**Title**: Effectiveness of Healthy Lifestyle-based interventions in Lung Cancer Survivors: a systematic review and meta-analysis

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**ABSTRACT**

**Purpose**: To assess the effectiveness of healthy lifestyle-based interventions in lung cancer survivors.

**Methods**: We performed a literature search using PubMed, Web of Science, and Science Direct (last search March 2022). Quality assessment and risk of bias were assessed using the Downs and Black scale and the Cochrane tool. A systematic review and meta-analysis of randomized controlled trials were performed. We included controlled trials testing the effect of healthy lifestyle-based interventions in lung cancer survivors versus a control intervention where lung cancer patients had no treatment, were receiving the usual care or had not an active role in the intervention. The data were pooled and a meta-analysis was completed for quality of life, psychological distress, and cancer-related symptoms.

**Results**: We selected 14 studies, which included 1519 patients with lung cancer. The treatment status of these patients was heterogeneous. Healthy lifestyle programs were applied isolated or in combination with usual care in most of the studies. The components of the healthy lifestyle programs were also heterogeneous. Results showed significant differences in favor of healthy lifestyle-based interventions in comparison to the control group for quality of life (p=0.01), psychological distress (p = 0.05), and cancer-related symptoms (p=0.03).

**Conclusions**: The findings indicated a beneficial effect of healthy lifestyle-based interventions for improving quality of life, psychological distress, and cancer-related symptoms in lung cancer patients. However, this review could not show any conclusion about the better treatment moment to apply healthy lifestyle-based interventions.

**Keywords**. Lung Cancer, Oncological Treatment, Healthy lifestyle, Quality of Life, Psychological distress, cancer-related symptoms.

**INTRODUCTION**

Lung cancer represents one of the most prevalent cancers in worldwide, being the leading cause of cancer deaths, with a median prognosis of less than one year [1]. The physiopathology of cancer development is associated with genetic and environmental components. The estimated genetic component for lung cancer only represents 14% of the cancer load, having environmental lifestyle factors [2] an effect that can be up to 95% [3].

Unhealthy lifestyle habits increase after the diagnosis and during cancer treatment [4], and are linked to the development of cancer and the overall survival rate of patients [5]. Lung cancer-related healthy lifestyle habits include smoking, physical activity, and diet among other lifestyle factors, being also associated with improved lung cancer risk, recurrence and survival [6,7].

There is growing evidence about the influence of lifestyle factors on the outcomes of lung cancer survivors [8]. In this line, the study of Holleand JC, et al. [9] showed a relationship between unhealthy lifestyle habits and the development of psychosocial distress with anxiety and depressive disorders. Another example is between healthy lifestyle habits and decreased symptoms, for this reason, several lifestyle interventions [10,11] have included symptom self-management in the healthy direction.

Healthy lifestyle-based interventions have been demonstrated to be beneficial for the quality of life in different cancer entities [12,13], however, the lung cancer patient is one of the cancer populations who can benefit most, taking into account that adults with lung cancer often experience lower HR-QOL [14] and high levels of distress [15] as compared to adults with other types of cancer.

For these reasons, achieving healthy lifestyles has become a priority for lung cancer healthcare professionals nowadays, being included as habitual recommendations for cancer prevention [16,17]. In this line, the self-management interventions provided for cancer patients are focussed on healthy directions for implementation in everyday life [16,17].

Several studies have proposed lifestyle-based interventions for cancer populations, however, to date; no study has summarized the effects of healthy lifestyles-based interventions in patients with lung cancer. We therefore, conducted a systematic review to summarize the available evidence on the effects of healthy lifestyle-based interventions in patients with lung cancer.

**METHODS**

**Study registration**

The protocol for this systematic review and meta-analysis was pre-registered on the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42021292152). This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [18] and the Cochrane Collaboration guidelines for reviewing interventions [19].

**Search strategy**

We systematically searched the articles indexed on Pubmed, Web of Science and Science Direct of randomized controlled trials databases from their inception to March 2022. A search strategy in MEDLINE was developed using the following steps: (1) a thorough examination of the MeSH Database, (2) development of keywords by examining relevant key terms used in existing systematic reviews, and (3) expert guidance and review by a specialist. This search strategy was tested and refined to claim it was the most effective strategy for this review. Then, this strategy was adapted to index across other databases. We screened the references of relevant reviews to screen for additional studies that can be potentially included in this review.

We applied the PICOS [20] model (Participants, Interventions, Comparisons, Outcome and Study design) to define the research question. The inclusion criteria were: (1) Lung Cancer survivors; (2) interventions with a focus on healthy lifestyle programs; (3) the exercise intervention had to be compared to a control intervention where patients do have not an active role, usual care or no-treatment; (4) Patient-reported outcomes were included; (5) only randomized clinical trials were included. Detailed information about the search strategy is provided in Appendix 1.

In this line, interventions with a focus on healthy lifestyle programs include any program which approaches any healthy lifestyle habit following the World Health Organization definition [21], which included any aspect that would lead to reducing the risk of being seriously ill or dying early, taking care of physical, mental, and social well-being, and helping to enjoy more aspects of the life.

The search process included removing duplicates and screening titles, abstracts, and eligible full texts. To reduce the selection bias potential, two investigators (A.H.; C.V.) independently performed the literature search and disagreements were resolved through a consensus discussion with a third independent investigator (J.M.).

Data extraction and quality assessment were performed when the articles were selected. We used the Downs and Black quality assessment method to assess the methodological quality of the included studies [22]. This method has 27 items comprising five subscales (study quality, external validity, study bias, confounding and selection bias, and study power), classifying methodological quality as ”excellent” if studies have a 26 o higher score, between 20 to 25 “good”, 15 to 19 “fair” and 14 or lower “poor”. This scale is ranked as one of the six highest-quality assessment scales suitable for use in systematic reviews, due to the high validity and reliability presented [23,24].

The risk of bias in each study was assessed using The Cochrane Collaboration Risk of Bias Tool for Randomized Controlled Trials [19]. This tool assesses seven aspects that may be subject to bias, classifying the quality assessment as high quality, when all domains obtained low risk; fair quality, when one criterion does not meet (i.e. high risk of bias for one domain) or two criteria are unclear but this is not a limitation that could invalidate the results; poor quality, when now there are important limitations that could invalidate the results, and when two or more criteria are listed as high or unclear risk of bias [25].

**Meta-analysis**

Quantitative synthesis was applied using The Review Manager 5 (RevMan 5) software on all studies that presented quality of life, psychosocial distress, and cancer-related symptoms post-intervention means and standard deviations. Data, including the final mean values, standard deviations, and the number of patients assessed at different endpoints for each treatment arm was extracted to estimate the overall mean differences between treatment arms. When the outcome was assessed at different time points during the same study, only the assessments performed at the end of the intervention were used, regardless of repeated evaluations throughout the trial.

When included articles presented insufficient data to calculate the effect size (e.g., no means provided, no standard deviation provided), their authors were contacted to obtain the required information. When p-values or 95% confidence intervals were given and standard deviations were missing, these were calculated via the embedded Review Manager calculator.

Standardized mean differences were used as all the scales were assumed to measure the same underlying symptom or condition, but some studies measured the outcomes on different scales. The overall mean effect sizes were estimated using random effect models or fixed effect models according to statistical heterogeneity I2 tests (for sizes of less than 50%, fixed effects models were used) [19]. Visual inspection of the forest plots for outlier studies was also undertaken. Sources of heterogeneity were explored, and sensitivity analyses were conducted by excluding trials that were at a high risk of detection or attrition bias.

Sensitivity analysis was conducted to investigate potential sources of heterogeneity and to determine how sensitive the conclusions of the study are to the particular method or study design feature that was used [26]. If the effect and confidence intervals in the sensitivity analysis lead to the same conclusion as the primary meta-analysis value, the results are deemed robust. Sensitivity analyses were performed in this study by the timing of the intervention.

**RESULTS**

**Study selection**

The flowchart of the search, screening and selection of study process is presented in Figure 1. A total of 4280 studies were obtained from the electronic databases. After removing duplicates, 2896 records remained. Screening based on the title and abstract resulted in the selection of 44 articles. From these 44 records, 32 articles were excluded following the evaluation of the full text, and 12 studies were finally included. Two studies were identified and included by other methods. Finally, a total of 14 studies were included in the qualitative syntheses [27–40], and 9 studies were included in the quantitative syntheses [27,28,30–32. 34-37].

**Fig 1.** PRISMAflow chart of literature search and study selection [18]

**Identification of studies via other methods**

**Identification of studies via databases and registers**

Records identified from:

Websites (n = 0)

Organisations (n = 0)

Citation searching (n = 3)

Records removed *before screening*:

Duplicate records removed (n = 1384)

Records marked as ineligible by automation tools (n = 0)

Records removed for other reasons (n = 0)

Records identified from:

Pubmed (n = 994 )

Web of Science (n = 1570)

Science Direct (n = 1716)

**Identification**

Records screened

(n = 2896)

Records excluded

(n = 2852)

Reports not retrieved

(n = 0)

Reports sought for retrieval

(n = 3)

Reports sought for retrieval

(n = 44)

Reports not retrieved

(n = 0)

**Screening**

Reports assessed for eligibility

(n = 2)

Reports excluded:

Excluded for not meeting the inclusion criteria (n = 1)

Reports assessed for eligibility

(n = 44)

Reports excluded:

Excluded for not meeting the inclusion criteria (n = 32)

**Included**

Studies included in review

(n = 14)

Reports of included studies

(n = 14)

**Study characteristics**

A total of 1519 lung cancer survivors have been included in this review, the majority of the sample men (60,50%), with an age range from 50 to 77 years old.

4 studies [29-31,38] included only non-small cell lung cancer patients, 6 studies [27,32,34-36,39] recruited a mixed sample of small and non-small cell lung cancer, and the resting studies [28,33,34,37] don´t report the etiology of the sample. The majority of the studies have [30,31,34,35,37] included patients with advanced stage (III-IV), and 3 studies [27, 32,39] with all cancer stages.

The treatment status of these patients was heterogeneous. 7 studies [28,31,32,34-37] included patients that were receiving oncological medical treatment, 4 studies [27,29,30,39] applied the intervention after oncological medical treatment. Additionally, 1 study [38] applied the intervention before receiving the cancer treatment, and 3 studies [32,38,40] included patients at the diagnosis. 12 studies [27-32,34-39] referred to included patients around coadjuvant treatment moment, which 4 [28,34,35,38] specified to include patients around chemotherapy treatment moment, and 1 study [37] during radiotherapy treatment moment. Only one study [29] included patients in a peri-surgical moment. The study of Yorke J, et al [33] doesn´t report the treatment status of the sample.

The study´s quality scores ranged from 9 to 23, with a mean of 18.86 ± 3.78. When the Cochrane Risk of Bias Assessment was applied, 9 studies presented poor quality [27-29,32-34,36,38,40], 4 studies presented fair quality [30,31,35,37] and the other one presented good quality [39].

**Table 1.** Characteristics of studies

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study (year)** | **Etiology****(Stage)** | **Treatment Status** | **Sample**(% Men) | **Sample Age**Years ± SD | **Quality Assessment****Downs and Black**(Risk of Bias) |
| **Sun. Y, et al. (2021)** [27] | NSCLC & SCLC (I-IV) | Post-Coadyuvant | n= 84 (69.04%) | **IG:** 61,5 ± 10,5**CG**: 60,5 ± 10,5 | 18 (Poor Quality) |
| **Halil-Günes I, et al. (2020)** [28] | NR | In-Chemo | n= 60 (91,66%) | **IG**: 60,96 ± 9,41 **CG**: 59,53 ± 13,30  | 22 (Poor Quality) |
| **Zhu X, et al. (2020)** [29] | NSCLC (I-III) | Post-Surgery | n= 70 (40%) | **IG**: 67,95 ± 4,81**CG**: 67,21 ± 4,68 |  17 (Poor Quality) |
| **Edbrooke L, et al. (2019)** [30] |  NSCLC (III-IV) | Post-Coadyuvant | n= 92 (55.43%) | **IG**: 64,6 ± 13,4**CG**: 62,5 ± 10,9 |  22 (Fair Quality) |
| **Huang CC, et al. (2017)** [31] | NSCLC (III-IV) | In-Coadyuvant | n= 55 (58,18%) | **IG**: 61.00 ± 2.04**CG**: 58.68 ± 1.77 |  20 (Fair Quality) |
| **Geerse OP, et al (2016) [**32] | NSCLC & SCLC (I-IV) | Dx OR In-Coadyuvant | n= 111 (57.84%) | **IG**: 60.6 ± 10.5**CG**: 62.3 ± 9.7 | 19 (Poor Quality) |
| **Yorke J, et al. (2015)** [33] | NR | NR | n= 101 (46.53%) | **IG**: 67.8 ± 10.1 **CG**: 67.6 ± 9.1 | 18 (Poor Quality) |
| **Yount SE, et al (2014)** [34] | NSCLC & SCLC (III-IV) | In-Chemo/Oral Therapy | n= 253 (49.4%) | **IG**: 61 ± 10.3**CG**: 60.2 ± 10.1 | 22 (Poor Quality) |
| **Fernández-Rodríguez C, et al. (2014)** [35] | NSCLC & SCLC (III-IV) | In- Chemo | n= 90 (81.11%) | **IG**: 61.64 ± 9.57**CG**: 60.92 ± 8.33 | 19 (Fair Quality) |
| **Study (year)** | **Etiology****(Stage)** | **Treatment Status** | **Sample**(% Men) | **Sample Age**Years ± SD | **Quality Assessment****Downs and Black**(Risk of Bias) |
| **Schofield P, et al (2013)** [36] | NSCLC & SCLC (NR) | In-Coadyuvant | n= 108 (60.18%) | **IG**: 62.3 ± 9.2**CG**: 63.8 ± 11.4 | 17 (Poor Quality) |
| **Chan CWH, et al (2011)** [37] | NR (III-IV) | In-Radio | n= 140 (83%) | **IG**: NR**CG**: NR | 23 (Fair Quality) |
| **Temel JS, et al (2011)** [38] | NSCLC(NR) | Dx OR Pre-Chemo | n= 151 (35.76%) | **IG**: 64.98 ± 9.7**CG**: 64.87 ± 9.4 | 15 (Poor Quality) |
| **Wilkie DJ, et al (2010)** [39] | NSCLC & SCLC (I-IV) | Post-Coadyuvant | n= 151 (74%) | **IG**: 60.1 ± 10.6**CG**: 63.2 ± 11 | 23 (Good Quality) |
| **Goldberg RJ, et al (1985)** [40] | NR | Dx | n= 53 (71.69%) | **IG**: 61 ± NR**CG**: 62 ± NR | 9 (Poor Quality) |

*NSCLC: Non-Small cell lung cancer; SCLC: Small cell lung cancer; Dx: Diagnosis; Chemo: Chemotherapy; Radio: Radiotherapy; NR: Non-Reported; SD: Standard Deviation; EG: Exercise Group; CG: Control Group.*

Details about applied interventions and obtained results are reported in table 2. Most of the intervention were applied in a hospital environment [27,28,30,32-38,40], including 2 studies [33,34] a domiciliary environment, however 4 studies [31,33,36,39] were conducted in a clinical center.

The components of the usual care were heterogeneous. These patients received standard medical treatment [27,29,30,32,36,37,38], general information [31,33,37,40], and periodic monitoring [30]. Additionally, Wilkie DJ, et al. [39] carried out a control group who received an intervention based on talking about the cancer experience.

Healthy lifestyle programs were applied isolated [27,28,31,34-36,39,40] or in a combination of usual care [29,30,33,38] in most of the studies. 2 studies [33,37] applied it in a combination of general information, and only one study [30] applied it in a combination on exercise. The interventions have been applied between 2 and 24 weeks [27-40], with a frequency from once every 2 weeks to 2 days per week [27-40]. The duration ranged from 10 minutes to 1 hour [27-40].

Many of the healthy lifestyle programs were performed in a face-to-face format [27-33,35,36,38-40], except for the study of Chan CWH, et al. [37] who only provided a leaflet and an audiotape, accompanied by a telephone reminder. 7 studies added written information in form of brochures [27], booklet [28,30,36], and written scripts [33,34,37]. This written information included preferentially general information about cancer, management of side effects, and psychological strategies. Three studies [29,37,39] accompanied the written information with video and audiotape materials. Other forms to provide the intervention were the use of a structural diary [29, 33], telephone interviews and reminder [28-30,36,37,39], or electronic educational technology [31].

The components of the healthy lifestyle programs were heterogeneous, but the most widely applied strategies were to provide information about condition and /or its management [27-31,33,36,38], training for symptom self-management strategies [30,31,33,36-39], training for practical self-management activities [29,30,35,37,39,40], and training for psychological strategies [27,28,30,31,33,35-37,40].

The most common outcomes explored in these studies were cancer-related symptoms [30,31,34,36], the psychosocial distress of the patients [27,30,32,35,37], and the health-related quality of life, which was evaluated by 10 of the 14 studies [27,28,30-32,34,35,37]. Concerning to baseline, the experimental group of most of the studies [27-29,31,33-35,37-39] showed an improvement of these variables after treatment intervention, but 4 studies [30,32,36,40] didn´t report significant differences. 11 studies [27-31,33-36,37-39] have shown significant differences between groups in favor to the experimental group, however the other 3 studies [32,36,40] didn´t report significant results. The study by Yorke J, et al. [33] published a significant improvement in the cancer-related symptoms that appeared 4 weeks after the end of the intervention, while a significant improvement in quality of life was reported at 12 weeks after completing the intervention.

Other outcomes like self-care [28,32,34], functionality [28,31], illness perception [38,40], or respiratory function [27] improved after healthy lifestyles interventions in the majority of the studies included.

**Tabla 2.** Characteristics of interventions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Sun. Y, et al. (2021)** [27] | Hospital | **EG:**  Healthy lifestyle programs**CG:**  Usual Care | BROCHURES + FACE-TO-FACE INTERVIEWS + GROUP INTERVIEWS - Information about condition and /or its  management - Training for nutritional strategies - Training for oral health strategies - Training for psychological strategies - Training for social strategies | 1-2 days / week | ·Quality of life (%)·Anxiety (HAMA)·Depression (HAMD)·Respiratory Function (SpO2, FEV-1, FVC, MVV) | Quality of life EG>CG (p<0,001)Anxiety and Depression EG< CG (p<0,001)Respiratory functionEG>CG (p<0,001) |
| **Halil-Günes I, et al. (2020)** [28] | Hospital | **EG:**  Healthy lifestyle programs**CG:**  No Intervention | FACE-TO-FACE INTERVIEWS + BOOKLET + TELEPHONE CALLS - Information about condition and /or its  management - Training for psychological strategies | 4 Weeks2 days / week | ·Self-Care (S-CAS)·Functionality (FLIS) | Self-CareEG>CG (p=0,001)FunctionalityEG>CG (p=0,038) |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Zhu X, et al. (2020)** [29] | NR | **EG:**  Healthy lifestyle programs Usual Care**CG:**  Usual Care | TELEPHONE CALLS + HOME INTERVIEWS + VIDEOTAPE + STRUCTURED DIARY - Information about condition and /or its  management - Information about specific clinical action - Regular visits with healthcare professionals - Training for practical self-management activities | 6 weeks | · Quality of Life (SF-36)·Self-efficacy Fatigue (PSEFSM fatigue)·Fatigue (BFS; RSEFSMD)·Exercise Capacity (6MWT) | Quality of life EG>CG (p<0,05)Fatigue EG<CG (p<0,05)Exercise CapacityEG>CG (p<0,05) |
| **Edbrooke L, et al. (2019)** [30] | Hospital | **EG:**  Healthy lifestyle programs Exercise Usual Care**CG:**  Usual Care | TELEPHONE CALLS + HOME INTERVIEWS + BOOKLET - Information about condition and /or its  management - Regular visits with healthcare professionals  - Training for symptom self-management  strategies - Training for practical self-management activities - Training for psychological strategies | 6 moths1 per week/ 1-8ª week1 per moth/ 9ªweek-6º moth | · Quality of Life (FACT-L; AQOL)· Anxiety (HADS-A)· Depression (HADS-D)· Symptoms (MDASi-LC)· Exercise Capacity (6MWT)· Physical Activity (Accelerometry; IPAQ)· Muscle Strength (handgrip and quadriceps)· Behavior Exercise (BREQ-2)· P.A.Self-efficacy (PAA-I)· Resilience (cRISC-10) | Quality of life EG>CG (p=0,005)SymptomsEG>CG (p=0,001)Anxiety and DepressionExercise CapacityPhysical ActivityMuscle Strength Behavior Exercise Resilience NS (p>0,05) |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Huang CC, et al. (2017)** [31] | Medical Center | **EG:**  Healthy lifestyle programs**CG:**  Usual Care Information about side-effects treatmentand management | ELECTRONIC EDUCATIONAL TECHNOLOGY + FACE-TO-FACE INTERVIEWS - Information about condition and /or its  management - Information about specific clinical action - Training for symptom self-management  strategies - Training for psychological strategies - Training for social strategies | 1 Session Pre-medical treatment (15-20min)+3 moths1/15 days | · Quality of Life (EORTC QLQ-C30)· Symptom distress (SDS)· Function (Ecog-PS) | Quality of life EG>CG (p<0,05)Symptoms distressEG<CG (p<0,001)Emotional FunctionEG>CG (p<0,001) |
| **Geerse OP, et al (2016)** [32] | Hospital | **EG:**  Healthy lifestyle programs Referral to healthcare professionals**CG:**  Usual Care | FACE-TO-FACE INTERVIEWS + REFERRAL TO HEALTHCARE PROFESSIONAL - Training for identifying and satisfying patients´ health needs  - Training for finding healthcare professional support when needed | 4 visit o more if patient considered necessary | · Quality of Life (EORTC QLQ-C30+LC13; Eq-5D)· Anxiety (HADS-A)· Depression (HADS-D)· Satisfaction (PSQ-III) | Quality of lifeAnxiety DepressionSatisfactionNS (p>0,05) |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Yorke J, et al. (2015)** [33] | Hospital & Cancer Center & Domiciliary | **EG:**  Healthy lifestyle programs Macmillan breathlessness andfatigue information booklets Usual Care**CG:**  Usual Care Macmillan breathlessness andfatigue information booklets | WRITTEN INFORMATION + FACE-TO-FACE INTERVIEWS + DIARY - Information about condition and /or its  management - Information about social support  - Training for symptom self-management  strategies - Training for everyday activities - Training for psychological strategies | 2 Informative Sessions + 12 weeks2 times per day | · Quality of Life (Eq-5D)· Anxiety (HADS-A)· Depression (HADS-D)· Symptoms (LCSS)· Dyspnea (NSR; D-12)· Cough (MCLC)· Fatigue (FACIT-F) | 4 weeks after intervention:SymptomsEG<CG (p=0,04)Quality of LifeAnxietyDepressionDyspneaCoughFatigueNS (p>0,05)12 weeks after intervention: Quality of LifeEG>CG (p=0,009)DyspneaEG<CG (p=0,026)AnxietyDepressionSymptomsCoughFatigueNS (p>0,05) |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Yount SE, et al (2014)** [34] | Hospital & Domiciliary | **EG:**  Healthy lifestyle programs**CG:**  No Intervention (Monitoring symptom) | WRITTEN INFORMATION + SCHEDULE CLINICAL REVIEW   - Regular visits with healthcare professionals - Knowledge of the self-condition via healthcare professional feedback  - Training for finding healthcare professional support when needed | 12 weeks1 day/week | · Quality of Life (FACT-G)· Symptoms (FLSI)· Symptom Burden (SDS)· Perceived Barriers to Symptom Management (SMBQ)· Self-Efficacy (own tool)· Treatment satisfaction (FACIT-TS-PS)· Clinical Interventions (Nº activities)· Medical utilizations (Checklist) | Treatment satisfactionEG<CG (p=0,027)Medical utilizationsEG>CG (p=0,022)Quality of LifeSymptoms Self-EfficacyClinical InterventionsNS (p>0,05) |
| **Fernández-Rodríguez C, et al. (2014)** [35] | Hospital | **EG:**  Healthy lifestyle programs**CG:**  No Intervention | FACE-TO-FACE INTERVIEWS - Training for everyday activities - Training for practical self-management activities - Training for psychological strategies - Training for social strategies | 4 seasons45min | · Quality of Life (EORTC-QLQ-C30)· Anxiety (HADS-A)· Depression (HADS-D)· Health Status (GSS; KPS; HSS)· Symptoms, mood, functionality in daily life (semi-structured interview) | Health StatusEG>CG (p=0,009)Anxiety and DepressionEG<CG (p<0,05)Quality of lifeSymptomNS (p>0,05) |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Schofield P, et al (2013)** [36] | Hospital & Cancer Center | **EG:**  Healthy lifestyle programs**CG:**  Usual Care | FACE-TO-FACE/TELEPHONE INTERVIEWS + BOOKLET - Information about condition and /or its  management - Training to communicate with health-care  professionals  - Training for symptom self-management  strategies - Training for psychological strategies - Training for social strategies | 2 seasons30min-1h | · Quality of Life (EORTC-QLQ-C30)· Mood (HADS)· Symptom distress(Distress Termometer)· Patient Needs (Needs Assessment for Advanced Lung Cancer Patients) | Quality of lifeMoodSymptom distressPatient NeedsNS (p>0,05) |
| **Chan CWH, et al (2011)** [37] | Hospital | **EG:**  Healthy lifestyle programs Information about side-effects treatmentand management**CG:**  Usual Care Information about side-effects treatmentand management | LEAFLETS + AUDIOTAPE + TELEPHONE REMINDER - Training for symptom self-management  strategies - Training for practical self-management activities  - Training for psychological strategies | 3-6 weeks | · Quality of Life (SF-36)· Anxiety (STAI)· Fatigue (Piper)· Dyspnoea (VAS) | 6 weeks after intervention:Quality of lifeEG>CG (p< 0,001)AnxietyEG<CG (p= 0,001)Fatigue EG<CG (p= 0,011)DyspnoeaEG<CG (p= 0,002)12 weeks after intervention: Quality of lifeEG>CG (p< 0,002)AnxietyEG<CG (p= 0,005)Fatigue NS (p>0,05)DyspnoeaEG<CG (p= 0,001) |
| **Study (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Temel JS, et al (2011)** [38] | Hospital | **EG:**  Healthy lifestyle programs Usual Care**CG:**  Usual Care | FACE-TO-FACE INTERVIEWS - Information about condition and /or its  management - Provision of/agreement on specific clinical action  plans to improve self-efficacy - Regular visits with healthcare professionals - Training for identifying and satisfying  patients´ health needs - Training for symptom self-management  strategies - Training for practical self-management activities - Training for social strategies | 6 weeks | · Illness perception (own questionnaire)· Therapy perception (own questionnaire) | Illness perceptionEG>CG (p= 0,02)Therapy perception EG<CG (p= 0,02) |
| **Wilkie DJ, et al (2010)** [39] | Clinical Center | **EG:**  Healthy lifestyle programs**CG:**  Talking about cancer experience | FACE-TO-FACE/TELEPHONE/MAIL INTERVIEWS + VIDEOTAPE - Training for symptom self-management  strategies - Training for practical self-management activities | 4 weeks5-10min | · Anxiety (STAI)· Depression (CES-D)· Pain (MPQ; PINS)· Pain Management (Audiotape Scoring Tool)· Actual Pain (VAS)· Pain Relief (MPQ; VAS)· Analgesic management (PMI)· Catastrophyzing Pain Coping (CSQ) | Pain Management EG>CG (p<0,01)AnxietyDepressionPainAnalgesic managementCatastrophzing copingNS (p>0,05) |
| **9tudy (year)** | **Setting** | **Interventions** | **Healthy lifestyle programs** | **Intervention****duration and****frequency**WeeksDays x weekMinutes session | **Outcomes** | **Main Results** |
| **Goldberg RJ, et al (1985)** [40] | Hospital | **EG:** Healthy lifestyle programs**CG:** Usual Care |  FACE-TO-FACE INTERVIEWS - Training for psychological strategies - Training for social strategies | 12 seasons | · Mood (POMS)· Physical Perfomance (KPS)· Adjustment Illness (PAIS) | Mood Physical Perfomance Adjustment Illness NS (p>0,05) |

*HAMA: Hamilton Anxiety Rating Scale; HAMD: Hamilton Depression Rating Scale;FEV-1: Flow Expiratory Volumen-1 second; FVC: Forced Vital Capacity; MVV: Maximum Voluntary Volume; S-CAS: Self-Care Agency Scale; FLIS: Functional Living Index Scale; SF-36: Short Form Health Survey; PSEFSM fatigue: perceived self-efficacy for fatigue self-management - fatigue; 6MWT: 6 Minutes Walking Test; FACT-L: Functional Assessment of Cancer Therapy-Lung; AQOL: Assessment of Quality of Life; HADS: Hospital Anxiety and Depression Scale; MDASi-LC: MD Anderson Symptom Inventory–Lung Cancer; IPAQ: International Physical Activity Questionnaire; BREQ-2: Behavioural Regulation of Exercise Questionnaire, version 2; PAA-I: Physical Activity Assessment Inventory; CD-RISC-10: Connor-Davidson Resilience Scale 10-item version; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; SDS: Symptom Distress Scale; Ecog-PS: Eastern Cooperative Oncology Group Performance Status Scale; EQ-5D-3L: Euroqol-5Dimenssion-3L; PSQ-III: Patient Satisfaction Questionnaire-III; LCSS: Lung Cancer Symptom Scale; NSR: Numerical Rating Scale; D-12: Dyspnoea-12; MCLC: Manchester Cough in Lung Cancer scale; FACIT-F: Functional Assessment of Cancer Therapy-Fatigue; FACT-G: Functional Assessment of Cancer Therapy -General; FLSI: Functional Assessment of Cancer Therapy [FACT] – Lung Symptom Index; SMBQ: Symptom Management Barriers Questionnaire; FACIT-TS-PS: Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-Patient Satisfaction; KPS: Karnofsky Performance Scale; GSS: General Status Scale; HSS: Health Status Scale; STAI: State-Trait Anxiety Inventory; Piper: Piper Fatigue Scale; VAS: Visual Analogue Scale; CES-Q: Center for Epidemiological Studies Depression Scale; MPQ: McGill-Pain Questionnaire; PINS: Pain Intensity Number Scale; PMI: Pain Management Index; CSQ: Pain Coping Strategies Questionnaire; POMS: Profile of Moods Scale; PAIS: Psychosocial Adjustment to Illness Scale; NR: Non-reported; EG: Exercise Group; CG: Control Group; NS: No Significant results.*

**Results obtained in meta-analysis**

Results obtained in Quality of Life have been analyzed as shown in Figure 2.

The pooled mean difference (MD) showed significant overall effect of healthy lifestyles-based interventions: experimental group compared with control group (MD = 0.73, 95% CI=0.17, 1.29; p=0.01). The results show heterogeneity, detecting significant variability of I2=92%, not attributable to chance.

**Fig 2**. Meta-analysis: Forest plot illustrating changes in Quality of Life.

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*NR: Non-Reported; FLIS:* *Functional Living Index Scale; FACT-L:* *Functional Assessment of Cancer Therapy-Lung; QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FACT-G: Functional Assessment of Cancer Therapy-General; SF-36: Short Form Health Survey; SD: Standard Deviation; CI: Coefficient Intervale.*

Figure 3 presents the results of the meta-analysis for psychosocial distress of lung cancer survivors divided by the different psychological disorders. For anxiety disorders, the pooled mean difference (MD) didn't show significant overall effect of healthy lifestyles-based interventionswhen compared to control group (MD = 0.61; 95% CI = -0.13, 1.36; p = 0.11). In the same line, for depression disorders, the pooled mean difference (MD) didn't show significant overall effect of healthy lifestyles-based interventions when compared to control group (MD = 0.49; 95% CI = -0.34, 1.33; p = 0.25). However, with respect to total psychosocial distress measure reported, the pooled mean difference (MD) showed significant overall effect of healthy lifestyles-based interventions when compared to control group (MD = 0.57; 95% CI = 0.01, 1.13; p = 0.05). The results show heterogeneity, detecting significant variability of I2=93%, not attributable to chance.

**Fig 3**. Meta-analysis: Forest plot illustrating changes in Psychological Distress.



*STAI: State-Trait Anxiety Inventory; HAD-A: Hospital Anxiety and Depression- Anxiety; HAMA: Hamilton Anxiety Rating Scale; HAD-D: Hospital Anxiety and Depression- Depression; HAMD: Hamilton Depression Rating Scale; SD: Standard Deviation; CI: Coefficient Intervale.*

Results obtained in cancer-related symptoms have been analyzed as shown in Figure 4.

The pooled mean difference (MD) showed significant overall effect of healthy lifestyles-based interventions: experimental group compared with control group (MD = 0.77, 95% CI=0.08, 1.45; p=0.03). The results show heterogeneity, detecting significant variability of I2=90%, not attributable to chance.

**Fig 4**. Meta-analysis: Forest plot illustrating changes in cancer-related symptoms.



*MDASI-LC: MD Anderson Symptom Inventory–Lung Cancer; SDS: Symptom Distress Scale; FLSI: Functional Assessment of Cancer Therapy [FACT] – Lung Symptom Index; SD: Standard Deviation; CI: Coefficient Intervale.*

**Results obtained in Sensitivity Analysis**

When we restricted the analysis to 8 studies [27,28,30,31,32,34,35,37] that used a group format for intervention, no different findings were found among the outcomes. Removal of any study with individual intervention did not significantly alter the heterogeneity or p-value. Moreover, a sensitivity analysis identified no significant differences between studies that recruited cancer patients who intervened during oncological treatment [28,31,32,34, 35,37] and those that intervened after oncological treatment [27,30].

**DISCUSION**

The current review aimed to examine the effects of healthy lifestyle-based interventions in the lung cancer patients. Our results suggest beneficial effects of implementing healthy lifestyle-based interventions in lung cancer patient, with significant improvement in quality of life, psychological distress, and cancer-related symptoms.

These results are in line with other cancer reviews as the study of Green AC et al. [41] who have reported positive results for the use of lifestyle-based interventions in adults with or at risk for cancer, however, the review only recruited breast, prostate and colorectal cancer patients.

The sample of our review is like the sample of other lung cancer reviews [42,43], in which clinical profile and timing of the interventions were heterogeneous. Previous studies [44,45] have reported that timing close to diagnosis is an opportunity to positively impact a patient’s health behaviours, but in contrast, other studies [8] concluded that the post-treatment moment is the optimal time to initiate lifestyle programs. Our systematic review results suggest that the moment around oncological treatment seems to be most helpful. These conclusions suggest that these interventions can be used in any treatment status, but further research is needed to clearly understand the intersection between the timing of the intervention and the delivery of interventions.

The heterogeneity among the program´s designs and contents leads to a high discrepancy in the assessed variables and the results of the interventions. For this reason, our systematic review is focused on the components of the programs, while the meta-analysis is focused on the results of the common assessed variables.

The components proposed in the interventions were heterogenous, but it was to be expected given the fact that there is no consensus about the components of a healthy lifestyle. Most of the current definitions [46] of healthy lifestyle habits only consider physical activity, nutritional aspects, smoking and alcohol cessation. However, as early as 1999, the World Health Organization [21] has taken into account a broader view of factors that could disturb a patient's well-being. In this line, previous reviews [47,48] about healthy lifestyle-based programs considered other components like psychological advice, health information seeking or shaping knowledge, in a similar way to our review.

The meta-analyzed results of this review are in line with the meta-analyzed results of similar reviews. Spei ME et al [49] implemented regular physical activity in breast cancer survivors, reporting beneficial effects on the cancer-related symptom, psychological distress and quality of life of these patients. Previous studies [50] have highlighted the use of the variable that assesses overall health outcomes and may have a cumulative effect on lifestyle-based interventions such as quality of life. It would be interesting to meta-analyze other variables like self-efficacy or illness adjustment, given the interest generated in other healthy lifestyle-based intervention reviews [51,52], however, it could not be possible because of the lack of results in the included studies.

**Limitations**

This review has several limitations to comment. Our analysis includes a relatively small number of studies, making it unfeasible to conduct subgroup analyses, nevertheless previous reviews on the cancer population have been conducted with a similar number of studies [53]. Additionally, the stage and treatment status of lung cancer patients were not homogeneous, making it difficult to categorize the results. Although we reviewed multiple electronic databases of published and unpublished studies, some trials may have been missed. The timing of the intervention was also heterogenous, impeding the determination of stable results from the conducted analysis. However, the sensitivity analysis suggested that the effect of lifestyle-based interventions was consistent across the timing of the treatment. Nevertheless, given the small number of studies included, the assessment of the publication bias was difficult in this exposure. It should be taken into account that the statistic method used for meta-analysis assumes that the differences in standard deviations among studies reflect differences in measurement scales and not real differences in variability among study populations, for this reason the overall intervention effect can also be difficult to interpret as it is reported in units of standard desviation rather than in units of any of the measurement scales used in the review. All this means that the result´s interpretation and the conclusions drawn in this review should be taken with caution for clinical application.

**CONCLUSIONS**

In conclusion, the results of this systematic review with meta-analysis suggest that healthy lifestyle-based interventions improved the quality of life, psychological distress, and cancer-related symptoms of lung cancer patients, and seem to be most helpful around oncological treatment moment. However, this review could not show any conclusion about the better treatment moment to apply healthy lifestyle-based interventions. Additional research is needed to analyze which stage and treatment status are more likely to be effective. Future analyses are also needed to clarify the effect of the timing of the intervention when it could be possible to improve the personalized approach of lung cancer patients.

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**Appendix 1.** Search strategy.

**Pubmed:**

(neoplas\*[Title/Abstract]) OR (metastat\*[Title/Abstract])) OR (cancer\*[Title/Abstract])) OR (carcino[Title/Abstract])) OR (carcinoma\*[Title/Abstract])) OR (onco\*[Title/Abstract])) OR (tumor\*[Title/Abstract])) OR (tumour\*[Title/Abstract])) OR (malignan\*[Title/Abstract])) AND (Lung[Title/Abstract])) OR (Lungs[Title/Abstract])) AND (self care[Title/Abstract])) OR (self-care[Title/Abstract])) OR (self manage[Title/Abstract])) OR (self-manage[Title/Abstract])) OR (self efficacy[Title/Abstract])) OR (self-efficacy[Title/Abstract])) OR (home base[Title/Abstract])) OR (home-base[Title/Abstract])) OR (health education[Title/Abstract])) OR (patient education[Title/Abstract])) OR (patient participation[Title/Abstract])) OR (health communication[Title/Abstract])) OR (health promotion[Title/Abstract])) OR (self concept[Title/Abstract])) OR (self-control[Title/Abstract])) OR (self concept[MeSH Terms])) OR (self-regulation[Title/Abstract])) OR (patient autonomy[Title/Abstract])) OR (patient compliance[MeSH Terms])) OR (health behavior[MeSH Terms])) OR (health attitude[Title/Abstract])) OR (illness attitude[Title/Abstract])) OR (patient attitude[Title/Abstract])) OR (choice behavior[MeSH Terms])) OR (illness behavior[MeSH Terms])) OR (Self-management[Title/Abstract])) OR (adaptation, psychological[MeSH Terms])) OR (adjustment disorders[MeSH Terms])) OR (disease management[MeSH Terms])) OR (Adjustment[Title/Abstract])

**Web of Science:**

(neoplas\* OR metastat\* OR cancer\* OR carcino\* OR carcinoma\* OR onco\* OR tumor\* OR tumour\* OR malignan\*) AND (“Lung” OR “Lungs”) AND ("self care" OR "self-care" OR "self manage" OR "self-manage" OR "self efficacy" OR "self-efficacy" OR "home base" OR "home-base" OR "health education" OR "patient education" OR "patient participation" OR "health communication" OR "health promotion" OR "self concept" OR “Self-control” OR “Self-regulation” OR Patient autonomy\* OR “health behavior” OR “Health attitude” OR “Illness attitude” OR Patient attitude\* OR “Self management” OR Adjustment\*) AND (RCT OR Randomized Controlled Trial)

**Science Direct:**

(\*neoplas OR \*metastat OR \*cancer OR \*carcino OR \*carcinoma OR \*onco OR \*tumor OR \*tumour OR \*malignan) AND (“Lung” OR “Lungs”) AND ("self care" OR "self-care" OR "self manage" OR "self-manage" OR "self efficacy" OR "self-efficacy" OR "home base" OR "home-base" OR "health education" OR "patient education" OR "patient participation" OR "health communication" OR "health promotion" OR "self concept" OR “Self-control” OR “Self-regulation” OR \*Patient autonomy OR “health behavior” OR “Health attitude” OR “Illness attitude” OR \*Patient attitude OR “Self management” OR \*Adjustment) AND (RCT OR Randomized Controlled Trial)