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Impact of platinum-based and non-platinum chemotherapy on quality of life in non-small cell lung cancer: A narrative review

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ABSTRACT

Chemotherapy remains one of the main therapeutic options for patients with advanced non-small cell lung cancer (NSCLC), a disease that continues to contribute significantly to global cancer-related mortality. The selection of platinum-based or non-platinum chemotherapy regimens has important clinical implications, as these approaches differ not only in antitumor efficacy but also in their impact on patients' health-related quality of life (HRQoL). This narrative review aimed to synthesize recent evidence regarding the effects of platinum-based and non-platinum chemotherapy on HRQoL among patients with NSCLC. Relevant studies published between 2020 and 2025 were identified through systematic searches of major scientific databases, including PubMed, Scopus, and Web of Science. The findings were narratively synthesized across commonly reported HRQoL domains using validated assessment instruments, such as the Functional Assessment of Cancer Therapy–Lung (FACT-L), the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and Lung Cancer Module (QLQ-LC13), as well as the EQ-5D-5L. Overall, platinum-based chemotherapy was associated with better disease control but also with greater toxicity-related deterioration in physical and emotional functioning. In contrast, non-platinum regimens demonstrated improved tolerability and more stable HRQoL outcomes. These differences have important implications for shared clinical decision-making, particularly in patients with advanced disease for whom symptom relief and quality of life often represent primary treatment goals. This review highlights the need to integrate HRQoL considerations alongside clinical efficacy when individualizing chemotherapy strategies for patients with advanced NSCLC.

ABSTRAK

K Kemoterapi masih menjadi salah satu pilihan terapi utama bagi pasien dengan non-small cell lung cancer (NSCLC) stadium lanjut, suatu penyakit yang tetap memberikan kontribusi besar terhadap angka kematian akibat kanker secara global. Pemilihan regimen kemoterapi berbasis platinum atau non-platinum memiliki implikasi klinis yang penting, karena kedua pendekatan tersebut tidak hanya berbeda dalam efektivitas antitumor, tetapi juga dalam dampaknya terhadap kualitas hidup terkait kesehatan (health-related quality of life/HRQoL) pasien. Tinjauan naratif ini bertujuan untuk mensintesis bukti terkini mengenai pengaruh kemoterapi berbasis platinum dan non-platinum terhadap HRQoL pada pasien NSCLC. Studi yang relevan dan dipublikasikan antara tahun 2020 hingga 2025 diidentifikasi melalui penelusuran sistematis pada basis data ilmiah utama, yaitu PubMed, Scopus, dan Web of Science. Temuan penelitian disintesis secara naratif berdasarkan domain HRQoL yang umum dilaporkan dengan menggunakan instrumen terstandar dan tervalidasi, seperti Functional Assessment of Cancer Therapy–Lung (FACT-L), European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) beserta modul kanker paru (QLQ-LC13), serta EQ-5D-5L. Secara umum, kemoterapi berbasis platinum dikaitkan dengan pengendalian penyakit yang lebih baik, namun juga dengan penurunan fungsi fisik dan emosional yang lebih besar akibat toksisitas terapi. Sebaliknya, regimen non-platinum menunjukkan tolerabilitas yang lebih baik dan profil HRQoL yang lebih stabil. Perbedaan ini memiliki implikasi penting dalam pengambilan keputusan klinis bersama, terutama pada pasien dengan penyakit stadium lanjut yang sering kali memprioritaskan pengendalian gejala dan kualitas hidup. Tinjauan ini menegaskan pentingnya mempertimbangkan aspek HRQoL selain efektivitas klinis dalam pemilihan strategi kemoterapi yang bersifat individual pada pasien NSCLC stadium lanjut.

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INTRODUCTION

Lung cancer remains one of the leading causes of cancer-related mortality worldwide and continues to pose a major global health challenge. According to GLOBOCAN 2022 data, lung cancer rank as the second leading cause of cancer death globally, following breast cancer.[1] Non-small cell lung cancer (NSCLC), which includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, accounts for approximately 85% of all lung cancer cases.[2] Most patients with NSCLC are diagnosed at an advanced stage, at which point curative treatment options are limited.[3] In this setting, chemotherapy plays a central role in prolonging survival and alleviating disease-related symptoms. The increasing availability of chemotherapy regimens has therefore underscored the importance of evaluating not only clinical efficacy but also their impact on patients' quality of life.[4]

Based on their principal drug components, chemotherapy regimens for NSCLC are broadly classified into platinum-based and non-platinum regimens.[5] Platinum-based regimens typically combine cisplatin or carboplatin with agents such as pemetrexed, paclitaxel, gemcitabine, docetaxel, or vinorelbine.[6] These combinations have demonstrated improved tumor response rates and survival outcomes in multiple clinical trials, but they are often associated with substantial treatment-related toxicity. In contrast, non-platinum regimens, including docetaxel monotherapy, single-agent pemetrexed, or combinations of gemcitabine and vinorelbine, have been developed as more tolerable alternatives, particularly for patients who are ineligible for platinum-based therapy due to comorbidities or poor clinical status.[7] Consequently, the selection of chemotherapy regimens increasingly considers not only disease control but also their effects on patients' quality of life during and after treatment.

The balance between antitumor efficacy and treatment tolerability is a critical determinant of quality of life among patients receiving chemotherapy for lung cancer. Common adverse effects, such as peripheral neuropathy, fatigue, nausea, and organ dysfunction, can markedly impair physical functioning and overall well-being during therapy.[8] In addition, psychological factors, including treatment-related stress, anxiety, and depression, influence how patients perceive and evaluate their quality of life.[9] Health-related quality of life in lung cancer is most commonly assessed using validated instruments such as the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) and its lung cancer–specific module, the QLQ-LC13. When combined with the EQ-5D-5L, these tools enable a comprehensive assessment of treatment-related changes across multiple dimensions of patient well-being.[10]

Using these instruments, differences in quality-of-life outcomes between platinum-based and non-platinum chemotherapy regimens in NSCLC can be examined more systematically. Several factors contribute to these differences, including variations in hematological, nephrotoxic, and neurotoxic adverse effects, which are more frequently associated with platinum-based agents. Differences in drug combinations, treatment duration, and patient-related characteristics such as age, performance status, and comorbid conditions also influence treatment tolerance.[11] Over successive treatment cycles, the cumulative burden of chemotherapy-related toxicity often becomes a major driver of quality-of-life deterioration. Although non-platinum regimens are generally associated with milder adverse effects, they may offer lower efficacy in disease control compared with platinum-based therapies.[7]

Several previous studies have

examined the correlation between different chemotherapy regimens and the quality-of-life profiles of individuals with NSCLC. Owens *et al*.,[12] showed that carboplatin-paclitaxel-based regimens led to significant improvement in respiratory symptoms, although these benefits were accompanied by increased fatigue and peripheral neuropathy. Similarly, Koda *et al*.,[13] compared single-agent pemetrexed with a cisplatin–pemetrexed combination and found that patients receiving the non-platinum regimen experienced better quality-of-life outcomes, particularly in physical and emotional domains. In addition, Chen *et al*.,[14] demonstrated that, among elderly patients, non-platinum regimens offered improved tolerability without significant differences in clinical efficacy. Despite these important findings, the existing studies were conducted independently and did not provide an integrated synthesis of health-related quality-of-life outcomes across different chemotherapy strategies.

Although evidence regarding chemotherapy-related outcomes continues to grow, relatively few studies have directly compared platinum-based and non-platinum regimens with a specific focus on health-related quality of life in patients with NSCLC. Many clinical investigations emphasize treatment efficacy and toxicity, whereas patient-reported HRQoL outcomes remain insufficiently synthesized. This gap limits the ability to comprehensively understand how different chemotherapy strategies affect patients' lived experiences during treatment.

Accordingly, this narrative review aims to address this gap by synthesizing recent evidence on HRQoL outcomes associated with platinum-based and non-platinum chemotherapy regimens in patients with NSCLC. Specifically, the review seeks to examine differences in physical, emotional, social, and functional well-being across treatment approaches and to discuss the clinical implications of HRQoL findings for individualized treatment selection and future research.

MATERIAL AND METHODS

A comprehensive literature search was conducted for this narrative review using Scopus, PubMed, and Web of Science to identify relevant studies. Articles were eligible for inclusion if they met the following criteria: (1) clinical studies involving patients with non-small cell lung cancer (NSCLC) who received either platinum-based or non-platinum chemotherapy regimens and reporting health-related quality of life (HRQoL) outcomes, (2) publication in English, and (3) availability of full-text articles.

Studies were excluded if they met any of the following criteria: (1) non-original research, including reviews, case reports, editorials, or commentaries; (2) study populations other than patients with NSCLC, (3) reporting of clinical outcomes without HRQoL assessment; or (4) absence of validated HRQoL measurement instruments.

The search strategy employed combinations of keywords and Medical Subject Headings (MeSH), including "NSCLC," "non-small cell lung cancer," "platinum-based chemotherapy," "non-platinum chemotherapy," "cisplatin," "carboplatin," "gemcitabine," "pemetrexed," "paclitaxel," and "quality of life," combined using Boolean operators. Duplicate records and clearly irrelevant articles were removed during the screening process. The literature search and screening procedures were informed by PRISMA principles to enhance transparency and reproducibility; however, this review was not conducted as a systematic review and did not follow a systematic review protocol.

Studies evaluating platinum-based chemotherapy alone were also included to provide contextual evidence on HRQoL outcomes and to support comparative interpretation in the absence of sufficient

direct head-to-head comparisons with non-platinum regimens. All included studies were qualitatively reviewed and narratively synthesized. In accordance with the narrative review design, no formal assessment of study quality or risk of bias was performed.

RESULTS

Study selection

The literature search yielded approximately 100 records from PubMed, Scopus, and Web of Science. After removal of duplicates and screening of titles and abstracts, a limited number of articles met the predefined eligibility criteria. Following full-text assessment, six studies were included in the qualitative synthesis. These studies comprised randomized controlled trials, subgroup analyses, and one single-arm study evaluating HRQoL outcomes in patients with advanced or metastatic NSCLC receiving platinum-based or non-platinum chemotherapy regimens. The stages of study identification, selection, and inclusion are summarized in FIGURE 1.

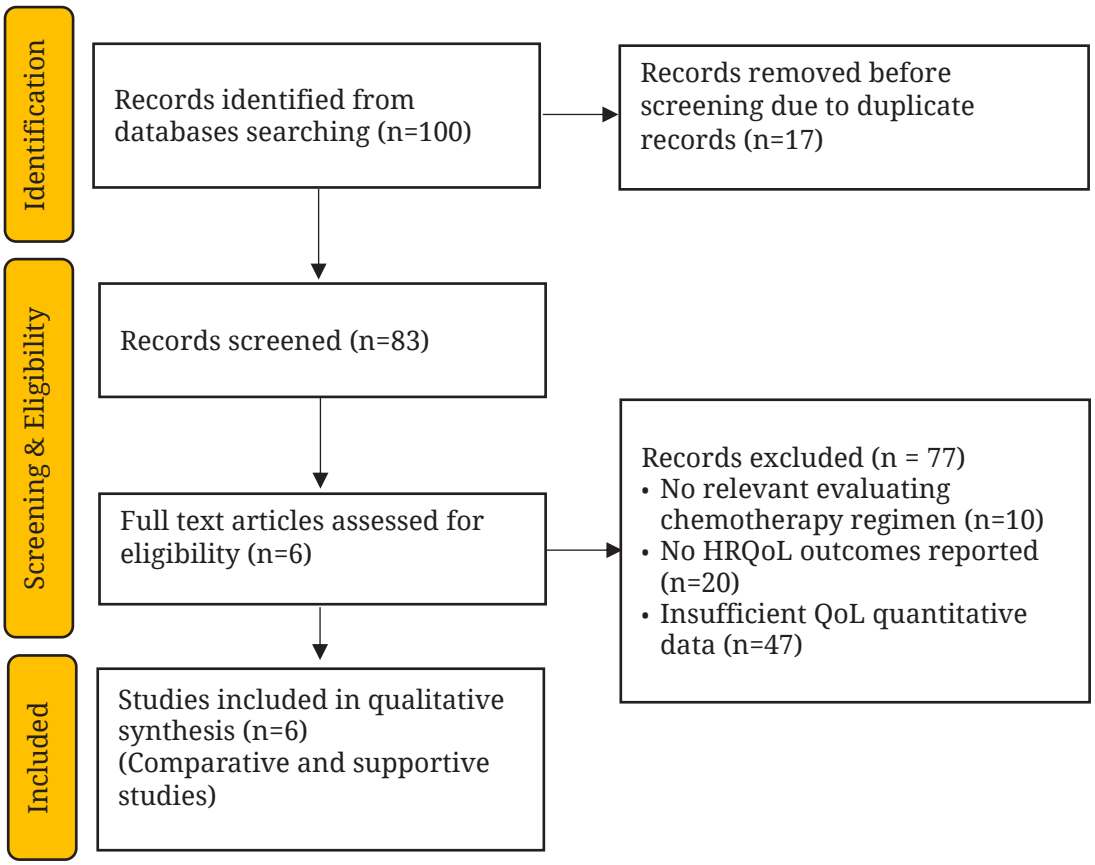

FIGURE 1. Article search process

Study characteristics

The baseline characteristics of the included studies are summarized in TABLE 1 and TABLE 2. Most studies were predominantly phase II and phase III clinical trials, with study populations predominantly consisting of elderly patients or individuals with advanced-stage NSCLC. Platinum-based chemotherapy regimens mainly involved carboplatin-based doublets, including carboplatin–pemetrexed and carboplatin-nab-paclitaxel combinations. In contrast, non-platinum regimens largely consisted of single-agent therapies, such as docetaxel, S-1, and pemetrexed-based treatments administered without platinum compounds. Health-related quality of life outcomes were evaluated using validated instruments, including the Functional Assessment of Cancer Therapy–Lung (FACT-L), the Lung Cancer Symptom Scale (LCSS), and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30).

Comparative HRQoL outcomes between chemotherapy regimens

Direct comparative evidence was obtained from randomized controlled trials comparing platinum-based and non-platinum chemotherapy regimens. In one randomized study comparing pemetrexed plus bevacizumab with docetaxel plus bevacizumab, patients receiving pemetrexed-based therapy experienced smaller declines in lung cancer–specific and physical well-being domains of FACT-L scores. Statistically significant differences were observed in selected domains ($p < 0.05$).[15]

Similarly, randomized trials comparing platinum-based carboplatin doublet chemotherapy with non-platinum docetaxel monotherapy in elderly patients demonstrated that changes in the platinum-based groups did not consistently reach clinically meaningful deterioration. In contrast, patients receiving non-platinum doxetacel monotherapy showed statistically significant worsening in symptom-related domains, including fatigue and appetite loss ($p<0.05$).[16,17] These findings suggest that symptom burden varied across regimens despite comparable global HRQoL.

HRQoL Patterns in Supportive and Non-Comparative Studies

Additional insights into HRQoL trajectories were derived from subgroup analyses and single-arm studies included as supportive evidence. In a subgroup analysis of previously treated elderly patients receiving non-platinum S-1 or non-platinum docetaxel, adjusted mean global health status scores favored S-1 by 7.41 points (95% CI 0.37-14.46), although HRQoL was not the primary endpoint of the study.[18]

In a single-arm phase II study evaluating platinum-based carboplatin plus pemetrexed combination with camrelizumab, increases in symptom scores, particularly fatigue and gastrointestinal symptoms, were observed during treatment. However, no statistically significant deterioration in global health status scores from baseline was reported ($p>0.05$).[19] These findings provide contextual information on HRQoL patterns during platinum-based combination therapy but do not represent direct comparative evidence.

Across these supportive studies, HRQoL outcomes varied according to regimen composition, toxicity profile, and patient characteristics. While platinum-based regimens were associated with increased treatment-related symptoms several studies, these effects did not consistently translate into significant deterioration in global HRQoL scores.[18-20]

TABLE 1. Main characteristics of studies included in the narrative review

Author	Country	Study design	Sample size	Chemotherapy regimen	Regimen type	Key characteristics
Kozuki *et al.*,[15]	Japan	Randomized controlled trial	103	Docetaxel + bevacizumab vs pemetrexed + bevacizumab	Non-platinum vs non-platinum	Evaluated HRQoL differences between two non-platinum regimens in elderly patients with advanced NSCLC, providing direct comparative evidence on HRQoL deterioration, fatigue, and treatment-related burden.
Okamoto *et al.*,[16]	Japan	Phase III randomized, open-label, non-inferiority trial	433	Carboplatin + pemetrexed (maintenance pemetrexed) vs docetaxel	Platinum-based vs non-platinum	Directly compared a platinum-based doublet regimen with non platinum docetaxel monotherapy in elderly patients with advanced nonsquamous NSCLC, with HRQoL and toxicity assessed as secondary outcomes.
Kogure *et al.*,[17]	Japan	Phase III randomized trial	196	Carboplatin + nab-paclitaxel vs docetaxel	Platinum-based vs non-platinum	Directly compared a platinum-based combination with non-platinum single-agent docetaxel in elderly patients with advanced squamous NSCLC, focusing on longitudinal patient-reported HRQoL outcomes.
Yang *et al.*,[18]	Multinational	Phase III randomized trial (subgroup analysis of EAST-LC)	189	S-1 vs docetaxel	Non-platinum vs non-platinum	Evaluated differences in HRQoL between non-platinum regimens in pretreated elderly patients with advanced NSCLC, providing supportive evidence on symptom burden and global health status.
Hou *et al.*,[19]	China	Phase II single-arm study	45	Carboplatin + pemetrexed + camrelizumab	Platinum-based	Assessed HRQoL trajectories and symptom-related outcomes in patients with advanced NSCLC treated with platinum-based chemoimmunotherapy, the single-arm design contributed complementary HRQoL data.
Yang *et al.*[20]	Multinational	Phase III randomized, double-blind trial	492	Platinum + pemetrexed ± pembrolizumab	Platinum-based	Evaluated treatment-related toxicity and survival outcomes in EGFR-mutant NSCLC following progression on tyrosine kinase inhibitors, with HRQoL considerations included as supportive contextual evidence.

TABLE 2. Summary of HRQol Outcomes Across Platinum-Based and Non-Platinum Chemotherapy Regimens

Author	Patients	Assessment Instrument	Results	Remarks
Kozuki *et al.*,[15]	Elderly patients (≥75 yr) with advanced NSCLC	FACT-L (Lung Cancer Subscale)	HRQoL questionnaires were completed by 32 patients (62.7%) in the docetaxel arm and 36 patients (69.2%) in the pemetrexed arm. Baseline HRQoL scores were comparable except for functional well-being (19.1 vs 16.1; p=0.022). After treatment, HRQoL declined in both groups; however, the mean decline in lung cancer subscale scores was significantly smaller with pemetrexed plus bevacizumab (-1.0 vs -3.8; p = 0.016). At 12 wk, declines in FACT-L total score, Trial Outcome Index, and physical well-being were also significantly smaller in the pemetrexed arm (p<0.05).	Among non-platinum regimens, pemetrexed plus bevacizumab was associated with less HRQoL deterioration than docetaxel plus bevacizumab.
Okamoto *et al.*,[16]	Elderly patients (≥75 yr) with advanced NSCLC	Symptom Score Questionnaire (LCSS)	Median OS was 18.7 mo with carboplatin–pemetrexed vs 15.5 mo with docetaxel. Median PFS was longer in the platinum-based arm (6.4 vs 4.3 mo). Symptom scores remained stable in the carboplatin-pemetrexed group, whereas the docetaxel group showed early and persistent deterioration from week 6 to 18 (p<0.05). Grade 3-4 neutropenia and febrile neutropenia were more frequent with docetaxel.	Platinum-based chemotherapy preserved symptomrelated HRQoL while providing better disease control compared with docetaxel.
Kogure *et al.*,[17]	Elderly patients (≥70 yr) with advanced squamous NSCLC	FACT-L (Lung Cancer Subscale)	HRQoL scores remained generally stable in both treatment arms. Although grade 3-4 adverse events were more frequent with carboplatin plus nab-paclitaxel, no statistically significant differences in global HRQoL scores were observed between groups (p > 0.05).	Higher toxicity with platinum-based therapy did not translate into worse HRQoL.
Yang *et al.*[18]	Elderly patients (≥70 yr) with pretreated advanced NSCLC	EORTC QLQ-C30	Median OS was 14.7 mo with S-1 vs 12.1 mo with docetaxel (HR 0.76; 95% CI 0.54-1.07). Median PFS was 4.1 mo in both arms (HR 0.84; 95% CI 0.60-1.18). Adjusted mean global health status scores favored S-1 by 7.41 points (95% CI 0.37-14.46).	Non-platinum S-1 was a more favorable HRQoL profile with comparable survival outcomes to docetaxel.
Hou *et al.*,[19]	Patients with advanced NSCLC	FACT-L, MoCA, MMSE	HRQoL assessed by FACT-L showed a significant improvement over time (p<0.001). Cognitive function measured by MoCA also improved significantly (p=0.025), while MMSE scores remained stable (p= 0.567).	Platinum-based chemo-immunotherapy increased symptoms without compromising overall HRQoL.
Yang *et al.*,[20]	EGFR-mutant, TKI-resistant metastatic nonsquamous NSCLC	EORTC QLQ-C30, EQ-5D-5L	Median PFS was 5.6 vs 5.5 mo (HR 0.80; 95% CI 0.65-0.97). Median OS was 15.9 vs 14.7 mo (HR 0.84; 95% CI 0.69-1.02). Grade ≥3 adverse events occurred in 43.7% vs 38.6% of patients. HRQoL scores remained stable with no clinically meaningful deterioration between groups.	Increased toxicity without clear survival benefit underscores the importance of HRQoL evaluation.

DISCUSSIONS

This narrative review highlights the differential impact of platinum-based and non-platinum chemotherapy regimens on HRQoL in patients with NSCLC. Across the included studies, HRQoL outcomes varied substantially according to regimen composition, toxicity profile, patient characteristics, and assessment instruments, underscoring the multifactorial nature of quality-of-life changes during systemic cancer therapy.[15-20]

Overall, platinum-based chemotherapy regimens were frequently associated with increased treatment-related symptoms, including fatigue, gastrointestinal discomfort, and hematologic toxicity, which may negatively affect physical and functional HRQoL domains. Although several studies demonstrated preserved global HRQoL scores despite higher toxicity rates, symptom-specific deterioration was consistently observed, particularly among elderly patients.[16,17] These findings suggest that global HRQoL measures alone may underestimate the true patient burden when symptom-level outcomes if symptom-level outcomes are not simultaneously evaluated.

In contrast, non-platinum regimens generally demonstrated a more favorable HRQoL profile, with smaller declines in lung cancer–specific, physical, and functional domains. Kozuki *et al.*,[15] reported significantly less deterioration in FACT-L lung cancer subscale and physical well-being scores among patients receiving pemetrexed plus bevacizumab compared with docetaxel plus bevacizumab, highlighting the clinical relevance of treatment tolerability on patient-perceived well-being. Supportive evidence from subgroup analyses indicated that non-platinum regimens, such as S-1 or docetaxel-based therapies, may better preserve global health status in elderly or pretreated patients.[18] These observations reinforce the importance of minimizing treatment-related symptom burden to maintain HRQoL during chemotherapy administered with palliative intent.

Interpretation of HRQoL outcomes across studies is complicated by substantial heterogeneity in study design, patient populations and HRQoL assessment tools. The included trials varied in chemotherapy line (first-line versus salvage therapy), age distribution, performance status, and disease stage, all of which are known to influence baseline HRQoL and symptom trajectories. In addition, the use of different HRQoL instruments (FACT-L, LCSS, EORTC QLQ-C30, EQ-5D-5L) limits direct quantitative comparisons because these tools capture distinct dimensions of quality of life.[15-20] This methodological heterogeneity necessitates cautious interpretation of cross-study comparisons and supports the narrative, rather than pooled, synthesis approach adopted in this review

Heterogeneity across the included studies is also evident in the variation of HRQoL outcomes reported for platinum-based and non-platinum chemotherapy regimens. Studies evaluating non-platinum regimens, such as that by Kozuki *et al.*,[15] documented only modest declines in lung cancer–specific and physical HRQoL domains, suggesting relative preservation of patient-reported well-being. In contrast, trials assessing platinum-based chemotherapy, including those conducted by Okamoto *et al.*[16] and Kogure *et al.*,[17] reported largely stable global HRQoL scores despite higher incidences of treatment-related toxicity. Among pretreated elderly patients, non-platinum regimens were associated with more favorable global health status, as demonstrated by Yang *et al.*[18] Conversely, studies that enrolled fitter or molecularly selected populations

described stable HRQoL outcomes even with more intensive platinum-based or chemoimmunotherapy regimens. 18-20 Taken together, these differences in reported HRQoL outcomes likely reflect variation in baseline patient characteristics treatment line, and the HRQoL instruments employed rather than inherent inconsistencies in regimen-specific effects.

Several potential confounding factors may also influence HRQoL outcomes independently of chemotherapy regimen. Advanced age, reduced baseline performance status, comorbid conditions, and prior systemic therapy are associated with diminished functional reserve and increased vulnerability to treatment-related toxicity.[16-18] Differences in supportive care strategies, dose adjustments, and treatment discontinuation rates across studies may further affect patient-reported outcomes. These considerations indicate that observed HRQoL differences cannot be attributed solely to platinum exposure and should be interpreted within the broader clinical context.

From a clinical perspective, the findings of this review emphasize that HRQoL should be integrated as a central consideration in chemotherapy selection for NSCLC, particularly in settings where survival differences between regimens are modest. For elderly or frail patients, regimens associated with lower symptom burden and better preservation of daily functioning may be preferable, even in the absence of superior oncologic efficacy.[15,18] Conversely, in patients with good performance status, platinum-based regimens may remain appropriate when potential benefits are balanced against anticipated toxicity and patient preferences. Incorporating HRQoL assessments into shared decision-making frameworks may help align treatment strategies with individual patient goals and improve patient-centered care.

In summary, this review demonstrates that chemotherapy-related HRQoL outcomes in NSCLC are shaped by regimen-specific toxicity profiles and patient-related factors rather than platinum exposure alone. Systematic evaluation of HRQoL provides essential insight into the real-world impact of chemotherapy and should be considered a core component of therapeutic decision-making in advanced NSCLC.

CONCLUSION

This review demonstrates that platinum-based and non-platinum chemotherapy regimens exert distinct effects on HRQoL in patients with NSCLC. Platinum-based combinations remain important for disease control but are more frequently associated with treatment-related symptoms that may impair physical and functional HRQoL, particularly in elderly patients or those with limited functional reserve. In contrast, non-platinum regimens generally exhibit better tolerability and more stable HRQoL profiles. In clinical practice, these differences have important implications for treatment selection, as HRQoL outcomes may guide regimen choice for patients who are vulnerable to toxicity or who prioritize preservation of functional status. These findings highlight the need to integrate HRQoL considerations alongside efficacy when individualizing chemotherapy strategies. Future studies should prioritize prospective, head-to-head comparative studies using standardized HRQoL instruments, longer follow-up periods, and stratification by age, performance status, and treatment line to better support patient-centered decision-making in NSCLC.

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