

Minimal Important Differences for Interpreting Health Related Quality of Life Scores from the EORTC QLQ-C30 in Lung Cancer Patients Participating in Randomized Clinical Trials

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BACKGROUND

The objective of this retrospective analysis was to determine the smallest changes in health related quality of life (HRQOL) scores on the European Organisation for Research and Treatment of Cancer quality of life core questionnaire (EORTC QLQ-C30) which could be considered as representing minimal important differences (MID).

The EORTC QLQ-C30 is a questionnaire developed to assess quality of life in cancer patients. The questionnaire consists of multi-item scales; five functioning scales (physical, role, emotional, cognitive, and social), three symptom scales (fatigue, pain, and nausea/ vomiting), and one global health status measure. The remaining single-item scales include dyspnea, appetite loss, sleep disturbance, constipation and diarrhea, and the perceived financial impact of the disease treatment. All scales range 0-100 and high scores on the global health status and functioning scales indicate better quality of life, while on the symptom scales they suggest worsening conditions, and thus poorer quality of life.

PATIENTS

Two closed EORTC randomized controlled clinical trials (RCTs) enrolling in total 812 palliative, locally advanced and/or metastatic non-small cell lung cancer (NSCLC) patients were jointly analyzed. One trial was a three arm study to compare paclitaxel plus cisplatin (arm A) versus gemcitabine plus cisplatin (arm B), and arm A versus paclitaxel plus gemcitabine (arm C), which enrolled 480 patients and used the EORTC QLQ-C30 version 3. The other trial was a RCT of two Cisplatin-based combination chemotherapies, which enrolled 332 patients and used version 1 of the EORTC QLQ-C30. HRQOL was measured longitudinally as a secondary endpoint at baseline, during treatment, and on several follow-up occasions after the end of treatment. Both trials involve the same cancer site, and have similar treatment modalities, it is appropriate to combine the data from the two trials.

METHODS

The WHO performance status (PS, scale 0-4) and weight loss (WL) were chosen as the clinical anchors to which changes in scores of the EORTC QLQ-C30 would be compared. Changes in PS were categorized into three groups; deterioration (PS worsening by 1 category), no change (PS stays the same), and improvement (PS improves by 1 category). Changes in weight were grouped as weight loss (5% or more loss), no weight change (not more than 5% loss or gain), and weight gain (5% or more gain). The EORTC QLQ-C30 scales chosen for study were; physical (PF), social (SF), and role (RF) functioning, global health status (GHS), fatigue (FA) and pain (PA). Patients who had both HRQOL scores and anchor values on at least two time points were considered, and the two most separated time points were used for analysis.

Differences in the anchor values and HRQOL scores between the two time points in question were calculated for each patient. The differences in HRQOL scores were then classified into 'clinically meaningful' categories, as defined a priori by the anchors. Differences in the HRQOL mean changes in scores between adjacent categories were then used to provide a range for the estimate of the MID. Analysis of variance (ANOVA) was used to assess if there existed any statistically significant differences at the 5% level in HRQOL scores between the anchor-defined groups.

RESULTS

The mean change scores for select EORTC QLQ C-30 domains are presented in Tables 1 and 2, categorized by anchor-defined groups for PS and weight loss, respectively.

Table 1: PS- Mean individual change scores (SD) in the anchor defined groups

Scale	Improvement n[56-57]	No change n[350-354]	Deterioration n[104-108]	Mean difference between adjacent categories
Physical	1.3 (23.6)	-5.6 (18.1)	-13.8 (23.5)	6.9, 8.2
Social	3.3 (22.8)	-1.2 (22.8)	-8.5 (29.0)	4.5, 7.3
Role	9.9 (31.8)	-4.5 (29.4)	-12.4 (33.3)	14.4, 7.9
GHS	8.2 (21.6)	-0.9 (19.7)	-4.5 (24.6)	9.1, 3.6
Fatigue	-7.5 (27.1)	6.6 (24.3)	12.3 (31.7)	14.1, 5.7
Pain	-15.8 (34.0)	0.0 (26.7)	-3.1 (27.2)	15.8, 3.1

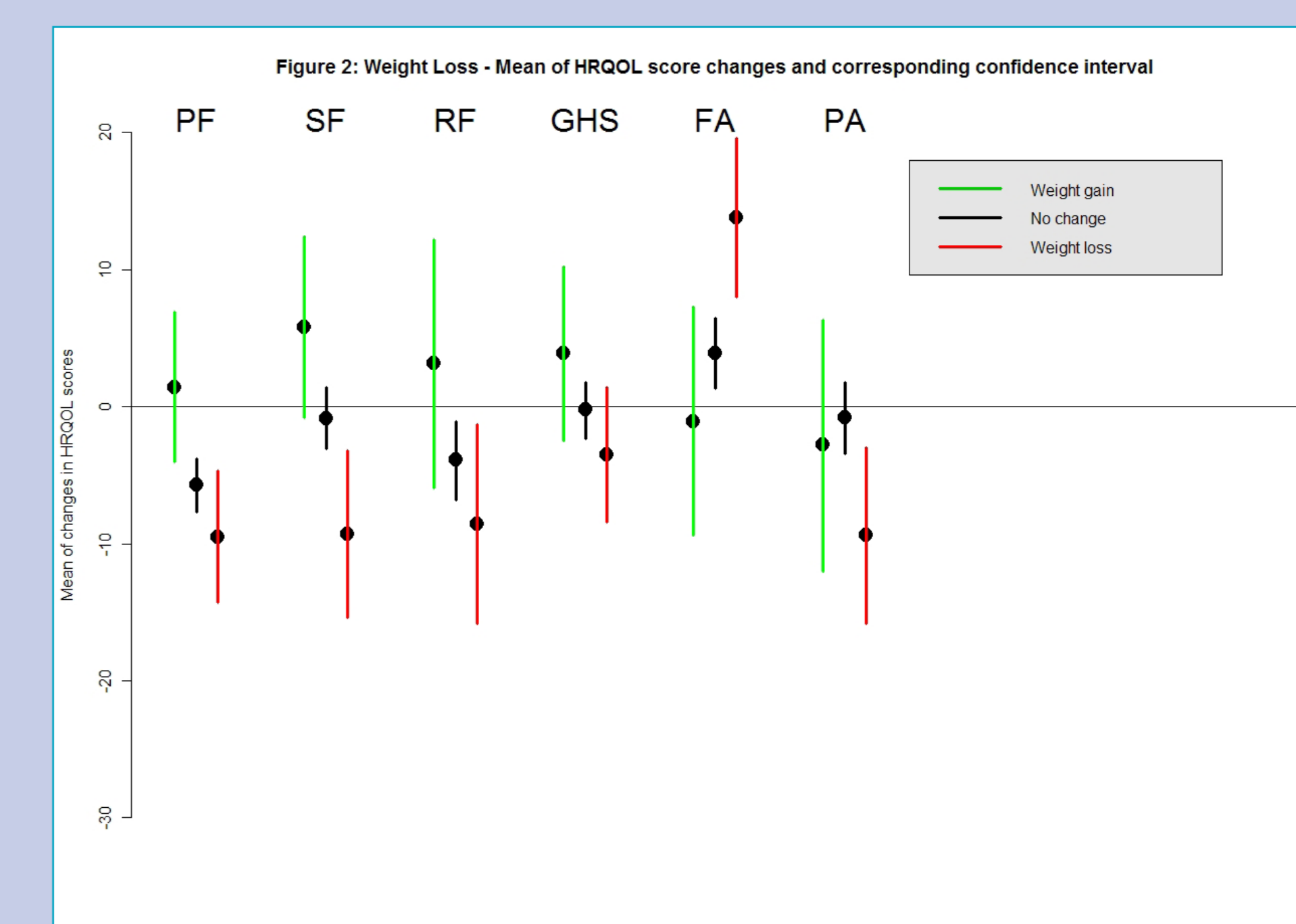
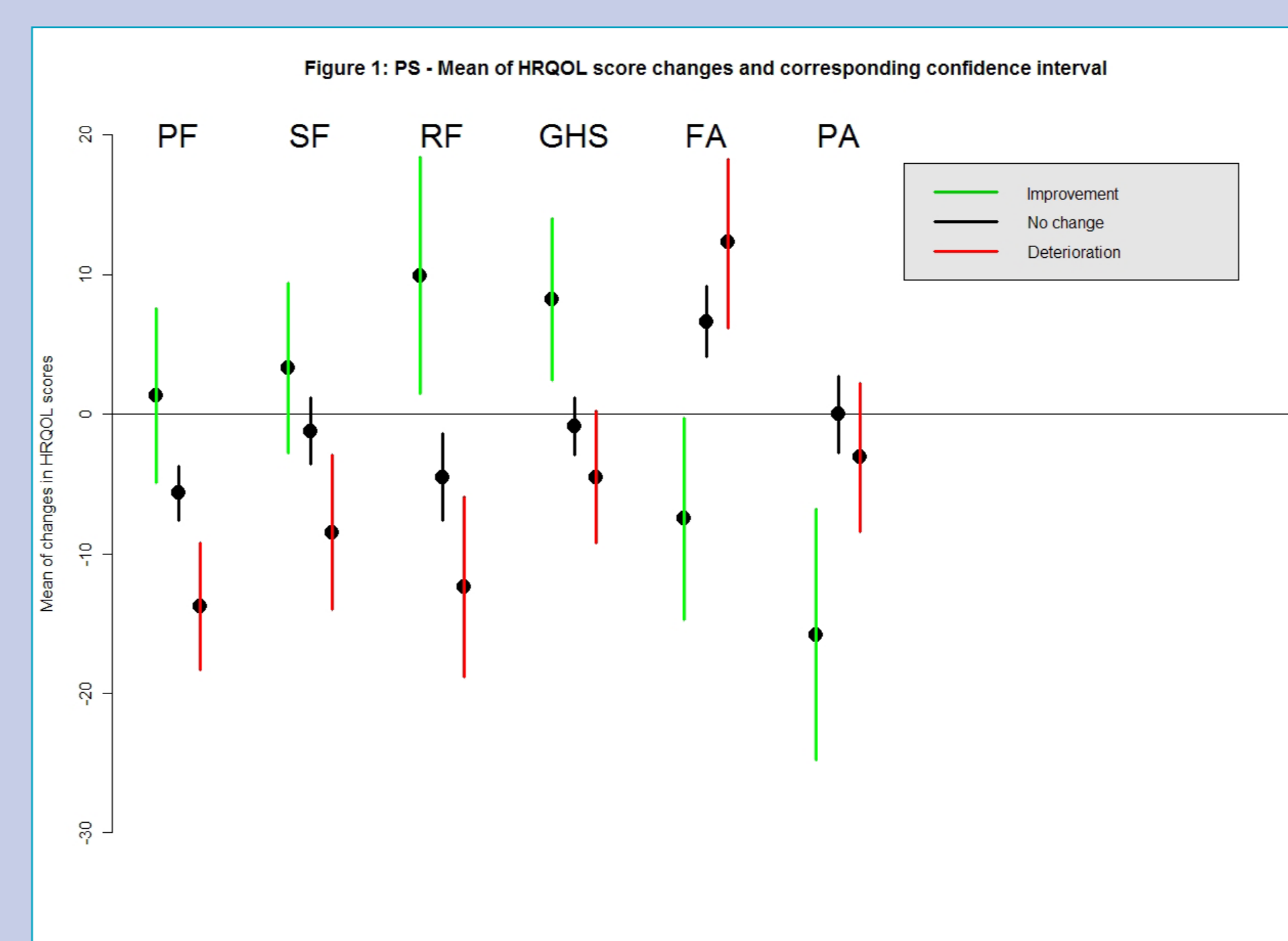
Table 2: WL- Mean individual change scores (SD) in the anchor defined groups

Scale	>=5% gain n[41-43]	No change n[360-367]	>=5% loss n[108-112]	Mean difference between adjacent categories
Physical	1.4 (17.7)	-5.7 (18.9)	-9.5 (23.3)	7.1, 3.8
Social	5.8 (21.5)	-0.9 (21.9)	-9.3 (32.1)	6.7, 8.4
Role	3.2 (29.0)	-3.9 (27.8)	-8.6 (38.7)	7.1, 4.7
GHS	3.9 (20.6)	-8.6 (38.7)	-3.5 (25.7)	4.1, 3.3
Fatigue	-1.1 (26.9)	6.6 (24.3)	13.8 (30.9)	5.0, 9.9
Pain	-2.8 (29.1)	0.0 (26.7)	-9.4 (34.3)	2.8, 8.6

The differences in mean values between the anchor-defined adjacent categories are presented Tables 1 and 2. For example, consider physical functioning in Table 1; the difference between the 'improvement' and 'no change' groups is 1.3-(-5.6)=6.9. These differences were then used to provide a range for the estimate of the MID for the various HRQOL domains.

The mean change scores and their 95% confidence intervals are graphically presented in Figures 1 and 2 for PS and weight loss respectively.

In general, the observed mean values of changes in HRQOL scores for the different scales were in the expected direction. In the example of role functioning in Table 1, on average the scores increased about 10 points for patients with improved performance status but decreased by about 12 points for patients with worsened performance. Generally, the mean values presented in Table 2 also appear to follow the expected directions.



From ANOVA, the PS results showed significant ($p < 0.05$) differences among anchor-defined groups for all the HRQOL scales.

For weight loss, significant differences in HRQOL scores between groups were observed except for role functioning and global health status.

CONCLUSION

In a pooled data of 812 NSCLC patients, the range of values determined to represent the minimal important differences for the functioning scales ranged as follows; physical (4-8), social (5-8) and role (5-14). For global health status the range was 3-9, for fatigue it was 5-14, and for pain it was 2-16. These estimates can help clinicians to evaluate changes in HRQOL over time and, in conjunction with other measures of efficacy, help to assess the value of a health care intervention or to compare treatments. Furthermore, the estimates can be useful in determining sample sizes in the design of future clinical trials. Although a one-category change in WHO PS seemed to be associated with statistically significant changes in HRQOL scores, weight changes of +/- 5% may not be an adequate clinical anchor.

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