Quality of Life and Economic Burden of Advanced Non-Small Cell Lung Cancer in Medium and Small Markets: A Systematic Literature Review

EE669

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BACKGROUND

- Lung cancer is one of the most lethal malignancies globally, comprising 14% of all cancer cases and 18% of all cancer-related deaths[1]
- Non-small cell lung cancer (NSCLC) accounts for over 80% of all lung cancer cases
  - A significant number of NSCLC patients are diagnosed at an advanced stage, resulting in overall survival periods of 9–34 months[2]
- Clinical trials are a crucial source of information for researchers studying patient quality of life (QoL) and economic burden (EB). However, these trials tend to favor enrollment from the top 9 (ie, large) pharmaceutical markets, encompassing more than 50% of all patients[3]
- The QoL and EB experienced by patients with advanced or metastatic NSCLC (aNSCLC) in medium-sized and small markets (Med&SM) remain poorly explored due to the limited research conducted in these regions

OBJECTIVES

- To delineate the humanistic burden of aNSCLC by examining QoL outcomes and EB in patients with advanced/metastatic NSCLC in Med&SM
- To assess any gaps in the existing literature on this topic

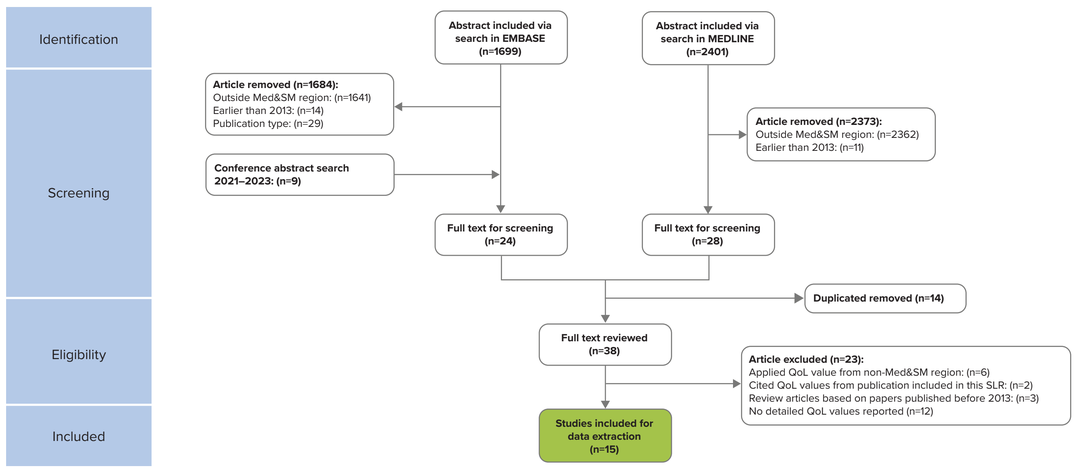
METHODS

- The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The design and execution of this review were guided by the Population, Intervention, Comparison, Outcomes, and Study (PICOS) criteria:
  - **Population:** Patients ≥18 years of age with aNSCLC (Stage III or IV)
    - Geographic regions: 14 countries were selected to represent the geographic and economic diversity of Med&SM: Argentina, Australia, Brazil, Indonesia, Israel, Malaysia, Mexico, New Zealand, Saudi Arabia, Singapore, South Korea, Thailand, Turkey, and United Arab Emirates
  - **Interventions:** All interventions for aNSCLC were included
  - **Comparison:** All interventions for aNSCLC were included
  - **Outcomes:** Original data of the QoL or EB of patients with aNSCLC
  - **Study types:** Prospective, retrospective, and cross-sectional studies
- Searches for English peer-reviewed journal articles and conference abstracts were conducted in EMBASE, MEDLINE®, including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE® Daily, and MEDLINE® Versions
- Journal articles published January 2013–April 2023 and conference abstracts published January 2021–April 2023 were included
- 2 independent researchers conducted the screening and data extraction process. In the event of disagreements, a third reviewer was consulted to reach a resolution

RESULTS

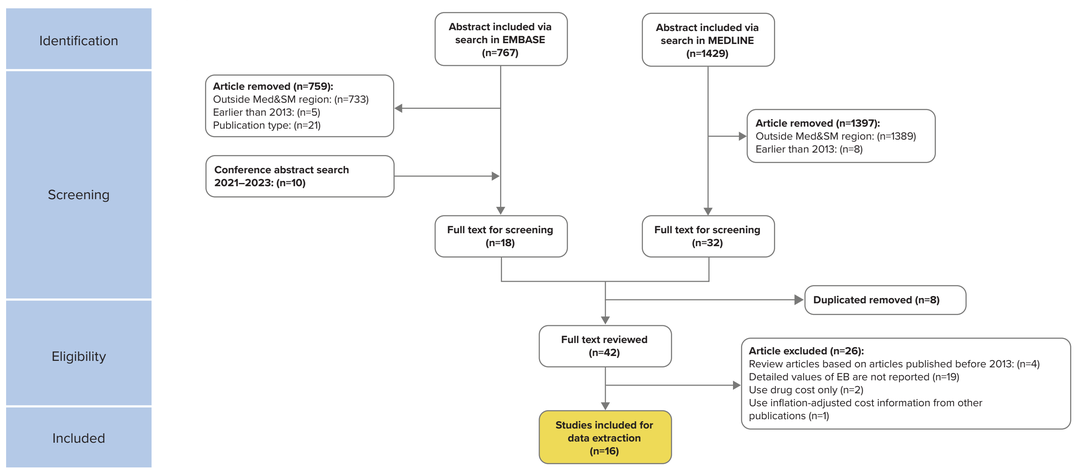
- 4100 publications were screened for QoL studies in patients with aNSCLC; 2196 publications were screened for EB studies in the same patient population
  - Among these, 15 manuscripts related to QoL and 16 manuscripts related to EB were identified and included in the final analysis (**Figure 1** and **Figure 2**)

Figure 1: PRISMA Diagram for SLR on QoL for Patients With aNSCLC



aNSCLC, advanced or metastatic non-small cell lung cancer; Med&SM, medium-sized and small market; QoL, quality of life; SLR, systematic literature review.

Figure 2: PRISMA Diagram for SLR on EB for Patients With aNSCLC

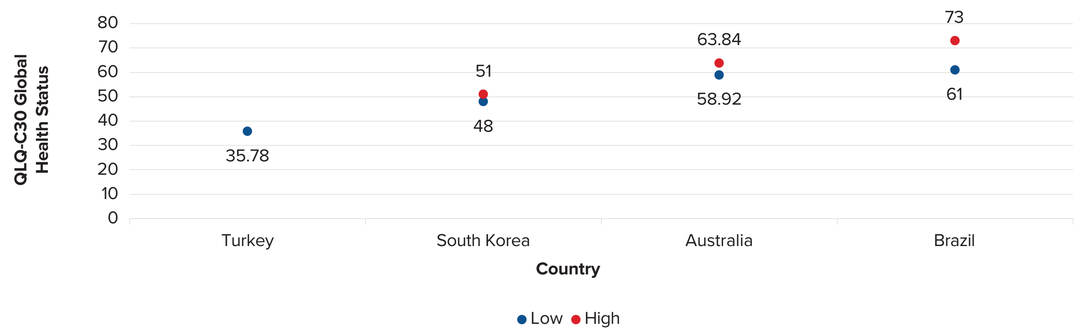


aNSCLC, advanced or metastatic non-small cell lung cancer; EB, economic burden; Med&SM, medium-sized and small market; SLR, systematic literature review.

QoL Outcomes

- We identified 15 studies that reported QoL information for 6 Med&SM countries: 5 for South Korea, 4 each for Australia and Turkey, 2 for Brazil, and 1 each for Indonesia and Thailand
- Among the identified QoL studies, 7 were cross-sectional surveys, 4 were prospective observational studies, 3 were prospective randomized trials, and 1 was a retrospective study
- Validated QoL instruments were employed in 14/15 studies conducted in Med&SM countries, with QLQ-C30 being the most commonly used instrument, followed by EQ-5D, QLQ-LC13, and MDASI-LC
- Among the selected QoL studies, male patients with a history of smoking were the predominant demographic. The average age of participants was 55–70 years, with the majority in their 60s
- Diverse histological characteristics were reported, with adenocarcinoma and squamous cell carcinoma being the most frequently observed subtypes
- While the QoL data exhibited significant heterogeneity, making systematic comparisons challenging, a naïve comparison revealed substantial differences among patients with aNSCLC across countries (**Figure 3**). Notably, patients with disease progression experienced poorer QoL compared with those with progression-free disease (**Figure 4**)
- QoL generally declined with successive treatment rounds. Even at later stages, progression-free patients reported better QoL compared with those with disease progression (**Figure 5**)

Figure 3: Ranges of QLQ-C30 Global Health Status/Quality of Life Scores for aNSCLC Patients by Country[4-8]

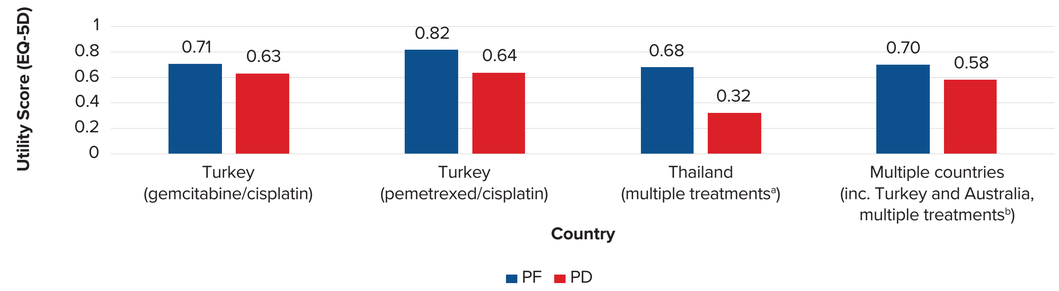


QLQ-C30 was created by the European Organization for Research and Treatment of Cancer (EORTC) to evaluate the QoL among cancer patients. A higher score with respect to the QLQ-C30 Global Health Status signifies a better quality of life. The terms 'high' and 'low' were used to represent the maximum and minimum QLQ-C30 Global Health Status scores reported within a given country. In cases where only a single score was accessible, it was categorized as 'low.'
QoL, quality of life.

CONCLUSIONS

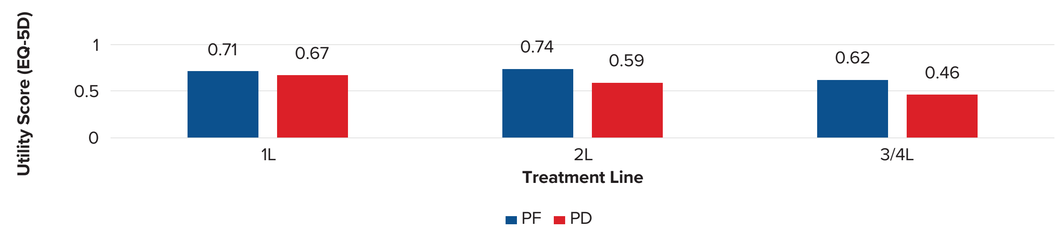
- Systematic assessment of QoL and EB in aNSCLC patients within Med&SM is challenging due to the limited data available. Nevertheless, it is evident that aNSCLC substantially impacts QoL and healthcare expenditures in these markets
- Preventing disease progression improves patient QoL, and the introduction of novel treatments for aNSCLC may potentially enhance patient QoL and reduce the EB

Figure 4: Comparison of Utility Scores by Disease Status[9-12]



EQ-5D is a standardized questionnaire developed by the EuroQol Group to measure health-related QoL.
[a]Patients were treated with platinum doublets or tyrosine kinase inhibitors (gefitinib, erlotinib, or afatinib).
[b]Results were based on patients on unspecified 1st to 4th lines of treatments.
PD, progressive disease; PF, progression-free; QoL, quality of life.

Figure 5: Utility Score by Lines of Treatment in a Multi-Country Study[9]

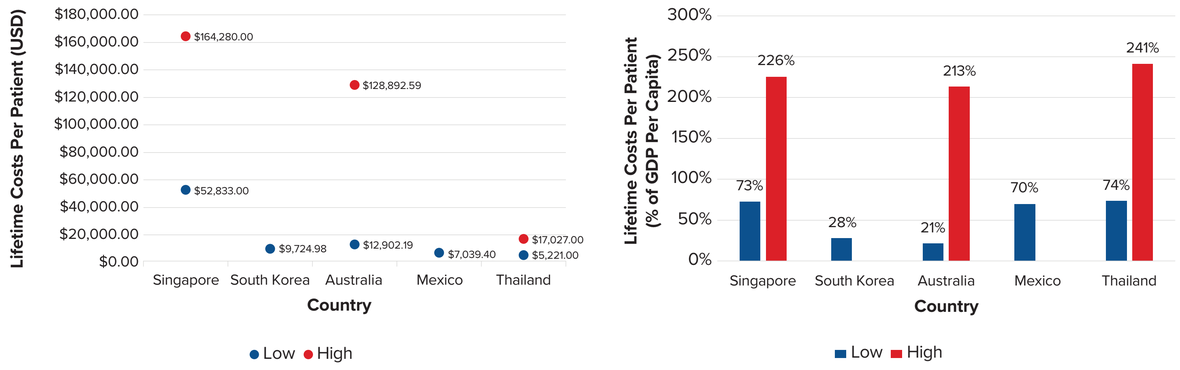


EQ-5D is a standardized questionnaire developed by the EuroQol Group to measure health-related QoL.
Australia and Turkey were included in this study. EQ-5D utility scores were not reported by countries.
1L, first-line treatments; 2L, second-line treatments; 3/4L, third- or fourth-line treatments. PD, progressive disease; PF, progression-free; QoL, quality of life.

EB Outcomes

- EB data based on original research were reported for 6 countries: Singapore, South Korea, Australia, Mexico, Thailand and Turkey
  - All 6 countries have established health technology assessment processes
- 9 of 16 identified EB studies described health economic models, while 6 of the remaining 7 were retrospective studies
  - These EB studies relied on government-published price listings, existing medical claims, hospital databases, and/or expert interviews to estimate the cost of managing aNSCLC
- Med&SM countries exhibit significant differences in their national economic development. When converting the EB of aNSCLC into US dollars (USD), there were substantial cost variations between these countries (**Figure 6A** and **Figure 7A**)
  - Lifetime costs per patient in Med&SM varied from $5,221 USD in Thailand to $164,280 USD in Singapore, depending on the treatment and country
- When the costs per patient were expressed as a percentage of GDP per capita, the lifetime management cost ranges of aNSCLC exhibited greater consistency across countries, primarily falling within 70% to 240% of GDP per capita (see **Figure 6B**)
- Singapore and South Korea had lower annualized aNSCLC costs in comparison with Mexico and Thailand (**Figure 7B**)

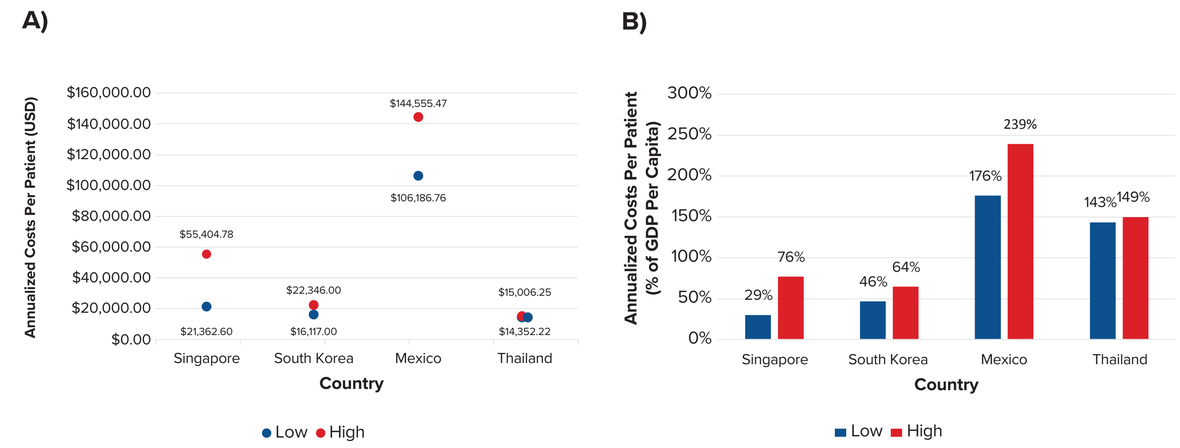
Figure 6: Lifetime Costs Per Patient of Managing aNSCLC by Country A) in USD and B) by % of GDP Per Capita[7,8,10-16]



Lifetime costs per patient of treating aNSCLC in USD. Conversion to USD was based on the exchange rates published on 4/5/2023. The terms 'high' and 'low' were used to represent the maximum and minimum costs reported within a given country. In cases where only a single cost was accessible, it was categorized as 'low.'
aNSCLC, advanced or metastatic non-small cell lung cancer; USD, US dollar.

Lifetime costs per patient of treating aNSCLC as percentages of 2021 GDP per capita. The terms 'high' and 'low' were used to represent the maximum and minimum costs reported within a given country. In cases where only a single cost was accessible, it was categorized as 'low.'
aNSCLC, advanced or metastatic non-small cell lung cancer; GDP, gross domestic product.

Figure 7: Annualized Costs Per Patient of aNSCLC A) in USD and B) by % of GDP Per Capita[17-23]



Annualized costs per patients of treating aNSCLC in USD. Conversion to USD was based on the exchange rates published on 4/5/2023. The terms 'high' and 'low' were used to represent the maximum and minimum costs reported within a given country. In cases where only a single cost was accessible, it was categorized as 'low.'
aNSCLC, advanced or metastatic non-small cell lung cancer; USD, US dollar.

Annualized costs per patient of treating aNSCLC as percentages of 2021 GDP per capita. The terms 'high' and 'low' were used to represent the maximum and minimum costs reported within a given country. In cases where only a single cost was accessible, it was categorized as 'low.'
aNSCLC, advanced or metastatic non-small cell lung cancer; GDP, gross domestic product.

REFERENCES

1. Sung H, et al. *CA Cancer J Clin.* 2021;71(3):209-49.
2. Casal-Mourino A, et al. *Transl Lung Cancer Res.* 2021;10(1):506-18.
3. US Food and Drug Administration. 2015-2019 Drug Trials snapshots summary report, in five-year summary and analysis of clinical trial participation and demographics 2020.
4. Araujo LA, et al. *Future Oncology.* 2021;17(14):1721-33.
5. Avelino CU, et al. *J Bras Pneumol.* 2015;41(2):133-42.
6. Dhillon HM, et al. *Ann Oncol.* 2017;28(8):1889-97.
7. Kivrak Bernardelli BG. *Marmara Pharm J.* 2013;2(17):120-30.
8. Yi Y.S, et al. *BMC Cancer.* 2018;18(1):1053.
9. Chouaid C, et al. *J Thorac Oncol.* 2013;8(8):997-1003.
10. Limwattananon C, et al. *Lung Cancer.* 2018;120:91-7.
11. Wulandari L, et al. *Asian J Oncol.* 2022;8:15-21.
12. Yalcin Balcik P, Sahin B. *Turk J Med Sci.* 2016;46(1):152-8.
13. Edbrooke L, et al. *Thorax.* 2019;74(8):787-96.
14. Kim EJ, et al. *BMC Cancer.* 2018;18(1):1081.
15. Lee MK. *Healthcare (Basel).* 2020. 9(1):28.
16. Nafees B, et al. *Asia Pac J Clin Oncol.* 2017;13(5):e195-e203.
17. Arrieta O, et al. *Tob Induc Dis.* 2014;12(1):25.
18. Aziz MIA, et al. *J Med Econ.* 2020;23(11):1330-39.
19. Aziz MIA, et al. *J Med Econ.* 2020;23(9):952-60.
20. Khoo T, Gao L. *Expert Rev Pharmacoecon Outcomes Res.* 2021;21(3):415-23.
21. Lim EA, et al. *PLoS One.* 2016;11(8):e0160155.
22. Shim YB, et al. *PLoS One.* 2022;17(9):e0274876.
23. Thongprasert S, Permsuwan U. *Curr Med Res Opin.* 2017;33(5):955-61.

DISCLOSURES

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