Cost-effectiveness of patient navigation for lung cancer – a systematic review [version 2; peer review: 1 approved]

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Abstract

Background: Patient navigation (PN) programs have been shown to increase patient satisfaction and quality of life among patients with lung cancer and to decrease time to treatment. However, the general cost-effectiveness of such programs in the context of lung cancer remains unknown. Hence, the aim of the present systematic review was to analyze the scientific literature and quantitatively assess the level of evidence on the cost-effectiveness of PN programs for patients diagnosed with lung cancer.

Methods: A systematic literature search was carried out in PubMed, EMBASE, CENTRAL, CINAHL and PsycINFO databases without time limitations. Randomized controlled trials written in English or German were eligible for inclusion if any results regarding the cost-effectiveness of personally delivered PN programs for patients after lung cancer diagnosis were reported. A manual search was carried out to supplement the systematic search. Additionally, the authors of ongoing or unpublished relevant research were contacted. The titles, abstracts and full texts of relevant citations were screened independently by two reviewers.

Results: The initial search yielded 814 articles, including four papers identified manually. Twenty-one articles were included in the full text screening. However, no study met the inclusion criteria. Contacting the authors of ongoing or unpublished research and cross-cancer studies did not yield any studies that met the inclusion criteria.

Conclusion: Since no study met the inclusion criteria, this study reveals a research gap in this area. Furthermore, no conclusive statement regarding the cost-effectiveness of patient navigation programs for patients diagnosed with lung cancer can be made.
cancer can be made. Since the implementation of new healthcare models such as PN at least partially depends on their cost-effectiveness, future attempts to evaluate PN programs for lung cancer patients should consider examining outcomes related to cost-effectiveness to overcome the identified research gap.

**Keywords**
Patient Navigation, Cost-Benefit Analysis, Lung Cancer, Systematic Review, Empty Review, Randomized Controlled Trials

This article is included in the [Oncology](#) gateway.

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**Competing interests:** No competing interests were disclosed.

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Amendments from Version 1

We appreciate the extensive review that our manuscript received and the insightful comments. We have edited the manuscript according to most of the recommendations of the reviewer. Especially, changes were made in the introduction, methods and discussion section to improve the quality of our review. Further, we have answered and commented upon all issues raised by the reviewer.

Any further responses from the reviewers can be found at the end of the article.

Introduction

Lung cancer remains the most commonly diagnosed cancer type worldwide, with 2.1 million new cases annually. It accounts for an estimated 1.8 million deaths per year and is thus the most common cause of cancer-related deaths in men and the second most common cause in women. Steady progress in the detection, treatment and prevention of lung cancer has led to increased survival as well as decreased incidence. However, more than 50 percent of lung cancer patients die within a year after diagnosis, and the 5-year survival rate is still lower than 21 percent for men and women combined. In addition to the poor prognosis, lung cancer patients often experience severe symptom burdens, such as fatigue, shortness of breath and pain. These symptoms, along with anxiety and depression, are associated with reduced quality of life in lung cancer patients.

Depending on patients’ overall health and their lung cancer stage, treatment patterns can be very complex and overwhelming for patients. Chemotherapy, immunotherapy, radiotherapy, surgery, or therapy combinations are possible treatment options in curative or palliative settings. Furthermore, targeted therapy can be applied. These care options are provided by numerous different health care professionals within and across health care sectors. Patients’ complex needs, the large number of involved caregivers and expensive treatment patterns result in a high economic burden of lung cancer, varying across disease stages, treatment patterns and health care systems.

A promising approach to improve patient-oriented outcomes (e.g., health-related quality of life) and to reduce health care costs (e.g. by reducing barriers to appropriate treatment at an earlier stage of disease in order to avoid advanced stages of the disease) for patients with cancer and chronic diseases is patient navigation (PN). PN was first introduced by Harold Freeman to address barriers to timely care among African-American women with breast cancer in Harlem, New York. While PN programs initially focused on barriers within breast cancer care, there is currently a wide range of different programs across the cancer care continuum and beyond, including programs for other chronic diseases. Typically, PN programs focus on the elimination of one or multiple barriers to appropriate health care services, such as financial and access barriers, information barriers, medical system barriers and emotional barriers. Components of PN programs to overcome these barriers include aiding in care coordination, transportation services, educational components, emotional support and assistance with financial barriers such as insurance coverage. Programs are situated across the care continuum, including screening, diagnosis, treatment and surveillance. Navigators are most often trained health care professionals. In some programs lay health workers are employed.

Within the context of lung cancer, the introduction of PN delivered by nurses reduced the time to treatment initiation after suspicion of a lung cancer diagnosis in different settings. PN carried out by lay health workers has been shown to improve lung cancer screening rates in current smokers who receive care in community health centers. In one study, newly diagnosed lung cancer patients highly appraised the provision of information, emotional support and care coordination delivered by trained volunteer lay navigators. Compared to a control group receiving enhanced standard care over a 12-month follow-up, patients in a 16-week PN support program who were newly diagnosed with lung, breast or colon cancer reported comparable cancer-related quality of life and cumulative direct costs as well as higher patient satisfaction. The authors found lower cumulative direct costs in the small subsample of 30 lung cancer patients; however, effectivenes measures were not reported separately for this diagnosis. However, the general cost-effectiveness of such PN programs in the context of patients diagnosed with lung cancer has not yet been evaluated. Therefore, to date, no systematic and quantitative assessment of the cost-effectiveness of PN programs for patients diagnosed with lung cancer is available. Hence, the aim of this review was to analyze the scientific literature to quantitatively assess the level of evidence on the cost-effectiveness of PN programs for patients diagnosed with lung cancer.

Methods

Systematic and comprehensive literature searches in the PubMed, EMBASE, CENTRAL, CINAHL and PsycINFO databases were conducted at January 15, 2020. Medical subject headings (MeSH) terms and keywords were used to identify cost-effectiveness analyses of PN focusing on lung cancer patients. Broad search terms for patient navigation, including potential synonyms (e.g., case management, case coordination, and community health workers),
cost-effectiveness and lung cancer, were applied. The PubMed search strategy (Table 1) was adapted to the other electronic databases. An extensive manual search, including screening of study registers, and reference lists of studies and reviews in the context of patient navigation and lung cancer was carried out to identify additional studies. The authors of study protocols and cross-cancer studies were contacted up to two times to retrieve unpublished lung cancer-specific results.

Retrieved citations from all databases and manual searches were merged using Endnote Version X9.2 for Windows (Clarivate Analytics, Boston, MA, USA). After the review and removal of duplicates, study titles and abstracts were screened for inclusion. The full texts of the remaining articles were assessed for eligibility. Each step was independently performed by two review authors (CD, BK) to verify the retrieved results. Studies were eligible for inclusion if the following criteria were met:

1) the study was a randomized controlled trial (RCT);
2) the study was published in English or German; and
3) the study reported results regarding the cost-effectiveness of PN for lung cancer patients after the diagnosis was confirmed.

Based on a modification of the definition by Wells et al. (2008), PN was defined as an intervention that is carried out personally (e.g., by nurses, care managers, lay health workers) for a defined episode of individual lung cancer-related care and focuses on the identification and resolution of individual barriers to receive appropriate healthcare services. To reduce the heterogeneity of the included programs and effectiveness outcomes, PN programs focusing on the screening and early detection of lung cancer were a priori excluded. No further restrictions regarding the interventions were made. Studies describing all possible PN program components applied after diagnosis were eligible. No restrictions regarding the publication date, age of participants, lung cancer classification and stage, follow-up lengths, evaluation perspectives or reported cost types were made. Studies were excluded if they did not meet all eligibility criteria.

Data extraction and quality assessment of the included studies were planned to be carried out independently by two review authors. Data extraction using the 3rd version of the Cochrane data collection form for intervention reviews (Cochrane, London, UK) or an adaption of this form as well as the Revised Cochrane tool for assessing risk of bias in randomized trials tool for quality assessment were considered. Disagreements of any kind regarding data extraction and quality assessment were resolved by consensus. The two review authors worked closely together with an experienced senior author (TR) through the entire process. The systematic selection and screening of studies followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.

Results
A total of 810 citations were identified through database searches (PubMed n = 447, EMBASE n = 122, CENTRAL n = 72, CINAHL n = 165, PsycINFO n = 4), and an additional four articles were found manually. The removal of duplicate citations resulted in the inclusion of 741 titles and abstracts for eligibility screening. In this first-stage screening, 720 articles did not meet the inclusion criteria and were excluded. The remaining 21 articles proceeded to the full text assessment. Eight articles did not investigate patient navigation programs; six articles did not focus on lung cancer or
did not present lung cancer-specific results \(^{36-41}\); three articles did not include an economic evaluation \(^{8,24,42}\); three articles were study protocols \(^{43-45}\); and one article focused on promoting lung cancer screening prior to the diagnosis.\(^{22}\) During the full text assessment, the interrater reliability between CD and BK was 100%. Figure 1 illustrates the described study identification and selection process according to the PRISMA guidelines.

Additional attempts have been made to contact the authors of eight study protocols or cross-cancer studies.\(^{24,33,39-42,44,46}\) The authors of four studies could not be reached or did not reply. One research group did not collect cost-related data in their study, and the remaining three groups did not perform lung cancer-specific analyses. Furthermore, the screening of reference lists of approximately matching reviews and studies did not yield any relevant record either. Since no eligible studies on the cost-effectiveness of PN in lung cancer patients were found, this review reveals a research gap in this area.

**Discussion**

The systematic review did not identify any RCTs examining the cost-effectiveness of PN programs for patients diagnosed with lung cancer, revealing a research gap. Hence, no conclusion about the cost-effectiveness of such programs can be drawn.

A Markov model by Shih et al. from 2016 is the only analysis in this field.\(^{47}\) These authors offer early evidence that PN might be cost-effective for lung cancer patients. However, since the Markov model is not based on an RCT, the study did...
not meet the inclusion criteria for the current review and in line with recommendations for empty reviews, its results will not be further discussed as they are not able to answer the research question at hand.48

During the review process, one RCT focusing on the cost-effectiveness of a lung cancer PN screening program was detected.22 A priori, heterogeneity concerns led to the exclusion of programs focusing on the time before lung cancer diagnosis. The personal circumstances prior to and after such a diagnosis and thus the needs of potential patients seemed too different for a systematic comparison of respective PN programs. Other systematic reviews regarding the effectiveness or cost-effectiveness of PN did not distinguish between programs that were conducted prior to diagnosis and those that were conducted after diagnosis.13,14,16,18,49 However, heterogeneity was an issue regarding the generalizability of the results.

The specificity of the investigated research question to overcome heterogeneity concerns and the comprehensive attempts to gather unpublished information were considered strengths of the present review. Nevertheless, heterogeneity concerns are irrelevant in the absence of studies meeting the inclusion criteria, and the contact attempts were unsuccessful since no findings could be included and only half of the contacted authors replied.

Considering the high mortality and particularly severe disease burden of lung cancer, as well as the potentially beneficial effects of PN in other clinical fields, we encourage further research regarding the cost-effectiveness of PN programs for lung cancer patients. The low survival rates of lung cancer patients indicate the need for individually tailored treatment and support (e.g., PN programs) but might also be a cause for reduced study participation. Additionally, such studies need short follow-up periods, which in turn requires a high compliance among patients. The disease severity might also result in small subsample sizes in studies examining different cancer types, which would lead to a main analysis among all cancer types rather than subsample analyses. This assumption was substantiated by the answers from the contacted authors. Moreover, patients in advanced stages of the disease might be less likely to participate in an RCT, in which the kind of intervention will be decided by chance. Nonetheless, we focused on RCTs to build on the best available evidence. Since no eligible studies were identified, the focus on RCTs could be seen as a limitation. However, our broad search strategies did not include a restriction by study type, and no further thematically relevant nonrandomized studies except for the above-mentioned Markov model were identified during the selection process. Therefore, even if we had loosened the inclusion criteria, e.g. to non-RCTs with a sufficiently high number of participants, no further studies would have been identified. Recently published systematic reviews and study protocols related to the cost effectiveness of PN in the context of other cancer types and chronic diseases, might be a good starting point to develop and conduct similar studies in the context of lung cancer and thereby help overcome the research gap.18,49–32

Against the background of striving for the strongest evidence, future evaluations of PN programs for lung cancer patients should focus on RCTs and incorporate the examination of cost-effectiveness related outcomes, like quality of life as well as direct and indirect cost measurements over the intervention, and a sufficient follow-up period.

Future review attempts could consider an a priori broader research question and less restrictive inclusion criteria. Hence, all attempts should weigh heterogeneity concerns and its attached problems of comparability against further potential inclusions.

Conclusions
No evidence meeting the inclusion criteria was detected. Hence, this systematic review reveals a research gap regarding the cost-effectiveness of PN programs for patients diagnosed with lung cancer. Furthermore, no conclusive statement regarding the cost-effectiveness of such PN programs can be made. Since the implementation of new healthcare models such as PN at least partially depends on their cost-effectiveness, future evaluation attempts of PN programs in the field should consider examining outcomes related to cost-effectiveness analyses to overcome this research gap and thus help stakeholders make informed decisions regarding the implementation of PN programs among lung cancer patients in routine care.

Data availability
All data underlying the results are available as part of the article and no additional source data are required.

Reporting guidelines
Acknowledgements
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References


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Derek Falk

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The authors have responded to all of my concerns.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Patient navigation and health equity

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 29 September 2021

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1. Introduction, 3rd Paragraph. How exactly would PN reduce costs for patients? Generally, it is accepted that PN improves timely screening and care.
2. Introduction, 3rd Paragraph. The last sentence seems repetitive compared to the barriers presented. Also, it can be simply stated that navigators include both trained health care professionals and lay health workers.

3. Methods. What was the start date of the literature review?

4. Why did the authors only include RCTs in the inclusion criteria? This would severely limit the available literature in this area.

5. I wonder if the definition of PN should be included in the introduction rather than Methods. Also, are case management, care coordination, and community health working interchangeable concepts?

6. Discussion. Could the authors explain how exactly the Shih et al. 2016 study did not meet inclusion criteria without extensive discussion?

7. Discussion. Perhaps explaining the design of an ideal study would help the reader to understand the type of study and rigor required for inclusion. Also, do the authors intend to perform such a study as a next step since the literature does not address it?

Are the rationale for, and objectives of, the Systematic Review clearly stated?
Yes

Are sufficient details of the methods and analysis provided to allow replication by others?
Yes

Is the statistical analysis and its interpretation appropriate?
Not applicable

Are the conclusions drawn adequately supported by the results presented in the review?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Patient navigation and health equity

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 08 Oct 2021

**Benjamin Kass**, Charité-Universitätsmedizin Berlin, Berlin, Germany

**Comment 1:**
Introduction, 3rd Paragraph. How exactly would PN reduce costs for patients? Generally, it
is accepted that PN improves timely screening and care.

**Response 1:**
Thank you for this helpful comment. PN generally aims to reduce barriers to appropriate care and has thereby the potential to reduce treatment costs e.g. for people who receive treatment at an earlier (more appropriate) stage of disease. As pointed out by Wells et al. 2008, PN has the potential to move a person to an earlier stage of tumor diagnosis with a potentially less severe degree of cancer and thereby potentially reduce future treatment costs.

A sentence has been rewritten for clarification (Introduction, 3rd Paragraph).

**Comment 2:**
Introduction, 3rd Paragraph. The last sentence seems repetitive compared to the barriers presented. Also, it can be simply stated that navigators include both trained health care professionals and lay health workers.

**Response 2:**
Thank you for pointing this out. We have rewritten the last part of the paragraph (Introduction, 3rd Paragraph).

**Comment 3:**
Methods. What was the start date of the literature review?

**Response 3:**
The literature review started with the systematic search at January 15th 2020. The first sentence of the methods section has been clarified (Methods, first sentence).

**Comment 4:**
Why did the authors only include RCTs in the inclusion criteria? This would severely limit the available literature in this area.

**Response 4:**
Thank you for this comment. We see the potential controversy of limiting our review to RCTs. In the process of planning this review, we a priori focused on RCTs, since it was our aim as authors to present the best available evidence. After revealing no relevant RCTs during the review process, this can be seen as a weakness of our review. However, our broad search strategy, which was not restricted to RCTs, could only identify one nonrandomized thematically relevant study, the briefly discussed Markov model by Shih et al. 2016.

We tried to elaborate on this topic at the 5th paragraph of the discussion section. Please let us know, if we should include further aspects to the discussion of the study selection.

**Comment 5:**
I wonder if the definition of PN should be included in the introduction rather than Methods.

**Response 5:**
Thank you very much for your comment. The topic was discussed prior to submission and we considered this point in detail once more.

Against the background of our rewritten general description of PN in the introduction, we would prefer to leave our specific PN definition in the Methods to give the audience a general overview about inclusion and exclusion criteria at one place.
Comment 6:
Also, are case management, care coordination, and community health working interchangeable concepts?

Response 6:
Our research has shown that these concepts are inconsistently labeled in the literature. Against this background, it was our aim to include all potentially relevant concepts to the search strategy and thereafter to check potentially relevant programs against the background of our PN definition.

Comment 7:
Discussion. Could the authors explain how exactly the Shih et al. 2016 study did not meet inclusion criteria without extensive discussion?

Response 7:
The Shih et al. publication is a Markow model based calculation without an underlying RCT. Hence, it did not meet the a priori defined suitable study type for inclusion. A sentence has been rewritten for clarification (Discussion, 2nd Paragraph).

Comment 8:
Discussion. Perhaps explaining the design of an ideal study would help the reader to understand the type of study and rigor required for inclusion.

Response 8:
Thank you for your suggestion. We included a sentence to the penultimate paragraph of the Discussion.

Comment 9:
Also, do the authors intend to perform such a study as a next step since the literature does not address it?

Response 9:
Yes, it is intended and has already started. As part of the NAVICARE project, some of the authors are working on a project that aims to evaluate a patient navigation program for stroke and lung cancer patients in Germany, which would fit the inclusion criteria for patient navigation of this review in the future. The study is called CoreNAVI - Feasability of a patient navigation programme, and is registered at the German registry for clinical studies (https://www.drks.de/drks_web/setLocale_EN.do). The study will also address the cost-effectiveness issues of patient navigation based on cost data provided by a cooperating statutory health insurance and effectiveness data collected during the trial.

Competing Interests: No competing interests were disclosed.
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