

REMOTE NURSING SUPPORT IN LUNG CANCER PATIENTS UNDERGOING CHEMOTHERAPY: A COMPREHENSIVE REVIEW

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Abstract: Objective: Patients with lung cancer patients report a worse quality of life than other cancer patients. Telenursing interventions should represent effective solutions in their clinical pathways. The study aims to provide an overview of telenursing interventions in lung cancer patients on chemotherapy.

Materials and Methods: A systematic review following the PRISMA Statement was performed. The following databases were consulted: PubMed, EMBASE, Cochrane Library, and CINAHL. The quality of the studies included was assessed through the GRADE method. Primary quantitative, qualitative, and mixed-method studies on telenursing intervention in lung cancer patients ≥ 18 years old, on chemotherapy, and in home-setting care were included (International Prospective Registry of Systematic Reviews Protocol ID: CRD42022332779).

Results: From the 801 studies retrieved, three were finally included in the review and resumed in a narrative synthesis.

Conclusions: Despite the increase in telenursing interventions during the pandemic, limited evidence was found in lung cancer patients on chemotherapy. The little evidence identified does not allow for drawing conclusive conclusions regarding effectiveness, usability, and satisfaction with the care provided, either in addition to or as an alternative to usual care. Telenursing interventions and the perceived satisfaction of patients with lung cancer are potentially consistent and should improve access and quality of care, healthcare costs and resources.

KEYWORDS: Telenursing, Cancer, Lung, Chemotherapy, Systematic Review.

INTRODUCTION

Cancer is a leading cause of death worldwide, with 10 million deaths and 19.3 million new cancer cases yearly¹, representing a strategic intervention sector in all healthcare settings. Lung and breast cancer have a higher prevalence in the population, and lung cancer is the leading cause of death for cancer worldwide¹. Late onset of symptoms in patients with lung cancer results in diagnostic delay, a 15% 5-year survival rate, and a generally



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1

poor prognosis². Furthermore, some studies suggest that the quality of life in patients with lung cancer is often worse than in patients with other types of cancer³. In the era of personalised medicine, lung cancer classification aims to link morphology to biological characteristics of cancer cells, increasing and improving therapeutic choices and clinical outcomes⁴. Predictive molecular biomarkers offer valuable insights into cancer aggressiveness and the best cancer treatments, including traditional chemotherapy, targeted therapies and immunotherapy⁵. Although cytotoxic chemotherapy has significantly increased the life of patients with lung cancer⁶, it has more significant risks, such as the high prevalence of overall side effects due to non-specific targets and a relatively short patient survival time, than targeted therapies and immunotherapy⁷. The technological innovation of recent decades, particularly telemedicine, can improve the reorganization of global health systems. Innovative patient-centered interventions should be implemented to improve access to healthcare services and clinical outcomes of patients with cancer, especially at home⁸. In the nursing field, the remote support of telenursing, a subset of telehealth, can improve the interaction between nurses and patients, overcoming obstacles such as distance and time, positively impacting quality and access to care even remotely⁹. Telenursing interventions aim to strengthen nursing activities with digital tools, enhance usual care (u.c.), and preserve the nurse-patient relationship¹⁰.

Especially for outpatient patients with cancer in-home care, telenursing could effectively improve care, reduce hospitalizations and optimize resource utilisation^{11,12}.

While several studies have shown that telenursing plays a role in chronic disease management¹³⁻¹⁶ and the rehabilitation of elderly patients¹⁷, to our knowledge, no study summarizes telenursing interventions and effectiveness in patients with lung cancer on chemotherapy. Given the increasing prevalence of this population and the development of this care model, this systematic literature review aims to provide an overview of telenursing interventions for patients with lung cancer on chemotherapy.

MATERIAL AND METHODS

Study design

For the aim of the study, a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was performed¹⁸ (**Supplementary Table 1**).

The framework PICOS shaped the study:

Population: Home-assisted lung cancer patients on chemotherapy.

Intervention: Telenursing interventions.

Comparison: Usual Care.

Outcomes: Samples' characteristics, interventions, efficacy on primary outcomes, tools. Setting: Home care.

Register protocol

The protocol was registered in the International Prospective Registry of Systematic Reviews (PROSPERO ID: CRD42022332779) on May 25, 2022.

Review question

Three review questions were used to describe the characteristics of the telenursing interventions, outcomes and timing implemented on home-assisted patients with lung cancer on chemotherapy:

What were the primary telenursing interventions used in patients with lung cancer on chemotherapy? What were the timing of the interventions? What were the primary outcomes used?

Inclusion and exclusion criteria

The following inclusion and exclusion criteria informed the search strategy. Inclusion criteria: patients with lung cancer ≥ 18 years old, on chemotherapy; patients in home-care setting; patients enrolled in primary quantitative, qualitative and mixed-method, experimental, quasi-experimental, observational, descriptive and cross-sectional studies on telenursing interventions with nurses' contribution, used to collect or provide information; studies in English published from 01st January 2000 and 30th April 2022. Exclusion criteria: grey literature and reviews

PubMed
((Telenursing[Title/Abstract] OR telehealth[Title/Abstract] OR telemedicine[Title/Abstract]) OR ("Telemedicine"[Mesh] OR "Telenursing"[Mesh]) AND (((Tumor*[Title/Abstract] OR Tumour*[Title/Abstract] OR Neoplas*[Title/Abstract] OR Cancer*[Title/Abstract] OR Malignant*[Title/Abstract] OR Carcin*[Title/Abstract] OR Adenocarcinoma*[Title/Abstract]) AND (lung*[Title/Abstract])) OR ("Lung Neoplasms"[Mesh] OR "adenocarcinoma of lung "[Mesh]))

(systematic, scoping, narrative, etc.); study protocols; case studies; studies including patients affected by other than lung cancer; studies in surgical, immunotherapy treatments or exclusive palliative care; studies on healthcare professional perspectives; articles with no or unclear nursing contribution; studies in languages other than English.

Search strategy

The following databases were consulted: PubMed, Excerpta Medica dataBASE (EMBASE), Cochrane Library, and Cumulative Index to Nursing and Allied Health Literature (CINAHL). The search strategy used in PubMed (Figure 1) was built and adapted to the other databases with the support of two librarians (F.S. and V.S.). RefWorks® bibliographic management software was used in the screening process.

Figure 1. PubMed search strategy.

Selection of studies

Two independent reviewers (A.D.L. and G.L.) assessed the papers for eligibility. The agreement was achieved by comparing the researchers' opinions or those of a third independent reviewer (E.D.S.) who supervised the study.

Certainty of the evidence

Confidence in the identified interventions was tested through the certainty of evidence of the GRADE approach¹⁹ (Grading of Recommendations Assessment, Development and Evaluation). This systematic process is used to identify the confidence and strength of evidence through the following five domains: risk of bias, inconsistency, indirectness of evidence, imprecision and publication bias.

Screening process

The screening process was performed from 01 June 2022 to 30 August 2022. Two independent reviewers (A.D.L. and G.L.) screened titles and abstracts of the eligible studies. Potentially eligible studies were subsequently subjected to full-text reading to assess their eligibility, and the included studies were finally summarized in narrative form (Figure 2).

RESULTS

The screening process led to the initial identification of 801 records (Figure 2)²⁰.

After eliminating duplicates, 685 articles were excluded after reading the title and abstract. The remaining 58 records were read in full text, which led to the final identification of the three studies included in the present review²¹⁻²³. The following information was collected for each study: authors and publication year, study design, aims, tools, sampling and timing intervention, outcomes, conclusions, and implications for clinical practice (Table 1).

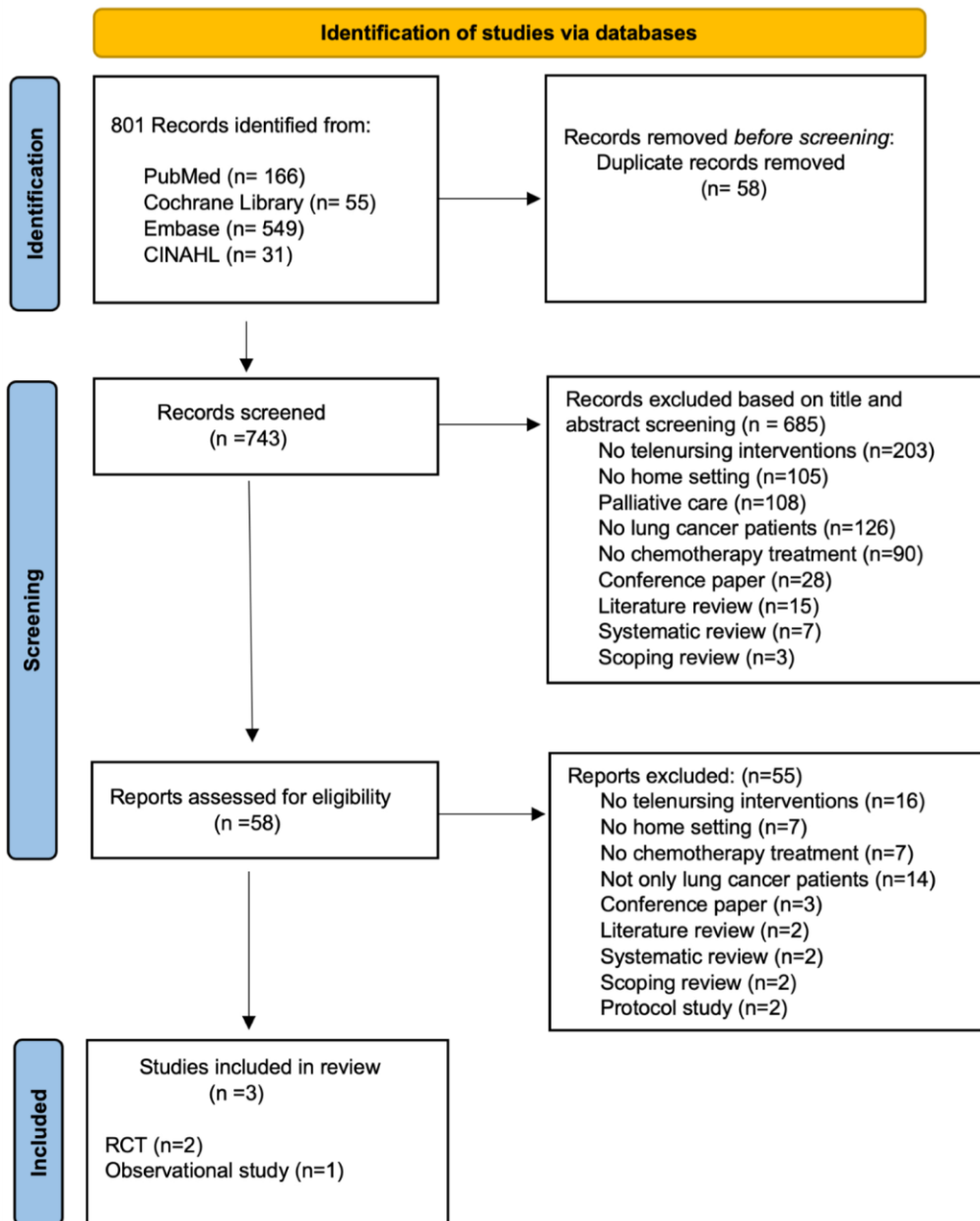


Figure 2. Prisma Flow Diagram for new systematic reviews which included searches of databases and registers only. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; 372 :n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>

The quality of the included studies was assessed through the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) method¹⁹ and summarized in the summary of findings (Table 2).

The three included studies²¹⁻²³ described educational remote vital signs monitoring and symptom management interventions in patients with lung cancer on chemotherapy. The exploratory, descriptive observational study by Petite et al²² focused on ten patients living in rural areas within 75 miles of the study hospital. The prospective Randomized Clinical Trial (RCT) by Yount et al²³ involved two hundred and fifty-three patients with lung cancer enrolled in three clinical centres. At the same time, Huang's RCT was a monocentric study on fifty-five patients²¹.

Two studies assessed the usability and acceptability of the tools and interventions used as primary objectives^{22,23}. In contrast, Huang's analysis focused on the effect of a web-educational program on Quality of Life (QoL) and symptom management²¹.

Table 1.Data extraction.

Authors (Publication year)	Study design	AIMS	Tools	Sampling / Timing intervention	Outcomes
Huang et al. (2019)	RCT	To assess the impact of web-ECOG-PS, SDS, EORTC C30	Twenty-seven patients with	Performance status; top t	
5	TELENURSING IN LUNG CANCER: A SYSTEMATIC REVIEW				
	based health educational	lung cancer be	weekly-3 months	symptom distress; global	
	program can improve global QoL,	interventions on QoL, QoL	subjected to a health		
	educational QoL; HRQoL on physical,	emotional function, and reduce	related function and		
	symptom	web-based program vs. Twenty-	role, emotional, cognitive	the distress of top ten	
	significant				
	burden in patient with	eight control group u.c. patients.	and social functions		
	symptoms in lung cancer patients				
	advanced lung cancer	Data collection: at diagnosis (T0),	on chemotherapy		
	on chemotherapy	and at 1 (T1), 2 (T2), and 3 (T3)			
	months after beginning				
	chemotherapy				
Petitte et al. (2014)	Exploratory,	To assess the feasibility and	Short-form Pulmonary	Two months	
follow-up in ten	Patients' enrollment and	Improvement and expansion of	descriptive, the		
impact of digital technology	Functional Status Scale,	discharged lung cancer patients	retention strategies;		
fourteen-	telemonitoring. Daily monitoring	observational	Honeywell		
LifeStream software	living at home within a 75-mile	day data transmission; nurse	could be useful for		
risk assessment.	study coaching intervention in rural	program, telephone-based	from the study		
center. Control	coaching intervention to	Changes in vital signs and symptoms	patients with		
lung cancer	coaching intervention from	group: five patients receiving	promote patients' self-		
are important for assessing changes in		the research nurse and	two home-visit (u.c.);		
management approach based	patients' health status and risk and	satisfaction	survey		
regarding	intervention group: five patients	on data	implementing the most appropriate		
	remote-care	telemonitored for 5 days	nursing coaching interventions		
	patients in addition to u.c.				
Yount et al. (2014)	Prospective,	To assess the efficacy of remote	Baseline questionnaires;	Two	
hundred fifty-three patients	Active monitoring and reporting	Remote symptom monitoring in lung			
multicenter RCT	symptom reporting and monitoring	weekly symptom surveys via	were enrolled at three		
centers	intervention failed to show	cancer patients effectively improves	to reduce the		
symptoms' burden	interactive voice response	and randomized to monitor	benefits in lowering		
symptom	patients' satisfaction and relationships				
	in advanced lung cancer patients	(IVR); severe symptom scores	and report (MR) or monitor		
burden vs. u.c. There was good	with health professional teams				
	send an email alert to the site	only (MA) for 12 weeks	adherence to the weekly calls		
	nurse for the most appropriate	in both groups. HRQoL declined			
nursing educational	over 12 weeks in both groups	intervention	($p <$		
.006 to $p < .025$); at week					
	12, treatment satisfaction was			higher	
in MA than in MR		patients ($p < .012$; $p < .027$)			
RCT = Randomized Control Trial; QoL = Quality of Life; ECOG-PS = Eastern Cooperative Oncology Group Performance Status Scale; SDS = symptom distress scale; EORTC C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 u.c. = usual care HRQoL = Health Related Quality of Life.					

Table 2. GRADE method quality assessment.

Authors	Study Design	Risk of Bias	Inconsistency	Indirectness	Indirect-considerations	Imprecision	Other considerations	Certainty
Huang et al. (2019)	Randomized Clinical Trial	Serious	Not serious	Not serious	Not serious	None	□□□□	LOW
Petit et al. (2014)	Exploratory Observational study	Serious	Not serious	Not serious	Serious	None	□□□□	VERY LOW
Yount et al. (2014)	Randomized Clinical Trial	Serious	Not serious	Not serious	Not serious	None	□□□□++	LOW

GRADE Working Group grades of evidence. **High certainty:** Very confident that the true effect could be close to that of the estimate of the effect; **Moderate certainty:** Moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but it could also be substantially different; **Low certainty:** Limited confidence in the effect estimate; the true effect may be substantially different from the estimate of the effect; **Very low certainty:** Very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Petit et al²² assessed the impact of a fourteen-day intervention, using digital technology and daily telephone nurse coaching on ten Appalachian rural patients with lung cancer discharged at home. The Genesis DM, approved by the United States America (USA) Food and Drug Administration, was used to telemonitor patients from a West Virginia University Hospital. The study's objectives were patient enrollment until the end of the study (two months), supporting patients in recognizing key symptoms and worsening health conditions, patient-nurse data transmission and using patients' data to improve patients' health status through self-management strategies and behaviors. To compare the groups, a hospital baseline assessment was done for all patients enrolled in the study. After discharge, five patients (control group) received two nurse visits; five patients were, in addition, home-monitored, receiving daily nurse telephone calls for two weeks to capture disease-related changes (intervention group). All patients completed the same surveys at the same time three times; the intervention group was assessed for satisfaction, too. One-on-five control group patients and three-on-five remote-monitored patients completed the study. All remote-monitored patients were followed for fourteen days post-discharge and completed study surveys. The system captured symptom changes referred from patients, and nurses helped patients to recognize and self-manage their conditions through motivational interviews. Patients appreciated the system's usability and utility.

The prospective multisite RCT study by Yount et al²³ assessed the efficacy of reporting and remote monitoring on symptom burden in patients with advanced lung cancer, using Symptom Monitoring and Reporting System for Lung Cancer (SyMon-L) in three USA medical center sites. Patients were randomly divided into a symptom monitoring and reporting group (MR) and a symptom monitoring alone (MA) group of 123 and 130 subjects. Both groups tracked their symptoms weekly and used a phone-based interactive voice response (IVR) system for SyMon-L. The severe symptoms of patients in the MR group generated alarms for nurses who implemented coaching interventions. In addition, the MR clinical team received reports of severe patient symptoms to discuss with patients during visits. No significant differences in study outcomes were observed in the intervention group at 3, 6, 9 and 12 weeks on the following primary outcomes: Symptom Distress Scale, SDS^{24,25}; Functional Assessment of Cancer Therapy, FACT - Lung Symptom Index, FLSI²⁶; Health-Related Quality of Life, HRQL with the FACT-General, FACT-G²⁷; Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-Patient Satisfaction, FACIT-TS-PS²⁸; Symptom Management Barriers Questionnaire, SMBQ based on previous studies^{29,30}. The system's usability and usefulness were assessed with a developed self-efficacy questionnaire. Similar benefits were reported in both groups, except for MR patients reported calling nurses more frequently than MA patients ($p = .022$) and higher treatment satisfaction in MA than MR patients at week 12 (respectively

$p < .012$, and $p < .027$). HRQL declined over 12 weeks in both groups ($p < .006$ to $p < .025$), adherence to weekly calls was 82%, and patient satisfaction was high.

The RCT by Huang et al²¹ tested a health educational program based on the *e-learning* theory^{31,32} and the Symptom Management Theory (SMT)^{33,34} to improve symptom management, QoL and reduce the primary ten symptom distress in patients from a medical center in northern Taiwan. Using the web-based intervention (intervention arm), twenty-seven patients with lung cancer on chemotherapy were compared with twenty-eight u.c. patients. Nurses, involving physicians as needed, supported both groups. The feasibility and acceptability of the program were preliminarily tested on two pilot patients. Data were collected at baseline before chemotherapy and subsequently monthly for three times. No differences were observed between groups at baseline; statistically significant differences were instead observed over time in the intervention arm in global QoL, emotional function and reduction in top ten symptom burden ($p < .05$).

DISCUSSION

The impact of cancer and cancer-related treatments forces healthcare systems to find new solutions to improve patient's QoL, burden, and care access. In particular, treatments and disease impact the therapeutic pathway and QoL of patients with lung cancer³, suggesting the need for rigorous studies in this large and fragile population. This systematic review explores the impact of telenursing interventions on patients with lung cancer on chemotherapy.

The literature search led to an initial identification of 801 records. The screening process led to the final identification of three articles dealing solely with patients with lung cancer on chemotherapy²¹⁻²³. Many articles, full-text read, dealt with patients with lung cancer and other cancer types, such as recurrent breast^{35,36} and colorectal cancer³⁷. Other studies have not involved patients with lung cancer on chemotherapy, or the contribution of nurses has not been predicted or described³⁸. For these reasons, although chemotherapy for patients with lung cancer is also used in other cancer types, considering the specific care needs of this population and the more significant impact on their QoL³, most of the articles were excluded from this review. Consistent with similar studies involving different cancer populations^{39,40}, the RCT by Yount et al²³ tested a nursing intervention to reduce symptom burden and improve Health-related Quality of Life (HRQoL), specifically in patients with lung cancer on chemotherapy. However, no statistically significant clinical differences were observed between groups in symptom burden reduction compared to u.c., except for the top ten symptom burden by Huang and colleagues²¹. In this regard, consistent with other studies⁴¹, the web-based nurse educational program in the RCT by Huang et al²¹ suggests improving global QoL, symptom distress and HRQoL related to emotional function in the intervention arm. The observed non-statistically significant improvement in physical dimension associated with QoL may suggest the need to add exercise in addition to information delivery, as recommended by recent cancer guideline⁴². Furthermore, the lack of significant impact on physical and role functions probably suggests the need for increased social and family support in this population, as shown in previous studies on older adults with osteoarthritic diseases¹⁷. In this regard, Petite et al²² observed a greater involvement and education in managing symptoms and stressful situations by both the patient and family members and a positive impact on caregivers, nurses, and patients' QoL. In fact, in line with the current literature⁴³, Petite²² suggested that patients provided nurses with an opportunity to enhance their skills and identify the potential benefits of helping patients develop self-management skills. The observed improvement in global QoL, emotional function and symptom distress 12 weeks after the initiation of chemotherapy²¹, as in the Yount et al²³ study, suggests the need for further studies to assess the impact of nursing intervention in the long term.

Consistent with previous^{40,43,44} and currently ongoing studies³⁹ in patients with cancer, telenursing interventions of the included studies used telephone calls, and patients were generally compliance and satisfied with the care provided^{22,23}, although in Yount et al²³ study, satisfaction at 12 weeks was higher in the control group²³. These findings could probably be explained by investigating patients' ability to seek and use information about health and treatments.

In the screening process, many articles were excluded because the nursing contribution in the studies, undoubtedly present in remote care, was not described³⁸, particularly in the Italian context^{45,46}. These findings suggest the need for increased engagement, research, and further studies by nurses. In the current literature process, two studies assessed the impact of age on the symptom management of patients with cancer, including patients with lung cancer, suggesting improvements in symptom management and HRQoL and not statistically significant age-related differences^{47,48}. However, they were excluded from the present systematic review because they concerned patients with different cancer types, and outcomes were not detectable for patients with lung cancer. To the authors' knowledge, no studies have been conducted exclusively on elderly patients with lung cancer to evaluate the efficacy of telenursing interventions on this fragile population.

In a multidisciplinary team, an Advanced Practice Lung Cancer Nurse (APNLC) could improve telenursing interventions, patient-reported outcome measures (PROMs) detection, and patient-centered care. However, further studies are needed to evaluate their impact, especially regarding costs and long-term workload⁴⁹.

An exciting study protocol by Ciani et al³⁹ assessed a supportive mobile app (LuCApp) for patients with metastatic lung cancer at three oncology sites in Northern Italy. Still, it was excluded despite addressing the same topic as the present review due to the study design.

Despite an uneven and non-widespread implementation of telenursing intervention in the oncology field, a growing trend is evident after the SARS-CoV-2 pandemic in many countries⁵⁰⁻⁵² also for patients with lung cancer⁵³, especially for surgical⁵⁴⁻⁵⁶ and immunotherapy treatments^{57,58} than chemotherapy. Increasing utilization of digital interventions was observed in palliative care settings too⁵⁹⁻⁶¹. However, palliative care settings were excluded from the present systematic review because, in patients with advanced disease, the effects of telenursing intervention could have been "hidden". Similarly, exciting studies using telenursing interventions on home patients after surgery for lung cancer were excluded from this systematic review⁵⁴.

The digital interventions of the included studies²¹⁻²³ aimed to improve the connection between nurses and patients and test the effect of telenursing interventions on patients' and caregivers' QoL and their symptom self-management. Patient compliance was high, although the intervention did not significantly reduce the symptom burden compared to u.c., except in Huang et al²¹ study.

Limited to the studies identified by this review²¹⁻²³, telenursing interventions for remote symptom monitoring in patients with lung cancer are feasible and effective in patients' satisfaction and relationships with the health care team.

Implications for clinical practice and future research

The limited studies identified by this review²¹⁻²³ suggest the need for future rigorous studies of telenursing interventions in patients with lung cancer. Considering telenursing's heterogeneity and great potential, future research could implement additional interventions overwhelming current nurse telephone follow-up^{12,40,62} to improve survival, coping strategies and QoL of patients with lung cancer. Two studies included in this review assessed the impact of the telenursing intervention over time, up to 12 weeks^{21,22}. In the authors' opinion, evaluating the long-term effect of nursing interventions on patients and care pathways through future studies may be exciting and valuable in cancer care. Despite the growing use of telenursing in the last three years and the challenge for nurses to improve their skills by increasing the self-care of patients with lung cancer, its diffusion is still uneven and not widespread⁵⁰⁻⁵². Further nursing studies are needed to highlight the impact of their specific contributions in improving outcomes, traditional care and helping relationships⁶³. Finally, many excluded studies identified medical interventions performed exclusively by different health care professionals, neglecting the nursing contribution, which was undoubtedly present within the care team⁶⁴. This publication bias suggests increasing nursing publications in the oncology field.

Limitations

The authors are aware of the limitations of the present study, primarily the small number of included studies²¹⁻²³. Secondly, non-English language papers and grey literature were excluded, potentially excluding studies on telenursing interventions in other languages. However, the choice was made considering English as the language

of the international scientific community. Furthermore, the low quality and heterogeneity of the studies did not allow for a meta-analysis. In particular, the quality of the included studies, assessed using the GRADE methodology¹⁹, reports quality levels of “low” and “very low” (Table 2). Finally, the authors are aware that the exclusive focus of this review on lung cancer patients may have likely excluded telenursing interventions in other cancer populations. However, the choice of such a narrow and specific population is due to the authors’ intention to evaluate the intervention’s effects on a homogeneous population with similar care needs, disease, and treatment.

CONCLUSIONS

The growing burden of patients with cancer and the limited available resources require global health systems to find effective and safe solutions, improving with the use of health technologies. Although this systematic review suggests implementing telenursing interventions in patients with lung cancer on chemotherapy, the studies identified do not allow conclusions regarding efficacy, usability, and satisfaction with the care provided²¹⁻²³. To assess and increase the effectiveness of telenursing interventions in caring for patients with lung cancer, more extensive and rigorous studies on efficacy, safety, QoL, quality of care, usability, and stakeholder satisfaction are needed. Telenursing interventions and remote care are essential challenges for nurses to improve their skills and identify the best strategies for patients with lung cancer to develop self-management skills⁶³. Consistent with similar findings⁶⁵, the present systematic review suggests that increased information about cancer and cancer-related treatments can reduce patients’ worry and fear throughout the care pathway. Finally, although the findings of this review do not allow definitive conclusions to be implemented in clinical practice, they suggest the need for further studies to evaluate and improve the significant contributions of nurses in the clinical pathways and coping strategies of patients with lung cancer.

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Ethics approval:

Approval from the local Ethics Committee was optional, considering the study design.

Informed Consent:

Not applicable.

Availability of data:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflict of interest:

The authors declare that they have no conflict of interest to disclose.

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Aurora De Leo: Research design, Methodology, Investigation, Formal analysis, Writing - original draft and Software. Gloria Liquori: Investigation, Data curation, Writing - original draft. Emanuele Di Simone: Methodology and Software. Fabrizio Petrone: Project administration. Alessandro Spano: Resources and Visualization. Laura Iacorossi: Data acquisition and validation. Nicolò Panattoni: Methodology and Writing - review & editing. Noemi Giannetta: Software and Resources. Marco Di Muzio: Methodology, Supervision, and Validation. Sara Dionisi: Writing - review & editing, Validation. The authors read and approved the submitted final version of the manuscript.

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