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 increase in the need to collect, and analyze Health Related Quality of Life (HRQOL) outcomes in cancer clinical trials is a key issue in recent times (Bottomley and Aaronson, 2007). However, we need a better understanding of how to interpret the results from such studies. The objective in this retrospective analysis was to determine the smallest changes in HRQOL scores on the European Organization for Research and Treatment of Cancer quality of life core questionnaire (EORTC QLQ-C30) which could be considered as representing minimal important differences (MID). Scores on scales on the EORTC QLQ-C30 range from 0 to 100.

**Patients:**
Two closed EORTC randomized controlled clinical trials enrolling in total 812 advanced non-small cell lung cancer (NSCLC) patients were merged and jointly analyzed in this study. The first trial was a three arm randomized study of two Cisplatin-based regimens and Paclitaxel plus Gemcitabine with an enrollment of 480 patients. The other trial was a randomized study of two Cisplatin-based combination chemotherapies involving 332 patients. In both trials, quality of life, collected using the EORTC QLQ-C30, was assessed in a longitudinal fashion; at baseline, during treatment, and on several follow-up occasions after end of treatment.

**Methods:**
An anchor-based approach (Lydick & Epstein, 1993; King, 1996) using World Health Organization performance status (scale 0-4) and weight loss as clinical anchors was applied. The HRQOL scales of interest 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 (baseline and on/after treatment) were included, and the two most separated time points were chosen for analysis. Changes in performance status between the two time points in question were calculated and categorized into three groups; improvement, no change, and deterioration. Changes in weight were grouped as weight loss (5% or more loss), no weight loss (not more than 5% loss or gain), and weight gain (5% or more gain). The differences in HRQOL scores between the two time points were then classified into the apriori set ‘clinically meaningful’ categories.
defined by the changes in the anchor. Differences in the mean of HRQOL 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 values of changes in HRQOL scores and corresponding confidence intervals in the anchor-defined groups are shown in Figure 1 and 2.

![Insert Figure 1](image1)

![Insert Figure 2](image2)

In Table 1 and 2, D1 denotes the difference in mean values between the ‘Improvement’ and ‘No change’ groups, and D2 represents the difference between the ‘No change’ and ‘Deterioration’ groups. For example, consider physical functioning in Table 1; D1 is obtained as $1.3 - (-5.6) = 6.9^+$, and D2 is calculated as $-5.6 - (-15.4) = 9.8^+$ where the superscript indicates whether the difference is positive or negative.

Statistically significant differences ($p<0.05$) in HRQOL scores across the anchor-defined groups were noted for all six scales implying HRQOL scores differ across the groups. For weight, significant differences were observed in all scales except for GHS and pain. For each HRQOL scale, the range of values for combined values of D1 and D2 from Table 1 and 2 is used to estimate a range for the MID.

![Insert Table 1](table1)

![Insert Table 2](table2)

**Conclusions:**
Our results suggest that for patients with advanced non-small cell lung cancer undergoing treatment, the following range of values represent estimates of the MID for the functioning scales; physical (4-10), social (5-9) and role (5-14). For the global health status, a range of 3-9 was obtained while for the symptom scales the ranges were obtained; fatigue (5-14) and pain (2-16). These estimates can be useful to clinicians to determine the proportion of patients benefiting from some treatment. The estimates could also be used as guidance for
classification of patients by changes in HRQOL and symptoms over time, and may aid sample size determination for future clinical trials.

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