT-P lends itself particularly well to this approach because the questionnaire consists of five domains (the same number used in SEIQoL-DW) and so no change is required to the SEIQoL-DW weighting discs. However, if one wished to use a QoL instrument consisting of eight QoL domains (such as the SF-36) then a direct-weighting disc consisting of the requisite number of overlapping circles could, in theory, be used to 'individualize' the responses.

One of the potential limitations of the Hybrid approach is that some respondents may find the process difficult to understand. We found that less than 1% (1 of 155) of men invited to participate in this study were unable to understand the direct-weighting procedure, whereas 3% (4 of 155) were unable to provide sufficient useable data for the FACT-P. This high response rate may have been a result of the 'convenience' nature of our sample. It is likely that a random population of men with prostate cancer would find the concept of 'direct weighting' more difficult to understand than the volunteers in our own study. However, provided that respondents found the direct-weighting procedure no more difficult to complete than the FACT-P itself, this should not contribute to data attrition in any future clinical studies.

Further work is required before the Hybrid approach can be recommended for general use. We have demonstrated the utility of the Hybrid measure in a convenience sample of generally fit men with prostate cancer. However, it will be important for future studies to include patients with different cancer types and stages of illness, undergoing different interventions. It would also be instructive to investigate how easily the Hybrid approach can be applied to other QoL questionnaires (such as the EORTC QLQc30 or the SF-36). Investigators could easily include the hybrid measure in the design of future clinical studies by 'piggy-backing' the direct-weighting process onto whichever investigator-derived questionnaire it is proposed to use.

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References

- Bottomley A, Flechtner H, Efficace F, Vanvoorden V, Coens C, Therasse P *et al*. Health related quality of life outcomes in cancer clinical trials. *Eur J Cancer* 2005; **41**: 1697-1709.
- Fallowfield L. Quality of life: a new perspective for cancer patients. *Nat Rev* 2002; **2**: 873-879.
- Cella D, Tulsky D, Gray G, Sarafian B, Linn E, Bonomi A *et al*. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol* 1993; **11**: 570-579.
- Esper P, Mo F, Chodak G, Sinner M, Cella D, Pienta KJ. Measuring quality of life in men with prostate cancer using the Functional Assessment of Cancer Therapy—Prostate instrument. *Urology* 1997; **50**: 920-928.
- Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR *et al*. Reliability and validity of the Functional Assessment of Cancer Therapy—Breast quality-of-life instrument. *J Clin Oncol* 1997; **15**: 974-986.
- List MA, D'Antonio LL, Cella DF, Siston A, Mumby P, Haraf D *et al*. The Performance Status Scale for Head and Neck Cancer Patients and the Functional Assessment of Cancer Therapy—Head and Neck Scale. A study of utility and validity. *Cancer* 1996; **77**: 2294-2301.
- Cella DF, Bonomi AE, Lloyd SR, Tulsky DS, Kaplan E, Bonomi P. Reliability and validity of the Functional Assessment of Cancer Therapy—Lung (FACT-L) quality of life instrument. *Lung Cancer* 1995; **12**: 199-220.
- Dijkers M. Individualization in quality of life measurement: instruments and approaches. *Arch Phys Med Rehabil* 2003; **84**: S3-S14.

- 9 Hays RD. Generic versus disease-targeted instruments. In: Fayers P, Hays R (eds). *Assessing Quality of Life in Clinical Trials*, 2nd edn. OUP: Oxford, 2005, pp 3–8.
- 10 Hickey AM, Bury G, O'Boyle CA, Bradley F, O'Kelly FD, Shannon W. A new short form individual quality of life measure (SEIQoL-DW): application in a cohort of individuals with HIV/AIDS. [see comments]. *BMJ* 1996; **313**: 29–33.
- 11 Stone PC, Murphy RF, Matar HE, Almerie MQ. Measuring the individual quality of life of patients with prostate cancer. *Prostate Cancer and Prostatic Diseases* 2008 doi: 10.1038/pcan.2008.16.
- 12 Browne JP, O'Boyle CA, McGee HM, McDonald NJ, Joyce CR. Development of a direct weighting procedure for quality of life domains. *Qual Life Res* 1997; **6**: 301–309.
- 13 Levack P, Graham J, Kidd J. Listen to the patient: quality of life of patients with recently diagnosed malignant cord compression in relation to their disability. *Palliat Med* 2004; **18**: 594–601.
- 14 Moons P, Marquet K, Budts W, De Geest S. Validity, reliability and responsiveness of the 'Schedule for the Evaluation of Individual Quality of Life-Direct Weighting' (SEIQoL-DW) in congenital heart disease. *Health Qual Life Outcomes* 2004; **2**: 28.
- 15 Mountain LA, Campbell SE, Seymour DG, Primrose WR, Whyte MI. Assessment of individual quality of life using the SEIQoL-DW in older medical patients. *QJM* 2004; **97**: 519–524.
- 16 Wettergren L, Bjorkholm M, Axdorph U, Langius-Eklöf A. Determinants of health-related quality of life in long-term survivors of Hodgkin's lymphoma. *Qual Life Res* 2004; **13**: 1369–1379.
- 17 Kazis LE, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. *Med Care* 1989; **27**: S178–S189.