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RESEARCH ARTICLE

Treatments for non-small cell lung cancer: a systematic quality assessment of clinical practice guidelines

Marcela Cortés-Jofré[1,2] · Meisser Madera[3] · Lesbia Tirado-Amador[4] · Claudia Asenjo-Lobos[5] · Xavier Bonfill-Cosp[6,7]

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Abstract

Aim To evaluate the methodological quality of clinical practice guidelines (CPGs) on treatments for non-small cell lung cancer (NSCLC).

Methods We searched MEDLINE, CPG developer websites, lung cancer societies, and oncology organizations to identify CPGs providing recommendations on treatments for NSCLC. The methodological quality for each CPG was determined independently by three appraisers using the AGREE II (Appraisal of Guidelines for Research and Evaluation II) instrument.

Results Twenty-two CPGs met the eligibility criteria. The median scores per AGREE II domain were: scope and purpose 90.7% (64.8–100%), stakeholder involvement 76.9% (27.8–96.3%); rigor of development 80.9% (27.1–92.4%); clarity of presentation 89.8% (50–100%); applicability 46.5% (12.5–87.5%); and editorial independence 91.7% (27.8–100%). Most of the CPGs (54.5%) were rated as "recommended with modifications" for clinical use.

Conclusions Overall, the methodological quality of CPGs proving recommendations on the management of NSCLC is moderate, but there is still room for improvement in their development and implementation.

Keywords Guidelines · Clinical guidelines · Non-small cells lung cancer · Lung cancer

Introduction

Lung cancer is one of the most common cancers worldwide and is considered a public health issue. According to the 2020 World Cancer Report, it had an incidence of 2.1 million new cases in 2018, and around 1.8 million deaths were reported for the same period [1]. It has been reported males have an incidence about 2 times higher than women and its incidence increases considerably with age [2]. One of the main risk factors for lung cancer is smoking, which could increase 20 times the chance of suffering lung cancer compared to non-smokers [3]. This risk could even increase when smoking is combined with other potential risk factors associated with lung cancers such as low physical activity, air pollution, vitamin A deficiency, child wasting, iron deficiency, exposition to asbestos and arsenic, unhealthy diet (high in sodium and low in vegetables and fruits), family history of lung cancer, and human immunodeficiency virus infection [4, 5]. Moreover, radon exposure is the leading risk factor for lung cancer among never-smokers and the second one in smokers [6].

✉ Meisser Madera
mmaderaa@unicartagena.edu.co

1 Doctoral Program in Research Methodology and Public Health, Universitat Autònoma de Barcelona, Barcelona, Spain

2 Facultad de Medicina, Universidad Católica de la Santísima Concepción, Concepción, Chile

3 Faculty of Dentistry, Department of Research, Universidad de Cartagena, Cartagena, Colombia

4 Programa de Odontología, Grupo GINOUS, Universidad del Sinú, Cartagena, Colombia

5 Centro de Estudios Clínicos, Instituto de Ciencias e Innovación en Medicina (ICIM), Facultad de Medicina Clínica Alemana, Universidad de Desarrollo, Santiago, Chile

6 Iberoamerican Cochrane Center, Institute of Biomedical Research Sant Pau (IIB Sant Pau), Barcelona, Spain

7 Public Health and Clinical Epidemiology Service, Hospital de la Santa Creu i Sant Pau, CIBER de Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain

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Non-small cell lung cancer (NSCLC) stands as the most prevalent lung tumor, accounting for around 85% of all lung neoplasms [7]. There are three subtypes of NSCLC: adenocarcinoma (40%), squamous cell carcinoma (25% to 30%), and giant cell carcinoma (10% to 15%) [8]. Although its 5-year survival rate has improved in recent decades, it remains a concern and can change depending on the stage of the disease. To illustrate, for people with localized NSCLC, the 5-year survival rate is 63%; for individuals with regional NSCLC, in which cancer has spread outside the lung to nearby lymph nodes, the 5-year survival rate is 35%; while it is just 7% for people with metastatic NSCLC. Moreover, its risk of relapse is high around 30% to 55% [9].

Due to the symptomatic manifestations of NSCLC are usually presented in advanced stages, the diagnosis is commonly established late when the disease has spread to other organs and its prognosis is poor [8]; consequently, the therapeutic interventions at this stage are limited. Overall, the management of NSCLC is stage-specific. To illustrate, people with stage I or II are usually treated with a surgical approach, while inoperable NSCLC are treated with radiotherapy or chemotherapy[10].

It is important to highlight that the most effective treatments are usually included in clinical practice guidelines (CPGs), which are systematically developed statements intended to help physicians and patients make decisions about appropriate medical care in specific circumstances[11]. Among the advantages of using CPGs are the improvement of clinical outcomes, adherence of clinicians and patients, promotion of a cost-effective and evidence-based practice[12]. Thus, using high-quality CPGs is a key approach to improving the survival rate and quality of life of people suffering from NSCLC.

Among the core aspects that strongly are recommended during the CPGs' development is that it must be based on a systematic review process, assessing the quality of the evidence, and translating the evidence into recommendations [11]. However, not all CGPs are developed with this evidence-based approach, which can lead to biased harmful recommendations [13]. Although the development, implementation, and systematic evaluation of CPGs have improved in recent years, they still have serious limitations in their methods, scope, and content.

In this sense, it is imperative to evaluate periodically the CPGs' development process, focusing on the standard methodology, reporting, quality, and the content of the CPGs to ensure that their recommendations are valid and reliable, and therefore, a useful and invaluable tool for decision-making [14]. Therefore, this study aimed to evaluate the methodological quality of CPGs proving recommendations on treatments for NSCLC.

Methods

Study design

A systematic assessment of the methodological quality of CPGs was conducted. The aim and all methods of this study were described in advance in a protocol.

Search strategy

We searched MEDLINE (via PubMed), CPGs developer websites, cancer scientific organizations, and lung cancer societies to identify CPGs proving recommendations on NSCLC. The Mesh term "Carcinoma, Non-Small-Cell Lung" was used in combination with terms related to CPGs such as "guidance", "practice guideline" and "recommendation". There was no restriction on languages. The last search was performed on 6th October 2022. The search strategy used, and the websites consulted are presented in detail in the Appendix A.

Eligibility criteria

We included CPGs providing recommendations for the management of primary or metastatic NSCLC in people aged 18 or over; CPGs had to have an explicit methodology chapter describing how their recommendations were formulated; publication in the last 10 years in English or Spanish, and the most updated version of the CPG. We excluded adaptations of CPGs and CPG retracted or archived by their developer.

Selection of CPGs

Initially, all records identified were retained and handled on the Covidence website. After removing duplicates, two authors independently revised titles/abstracts to identify potential CPGs, then the full texts were gathered to decide on the final inclusion of eligible CPGs. Discrepancies were resolved by discussion, with the participation of a third author, whether was needed.

Instrument to assess of methodological quality of CPGs

We used the AGREE II (Appraisal of Guidelines for Research and Evaluation II) instrument [15], which contains 23 items using a seven-point Likert scale and considered six domains: (a) Scope and purpose: this focuses on the aim, the target population and clinical questions addressed in the CPG; (b) Stakeholder involvement; this focuses on the extent to which the CPG was developed by the appropriate

stakeholders and represents the views of its intended users; (c) Rigor of development; this focuses on the methods used to formulate the recommendations and how evidence was gathered and summarized; (d) Clarity and presentation; this evaluates the way how recommendations are presented, if they are easily recognizable, unambiguous and clear, and whether there are various alternatives to the management of the disease; (e) Applicability; dealing with implementation issues, such as the assessment of organizational facilitators and barriers, the development of educational sources, economic implications, and monitoring or audit criteria; (f) Editorial independence; assessing whether the views or interests of the funding sources have influenced the recommendations, and if the conflicts of interest statement reports all information about the CPG developer team. In addition, the AGREE II instrument also contains two overall quality items for each CPG: an overall score of 1 to 7, and whether the assessor would recommend using the CPG, rating it as "recommended", "recommended with modifications" or "not recommended". The methodological quality assessment was independently conducted by three reviewers.

Data extraction and analysis

We extracted data on general characteristics from each CPG such as title, publication year, authoring organization, country, language, level of development, funding source, whether or not it is an update, methods used to formulate recommendations, level of evidence, and grading of the recommendations. This process was conducted independently by two authors. Discrepancies were resulted by discussion with the participation of a third author if necessary. We performed a descriptive analysis of these characteristics using tables and a synthesis narrative. Statistical analyses were performed with SPSS® version 27.0 software (SPSS Inc, Chicago, IL). Initially, we calculated the intraclass correlation coefficient (ICC) with its 95% confidence interval (95% CI) as an indicator of agreement between reviewers. Then, we calculated the domain scores by adding up all the scores of the individual items within a domain and calculated the percentage of the maximum possible score for that domain. Standardized scores (range, 0% to 100%) for each domain were calculated as follows: [(obtained score − minimum possible score)/(maximum possible score − minimum possible score)] × 100%. We assumed a threshold of 60% as an indicator of adequate quality. Median and minimum–maximum values were calculated for each domain score for each CPG. Moreover, to determine if the methodological quality of CPGs has improved in recent years, we compare the AGREE II scores between recent CPGs (published in last 5 years) and not recent CPGs (published before 2018) using the Mann–Whitney U test with a significance level of 0.05.

Results

CPGs identified

After removing duplicates, 498 titles/abstracts were reviewed, then 46 full-text documents were reviewed and 22 [16–37] of them met the eligibility criteria (Fig. 1). All documents considered relevant, and their reasons for exclusion are presented in the Appendix B.

General characteristics of the included CPGs

All included CPGs [16–37] were published between 2012 and 2022, 19 [16–21, 23, 24, 26–29, 31–37] of them were published in English, and three [22, 25, 30] in the Spanish language. All CPGs [16–37] provided recommendations for the management of NSCLC, whereas some of them also provided recommendations about diagnosis and follow-up [17–19, 22, 32, 33]. Sixteen [16–20, 23, 25–28, 31–33, 35–37] CPGs were an update of previous versions. There were eight CPGs [17–19, 27, 34–37] from the United States, five CPGs [16, 21, 23, 24, 26] were from Canada, three CPGs [22, 25, 28] from Spain, two CPGs [32, 33] from Europe, while the others were one from each one of the following countries: Mexico [30], Japan [31], Scotland [20], and Italy [29]. Nineteen CPGs [17–19, 21–35, 37] were developed by a professional organization, while three CPGs [16, 20, 36] were developed by a government agency. Five CPGs [21, 23, 29, 31, 34] used the GRADE (The Grading of Recommendations Assessment, Development and Evaluation) approach to develop their recommendations, whereas most of the CPGs [16–20, 22, 25, 27, 28, 30, 32, 33, 35–37] used a systematic review of the literature and critical appraisal of evidence (Table 1).

The methodological quality of CPGs

The overall agreement between appraisers was substantial (ICC: 0.72; 95% IC = 0.68–0.8). The median scores per AGREE II domain were: scope and purpose 90.7% (ranging from 64.8% to 100%), stakeholder involvement 76.9% (ranging from 27.8% to 96.3%); rigor of development 80.9% (ranged from 27.1% to 92.4%); clarity of presentation 89.8% (ranging from 50% to 100%); applicability 46.5% (ranging from 12.5% to 87.5%); and editorial independence 91.7% (ranging from 27.8% to 100%). Among all CPGs [16–37] evaluated, six CPGs [17, 18, 20, 21, 34, 37] (27.3%) were "recommended" by the reviewers for cline use; 12 CPGs [19, 22–27, 30, 31, 33, 35, 36] (54.5%) were "recommended with modifications"; and four CPGs [16, 28, 29, 32] (18.2%) were "not recommended". The median of the overall rate was 5

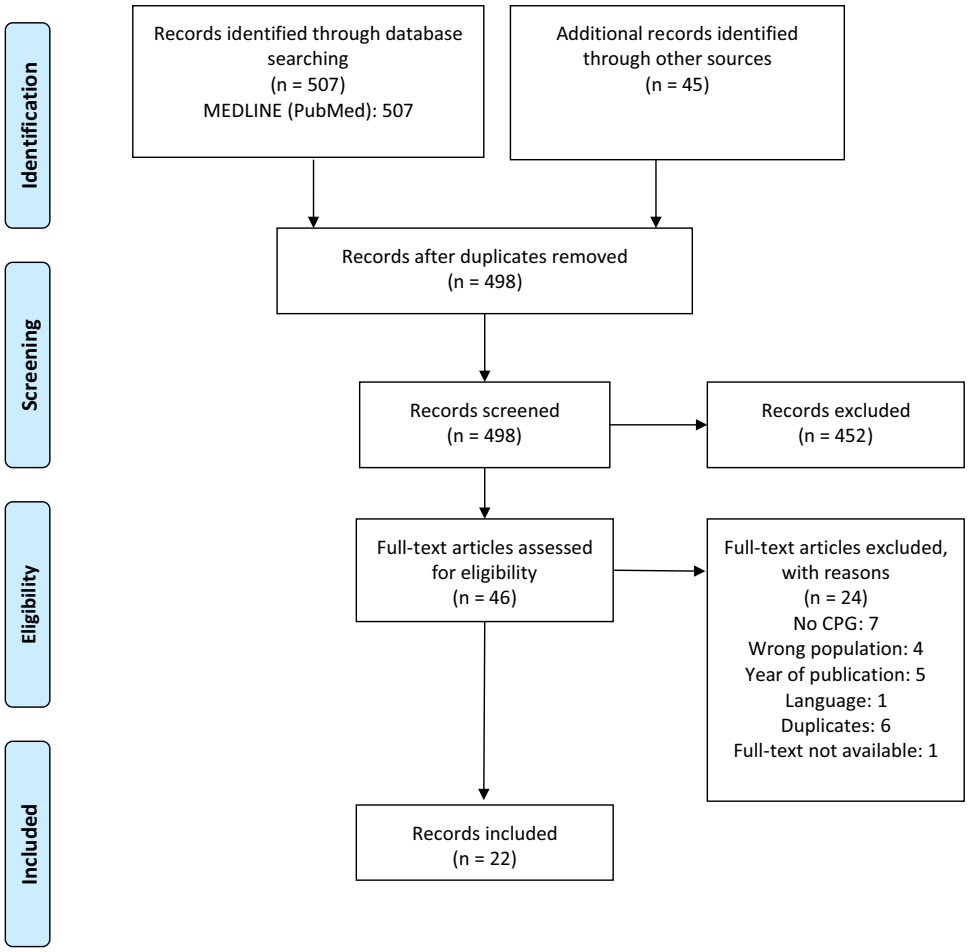

Fig. 1 The selection process of CPGs

(minimum 3, maximum 6) points. The standardized scores across CPGs by domain in detail and the overall recommendation for clinical use of the included CPGs are presented in Table 2.

Table 3 shows the comparison of the AGREE II scores by publication period. Overall, our analysis found no statistically significant differences between the methodological quality of recent CPGs (published in 2018–2022) and not recent CPGs (published in 2012–2017) using the overall AGREE II scores or by domains.

Discussion

CPGs are essential to provide evidence-based health services, thus identifying high-quality CPGs in a specific clinical area will contribute to their implementation and clinician´s adherence. Therefore, this study looked to appraise the methodological quality of CPGs on NSCLC, to help clinicians and patients about the most suitable treatments. Likewise, based on our knowledge, this study could be considered the first one assessing CPGs on treatments for NSCLC, using the AGREE II instrument.

Overall, the quality of CPGs providing recommendations on therapeutic interventions for NSCLC is moderate with most CPGs [19, 22–27, 30, 31, 33, 35, 36] being rated as "recommended with modifications" for clinical use. It suggests that there is room for improving the methodological quality of CPGs on NSCLC if their weaknesses are addressed. Among the deficiencies that need to be addressed are: a) the lack of information on sources and barriers to CPGs' implementation; (b) the incorporation of patients and other stakeholders in the CPG development process, (c) the deficiency of patients' views and their preferences; and (c) the inadequate critical appraisal of supporting evidence, especially of its limitations and strengths. These findings are similar to previous reports evaluating of methodological quality of CPGs in oncology[38–41] and other medical disciplines [42–48], which have concluded the quality of CPGs is substantially variable, suggesting a huge chance for improvement. Similarly, there are two previous studies[49, 50] evaluating CPGs on lung cancer suggesting that CPGs in this field must be improved, one[49] of them focused on the quality of CPGs proving recommendations on complementary and integrative medicine therapy such as social and spiritual support,

Table 1 General characteristics of the included CPGs

CPG	Year	Organization	Country/ Region	Language	Level of development	Funding source	CPG is an update	Methods	Level of evidence	Grading the recommendation
Non-small cell lung cancer: stage III [16]	2012	AHS	Canada	English	GA	NR	Yes	SR and CAE	NR	NR
Treatment of stage I and II non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines [17]	2013	ACCP	USA	English	Professional organization	Professional society	Yes	SR and CAE	NR	1A, 1B, 1C, 2A, 2B, 2C
Treatment of stage IV non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines [18]	2013	ACCP	USA	English	Professional organization	Professional society	Yes	SR and CAE	NR	1A, 1B, 1C, 2A, 2B, 2C

Table 1 (continued)

CPG	Year	Organization	Country/ Region	Language	Level of development	Funding source	CPG is an update	Methods	Level of evidence	Grading the recommendation
Treatment of stage III non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines [19]	2013	ACCP	USA	English	Professional organization	Professional society	Yes	SR and CAE	NR	1A, 1B, 1C, 2A, 2B, 2C
Management of lung cancer [20]	2014	SIGN	Scotland	English	GA	Government	Yes	SR and CAE	1 + + /1 + /1-/2 + + /2 + /2-/3/4	A/B/C/D/ GPP
The use of systemic treatment in the maintenance of patients with non-small cell lung Cancer [21]	2015	CCO	Canada	English	Professional organization	Government	No	GRADE	High/Moderate/Low/ Very low	NR
The SEPAR recommendations for the diagnosis and treatment of non-small cell lung cancer [22]	2016	SEPAR	Spain	Spanish	Professional organization	Professional society	No	SR and CAE	NR	1A, 1B, 1C, 2A, 2B, 2C
Systemic treatment for patients with advanced non-small cell lung cancer [23]	2016	CCO	Canada	English	Professional organization	Government	Yes	GRADE	High/Moderate/Low/ Very low	NR

Table 1 (continued)

CPG	Year	Organization	Country/ Region	Language	Level of development	Funding source	CPG is an update	Methods	Level of evidence	Grading the recommendation
Radiotherapy with curative intent in patients with early stage, medically inoperable, non-small cell lung cancer [24]	2016	CCO	Canada	English	Professional organization	Government	No	AGREE II	NR	NR
ICOPractice: treatment for non-small cell lung cancer [25]	2016	ICO	Spain	Spanish	Professional organization	Professional society	Yes	SR and CAE	I, II, III, IV, V	A/B/C/D
Treatment of patients with stage III (N2 or N3) non-small cell lung cancer [26]	2017	CCO	Canada	English	Professional organization	Government	Yes	AGREE II	NR	NR
Palliative thoracic radiation therapy for non-small cell lung cancer: 2018 Update of an American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline [27]	2018	ASTRO	USA	English	Professional organization	NR	Yes	SR and CAE	High/Moderate/Low	Strong/Conditional
SEOM clinical guidelines for the treatment of non-small cell lung cancer (2018) [28]	2019	SEOM	Spain	English	Professional organization	NR	Yes	SR and CAE	I, II, III, IV, V	A/B/C/D/

Table 1 (continued)

CPG	Year	Organization	Country/ Region	Language	Level of development	Funding source	CPG is an update	Methods	Level of evidence	Grading the recommendation
Treatment of metastatic non-small cell lung cancer: 2018 guidelines of the Italian Association of Medical Oncology (AIOM) [29]	2019	AIOM	Italy	English	Professional organization	Professional society	No	GRADE and SIGN	High/Moderate/Low/ Very low	A/B/C/D/ OR Strong for to Strong against
National Clinical Practice Guidelines for the management of non-small cell lung cancer in early, locally advanced and metastatic stages [30]	2019	SMO CENETEC	Mexico	Spanish	GA and professional organization	NR	No	SR and CAE	$1^{++}/1^{+}/1^{-}/2^{++}/2^{+}/2^{-}/3/4$	A/B/C/D/
The Japanese Lung Cancer Society Guideline for non-small cell lung cancer, stage IV [31]	2019	JLCS	Japan	English	Professional organization	Professional society	Yes	GRADE	High/Moderate/Low/ Very low	Strong/Weak
Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up [32]	2020	ESMO	Europe	English	Professional organization	NR	Yes	SR and CAE	I, II, III, IV, V	A/B/C/D/

Table 1 (continued)

CPG	Year	Organization	Country/ Region	Language	Level of development	Funding source	CPG is an update	Methods	Level of evidence	Grading the recommendation
Early and locally advanced non-small cell lung cancer: an update of the ESMO Clinical Practice Guidelines focusing on diagnosis, staging, systemic and local therapy [33]	2021	ESMO	Europe	English	Professional organization	NR	Yes	SR and CAE	I, II, III, IV, V	A/B/C/D/
Management of Stage III Non–Small-Cell: ASCO Guideline [34]	2022	ASCO	USA	English	Professional organization	Professional society	No	GRADE	high, moderate, low, and very low	Strong/moderate/ weak
Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stage I-IIIA Completely Resected Non-Small-Cell Lung Cancer: ASCO Guideline Rapid Recommendation Update [35]	2022	ASCO	USA	English	Professional organization	NR	Yes	SR and CAE	NR	NR
Non-Small-Cell Lung Cancer [36]	2022	NCCN	USA	English	GA	Government	Yes	SR and CAE	1, 2A, 2B, 3	NR

Table 1 (continued)

CPG	Year	Organization	Country/ Region	Language	Level of development	Funding source	CPG is an update	Methods	Level of evidence	Grading the recommendation
Therapy for Stage IV Non-Small-Cell Lung Cancer Without Driver Alterations: ASCO Living Guideline [37]	2022	ASCO	USA	English	Professional organization	Professional society	Yes	SR and CAE	High/Intermediate /Low	Strong/moderate/weak

ACCP American College of Chest Physicians; *AGREE II* Appraisal of Guidelines for Research and Evaluation II instrument; *AHS* Alberta Health Services, *AIOM* The Italian Association of Medical Oncology, *ASCO* American Society of Clinical Oncology, *ASTRO* American society for radiation oncology, *CAE* critical appraisal of evidence, *CCO* Cancer Care Ontario, *CENETEC* National Center for Technological Excellence in Health, *ESMO* European Society for Medical Oncology, *GA* Government agency, *GRADE* The grading of recommendations assessment, development and evaluation; *ICO* Catalan institute of oncology, *JLCS* Japan Lung Cancer Society, *NCCN* National comprehensive cancer network; *NR* not reported, *SEOM* the Spanish Society of medical oncology, *SEPAR* The Spanish Society of Pneumology and Thoracic Surgery, *SIGN* Scottish Intercollegiate Guidelines Network, *SMO* The Mexican Society of Oncology, *SR* systematic review of literature, *USA* United States of America

self-care strategies, yoga, massage therapy, exercise, acupuncture, and nutrition/dietary supplements; whereas the other[50] assessed the reporting quality of CPGs on lung cancer using the International Reporting Items for Practice Guidelines in Health Care (RIGHT) instrument. It is useful to highlight that our findings might not be comparable to these studies because they had other aims; to illustrate, they did not focus on NSCLC treatments, exclusively; moreover, one[50] of them used an instrument that captures different spheres of a CPG, thus, it is not comparable to AGREE II tool[51].

Regarding the domain scoring, we would like to highlight that the majority (5 out of 6) of AGREE II domains scored over the threshold of adequate quality (60%); only the "applicability" domain scored under this cut-off point, so it was the domain with the lowest scores, while the "editorial independence" and "scope and purpose" domains had the highest scores. These findings could be considered similar to some previous assessments of CPGs on cancers [38, 39, 49, 52] and other medical specialties[43, 44, 46, 47, 53–57], which support that "applicability" and "scope and purpose" domains are the ones with the lowest and highest scores, respectively. Conversely, some reports suggest that domains such as "rigor of development" [58] and "editorial independence" [59] stand among those with the lowest scores. Thus, it suggests that domain scores can vary depending on fields or topics addressed in the CPGs. Overall, our findings suggest that nowadays the CPCs including recommendations on NSCLC therapies usually do not provide explicit instructions about financial sources, costs, barriers, facilitators, additional materials, and other key factors to ensure the implementation of their recommendations, whereas they fully described their aims, the target population, potential users, developers' conflict of interest, funding sources, and clinical questions to be addressed into the CPG. Therefore, greater efforts are essential to improve their applicability issues. Likewise, to improve clinicians' adherence to these CPGs and decrease the variability of decisions in clinical practice, it is needed to disseminate appropriately the quality of available CPGs in this area.

The main implications of this study are linked to improving CPGs' development in this field, especially their applicability, which can contribute with provide better evidence-based practice and improve clinical outcomes of people suffering from NSCLC. Likewise, the variation in the methodological quality of the included CPGs highlights the need to identify high-quality CPGs before implementing their recommendations. To illustrate, it is widely known that implementing recommendations from low-quality CPGs can lead to negative effects on patients. Therefore, it is important to make available high-quality CPGs on NSCLC that could be a practical and genuine instrument for clinical decision-making.

Table 2 Standardized scores across CPGs by AGREE II domain

CPG	Scope and purpose	Stakeholder involvement	Rigour of development	Clarity of presentation	Applicability	Editorial independence	Overall rate	Overall recommendation
	%	%	%	%	%	%		
Non-small cell lung cancer: stage III [16]	90.7	77.8	66.7	79.6	27.8	88.9	4	Not recommended
Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cancer. 3rd ed: american college of chest physicians evidence-based clinical practice guidelines [17]	85.2	72.2	82.6	92.6	62.5	88.9	5	Recommended
Treatment of stage IV non-small cell lung cancer: diagnosis and management of lung cancer. 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines [18]	92.6	75.9	83.3	94.4	70.8	94.4	6	Recommended
Treatment of stage III non-small cell lung cancer: diagnosis and management of lung cancer. 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines [19]	83.3	81.5	79.2	85.2	62.5	94.4	5	Recommended with modifications
Management of lung cancer [20]	100	81.5	91.7	98.1	76.4	100	6	Recommended
The use of systemic treatment in the maintenance of patients with non-small cell lung cancer [21]	98.1	90.7	92.4	100	70.8	91.7	6	Recommended
The SEPAR recommendations for the diagnosis and treatment of non-small cell lung cancer [22]	87.0	68.5	75.0	87.0	27.8	94.4	5	Recommended with modifications
Systemic treatment for patients with advanced non-small cell lung cancer [23]	98.1	77.8	85.4	90.7	30.6	88.9	5	Recommended with modifications
Radiotherapy with curative intent in patients with early stage. medically inoperable. non-small cell lung cancer [24]	98.1	74.1	78.5	88.9	47.2	97.2	5	Recommended with modifications
ICOPractice: treatment for non-small cell lung cancer [25]	83.3	83.3	78.5	75.9	48.6	91.7	5	Recommended with modifications
Treatment of patients with stage III (N2 or N3) non-small cell lung cancer [26]	96.3	75.9	81.3	92.6	30.6	97.2	5	Recommended with modifications
Palliative thoracic radiation therapy for non-small cell lung cancer: 2018 Update of an American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline [27]	81.5	61.1	79.9	88.9	38.9	88.9	5	Recommended with modifications
SEOM clinical guidelines for the treatment of non-small cell lung cancer (2018) [28]	64.8	27.8	27.1	50.0	12.5	52.8	3	Not recommended
Treatment of metastatic non-small cell lung cancer: 2018 guidelines of the Italian Association of Medical Oncology (AIOM) [29]	64.8	57.4	54.9	64.8	25.0	86.1	4	Not recommended

Table 2 (continued)

CPG	Scope and purpose	Stakeholder involvement	Rigour of development	Clarity of presentation	Applicability	Editorial independence	Overall rate	Overall recommendation
	%	%	%	%	%	%		
National Clinical Practice Guidelines for the management of non-small cell lung cancer in early. locally advanced and metastatic stages [30]	92.6	96.3	80.6	90.7	45.8	27.8	5	Recommended with modifications
The Japanese lung cancer society guideline for non-small cell lung cancer. stage IV [31]	88.9	70.4	81.3	92.6	23.6	97.2	5	Recommended with modifications
Metastatic non-small cell lung cancer: ESMO Clinical practice guidelines for diagnosis. treatment and follow-up [32]	68.5	48.1	59.0	85.2	27.8	83.3	5	Not recommended
Early and locally advanced non-small cell lung cancer: an update of the ESMO Clinical practice guidelines focusing on diagnosis. staging. systemic and local therapy [33]	90.7	61.1	64.6	94.4	37.5	88.9	5	Recommended with modifications
Management of stage III Non–small cell: ASCO Guideline [34]	98.1	85.2	86.8	81.5	75.0	88.9	6	Recommended
Adjuvant systemic therapy and adjuvant radiation therapy for stage I-IIIA completely resected non-small cell lung cancer: ASCO guideline rapid recommendation update [35]	100	79.6	86.1	90.7	70.8	97.2	5	Recommended with modifications
Non-small cell lung cancer [36]	85.2	81.5	81.3	83.3	68.1	97.2	5	Recommended with modifications
Therapy for stage IV non-small cell lung cancer without driver alterations: ASCO living guideline [37]	100	94.4	88.2	94.4	87.5	100	6	Recommended
Median	90.7	76.9	80.9	89.8	46.5	91.7	5	
Minimum–maximum	64.8–100	27.8–96.3	27.1–92.4	50–100	12.5–87.5	27.8–100	3–6	

Table 3 Comparison of the AGREE II scores by publication period

AGREE II domains	Not recent CPGs ($n=11$)		Recent CPGs ($n=11$)		p value*
	Median (%)	IQR (%)	Median (%)	IQR (%)	
Scope and purpose	92.6	13.0	88.9	29.6	0.365
Stakeholder involvement	77.8	7.4	70.4	27.8	0.438
Rigour of development	81.2	6.9	80.5	27.1	0.438
Clarity of presentation	90.7	9.3	88.9	11.1	0.365
Applicability	48.6	40.3	38.9	45.8	0.562
Editorial independence	94.4	8.3	88.9	13.9	0.243
Overall median	5.3	0.7	5.3	1.0	0.652

Mann–Whitney *U* test; *IQR* The interquartile range

Among the limitations of this study are the language barriers since we only included CPGs published in English and Spanish, which limits the external validity of our results to CPGs published in other languages. Likewise, another limitation could be our incapacity to identify non-indexed CPGs. However, it has been reported that CPGs that are not indexed have poorer quality compared to those indexed [60]. This study also has some strengths, such as the assessment of all CPGs was independently performed by three appraisers with a substantial agreement using a validated and reliable instrument. Moreover, a comprehensive search was carried out to identify all relevant CPGs, so it is not likely that relevant CPGs are missing. Thus, all these processes provide trustworthiness to our findings.

Conclusion

Overall, the methodological quality of CPGs proving recommendations on the management of NSCLC is moderate. Most CPGs were rated as "recommended with modifications" for clinical use, and the "applicability" domain scored lowest; thus, great efforts are needed to improve the development and implementation of CPGs in this field, which could contribute to the decision-making process and lead better clinical outcomes in people suffering from NSCLC.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Wild CP, Weiderpass E, Stewart BW. 2020 World Cancer Report: cancer research for cancer development: In Wild CP, Weiderpass E Stewart BW, (eds). International Agency for Research on Cancer. Lyon
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71:209–49.
3. Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. Eur Respir J. 2016;48:889–902.
4. Wu X, Denise B-B, Zhan F, Zhang J. Determining association between lung cancer mortality worldwide and risk factors using fuzzy inference modeling and random forest modeling. Int J Environ Res Public. 2022. https://doi.org/10.3390/ijerph192114161.
5. Cortés-Jofré M, Rueda JR, Asenjo-Lobos C, Madrid E, Bonfill CX. Drugs for preventing lung cancer in healthy people. Cochrane Database Syst Rev. 2022. https://doi.org/10.1002/14651858.CD002141.pub3.
6. Cheng ES, Egger S, Hughes S, Weber M, Steinberg J, Rahman B, et al. Systematic review and meta-analysis of residential radon and lung cancer in never-smokers. Eur Respir Rev. 2021;30:1–14.
7. Relli V, Trerotola M, Guerra E, Alberti S. 2019 Abandoning the notion of non-small cell lung cancer. Trends Mol Med. 2019;25:585–94.
8. Chansky K, Detterbeck FC, Nicholson AG, Rusch VW, Vallières E, Groome P, et al. The IASLC lung cancer staging project: external validation of the revision of the TNM stage groupings in the of the TNM classification of lung cancer. J Thorac Oncol. 2017;12:1109–21.
9. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics. CA Cancer J Clin. 2023;73:17–48.
10. Duma N, Santana-Davila R, Molina JR. Non-small cell lung cancer: epidemiology, screening, diagnosis, and treatment. Mayo Clin Proc. 2019;94:1623–40.
11. Hassan Murad M. Clinical practice guidelines a primer on development and dissemination. Mayo Clin Proc. 2017;92(423):33.
12. Hollon SD, Teachman BA. Advantages of developing clinical practice guidelines using international standards. Psychotherapy. 2019;56:340–6.
13. McAlister FA, Van Diepen S, Padwal RS, Johnson JA, Majumdar SR. How evidence-based are the recommendations in evidence-based guidelines? PLoS Med. 2007;4:1325–32.
14. Eikermann M, Holzmann N, Siering U, Rüther A. Tools for assessing the content of guidelines are needed to enable their effective use–a systematic comparison. BMC Res Notes. 2014;7(1):853.
15. Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. Development of the AGREE II, part 2: assessment

of validity of items and tools to support application. CMAJ. 2010. https://doi.org/10.1503/cmaj.091716.
16. Alberta Health Services (AHS). Non-small cell lung cancer stage III. Clinical practice guideline LU-003. Alberta. 2012. www.albertahealthservices.ca
17. Howington JA, Blum MG, Chang AC, Balekian AA, Murthy SC. Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cáncer american college of chest physicians evidence-based clinical practice guidelines. Chest. 2013. https://doi.org/10.1378/chest.12-2359.
18. Socinski MA, Evans T, Gettinger S, Hensing TA, Van Dam SL, Ireland B, et al. Treatment of stage IV non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: american college of chest physicians evidence-based clinical practice guidelines. Chest. 2013. https://doi.org/10.1378/chest.12-2361.
19. Ramnath N, Dilling TJ, Harris LJ, Kim AW, Michaud GC, Balekian AA, et al. Treatment of stage III non-small cell lung cancer: diagnosis and management of lung cáncer american college of chest physicians evidence-based clinical practice guidelines. Chest. 2013. https://doi.org/10.1378/chest.12-2360.
20. Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer a national clinical guideline. 2014. www.sign.ac.uk/pdf/sign50eqia.pdf.
21. Kulkarni S, Vella E, Coakley N, Cheng S, Gregg R, Ung YC, et al. Guideline the use of systemic treatment in the maintenance of patients with non-small cell lung cancer. J Thor Oncol. 2015. https://doi.org/10.1016/j.jtho.2016.03.007.
22. Álvarez FV, Trueba IM, Sanchis JB, López-Rodó LM, Rodríguez Suárez PM, de Cos Escuín JS, et al. Recommendations of the Spanish society of pneumology and thoracic Surgery on the diagnosis and treatment of non-small-cell lung cancer. Arch Bronconeumol. 2023;52(Suppl 1):2–62.
23. Ellis PM, Vella ET, Ung YC. Systemic treatment for patients with advanced non-small cell lung cáncer program in evidence-based care guideline version 3. Amsterdam: Elsevier; 2016.
24. Falkson CB, Vella ET, Yu E, El-Mallah M, Mackenzie R, Ellis PM, et al. Radiotherapy with curative intent in patients with early stage, medically inoperable, non-small cell lung cáncer Program in evidence-based care evidence-based Series. Current Oncol. 2017. https://doi.org/10.3747/co.24.3358.
25. Instituto Catalan de Oncología. ICOpraxis para el tratamiento médico de cáncer de pulmón de célula no pequeña. ICO. 2016;2:1–125.
26. Swaminath A, Vella ET, Ramchandar K, Robinson A, Simone C, Sun A, et al. Treatment of patients with stage III (N2 or N3) non-small cell lung cancer. guideline 7–3 version 3 a quality initiative of the program in evidence-based care (PEBC). Cancer Care Ontario. 2017. Available from: http://www.cancercare.on.ca/.
27. Moeller B, Balagamwala EH, Chen A, Creach KM, Giaccone G, Koshy M, et al. Palliative thoracic radiation therapy for non-small cell lung cancer: 2018 update of an american society for radiation oncology (ASTRO) evidence-based guideline. Pract Radiat Oncol Pract Radiat Oncol. 2018;8:245–50.
28. Majem M, Juan O, Insa A, Reguart N, Trigo JM, Carcereny E, et al. SEOM clinical guidelines for the treatment of non-small cell lung cancer. Clin Transl Oncol. 2018;21:3–17.
29. Facchinetti F, Pilotto S, Metro G, Baldini E, Bertolaccini L, Cappuzzo F, et al. Treatment of metastatic non-small cell lung cancer: 2018 guidelines of the Italian association of medical oncology (AIOM). Tumori. 2016;105:3–14.
30. Barrón-Barrón F, Guzmán-De Alba E, Alatorre-Alexander J, Aldaco-Sarvide F, Bautista-Aragón Y, Blake-Cerda M, et al. Guía de Práctica Clínica Nacional para el manejo del Cáncer de Pulmón de células no pequeñas en estadios tempranos, localmente avanzados y metastásicos. Salud Publica Mex. 2019;61:359.
31. Akamatsu H, Ninomiya K, Kenmotsu H, Morise M, Daga H, Goto Y, et al. The japanese lung cancer society guideline for non-small cell lung cancer, stage IV. Int J Clin Oncol. 2019;24:731–70.
32. Planchard D, Popat S, Kerr K, Novello S, Smit EF, Faivre-Finn C, et al. Metastatic non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up the ESMO guidelines committee. Ann Oncol. 2020;3(1):71.
33. Remon J, Soria JC, Peters S. Early and locally advanced non-small-cell lung cancer: an update of the ESMO clinical practice guidelines focusing on diagnosis, staging, systemic and local therapy. Ann Oncol Ann Oncol. 2021;32:1637–42.
34. Daly ME, Singh N, Ismaila N, Antonoff MB, Arenberg DA, Bradley J, et al. Management of stage III non-small-cell lung cancer: ASCO guideline. J Clin Oncol. 2022;40:1356–84.
35. Pisters K, Kris MG, Gaspar LE, Ismaila N. Adjuvant systemic therapy and adjuvant radiation therapy for stage I-IIIA completely resected non-small-cell lung cancer: asco guideline rapid recommendation update. J Clin Oncol. 2022;40:1127–9.
36. Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman JR, Bharat A, et al. Non-small cell lung cancer, version 3.2022, NCCN clinical practice guidelines in oncology. Natl Compr Canc Netw. 2022;20:497–530.
37. Singh N, Temin S, Baker S, Blanchard E, Brahmer JR, Celano P, et al. Therapy for stage IV non-small-cell lung cancer without driver alterations: ASCO living guideline. J Clin Oncol. 2022;40:3323–43.
38. Madera M, Franco J, Solà I, Bonfill X, Alonso-Coello P. Screening and diagnosis of oral cancer: a critical quality appraisal of clinical guidelines. Clin Oral Investig. 2019;23:2215–26.
39. Madera Anaya MV, Franco JV, Merchán-Galvis ÁM, Gallardo CR, Bonfill CX. Quality assessment of clinical practice guidelines on treatments for oral cancer. Cancer Treat Rev. 2018;65:47–53.
40. Santero M, Meade AG, Acosta-Dighero R, González L, Melendi S, Solà I, et al. European clinical practice guidelines on the use of chemotherapy for advanced oesophageal and gastric cancers: a critical review using the AGREE II and the AGREE-REX instruments. Clin Transl Oncol. 2022;24:1588–604.
41. Zhou X, Yang Y, Li C, Gu S, Hou W, Lai X, et al. What information can we gain from the quality appraisal of guidelines with physical activity recommendations for cancer patients A systematic review using the AGREE II and AGREE-REX tools. Supportive Care Cancer. 2023. https://doi.org/10.1007/s00520-022-07567-5.
42. Noyahr JK, Tatucu-Babet OA, Chapple LAS, Barlow CJ, Chapman MJ, Deane AM, et al. Methodological rigor and transparency in clinical practice guidelines for nutrition care in critically ill adults: a systematic review using the AGREE II and AGREE-REX tools. Nutrients. 2022. https://doi.org/10.3390/nu14132603.
43. Hoydonckx Y, Kumar P, Flamer D, Costanzi M, Raja SN, Peng P, et al. Quality of chronic pain interventional treatment guidelines from pain societies: assessment with the AGREE II instrument. Eur J Pain. 2020;24:704–21.
44. Al Wattar BH, Fisher M, Bevington L, Talaulikar V, Davies M, Conway G, et al. Clinical practice guidelines on the diagnosis and management of polycystic ovary syndrome: a systematic review and quality assessment study. J Clin Endocrinol Metab. 2021;6:2436–46.
45. Rabassa M, Hernández Ponce Y, Garcia-Ribera S, Johnston BC, Salvador Castell G, Manera M, et al. Food-based dietary guidelines in Spain: an assessment of their methodological quality. Eur J Clin Nutr. 2022;76:350–9.
46. Angel G, Trujillo C, Mallama M, Alonso-Coello P, Klimek M, Calvache JA. Methodological transparency of preoperative clinical practice guidelines for elective surgery. PLoS ONE. 2023. https://doi.org/10.1371/journal.pone.0272756.

47. Merchan-Galvis AM, Caicedo JP, Valencia-Payán CJ, Calvache JA. Methodological quality and transparency of clinical practice guidelines for difficult airway management using the appraisal of guidelines research & evaluation II instrument: a systematic review. Eur J Anaesthesiol. 2020;37:451–6.
48. Deana NF, Zaror C, Seiffert A, Aravena-Rivas Y, Muñoz-Millán P, Espinoza-Espinoza G, et al. Quality appraisal of clinical practice guidelines on provision of dental services during the first months of the COVID-19 pandemic. J Evid Based Dent Pract. 2021. https://doi.org/10.1016/j.jebdp.2021.101633.
49. Ng JY, Nault H, Nazir Z. Complementary and integrative medicine mention and recommendations: A systematic review and quality assessment of lung cancer clinical practice guidelines. Integr Med Res. 2021. https://doi.org/10.1016/j.imr.2020.100452.
50. Yang Y, Lu J, Ma Y, Xi C, Kang J, Zhang Q, et al. Evaluation of the reporting quality of clinical practice guidelines on lung cancer using the RIGHT checklist. Transl Lung Cancer Res. 2021;10:2588–602.
51. Yao X, Ma J, Wang Q, Kanters D, Ali MU, Florez ID. A comparison of agree and right: which clinical practice guideline reporting checklist should be followed by guideline developers? J Gen Intern Med. 2020;35:894–8.
52. Chen YP, Wang YQ, Li WF, Chen L, Xu C, Lu TX, et al. Critical evaluation of the quality and recommendations of clinical practice guidelines for nasopharyngeal carcinoma. J Natl Compr Canc. 2017;15:336–44.
53. Seiffert A, Zaror C, Atala-Acevedo C, Ormeño A, Martínez-Zapata MJ, Alonso-Coello P. Dental caries prevention in children and adolescents: a systematic quality assessment of clinical practice guidelines. Clin Oral Investig. 2018;22:3129–41.
54. Jolliffe L, Lannin NA, Cadilhac DA, Hoffmann T. Systematic review of clinical practice guidelines to identify recommendations for rehabilitation after stroke and other acquired brain injuries. BMJ Open. 2018. https://doi.org/10.1136/bmjopen-2017-018791.
55. Yadav P, Alsabban A, de Los RT, Varghese A, Ming JM, Milford K, et al. A systematic review of paediatric neurogenic lower urinary tract dysfunction guidelines using the appraisal of guidelines and research evaluation (AGREE) II instrument. BJU. 2018;13(5):520.
56. Simancas-Racines D, Montero-Oleas N, Vernooij RWM, Arevalo-Rodriguez I, Fuentes P, Gich I, et al. Quality of clinical practice guidelines about red blood cell transfusion. J Evid Based Med. J Evid Based Med. 2019;12:113–24.
57. Alarcon JD, Rubiano AM, Chirinos MS, Valderrama A, Gich I, Bonfill X, et al. Clinical practice guidelines for the care of patients with severe traumatic brain injury: a systematic evaluation of their quality. J Trauma Acute Care Surg. 2013;75:311–9.
58. Alonso-Coello P, Irfan A, Solà I, Gich I, Delgado-Noguera M, Rigau D, et al. The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. Qual Saf Health Care. 2022. https://doi.org/10.1136/qshc.2010.042077.
59. Kwah LK, Green J, Butler J, Lam L. Quality of clinical practice guidelines for management of limb amputations: a systematic review. Phys Ther. 2019;99:577–90.
60. Fuentes Padilla P, Martínez G, Vernooij RWM, Cosp XB, Alonso-Coello P. Nutrition in critically ill adults: a systematic quality assessment of clinical practice guidelines. Clin Nutr. 2016;35:1219–25.