# Gaps in Evidence on Burden and Health-Related Quality of Life in Small-Cell Lung Cancer: Findings from a Targeted Literature Review

PCR 101

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## INTRODUCTION

- Small-cell lung cancer (SCLC) represents ~13–15% of all lung cancers and is marked by rapid progression, early metastasis, and poor prognosis.
- Patients face a heavy health-related quality of life (HRQoL) burden due to severe fatigue, breathlessness, pain, and psychological distress.
- Nearly two-thirds present with extensive-stage disease, leaving limited curative options.
- Despite initial chemo-sensitivity and newer immunotherapies (atezolizumab, durvalumab), survival gains remain modest, with median overall survival below 12 months.
- HRQoL evidence in SCLC is scarce, inconsistently assessed, and rarely stratified by disease stage.
- Epidemiological data are similarly limited and variable, creating uncertainty around the true magnitude of disease burden.
- This evidence gap limits understanding of patient experience and hinders value-based, patient-centered care—highlighting the need for standardized, longitudinal HRQoL and epidemiological research in SCLC.

## OBJECTIVE

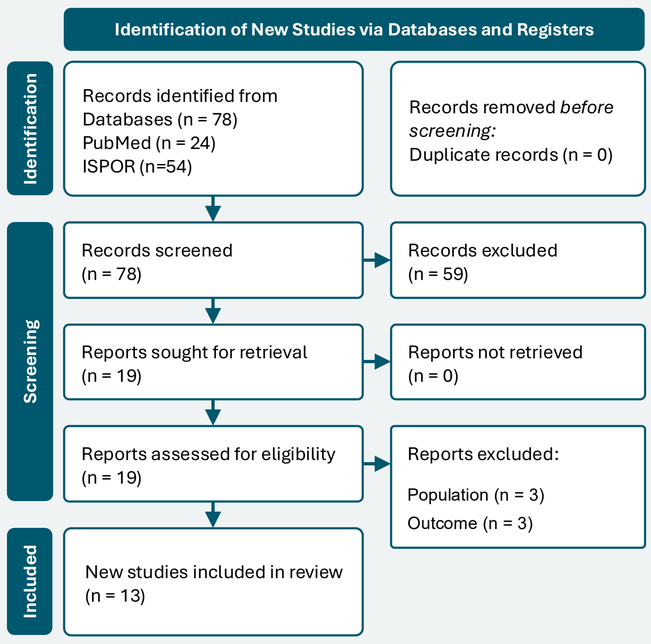
To perform a targeted literature review to identify and characterize evidence gaps in the reporting of clinical burden and HRQoL) among patients with SCLC.

## METHODS

- Targeted literature review in PubMed and ISPOR (2016–2025) of English-language studies.
- Included clinical trials, observational studies, registries, real-world analyses, and systematic reviews reporting disease burden or HRQoL outcomes in adults with SCLC.
- Search terms combined MeSH and free-text keywords for "small-cell lung cancer," "SCLC," "extensive-stage," "limited-stage," "disease burden," "survival," "EQ-5D," "EORTC QLQ-C30," and "health-related quality of life."
- Two-stage PRISMA screening applied; eligible full texts reviewed for data extraction.

| PICOS Element | Inclusion Criteria | Exclusion Criteria |
|---|---|---|
| **Patients** | Adults (≥18 years) with histologically or cytologically confirmed SCLC | Studies focusing exclusively on non–small-cell lung cancer (NSCLC) or other cancer types |
| **Intervention/ Comparator** | Any clinical management or disease state relevant to SCLC, including surgery, chemotherapy, radiotherapy, supportive care, or no treatment | NA |
| **Outcomes** | Disease burden (incidence, prevalence, survival, mortality) and/or HRQoL outcomes derived from validated instruments (e.g., EQ-5D, EORTC QLQ-C30). | Studies lacking epidemiological or HRQoL data |
| **Study Design** | Observational studies (prospective or retrospective), RCTs, registries, real-world analyses, and systematic reviews reporting empirical data. | Not empirical studies (e.g., commentaries, editorials, narrative reviews) |

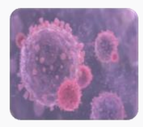
## RESULTS




**Study designs**
- Included prospective, retrospective, RCT, and observational studies

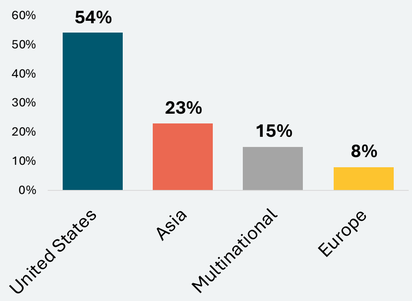
**HRQoL tools**
- Varied widely (EQ-5D, QLQ-30, SF-36, MDASI), limiting comparability

**Sample sizes**
- Ranged from small single-center to large multicenter cohorts, affecting generalizability



**Stage Stratification**
- Applied inconsistently; many lacked stage-specific HRQoL analysis

**Geographic Distribution of Included Studies**



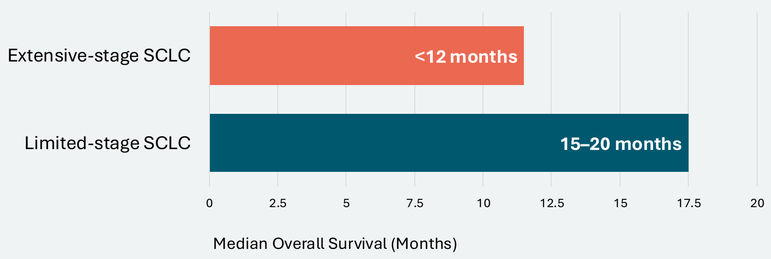

- Studies mainly from **North America and East Asia**.
- **Sparse data** from low- and middle-income regions.
- Highlights a **global evidence gap** in SCLC HRQoL research

| Author (Year) | Design | Sample for SCLC | HRQol Outcomes | HRQoL Tool |
|---|---|---|---|---|
| Mendoza et al. (2019) | Retrospective | 30 | Overall QoL Mean (SD) 5.8 (2.4)<br>Social support 7.5 (3.4) Emotional well-being 6.2 (2.8) Physical well-being 5.7 (2.5) | MDASI (Measures symptom severity and interference with daily life in cancer patients) |
| Vedadi et al. (2021) | Prospective cohort | 75 | HUS Mean (SE)-0.69<br>EQ-VAS Mean(SE)-61.5 | EQ-5D-5L, EQ-VAS, ESAS |
| Lipka et al. (2020) | Observational | 82 | Mean HRQOL composite scores PCS: 51.0; MCS: 74.3 | SF-36 |
| Yang et al. (2019) | Prospective longitudinal | 82 | Limited stage: 0.87 (<65y), 0.84 (≥65y)<br>Extensive stage: 0.84 (both age groups) | EQ-5D (Taiwan tariff), WHOQOL-BREF |
| Kim et al. (2023) | Phase 3 RCT | 453 | EORTC QLQ-C30 GHS/QoL Scale score at Baseline mean (SD) were 60.5 (22.6) points in the pembrolizumab plus EP group and 58.4 (20.6) points in the placebo plus EP group. | QLQ-C30 + LC13 |
| Stone et al. (2018) | Prospective cohort | 155 | Not assessed | None |
| Koller et al. (2020) | Observational field | 81 | Domain-level scores for SCLC were not separately reported | QLQ-C30 + LC29 |
| Yaghi et al. (2023) | Registry analysis | 21,925 | Not assessed | None (proxy: pain referral) |
| Bennet et al. (2017) | Systematic review of 27 studies | Not specified; pooled data from 27 studies | Global HRQoL Scores:<br>Untreated extensive-stage (ED) SCLC: 44.7 (EORTC QLQ-C30)<br>Limited-stage (LD) SCLC: up to 55.4 | EORTC QLQ-C30, QLQ-LC13, LCSS, EQ-5D, FACT-L, others |
| Richards et al. (2018) | Prospective observational study | 338 | EQ-5D Index: Mean baseline scores ranged from 0.70 to 0.76<br>EQ-5D VAS: Mean baseline scores ranged from 66.3 to 73.5<br>Total LCSS: Mean baseline scores ranged from 30.9 to 31.7 | LCSS and EQ-5D scores |
| Dasari et al. (2021) | Systematic literature review of 10 studies | 527 | HUS (EQ-5D Index) Stable ED-SCLC 0.72–0.76<br>Progressive ED- SCLC 0.37–0.53 | EQ-5D (Index) |
| Orfanos, P. et al.(2021) | Prospective trial-based utility analysis (IMpower133 Trial) | 403 | HUS (EQ-5D Index) Tecentriq + Chemo 0.730-0.762 Chemo Alone 0.723-0.756 | EQ-5D-5L |
| Cheng et al. (2024) | Phase 3 randomized, double-blind trial (ASTRUM-005) | 585 | Global health status/quality of life (HR 0.90, 95% CI 0.59–1.39), physical functioning (HR 1.01, 95% CI 0.61–1.65), and role functioning (HR 1.17, 95% CI 0.74–1.87) | EORTC QLQ-C30, QLQ-LC13, EQ-5D-5L |

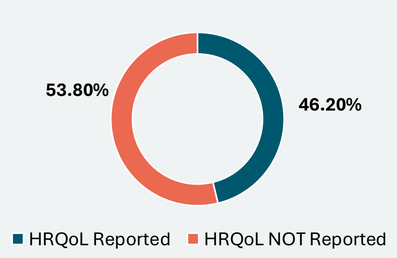
### Epidemiological Burden

**Incidence:** ranged from **2.3–7.4 per 100,000 population** annually.

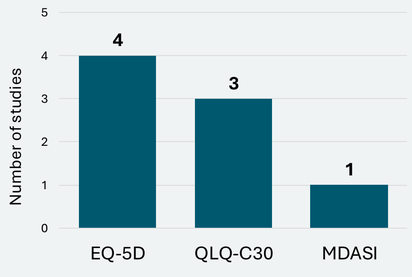
### Median Overall Survival (OS) by SCLC Disease Stage




### HRQoL Reporting Rate




### Instrument Usage




### Survival and HRQoL Context in SCLC

- **Limited-stage SCLC:** Median OS 15–20 months with combined chemoradiation.
- **Extensive-stage SCLC:** Median OS < 12 months despite immunotherapy, reflecting aggressive disease biology.
- **Implication:** Highlights need for early detection, stage-specific care, and integration of **HRQoL** with survival to guide value-based decisions.

### Key Gaps in SCLC HRQoL Evidence and Methodological Heterogeneity

### Methodological Rigor


**Heath Utility Range (EQ-5D):**
**0.73 - 0.87**
Indicates Moderate Impairment

**Dominant Symptom Burden:**
**Fatigue & Dyspnea**
(Consistently reported as most burdensome)

## DISCUSSION

- The targeted literature review highlights the persistently high clinical and humanistic burden associated with SCLC.
- HRQoL evidence remains limited, fragmented, and largely trial-based with few real-world insights.
- Geographic bias towards United States studies restricts global generalizability.
- Stage-specific HRQoL data are sparse, limiting understanding of disease progression and treatment impact.
- Inconsistent use of validated tools and variable reporting reduce comparability and interpretability.
- Recognizing these limitations is critical, as HRQoL metrics increasingly inform cost-utility analyses, HTAs, and patient-centered policy decisions.
- Adoption of standardized, validated, and longitudinal HRQoL is essential to improve evidence reliability and inform value-based, patient-centered care.

## CONCLUSION AND RECOMMENDATIONS

- HRQoL evidence in SCLC remains limited and fragmented, despite the disease's high symptom burden and poor prognosis.
- Lack of standardized and longitudinal HRQoL assessment constrains patient-centered and value-based care.
- Consistent use of validated instruments can enhance data comparability and strengthen evidence for clinical and policy decisions.
- Integration of HRQoL outcomes into real-world registries and HTA frameworks can bridge the evidence gap.
- Linking HRQoL insights with treatment patterns may help uncover drivers of patient well-being beyond survival metrics.
- Strengthening HRQoL measurement across the treatment continuum can advance value-based oncology and improve patient quality of life.

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