EE702

Economic Burden, Healthcare Resource Utilisation, and Health-Related Quality of Life Outcomes for Previously Treated Nonsquamous Nonsmall Cell Lung Cancer: A Series of Systematic Literature Reviews

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Previously treated advanced NSQ-NSCLC is associated with substantial economic and patient burden, including considerable HCRU, direct medical costs, and persistent HRQoL/symptom burden.

- Hospitalisation was the most frequently reported HCRU outcome across multiple healthcare settings.
- HRQoL evidence demonstrated persistent symptom and functional burden; several newer treatments delayed deterioration in selected patient-reported outcomes.
- Utility estimates varied by disease status, treatment, line of therapy, population, and valuation methodology.
- Additional utility evidence for progressive disease/biomarker-defined populations and real-world costs/HCRU evidence in biomarker-defined populations are needed to strengthen future economic evaluations in NSQ-NSCLC.

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Background

- Patients with previously treated, locally advanced, unresectable, or metastatic nonsquamous nonsmall cell lung cancer (NSQ-NSCLC) continue to experience substantial clinical and economic burden.
- Evidence on healthcare resource utilisation (HCRU), costs, health-related quality of life (HRQoL), and health-state utilities is needed to characterise the overall burden of disease and inform future economic evaluations.

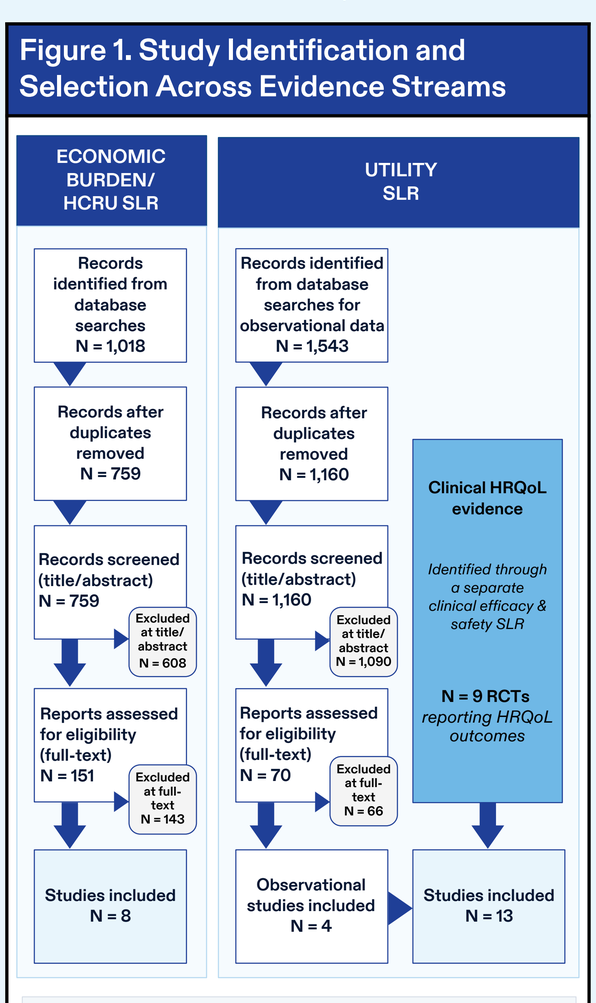
Objective

- To systematically identify and synthesise evidence on the economic burden, HCRU, HRQoL, and health-state utilities in previously treated locally advanced, unresectable, or metastatic NSQ-NSCLC.

Materials and Methods

- Economic burden/HCRU and utility systematic literature reviews (SLRs): MEDLINE, Embase, and Evidence-Based Medicine Reviews were searched for all SLRs; EconLit was additionally searched for economic burden/HCRU and PsycINFO for utilities. Searches covered the period from database inception to 10 December 2025 and were supplemented by grey literature.
- Eligible populations: Adults with locally advanced, unresectable, or metastatic NSQ-NSCLC previously treated with ≥1 systemic therapy.
- The economic burden/HCRU and utility SLRs identified evidence from real-world observational studies; clinical HRQoL evidence was incorporated from randomised controlled trials (RCTs) identified through a separate clinical SLR.
- Two independent reviewers performed study selection; disagreements were resolved by a third reviewer, and extracted data underwent independent validation.

Figure 1. Study Identification and Selection Across Evidence Streams



Abbreviations: HCRU = healthcare resource utilisation; HRQoL = health-related quality of life; RCT = randomised controlled trial; SLR = systematic literature review.

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*Former employee of Pfizer Inc., affiliation at the time of the study.

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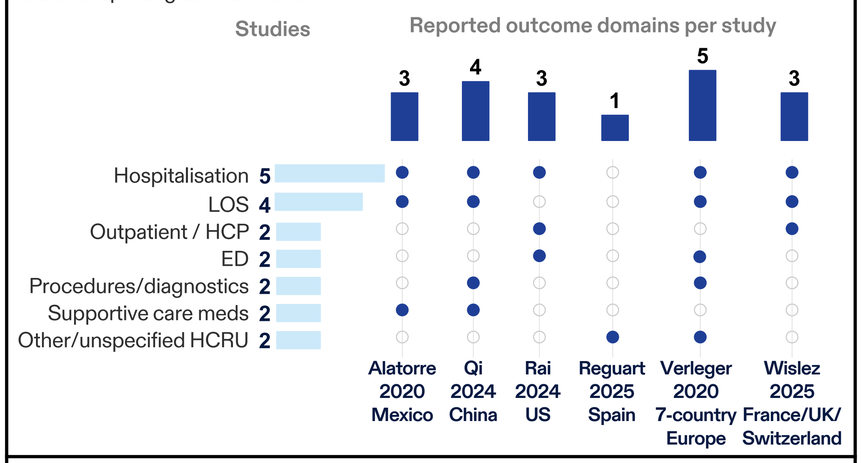
Results

Economic Burden and HCRU

- Eight retrospective cohort studies evaluated HCRU and/or costs; five were restricted to NSQ-NSCLC and three enrolled mixed NSCLC populations in which NSQ histology predominated.
- HCRU outcomes varied across studies, with hospitalisation and length of stay the most frequently reported domains (**Figure 2**).

Figure 2. Reported HCRU Outcome Overlap Across Six Retrospective Cohort Studies

Each dot indicates that the study reported the outcome domain; bars show the number of studies reporting each domain.



Abbreviations: ED = emergency department; HCP = healthcare professional; HCRU = healthcare resource utilisation; LOS = length of stay

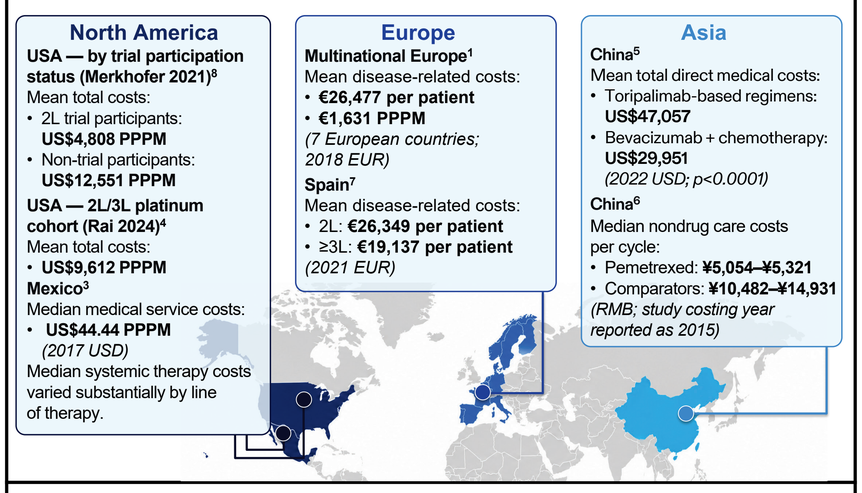
Hospitalisation Was the Most Frequently Reported HCRU Outcome

- Hospitalisation was reported in five of eight studies across North America, Europe, and Asia.
  - Europe: ≥1 hospitalisation was reported in 17.5% of patients in a seven-country study[1] and 70.1% in a France/UK/Switzerland study; with higher rates in the third line.[2] Disease-related complications and grade 3/4 adverse events (AEs) accounted for 54.2% and 24.4% of hospitalisations, respectively.[2]
  - North America: 51.3% of patients in a Mexican study experienced ≥1 hospitalisation; 76.3% of those hospitalised had >1 hospitalisation.[3] A US study reported 0.24 all-cause and 0.23 NSCLC-related inpatient admissions per patient per month (PPPM).[4]
  - Asia: Mean hospitalisations were higher with toripalimab-based regimens than bevacizumab + chemotherapy in a Chinese study (11.4 vs. 9.5; p=0.004).[5]
- Regional estimates should not be directly compared because populations, follow-up, treatment regimens, clinical practice, and outcome definitions differed.

Direct Medical Costs Were Substantial Across Multiple Studies and Regions

- Direct medical costs were reported in seven of eight studies conducted in North America, Europe, and Asia, with total costs reported in five studies.
- Costs accrued across systemic treatment, hospitalisation, diagnostics/procedures, AE management, supportive care, postprogression care, and end-of-life care.[1,3-7]
- Drug-related costs represented a major component of healthcare expenditure.[1,3,5-7]

Figure 3. Reported Direct Medical Cost Outcomes in Previously Treated Advanced NSCLC, by Study and Region



Cost definitions and reporting metrics varied across studies; estimates should not be directly compared because of differences in populations, treatments, follow-up, settings, currencies, costing years, and methodologies. Abbreviations: 2L = second line; 3L = third line; EUR = euro; NSCLC = nonsmall cell lung cancer; PP = per patient; PPPM = per patient per month; RMB = renminbi

- No eligible studies reported indirect or societal costs, including productivity loss or caregiver burden.

HRQoL and Symptom Burden

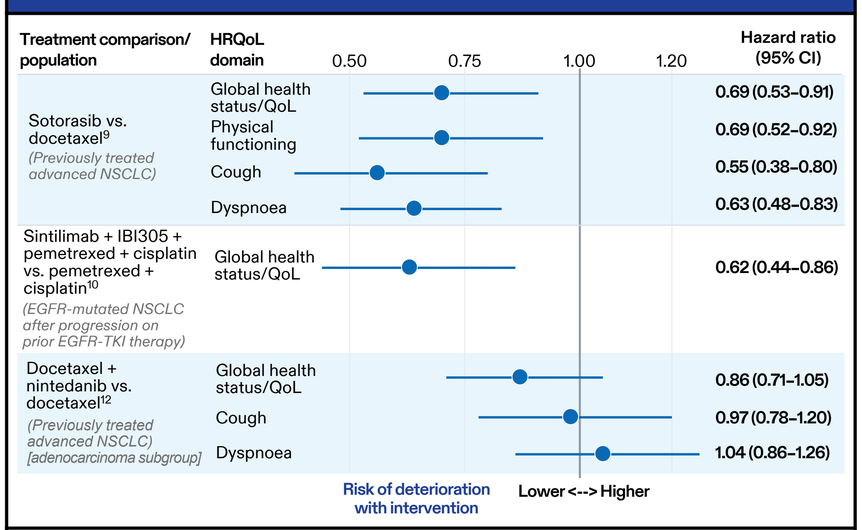
- Nine RCTs reported HRQoL outcomes, including global health status/QoL, physical functioning, cough, dyspnoea, and pain (**Table 1**).
- Several newer treatments delayed deterioration in selected HRQoL/symptom domains versus chemotherapy-based comparators, although findings varied across treatments and outcomes.
  - Sotorasib vs. docetaxel: significant delays in deterioration were reported for global health status/QoL, physical functioning, cough, and dyspnoea.[9]
  - Sintilimab + IBI305 + pemetrexed + cisplatin vs. pemetrexed + cisplatin: significantly delayed deterioration in global health status/QoL;[10] other comparisons showed mixed findings.

Table 1. Summary of Key EORTC QLQ Findings

Treatment Comparison	Instrument	HRQoL Domain	Median TTD (intervention vs. comparator)
Sotorasib vs. docetaxel[9]	EORTC QLQ-C30	Global health status/QoL	9.3 vs. 6.6 weeks
	EORTC QLQ-C30	Physical functioning	15.1 vs. 9.4 weeks
	EORTC QLQ-LC13	Cough	49.3 vs. 15.2 weeks
	EORTC QLQ-LC13	Dyspnoea	12.1 vs. 6.6 weeks
Sintilimab + IBI305 + pemetrexed + cisplatin vs. pemetrexed + cisplatin[10]	EORTC QLQ-C30	Global health status/QoL	5.7 vs. 3.0 months
Sacituzumab tirumotecan vs. chemotherapy[11]	EORTC QLQ-C30	Global health status/QoL	5.6 vs. 4.2 months
	EORTC QLQ-LC13	Cough	13.7 vs. 7.3 months
	EORTC QLQ-LC13	Dyspnoea	5.7 vs. 4.6 months
	EORTC QLQ-LC13	Chest pain	22.5 vs. 9.7 months
Docetaxel + nintedanib vs. docetaxel[12]	EORTC QLQ-C30	Global health status/QoL	No significant difference in TTD
	EORTC QLQ-LC13	Cough	No significant difference in TTD
	EORTC QLQ-LC13	Dyspnoea	No significant difference in TTD

Abbreviations: EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; EORTC QLQ-LC13 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Lung Cancer 13; HRQoL = health-related quality of life; NR = not reported; PRO = patient-reported outcome; QoL = quality of life; TTD = time to deterioration. QLQ-C30 functional/global health status scores are coded so higher scores indicate better status; symptom scores indicate greater burden. Minimally important differences vary by domain; a commonly used range for deterioration in lung cancer populations is approximately 5–15 points for QLQ-C30 and ~5–10 points for QLQ-LC13. TTD definitions varied by study and were not always reported explicitly. Regulatory approvals vary by region, biomarker status, and treatment line; some regimens are approved only for specific NSCLC subpopulations or treatment settings.

Figure 4. Time to HRQoL Deterioration in RCTs



HR <1 indicates lower risk of deterioration with the intervention versus comparator. Regulatory approvals vary by region, biomarker status, and treatment line; some regimens are approved only for specific NSCLC subpopulations or treatment settings. Abbreviations: CI = confidence interval; EGFR = epidermal growth factor receptor; EGFR-TKI = epidermal growth factor receptor-tyrosine kinase inhibitor; HRQoL = health-related quality of life; NSCLC = non-small cell lung cancer; QoL = quality of life; RCT = randomised controlled trial.

Health-state Utilities

- Four observational studies reported EQ-5D utilities ranged from 0.49 to 0.94 (**Table 2**).
- Thailand: Chemotherapy utilities were lower in progressive versus progression-free disease (0.49–0.72 vs. 0.83–0.87); this pattern was not observed with immune checkpoint inhibitors (ICIs).[13]
- Utilities also varied by line of therapy, treatment, and valuation tariff.[14,15]
- No disutility data were reported in the identified literature.

Table 2. Summary of Health-state Utility Evidence

Study Setting/Region	Population/Health State	Reported EQ-5D Utility Values
France/Germany[16]	Advanced NSCLC	0.76–0.81, depending on population/tariff
Multinational[14]	EGFRm+ advanced NSCLC, 2L	0.70
	EGFRm+ advanced NSCLC, 3L	0.80
Thailand[13]	Progression-free	Chemotherapy: 0.83–0.87 ICI: 0.74–0.87
	Progressive disease	Chemotherapy: 0.49–0.72 ICI: 0.94
Taiwan[15]	2L targeted therapy	0.88–0.90
	2L chemotherapy	0.80–0.85

Values originate from different studies, populations, time points, treatments, and valuation approaches and should not be directly compared. Abbreviations: 2L = second line; 3L = third line; EGFRm+ = epidermal growth factor receptor mutation-positive; EQ-5D = EuroQol 5-Dimension; ICI = immune checkpoint inhibitor; NSCLC = nonsmall cell lung cancer.

Evidence Gaps, Limitations, and Interpretation

- Heterogeneity in populations, treatments, outcome definitions, study years, follow-up, and healthcare settings limited cross-study comparisons.
- Utility evidence was limited, particularly for progressive disease and relevant biomarker-defined populations; no disutility data were identified.
- Real-world costs/HCRU evidence was limited in biomarker-defined populations; some estimates were derived from mixed NSCLC populations in which NSQ histology predominated.
- No evidence was identified stratified by integrin beta-6 expression or reporting indirect/societal costs.

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