Statistical methods used to analyse quality of life scores derived from EORTC QLQ-C30 and QLQ-LC13 questionnaires measured over time: a scoping review protocol

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Background and review question

Studies evaluating interventions for the treatment of lung cancer often assess quality of life (QoL) using the patient reported European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaires Core 30 (QLQ-C30), and Lung Cancer 13 (QLQ-LC13). These questionnaires produce multiple scores and are often completed by participants multiple times throughout a study to assess the change in QoL over time.

A range of statistical methods can be used to analyse QoL over time, all providing varying levels of precision and bias, resulting in varying effect sizes, p values, and potentially different conclusions being drawn. In addition, due to the patient population, missing questionnaires due to sickness/death are often an issue. Methods to account for missing data due to death are available but it is unknown how often these are implemented in practice.

This scoping review aims to identify the different statistical methods used to analyse changes in QoL over time assessed using the QLQ-C30 and/or QLQ-LC13 questionnaires.

Prior to developing this scoping review protocol, a preliminary search for existing scoping and systematic reviews on the topic was conducted. MEDLINE, Embase, Cochrane Database of Systematic Reviews, and JBI Evidence Synthesis were searched. No relevant reviews considering statistical methods for analysing these QoL scores were identified. The scoping review methodology was chosen due to the broad nature of the proposed topic, with an aim to comprehensively describe the types of statistical methods used to analyse QoL scores derived from these questionnaires in randomised controlled trials (RCTs) and prospective observational studies published in the literature. A secondary aim if possible, based on the resources available, is to produce a set of recommendations for the statistical analyses of these data in future studies.

Eligibility criteria

Participants

No restriction will be imposed on the type of participants of interest for this review, however the QoL questionnaires to be included in the review will mean participants included are current or previous individuals with cancer of any type. The review will not be restricted to patients with lung cancer as the focus is on statistical methods applied and these are not cancer-type dependent.

Concept

Methods of analysing scores derived from the QLQ-C30 and QLQ-LC13 questionnaires will be identified and reviewed. QoL must be assessed using the QLQ-C30 or QLQ-LC13 questionnaires. QoL must be collected longitudinally at more than one post-baseline/randomisation time point. Studies collecting QoL at multiple post-baseline/randomisation time points but not at baseline/randomisation will be included. Studies only collecting QoL 1x pre- and 1x post-baseline/randomisation/intervention will be excluded. The QoL score must be the outcome measure; studies where the QoL score is not treated as the outcome measure (e.g., used as a covariate or to calculate a propensity score) will be excluded. The scores derived from the QoL questionnaires of interest must be formally compared (i.e., analysed using a statistical model). No restriction is placed on the type of analyses used in the study. Any studies that do not report the

statistical methods used for QoL analyses will also be excluded, as the aim of the review is to identify the types of statistical methods used to analyse these data.

Context

The context of this review will be any setting where the QLQ-C30 and/or QLQ-LC13 questionnaires have been used to assess QoL at multiple post-baseline time points throughout a study. No restriction is placed on the number of participants included in each study (i.e., studies of any sample size will be included).

Types of sources

This scoping review will consider both experimental and quasi-experimental study designs including randomised controlled trials and observational studies that collect QoL data prospectively. Cross-sectional and descriptive study designs such as case series will not be included. Meta-analyses (unless using individual patient data) will be excluded. Text and opinion papers, conference abstracts, and clinical trial protocols will also be excluded.

Methods

The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews. (1)

Search strategy

The search strategy will aim to locate published studies. Prior to the full search, an initial limited search of MEDLINE and Embase was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles were used to develop a full search strategy. The search strategy, including all identified keywords and index terms, will be adapted for each included database.

Studies not published in English will be excluded. Studies published between 01 January 2021 and 31 December 2022 will be included to capture recent statistical methods used.

The databases to be searched include MEDLINE and Embase via OvidSP. The search strategy that will be used when searching Embase is presented in Appendix I. Sources of unpublished studies/grey literature will not be searched as the review is focused on statistical methods used in published studies.

Study/Source of evidence selection

Following the search, all identified citations will be collated and uploaded into EndNote X9.3.3 and duplicates removed. Titles and abstracts will be screened by the primary researcher for assessment against the inclusion criteria for the review. Potentially relevant sources will be retrieved in full. The full text of a subset of randomly selected citations will be assessed in detail against the inclusion criteria by two or more independent reviewers. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any

disagreements that arise between the reviewers will be resolved through discussion. The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRIMSA-ScR) flow diagram. (2)

Data extraction

Data will be extracted from papers included in the scoping review by the primary researcher using a data extraction tool developed by the primary researcher. Data will be extracted for a subset of papers included in the review by one or more independent reviewers. The level of agreement will be reported, and the data extraction form modified if required. The data extracted will include specific details about the study design, QoL scores analysed, statistical methods used, and results reported.

A REDCap database will be developed to collect the extracted information of interest. The data items to be extracted will be modified and revised as necessary during the process of extracting data from each included evidence source. Modifications will be detailed in the scoping review. Any disagreements that arise between the reviewers will be resolved through discussion.

Data analysis and presentation

Summaries of data extracted from the articles included in this review will be presented in tabular and/or graphical form. A narrative summary will accompany the results. This review will provide a detailed overview of the type of studies included in the review and the various statistical methods used to analyse the QoL scores. The number of different statistical methods applied in each study will be summarised and any patterns related to the type of study and methods used will be explored descriptively.

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Conflicts of interest

The authors confirm there are no conflicts of interest to declare.

References

1. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis, JBI, 2020. Available from https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-20-12
2. Tricco, AC, Lillie, E, Zarin, W, O'Brien, KK, Colquhoun, H, Levac, D, Moher, D, Peters, MD, Horsley, T, Weeks, L, Hempel, S et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 2018,169(7):467-473. doi:10.7326/M18-0850.

Appendices

Appendix I: Search strategy

Search strategy for Embase:

1. Randomized Controlled Trials as Topic/
2. random allocation/
3. double-blind method/
4. single-blind method/
5. random*.tw.
6. ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).tw.
7. (crossover* or cross-over).tw.
8. ((random* or control*) adj5 trial*).tw.
9. cohort studies/
10. cohort.tw.
11. or/1-10
12. cross-sectional study.tw. or cross-sectional study/ or (cross-sectional adj2 study).tw.
13. clinical protocol/ or protocol.ti.
14. statistical analysis plan.ti. or statistical analysis plan/ or economic evaluation/ or economic evaluation.kw. or systematic review/ or corrigendum.ti.
15. 12 or 13 or 14
16. 11 not 15
17. (EORTC Core-30 or EORTC Lung cancer-13 or Questionnaire-Core 30 or Questionnaire-Lung cancer 13 or QLQ-C30 or QLQ-LC13 or QLQ C30 or QLQ LC13 or QLQC30 or QLQLC13 or EORTC-QLQ-C30 or EORTC-QLQ-LC13 or EORTC-C30 or EORTC-LC13).af.
18. 16 and 17
19. (editorial or review or letter or conference abstract or note).pt.
20. 18 not 19
21. limit 20 to english language
22. limit 23 to yr=”2021 -2022”

Removed from search as deemed not necessary:

(neoplasm* or mesothelioma).sh. or (cancer or neoplastic or mesothelioma or neoplasm* or tumo?r* or carcinoma*).tw,kw.

Added to search after the terms were indexed in several records:

(or EORTC-C30 or EORTC-LC13).af