# Quality of life assessment in lung cancer clinical trials

HOT SPOT

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## Background

Clinical trials in lung cancer patients have historically focused on survival and/or disease progression as primary endpoints. In the advanced, palliative setting, especially, assessment of patient reported outcomes such as quality of life (QOL) are important and can add support to treatment efficacy or be part of a composite endpoint to demonstrate clinical benefits. A recent meta-analysis of QOL in non-small cell lung cancer (NSCLC) randomized controlled trials showed that 50% of trials demonstrating no survival benefit reported significant differences in QOL scores between arms. Routine assessment of QOL has also been shown to improve patient well being.

Validated QOL questionnaires have been developed specifically for patients with lung cancer, which assess symptoms and issues expected in this population. Both the European Organization for Research and Treatment of Cancer (EORTC) and Functional Assessment of Cancer Therapy (FACT) groups offer such questionnaires (the EORTC QLQ-LC13 and FACT-L, respectively), along with others tailored for various neoplasms. Often, these instruments accompany a "core" questionnaire that assesses more generalized QOL issues. Other less commonly used and rigorously validated instruments are available, which have been applied for this population. In response to the growing recognition of the importance of evaluation of QOL and the number of potential instruments, knowledge of the characteristics of common tools may assist investigators in choosing one best suited to their study.

Three tools are commonly used in the lung cancer population: the EORTC QLQ-LC13, FACT-L and Lung Cancer Symptom Scale (LCSS). At present, the EORTC QLQ-LC13 seems to be the preferred instrument in randomized, controlled NSCLC trials. Since 2002, 57% of trials have used this tool, while 23% and 13% use the questionnaires from the FACT group and the LCSS, respectively.



## EORTC QLQ-LC13

The EORTC QLQ-LC13 is a 13-item instrument meant for assessment of patients with lung cancer of various stages. It was created according to the EORTC guidelines and is designed to be used in conjunction with a "core" measure such as the QLQ-C30 or QLQ-C15-Pal. Along with functional scales assessed by the core instrument, the QLQ-LC13 allows for assessment of dyspnea (through a three-item scale) and pain (three total: chest, arm/shoulder, other), coughing, sore mouth, dysphagia, peripheral neuropathy, alopecia and hemoptysis, via single-item scales. All scores are rated in reference to the past week on a scale of 1 "not at all" to 4 "very much" and are converted to a 0-100 scale, with higher scores representing greater severity for symptom scales or better functioning in functional scales.

## FACT-L

Similar to the EORTC group, the FACT-L contains a nine-item lung-cancer specific subscale and the 27-item core FACT-G questionnaire, which is commonly used to assess more general QOL issues; validation studies have similarly been conducted. All items are scored from 0 "not at all" to 4 "very much" and are in reference to the past week. The FACT-L subscale is reported as a composite score of all nine items relevant to these patients such as shortness of breath, coughing and tightness of the chest. This accompanies the general subscales of physical well-being, social well-being, emotional well-being and functional well-being covered by the FACT-G.

## Lung Cancer Symptom Scale (LCSS)

As an individual assessment, the LCSS has commonly been included in clinical trials to assess symptomatic distress, functional well-being and global quality of life. It is different from the QLQ-LC13 and FACT-L, as items are rated on a visual analogue scale (VAS) from 0 to 100 mm. Patients provide their response to nine items, and health care professionals (observers) have an optional six-item categorically rated scale to complete to provide context. An average of either six major symptoms (cough, dyspnea, hemoptysis, pain, fatigue, appetite) or all nine items (six symptoms plus symptom distress, activity level, and overall quality of life) is taken to establish the average symptom burden index or total score. Reliability, validity and responsiveness have been established previously.

## Other instruments

Though the aforementioned instruments are most often used in the literature, other more generalized scales or study-specific instruments have been created where existing ones were felt not to adequately encompass study goals.

The Rotterdam Symptom Checklist, Brief Fatigue Inventory, EuroQol and core instruments (QLQ-C30 or FACT-G) alone have been used previously. Obvious disadvantages of using non-standard instruments include the lack of psychometric validation and cross-study future comparisons. An interesting point of note in NSCLC trials is that only 8% of studies report rationales for instrument selection.

## Next steps

Inclusion of QOL assessments in clinical trials involving patients with lung cancer is an important step in evaluating patient reported outcomes for various treatments and should continue. Within trials involving large cohorts, statistically significant differences in QOL can be achieved with minimal differences, though the true clinical relevance is unknown. An important consideration that should be explored in the future in subpopulations is the *minimal clinically important difference*, which assesses the magnitude of change required to be clinically relevant.

Clinical trials in lung cancer should continue to assess QOL to determine clinical benefits through analyzing patient reported outcomes. The EORTC QLQ-LC13, FACT-L and LCSS allow for assessment of QOL issues relevant to patients with lung disease. The choice between instruments ultimately depends on the study design and goals, though all three have been validated in large cohorts. Additional questionnaires are also available for use if investigators wish to evaluate more general or other issues.

**Table 1. Comparison of the EORTC QLQ-LC13 and FACT-L characteristics**

| | EORTC QLQ-LC13 | FACT-L | LCSS |
|---|---|---|---|
| **Lung-specific items** | 13 | 9 | 9 (patients)<br>6 (observers) |
| **Total items (inc. core QLQ)** | 43 | 36 | 15 |
| **Recall period** | Last week | Last week | Past day |
| **Response options** | Likert scale (1–4 inclusive) | Likert scale (0–4 inclusive) | Visual Analogue Scale, 0–100 mm (patients)<br>Categorical scale 0 to 100 (observers) |
| **Item format** | Questions | Statements | Questions |
| **Item organization** | Grouped into subscales | Grouped into one large scale | Grouped into large scales |
| **Subscales** | Dyspnea<br>Pain (chest, arm/shoulder, other)<br>Coughing<br>Sore mouth<br>Dysphagia<br>Peripheral neuropathy<br>Alopecia<br>Hemoptysis | Lung cancer subscale (includes all items) | Total symptom severity (9 items)<br>Symptom burden (6 items) |
| **Scoring** | All scale scores are converted to a 0–100 scale with higher scores representing worse symptoms | A summed score of all items ranging from 0–28 with higher scores representing worse QOL | Average of 9 items or 6 items to create subscale scores. Single items can also be analyzed. |

*QLQ: quality of life questionnaire; QOL: quality of life; LCSS: Lung Cancer Symptom Scale*

## References


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