BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2021-057801
Article Type:	Protocol
Date Submitted by the Author:	27-Sep-2021
Complete List of Authors:	Fu, Liang; Jinhua Hospital of Zhejiang University, Department of Nursing/Central Laboratory Zhuang, Minling; Jinhua Hospital of Zhejiang University Luo, Chengcan; Jinhua Hospital of Zhejiang University Zhu, Ruiyun; Jinhua Hospital of Zhejiang University Wu, Bei; Jinhua Hospital of Zhejiang University Xu, Wenxia; Jinhua Hospital of Zhejiang University, Central Laboratory Ye, Xianghong; Jinhua Hospital of Zhejiang University, Department of Nursing
Keywords:	Adult oncology < ONCOLOGY, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Financial Toxicity in Patients with Lung Cancer: A Scoping Review Protocol

Liang Fu,[1, 2] Minling Zhuang,[1] Chengcan Luo,[1] Ruiyun Zhu,[1] Bei Wu, [1] Wenxia Xu,[2] Xianghong Ye[1]

[1]Department of Nursing, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China

[2]Central Laboratory, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China

Correspondence to

Xianghong Ye;

13868992616@163.com

ABSTRACT

Introduction Lung cancer has the second-ranked morbidity rate and the first-ranked mortality rate worldwide. With the progression of the cancer condition and the advance of new treatments, the corresponding medical expenses have risen sharply. Nowadays, financial toxicity has become one of the most common concerns in cancer patients. However, the full landscape of studies on financial toxicity is unclear in lung cancer patients by far. Thus, this scoping review aims to summary the degree, affecting factors, outcomes and intervention strategies of financial toxicity in patients with lung cancer.

Methods and analysis This scoping review will be developed following the methodology described in the JBI Manual for Evidence Synthesis on scoping review protocol, which was based on Arksey and O'Malley's methodological framework, Levac et al's recommendations for applying this framework and Peters' enhancements of the framework. From the day of database building to December 31, 2021, nine English databases will be searched in "Abstract" field with three parts of search terms "Lung", "Cancer" and "Financial toxicity". The studies screening and data extraction will be independently performed by two reviewers. Any disagreements between the two reviewers will be resolved by consensus, and a third reviewer will be invited if necessary. The results will be analyzed and presented using tables and figure. This scoping review will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist (PRISMA-ScR).

Ethics and dissemination An ethical approval is not required for this scoping review protocol, nor for the scoping review. The results of this scoping review will be disseminated through publication in a peer-reviewed journal, or presentation at conferences.

Registration This scoping review protocol has been registered in the Open Science Framework (https://osf.io/ub45n/?view_only=bb93eb94e1434a0f8196b3b61cffcec2).

Strengths and limitations of this study

- There was hardly any review on financial toxicity in patients with lung cancer.
- This scoping review will be developed following the methodology described in the JBI Manual for Evidence Synthesis on scoping review protocol.
- This scoping review will explore and illustrate the degree, affecting factors, outcomes and intervention strategies of financial toxicity in patients with lung cancer.
- This scoping review will focus on financial toxicity of lung cancer patients, and the results may not to be generalizable to other cancers.
- This scoping review will be limited to include studies published in English.

INTRODUCTION

Lung cancer (LC), or bronchogenic carcinoma, is a proliferative malignant neoplasm arising from the primary respiratory epithelium.[1] Lung cancer is generally divided into two major histologic groups: non small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). As one of the most commonly diagnosed cancers globally, lung cancer has

the second-ranked morbidity rate and the first-ranked mortality rate. In 2020, GLOBOCAN has reported there were an estimated 2, 206, 771 (11.4%) new cases and 1, 796, 144 (18.0%) cancer deaths of lung cancer worldwide.[2] Furthermore, a higher incidence (14.3%) and a higher mortality (21.5%) of lung cancer were found in males than the incidence (8.4%) and mortality (13.7%) in females.[2] Currently, lung cancer cannot be completely cured, which generally controlled by medication and treatment to prolong life. As a result, most of the time it is an ongoing process. With the progression of the cancer condition and the advance of new treatments, the increase of medical expenses is also inevitable.[1, 3-6]

Financial toxicity (FT) is objective financial burden on and subjective financial distress experienced by cancer patients as a result of their treatment.[7] As a new concern that has emerged in the last decade, high prevalence of financial toxicity was reported in patients with various cancers worldwide.[7-9] Factors related to financial toxicity were identified, involving baseline factors, cancer-related factors, medical insurance status, treatments, end of life care and so on.[8, 10] Furthermore, financial toxicity negatively affects the patient's treatment, prognosis, quality of life (QoL), symptom burden and so on.[7-10] And strategies to reduce financial toxicity have also been proposed at multiple levels (provider, clinic, hospital, and insurance and governmental).[7, 8]

The status of financial toxicity in patients with lung cancer is similar to

the above situation. Study from Hazell et al. explored financial toxicity in lung cancer patients, demonstrating 38.2% participants were either "just getting on" or "struggling" financially, inability to afford basic necessities, <1 month of savings and being employed but on sick leave were identified as risk factors of financial toxicity, and increased financial toxicity was correlated with a decrease in QoL.[11] Chen et al.'s study indicated 72.7% and 37.0% lung cancer patients reported catastrophic health spending and healthcare costs exceeded annual household income respectively, 83.7% participants perceived financial difficulty, and healthcare costs exceeding total annual household income and perceived financial difficulty were associated with poorer QoL.[12] However, the full landscape of studies on financial toxicity is unclear in lung cancer patients by far. Therefore, to identify the knowledge gaps between practice and evidence and propose recommendations for future studies, it's crucial to review and summarize the current literature regarding financial toxicity in lung cancer patients.

OBJECTIVES

The objectives of this scoping review are to illustrate: (1) the degree of financial toxicity in lung cancer patients; (2) the contributing factors of financial toxicity in patients with lung cancer; (3) the impacts of financial toxicity on lung cancer patients; (4) the strategies to reduce financial toxicity in patients with lung cancer.

METHODS

This protocol will be developed following the methodology described in the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis on scoping review protocol,[13] which was based on Arksey and O'Malley's methodological framework,[14] Levac et al's recommendations for applying this framework [15] and Peters' enhancements of the framework.[16] The proposed scoping review will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist (PRISMA-ScR).[17] The present protocol has been registered within the Open Science Framework (https://osf.io/).

Stage 1: identifying the research questions

According to the objectives, this scoping review is plan to answer the following main questions: (1) What evidence is available on degree of financial toxicity in patients with lung cancer; (2) What are the factors that affect financial toxicity in lung cancer patients; (3) What are the outcomes of financial toxicity on lung cancer patients; (4) What are the intervention strategies to deal with financial toxicity in patients with lung cancer.

Stage 2: identifying relevant studies

The participants of considering studies will be: (1) human being, (2) 18 years of age or older, (3) confirmed with a pathologic diagnosis of lung cancer, (4) reported financial toxicity. The concept, financial toxicity, was

defined as the objective financial burden and subjective financial distress of patients with cancer, as a result of treatments using innovative drugs and concomitant health services.[7, 18, 19] Objective financial burden stems from out-of-pocket spending on cancer drugs as well as the services that make up the treatment regimen, including medical imaging, radiotherapy, surgery, and other procedures.[7, 19, 20] Subjective financial distress results from the accumulation of out-of-pocket spending from the time of diagnosis, the erosion of the household's wealth and nonmedical budget, and worry about the effectiveness of coping strategies available to and used by the patient.[7, 19, 21] The context of studies will be globally acute care, primary health care, community care and so on. The type of studies will be primary quantitative studies, including randomized controlled trials, nonrandomized controlled trials, quasi-experimental studies, before and after studies, prospective and retrospective cohort studies, case-control studies, and cross-sectional studies. Qualitative studies, reviews, and conference abstracts were excluded.

The search strategy will be developed as follows: The nine databases, The Cochrane Library, MEDLINE, Embase, CINAHL, Web of Science, Scopus, ProQuest, PsycINFO and Google Scholar, will be searched. The search terms will be divided into three parts, namely "Lung", "Cancer" and "Financial toxicity". The search field will be Title/Abstract. The language will be limited to English. The time period will be set as the day

of database building to December 31, 2021. In addition, hand search will be performed for reference lists of the included literatures. The corresponding author will be contacted if necessary. A draft search strategy in MEDLINE was shown in online Supplemental Table S1.

Stage 3: study selection

All literatures identified by the search strategies will be exported from the databases/journals and imported into the EndNote respectively. After removing duplicates, the references will then be transferred into Rayyan.[22] A two-step process will be performed independently to select studies by two reviewers. According to the inclusion criteria described in Stage 2, the two reviewers will screen titles and abstracts of considering studies firstly, and then screen full-texts. All disagreements between the above-mentioned two reviewers will be resolved by consensus, and a third reviewer will be invited if necessary. Pilot tests of study selection will be performed in 10% of all references. The formal study selection will begin until 75% agreement or greater of is achieved among reviewers. A PRISMA-ScR flow diagram (Figure 1) will be provided to show details of studies included and excluded during the study selection process.

Stage 4: charting the data

A structured data recording form will be used on Microsoft Excel to capture the data of interest from the selected studies. The detailed data

will include author, year of publication, country, study design, setting, population and sample size, measure of financial toxicity, financial toxicity (financial burden and financial distress), affecting factor, outcome, intervention strategy and reference. To ensure consistency in data extraction, two reviewers will pilot test the form independently on a random sample of the included studies (10%). The form will be revised by an iterative process if necessary. In the formal data extraction stage, data will be extracted by one reviewer according to the objectives of this scoping review, and verified by another reviewer. Any disagreements between the two reviewers will be resolved by consensus, and a third reviewer will be invited if necessary. A daft data extraction form was presented in Table S2.

Stage 5: collating, summarizing and reporting the results

The synthesis will be performed using narrative summaries and thematic analyses of the extracted data. Meanwhile, frequency distributions and descriptive statistics will be used to present year of publication, country, study design, setting, population and sample size, measure of financial toxicity, financial toxicity (financial burden and financial distress), affecting factor, outcome and intervention strategy. In addition, the degree of financial toxicity (financial burden and financial distress) will be summarized and analyzed according to the measurement methods. The affecting factors, outcomes and intervention strategies of financial

toxicity (financial burden and financial distress) will be classified on the basis of the results. For the contributing factors, the categories may be demographic and socioeconomic factors, cancer related factors, medical insurance, treatments and so on. The outcomes may involve survival, mortality, treatment nonadherence, quality of life and symptom burden. The intervention strategies may be summarized from the level of healthcare providers, institutions and medical systems. See Table S3-S6.

Stage 6: consultation

A stakeholder consultation will be held to validate the findings in this scoping review, and identify knowledge gaps for further research. Stakeholders will include clinicians, nurses, accountants, public servants and methodological experts of evidence-based medicine. Their suggestions will be incorporated into our final manuscript of scoping review.

Patient and public involvement

Patients or the public will not be directly involved in the design, or conduct, or reporting, or dissemination plans of our research.

Ethics and dissemination

An ethical approval is not required for this scoping review protocol, nor for the scoping review. The results of this scoping review will be disseminated through publication in a peer-reviewed journal, or presentation at conferences.

Contributors XY conceived the study; LF, MZ, CL, RZ, BW and WX conceptualized the research questions; LF, WX and XY refined the research questions; LF, CL and XY drafted the scoping review protocol. All authors contributed to the refining of the study design, as well as to the editing and revising of this protocol.

Funding This work was supported by the General Project of Zhejiang Province Medical Science and Technology Plan (grant number: 2021KY1181), the Major Project of Jinhua City Science and Technology Research Plan (grant number: 2021-3-051) and the General Project of Jinhua Municipal Central Hospital Young and Middle-aged Scientific Research Start-up Fund (grant number: JY2020-2-05).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Figure 1 Flow diagram of study selection process

REFERENCES

1. Goldman L, Schafer AI. **Goldman-Cecil Medicine 26th Edition**. Philadelphia: Elsevier; 2020.
2. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. **CA Cancer J Clin**. May 2021;71(3):209-249.
3. Sanaei MJ, Pourbagheri-Sigaroodi A, Kaveh V, et al. Recent advances in immune checkpoint therapy in non-small cell lung cancer and opportunities for nanoparticle-based therapy. **Eur J**

Pharmacol. Aug 4 2021;909:174404.

4. Reuss JE, Gosa L, Liu SV. Antibody Drug Conjugates in Lung Cancer: State of the Current Therapeutic Landscape and Future Developments. **Clin Lung Cancer**. Jul 25 2021.
5. Wang Z, Liu Z, Mei J, Xu S, Liu Y. The next generation therapy for lung cancer: taking medicine by inhalation. **Nanotechnology**. 2021;32(39).
6. Giuliani J, Bonetti A. Financial Toxicity and Non-small Cell Lung Cancer Treatment: The Optimization in the Choice of Immune Check Point Inhibitors. **Anticancer Res**. Jul 2019;39(7):3961-3965.
7. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. **CA Cancer J Clin**. Mar 2018;68(2):153-165.
8. Lentz R, Benson AB, 3rd, Kircher S. Financial toxicity in cancer care: Prevalence, causes, consequences, and reduction strategies. **J Surg Oncol**. Jul 2019;120(1):85-92.
9. de la Cruz M, Delgado-Guay MO. Financial Toxicity in People Living with Advanced Cancer: A New, Deadly, and Poorly Addressed Effect of Cancer and Necessary Treatment. **Semin Oncol Nurs**. Aug 2021;37(4):151171.
10. Urek D, Ugurluoglu O. Predictors of financial toxicity and its associations with health-related quality of life and treatment non-adherence in Turkish cancer patients. **Support Care Cancer**. Aug 15 2021.
11. Hazell SZ, Fu W, Hu C, et al. Financial toxicity in lung cancer: an assessment of magnitude, perception, and impact on quality of life. **Ann Oncol**. Jan 2020;31(1):96-102.
12. Chen JE, Lou VW, Jian H, et al. Objective and subjective financial burden and its associations with health-related quality of life among lung cancer patients. **Support Care Cancer**. Apr 2018;26(4):1265-1272.
13. Aromataris E, Munn Z. *JBI Manual for Evidence Synthesis*. Adelaide: Joanna Briggs Institute; 2020.
14. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. **International Journal of Social Research Methodology**. 2005;8(1):19-32.
15. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. **Implement Sci**. Sep 20 2010;5:69.
16. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. **Int J Evid Based Healthc**. Sep 2015;13(3):141-146.
17. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. **Ann Intern Med**. Oct 2 2018;169(7):467-473.
18. Carrera PM. The financial hazard of personalized medicine and supportive care. *Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) 2017 Annual Meeting*. Washington, DC; 2017.
19. Olver I. **The MASCC Textbook of Cancer Supportive Care and Survivorship. 2nd ed**. New York: Springer; 2018.
20. Landwehr MS, Watson SE, Macpherson CF, Novak KA, Johnson RH. The cost of cancer: a retrospective analysis of the financial impact of cancer on young adults. **Cancer Med**. May 2016;5(5):863-870.
21. Barbaret C, Brosse C, Rhondali W, et al. Financial distress in patients with advanced cancer. **PLoS One**. 2017;12(5):e0176470.
22. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. **Syst Rev**. Dec 5 2016;5(1):210.

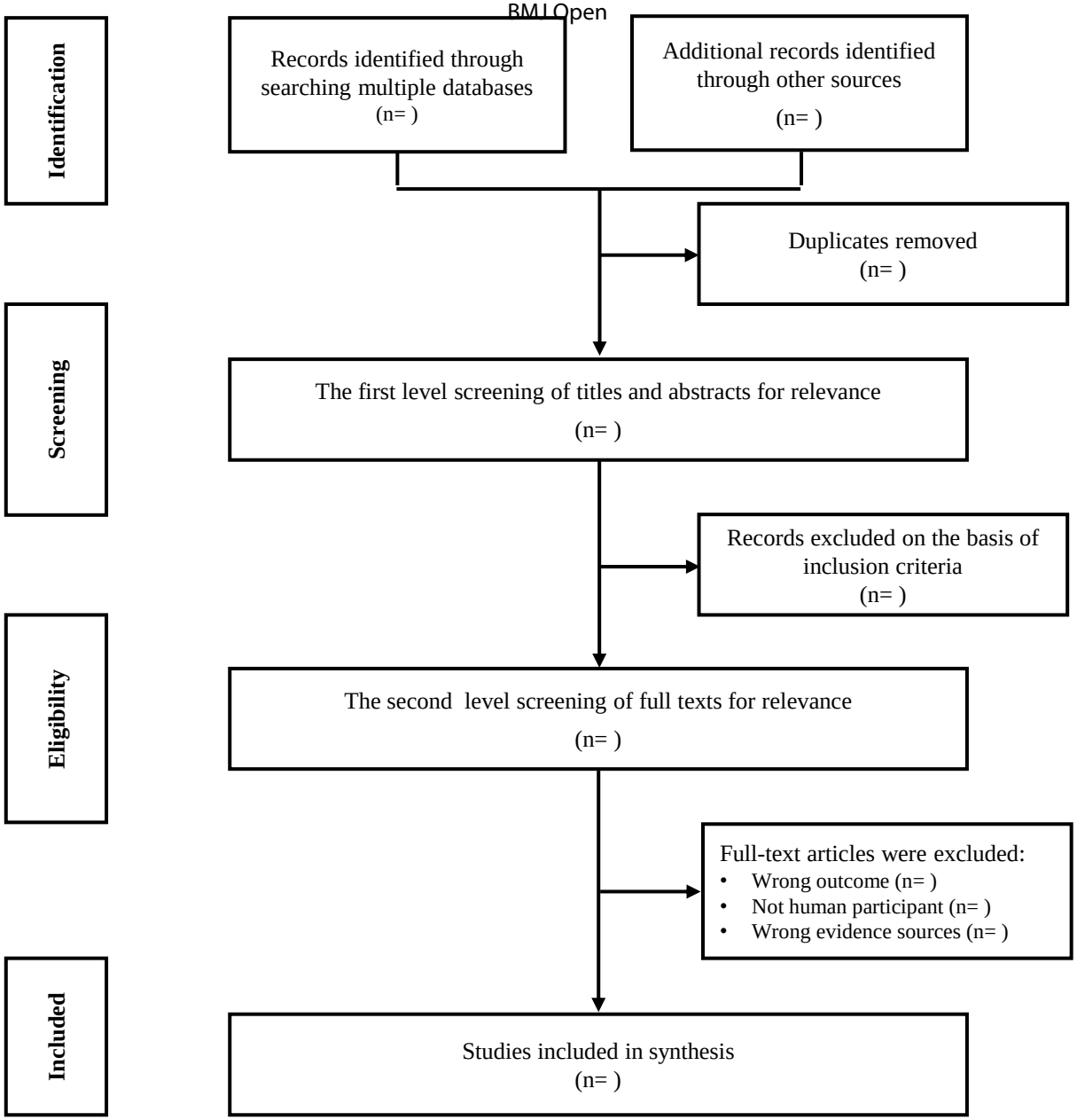

Figure 1 Flow diagram of study selection process

Table S1 Search strategy of MEDLINE

#	Search strings
1	(lung* OR bronch* OR pulmonary*).ab.
2	(cancer* OR tumor* OR tumour* OR neoplas* OR malignan* OR carcinoma*).ab.
3	(financial stress* OR financial toxicit* OR financial distress* OR financial burden* OR financial hardship* OR financial pressure* OR financial challenge* OR economic stress* OR economic toxicit* OR economic distress* OR economic burden* OR economic hardship* OR economic pressure* OR economic challenge*).ab.
4	#1 and #2 and #3

Table S2 The general information of included studies

No.	Author	Year of publication	Country	Study design	Setting	Population and sample size	Measure of financial toxicity	Financial toxicity	Financial burden	Financial distress	Affecting factor	Outcome	Intervention strategy	Reference
1														
2														
3														

Table S3 The degree of financial toxicity in lung cancer patients according to different measures

No.	Measure	Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

Table S4 The contributing factors of financial toxicity in lung cancer patients after classification

No.	Category	Contributing factor			
		Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

Table S5 The outcomes of financial toxicity in lung cancer patients after classification

No.	Category	Outcome			
		Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

Table S6 The intervention strategies of financial toxicity in lung cancer patients after classification

No.	Category	Intervention strategy			
		Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

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Manuscript ID	bmjopen-2021-057801.R1
Article Type:	Protocol
Date Submitted by the Author:	06-Apr-2022
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Primary Subject Heading:	Oncology
Secondary Subject Heading:	Health economics, Nursing
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[1]Department of Nursing, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China

[2]Central Laboratory, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China

[3]Department of Thoracic Surgery, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China

[4]Department of Teaching, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang, China

Correspondence to

Ruiyan Xu;

xry1234567890@163.com and

Xianghong Ye;

13868992616@163.com

ABSTRACT

Introduction Lung cancer has the second-ranked morbidity rate and the first-ranked mortality rate worldwide. With the progression of the cancer condition and the advance of new treatments, the corresponding medical

expenses have risen sharply. Nowadays, financial toxicity has become one of the most common concerns in cancer patients. However, the full landscape of studies on financial toxicity is unclear in lung cancer patients by far. Thus, this scoping review aims to summarize the degree, affecting factors, outcomes, and intervention strategies of financial toxicity in patients with lung cancer.

Methods and analysis This scoping review will be developed following the methodology described in the JBI Manual for Evidence Synthesis on scoping review protocol, which was based on Arksey and O'Malley's methodological framework, Levac et al's recommendations for applying this framework, and Peters' enhancements of the framework. From the day of database building to December 31, 2021, ten English databases will be searched in the "Abstract" field with three key search terms "Lung", "Cancer" and "Financial toxicity". The studies screening and data extraction will be independently performed by two reviewers (MZ and RZ). Any disagreements between the two reviewers (MZ and RZ) will be resolved by consensus, and a third reviewer (BW) will be invited if necessary. The results will be analyzed and presented using tables and figures. This scoping review will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist (PRISMA-ScR).

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Registration This scoping review protocol has been registered in the Open Science Framework (https://osf.io/ub45n/?view_only=bb93eb94e1434a0f8196b3b61cffcec2).

Strengths and limitations of this study

- This scoping review will be developed following the methodology described in the JBI Manual for Evidence Synthesis on scoping review protocol.
- To include as many relevant studies as possible, we plan to use a broad search strategy.
- We plan to perform the optional sixth stage (consultation) in our review.
- This scoping review will be limited to include studies published in English.
- The quality of studies in this scoping review will not be assessed.

INTRODUCTION

Lung cancer (LC), or bronchogenic carcinoma, is a proliferative malignant neoplasm arising from the primary respiratory epithelium.[1]

Lung cancer is generally divided into two major histologic groups: non small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). As one of the most commonly diagnosed cancers globally, lung cancer has the second-ranked morbidity rate and the first-ranked mortality rate. In 2020, GLOBOCAN has reported there were an estimated 2, 206, 771 (11.4%) new cases and 1, 796, 144 (18.0%) cancer deaths of lung cancer worldwide.[2] Furthermore, a higher incidence (14.3%) and a higher mortality (21.5%) of lung cancer were found in males than the incidence (8.4%) and mortality (13.7%) in females.[1] Currently, lung cancer cannot be completely cured, but is generally controlled by medication and treatment to prolong life. As a result, most of the time it is an ongoing process. With the progression of the cancer condition and the advance of new treatments, the increase in medical expenses are also inevitable.[1, 3-6]

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financial toxicity have also been proposed at multiple levels (provider, clinic, hospital, insurance and governmental, and so on).[7, 8, 11]

The status of financial toxicity in patients with lung cancer is similar to the above situation. The study from Hazell et al. explored financial toxicity in lung cancer patients, demonstrating 38.2% of participants were either "just getting on" or "struggling" financially, inability to afford necessities, <1 month of savings and being employed but on sick leave were identified as risk factors of financial toxicity, and increased financial toxicity was correlated with a decrease in QoL.[12] Chen et al.'s study indicated 72.7% and 37.0% of lung cancer patients reported catastrophic health spending and healthcare costs exceeded annual household income respectively, 83.7% of participants perceived financial difficulty, and healthcare costs exceeded total annual household income and perceived financial difficulty were associated with poorer QoL.[13] However, the full landscape of studies on financial toxicity is unclear in lung cancer patients by far. Therefore, to identify the knowledge gaps between practice and evidence and propose recommendations for future studies, it's crucial to review and summarize the current literature regarding financial toxicity in lung cancer patients.

OBJECTIVES

The objectives of this scoping review are to illustrate: (1) the degree of financial toxicity in lung cancer patients; (2) the contributing factors of

financial toxicity in patients with lung cancer; (3) the impacts of financial toxicity on lung cancer patients; (4) the strategies to reduce financial toxicity in patients with lung cancer.

METHODS

This protocol will be developed following the methodology described in the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis on scoping review protocol,[14] which was based on Arksey and O'Malley's methodological framework,[15] Levac et al's recommendations for applying this framework and Peters' enhancements of the framework.[16, 17] The proposed scoping review will be reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews checklist (PRISMA-ScR).[18] The present protocol has been registered within the Open Science Framework (https://osf.io/).

Stage 1: identifying the research questions

According to the objectives, this scoping review is planning to answer the following main questions: (1) What evidence is available on the degree of financial toxicity in patients with lung cancer; (2) What are the factors that affect financial toxicity in lung cancer patients; (3) What are the outcomes of financial toxicity on lung cancer patients; (4) What are the intervention strategies to deal with financial toxicity in patients with lung cancer.

Stage 2: identifying relevant studies

The participants of considering studies will be: (1) human being, (2) 18 years of age or older, (3) confirmed with a pathologic diagnosis of lung cancer, (4) reported financial toxicity. The concept, financial toxicity, was defined as the objective financial burden and subjective financial distress of patients with cancer, as a result of treatments using innovative drugs and concomitant health services.[7, 19, 20] Objective financial burden stems from out-of-pocket spending on cancer drugs as well as the services that make up the treatment regimen, including medical imaging, radiotherapy, surgery, lost wages for patients or caregivers, and other procedures.[7, 20,21] Subjective financial distress results from the accumulation of out-of-pocket spending from the time of diagnosis, the erosion of the household's wealth and nonmedical budget, and worry about the effectiveness of coping strategies available to and used by the patient.[7, 20, 22] The context of studies will be globally acute care, primary health care, community care and so on. The type of studies will be primary quantitative studies, including randomized controlled trials, nonrandomized controlled trials, quasi-experimental studies, before and after studies, prospective and retrospective cohort studies, case-control studies, and cross-sectional studies. Qualitative studies, reviews, and conference abstracts were excluded.

The search strategy will be developed as follows: The ten databases, The Cochrane Library, MEDLINE, Embase, CINAHL, Web of Science,

Scopus, ProQuest, PsycINFO, EconLit and Google Scholar, will be searched. The search terms will be based on three key terms, namely "Lung", "Cancer" and "Financial toxicity". The search field will be Title/Abstract. The language will be limited to English. The period will be set as the day of database building to December 31, 2021. In addition, hand search will be performed for reference lists of the included literature. The corresponding author will be contacted if necessary. A draft search strategy in MEDLINE was shown in online Supplemental Table S1.

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All literature identified by the search strategies will be exported from the databases/journals and imported into the EndNote respectively. After removing duplicates, the references will then be transferred into Rayyan.[23] A two-step process will be performed independently to select studies by two reviewers (MZ and RZ). According to the inclusion criteria described in Stage 2, two reviewers (MZ and RZ) will screen titles, and in the next step will screen abstracts of considering studies firstly, and then screen full texts. All disagreements between the above-mentioned two reviewers (MZ and RZ) will be resolved by consensus, and a third reviewer (BW) will be invited if necessary. Pilot tests of study selection will be performed in 10% of all references. The formal study selection will begin until 75% agreement or greater is

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Stage 4: charting the data

A structured data recording form will be used on Microsoft Excel to capture the data of interest from the selected studies. The detailed data will include author, year of publication, country, study design, setting, population and sample size, measure of financial toxicity, financial toxicity (financial burden and financial distress), affecting factor, outcome, intervention strategy and reference. To ensure consistency in data extraction, two reviewers (MZ and RZ) will pilot test the form independently on a random sample of the included studies (10%). The form will be revised by an iterative process if necessary. In the formal data extraction stage, data will be extracted by one reviewer (MZ) according to the objectives of this scoping review and verified by another reviewer (RZ). Any disagreements between the two reviewers (MZ and RZ) will be resolved by consensus, and a third reviewer (BW) will be invited if necessary. A draft data extraction form was presented in Table S2.

Stage 5: collating, summarizing and reporting the results

The synthesis will be performed using narrative summaries and thematic analyses of the extracted data. Meanwhile, frequency distributions and

descriptive statistics will be used to present the year of publication, country, study design, setting, population and sample size, the measure of financial toxicity, financial toxicity (financial burden and financial distress), affecting factor, outcome and intervention strategy. In addition, the degree of financial toxicity (financial burden and financial distress) will be summarized and analyzed according to the measurement methods. The affecting factors, outcomes and intervention strategies of financial toxicity (financial burden and financial distress) will be classified based on the results. For the contributing factors, the categories may be demographic and socioeconomic factors, cancer related factors, medical insurance, treatments and so on. The outcomes may involve survival, mortality, treatment nonadherence, quality of life and symptom burden. The intervention strategies may be summarized from the level of healthcare providers, institutions and medical systems. See Table S3-S6.

Stage 6: consultation

Stakeholder consultation will be held to validate the findings in this scoping review and identify knowledge gaps for further research. Stakeholders will include clinicians, nurses, accountants, public servants and methodological experts of evidence-based medicine. Their suggestions will be incorporated into our final manuscript of scoping review.

Patient and public involvement

Patients or the public will not be directly involved in the design, conduct, reporting, or dissemination plans of our research.

Ethics and dissemination

Ethical approval is not required for this scoping review protocol, nor for the scoping review. The results of this scoping review will be disseminated through publication in a peer-reviewed journal, or presentation at conferences.

Contributors RX and XY conceived the study; LF, MZ, CL, RZ, BW, WX and BX conceptualized the research questions; LF, WX, BX, RX and XY refined the research questions; LF, CL, RX and XY drafted the scoping review protocol. All authors contributed to the refining of the study design, as well as to the editing and revising of this protocol.

Funding This work was supported by the Key Project of Jinhua City Science and Technology Research Plan (grant number: 2020-3-040).

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Figure 1 Flow diagram of study selection process

REFERENCES

1. Goldman L, Schafer AI. Goldman-Cecil Medicine 26th Edition. Philadelphia: Elsevier; 2020.
2. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. May 2021;71(3):209-249.
3. Sanaei MJ, Pourbagheri-Sigaroodi A, Kaveh V, et al. Recent advances in immune checkpoint therapy in non-small cell lung cancer and opportunities for nanoparticle-based therapy. Eur J Pharmacol. Aug 4 2021;909:174404.
4. Reuss JE, Gosa L, Liu SV. Antibody Drug Conjugates in Lung Cancer: State of the Current Therapeutic Landscape and Future Developments. Clin Lung Cancer. Jul 25 2021.
5. Wang Z, Liu Z, Mei J, Xu S, Liu Y. The next generation therapy for lung cancer: taking medicine by inhalation. Nanotechnology. 2021;32(39).
6. Giuliani J, Bonetti A. Financial Toxicity and Non-small Cell Lung Cancer Treatment: The Optimization in the Choice of Immune Check Point Inhibitors. Anticancer Res. Jul 2019;39(7):3961-3965.
7. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. CA Cancer J Clin. Mar 2018;68(2):153-165.
8. Lentz R, Benson AB, 3rd, Kircher S. Financial toxicity in cancer care: Prevalence, causes, consequences, and reduction strategies. J Surg Oncol. Jul 2019;120(1):85-92.
9. de la Cruz M, Delgado-Guay MO. Financial Toxicity in People Living with Advanced Cancer: A New, Deadly, and Poorly Addressed Effect of Cancer and Necessary Treatment. Semin Oncol Nurs. Aug 2021;37(4):151171.
10. Urek D, Ugurluoglu O. Predictors of financial toxicity and its associations with health-related quality of life and treatment non-adherence in Turkish cancer patients. Support Care Cancer. Aug 15 2021.
11. Giuliani J, Fiorica F, Albanese V, Bonetti A. Financial toxicity and cancer treatments: Help from biosimilars - The explanatory case of bevacizumab. Eur J Cancer. 2021; 143(2021):40-42.
12. Hazell SZ, Fu W, Hu C, et al. Financial toxicity in lung cancer: an assessment of magnitude, perception, and impact on quality of life. Ann Oncol. Jan 2020;31(1):96-102.
13. Chen JE, Lou VW, Jian H, et al. Objective and subjective financial burden and its associations with health-related quality of life among lung cancer patients. Support Care Cancer. Apr 2018;26(4):1265-1272.
14. Aromataris E, Munn Z. JBI Manual for Evidence Synthesis. Adelaide: Joanna Briggs Institute; 2020.
15. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology. 2005;8(1):19-32.
16. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci. Sep 20 2010;5:69.
17. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc. Sep 2015;13(3):141-146.
18. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. Oct 2 2018;169(7):467-473.
19. Carrera PM. The financial hazard of personalized medicine and supportive care. Multinational

Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) 2017 Annual Meeting. Washington, DC; 2017.

20. Olver I. The MASCC Textbook of Cancer Supportive Care and Survivorship. 2nd ed. New York: Springer; 2018.
21. Landwehr MS, Watson SE, Macpherson CF, Novak KA, Johnson RH. The cost of cancer: a retrospective analysis of the financial impact of cancer on young adults. Cancer Med. May 2016;5(5):863-870.
22. Barbaret C, Brosse C, Rhondali W, et al. Financial distress in patients with advanced cancer. PLoS One. 2017;12(5):e0176470.
23. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. Dec 5 2016;5(1):210.

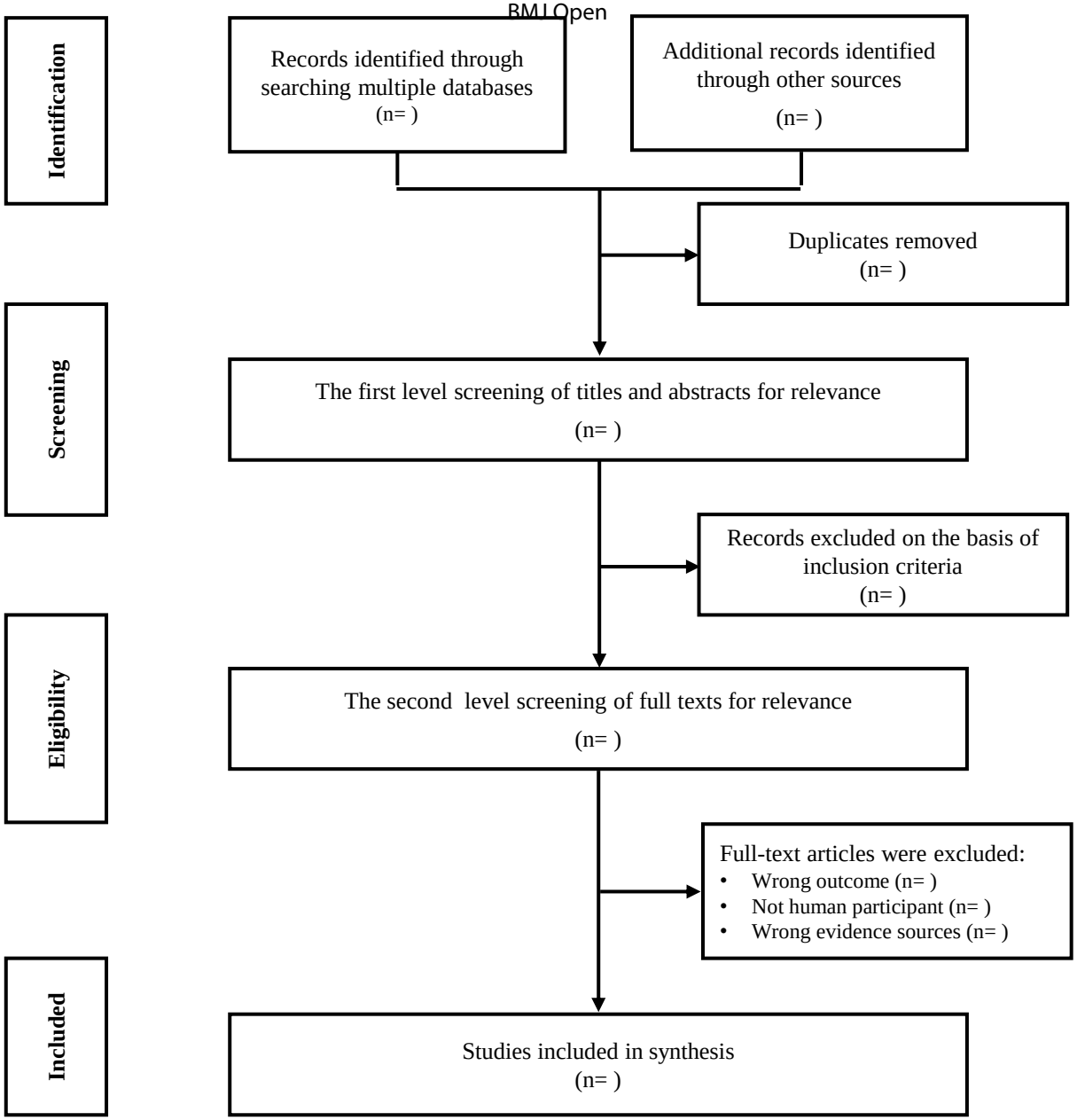

Figure 1 Flow diagram of study selection process

Table S1 Search strategy of MEDLINE

#	Search strings
1	(lung* OR bronch* OR pulmonary*).ab.
2	(cancer* OR tumor* OR tumour* OR neoplas* OR malignan* OR carcinoma*).ab.
3	(financial stress* OR financial toxicit* OR financial distress* OR financial burden* OR financial hardship* OR financial pressure* OR financial challenge* OR economic stress* OR economic toxicit* OR economic distress* OR economic burden* OR economic hardship* OR economic pressure* OR economic challenge*).ab.
4	#1 and #2 and #3

Table S2 The general information of included studies

No.	Author	Year of publication	Country	Study design	Setting	Population and sample size	Measure of financial toxicity	Financial toxicity	Financial burden	Financial distress	Affecting factor	Outcome	Intervention strategy	Reference
1														
2														
3														

Table S3 The degree of financial toxicity in lung cancer patients according to different measures

No.	Measure	Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

Table S4 The contributing factors of financial toxicity in lung cancer patients after classification

No.	Category	Contributing factor			
		Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

Table S5 The outcomes of financial toxicity in lung cancer patients after classification

No.	Category	Outcome			
		Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					

Table S6 The intervention strategies of financial toxicity in lung cancer patients after classification

No.	Category	Intervention strategy			
		Financial toxicity	Financial burden	Financial distress	Reference
1					
2					
3					