BMJ Open

Approaches for thoracoabdominal oesophagectomy for oesophageal cancer: a network meta-analysis – study protocol

Artur Rebelo ,[1] Juliane Friedrichs ,[1] Maurizio Grilli,[2] Johannes Vey,[3] Johannes Klose,[1] Marie Merling,[3] Joerg Kleeff,[1] Ulrich Ronellenfitsch [1]

To cite: Rebelo A, Friedrichs J, Grilli M, *et al*. Approaches for thoracoabdominal oesophagectomy for oesophageal cancer: a network meta-analysis – study protocol. *BMJ Open* 2025;**15**:e093561. doi:10.1136/bmjopen-2024-093561

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-093561).

Received 10 September 2024
Accepted 27 February 2025

[1]Department of Visceral, Vascular and Endocrine Surgery, Martin Luther University of Halle Wittenberg Faculty of Medicine, Halle (Saale), Germany
[2]Library of the Medical Faculty, Mannheim, Heidelberg University, Mannheim, Germany, UK
[3]University Hospital Heidelberg, Germany, Institute of Medical Biometry, Heidelberg, Germany, Heidelgerg, Germany

Correspondence to
Dr Artur Rebelo;
artur.rebelo@uk-halle.de

ABSTRACT

Introduction Oesophageal cancer is the seventh most frequently diagnosed cancer and the sixth leading cause of cancer-related deaths worldwide. Oesophagectomy remains the main curative treatment option. The effect of different surgical approaches (completely open, hybrid, completely minimally invasive and robot-assisted) on patients undergoing thoracoabdominal oesophagectomy (Ivor-Lewis's procedure) for oesophageal cancer is evaluated, focusing on overall survival, postoperative mortality and morbidity.

Methods and analysis A systematic literature search will be conducted in PubMed/Medline, Cochrane Library, Embase, Cumulated Index in Nursing and Allied Health Literature, ClinicalTrials.gov and International Clinical Trials Registry Platform using predefined search terms. A random-effects (network) meta-analysis using the frequentist framework will be performed.

Ethics and dissemination As this study is based on previously published data, no ethical approval is required. Findings will be disseminated through peer-reviewed publications and conference presentations to inform clinical decision-makers (eg, surgeons, gastroenterologists).

Trail registration number CRD42024564915.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This network meta-analysis will integrate all available evidence on oesophagectomy approaches for oesophageal cancer.
⇒ A systematic comparison of different surgical strategies will be conducted using a robust analytical framework.
⇒ Expected heterogeneity across studies may affect the consistency of results.
⇒ The absence of individual patient data may limit subgroup analyses.
⇒ Transhiatal surgical access and McKeown oesophagectomy are excluded due to their distinct indications compared with thoracoabdominal access.

INTRODUCTION

With an estimated 604 000 new cases and more than 544 000 deaths in 2020, oesophageal cancer is the seventh most frequently diagnosed cancer and the sixth leading cause of cancer-related deaths in the world.[1] 5-year survival ranges from 36.9% for locally confined tumours without nodal spread to 9.6% for node-positive disease and 2.6% for metastatic disease.[2] Oesophageal cancer involves two epidemiologically and pathologically distinct diseases with different aetiology, pathology, tumour location, medical therapies, prognosis, risk factors and incidence trends: squamous cell carcinoma and adenocarcinoma.[3 4] Squamous cell carcinoma has become less common in Western countries because of the reduced tobacco and alcohol use, representing less than 30% of all oesophageal cancers in these countries. On the other hand, oesophageal adenocarcinoma is more common in Western countries nowadays, as participants are more likely to be obese and to have chronic gastro-oesophageal reflux disease.[3 5]

In the treatment of oesophageal cancer, oesophagectomy is the main available treatment with curative intent, with abdominothoracic oesophagectomy being favoured from an oncological point of view. Oesophagectomy should be considered for all patients with oesophageal cancer who are physically fit.[6] For squamous cell carcinoma and Siewert type I and II adenocarcinoma (Esophagastric Junction Cancers), a thoracoabdominal approach is generally recommended over a transhiatal approach.[6] There are several possible surgical access techniques for this. Both the abdominal access and the thoracic access can be open or minimally invasive.[6] In addition, robotic techniques have found their way into everyday clinical practice in recent years.[7]

As mentioned above, several thoracoabdominal approaches for oesophagectomy

are available. These access routes can be used in various combinations (completely open, hybrid procedure: abdominally minimally invasive and thoracically open, thoracically minimally invasive and abdominally open or completely minimally invasive; the minimally invasive access can also be carried out robotically), and no clear advantage for one of these techniques has been shown, despite several randomised controlled trials (RCTs) comparing two of the referred techniques having been conducted on this topic.

From the currently available evidence, it remains unclear which surgical approach is the most effective and safest in thoracoabdominal oesophagectomy. The available meta-analyses only compared two of the access routes[8–15] or performed a network meta-analysis (NMA) that included transhiatal resections and non-randomised studies.[7]

In our meta-analysis, we will include only thoracoabdominal resections and differentiate them based on the type of surgical approach. Although not all combinations may be present, each surgical access method will be treated as an individual node in the network. This approach ensures that every combination is considered while maintaining methodological rigour. We specifically focus on the Ivor-Lewis oesophagectomy, as it is a widely performed thoracoabdominal approach for oesophageal cancer, while the McKeown oesophagectomy is excluded due to its distinct three-stage technique, including cervical anastomosis. We will also exclude transhiatal surgical access from our analysis due to its distinct indications compared with thoracoabdominal access and the resulting lack of transitivity in the NMA.

OBJECTIVES

Main objective

To assess the effects of different surgical approaches (completely open, hybrid procedure: abdominally minimally invasive and thoracically open, thoracically minimally invasive and abdominally open or completely minimally invasive; the minimally invasive access can also be carried out robotically) on participants undergoing abdominothoracic oesophagectomy for oesophageal cancer, in terms of overall survival and postoperative mortality and morbidity, by conducting a NMA.

Additional objectives

To assess the effects of different surgical approaches (completely open, hybrid procedure: abdominally minimally invasive and thoracically open, thoracically minimally invasive and abdominally open or completely minimally invasive; the minimally invasive access can also be carried out robotically) on participants undergoing abdominothoracic oesophagectomy for oesophageal cancer, in terms of disease-free survival, local-recurrence-free survival, distant-recurrence-free survival, serious adverse events, achievement of tumour-free resection margins, number of lymph nodes resected, length of hospital stay, pathological tumour stage and quality of life, by conducting an NMA. Reconstruction methods (eg, gastric pull-up, colonic interposition and jejunal interposition) will not be included in the sensitivity analysis, as the focus of this study is on comparing surgical approaches for thoracoabdominal oesophagectomy rather than variations in reconstruction techniques, which are primarily dictated by patient-specific factors.

METHODS

Types of studies

In this systematic review with NMA, we will only include RCTs. There will be no restrictions regarding minimal time of follow-up or number of included participants. There will be no restrictions regarding language.

Crossover trials and cluster RCTs are not suitable to answer our research question and therefore will not be included. Both published and unpublished studies, full articles and abstracts, satisfying the criteria listed below, will be included.

Types of participants

Previously untreated participants with resectable non-metastatic oesophageal cancer, both adenocarcinoma and squamous cell carcinoma, who underwent abdominothoracic oesophagectomy with curative intent will be included in this NMA. No restrictions regarding multimodal treatments will be applied.

The transitivity assumption is a fundamental concept in NMA and is mandatory for a valid estimation.[16 17] In this review, all the included treatments are legitimate alternatives that are not systematically applied or not applied to participants of different demographics or morbidities. In specific cases, it can be assumed that all the treatment options are commonly used in participants with resectable tumours requiring a thoracoabdominal resection. Thus, we assume that the transitivity assumption will be given.

Types of interventions

To be included in this NMA, trials have to compare at least two of the following interventions

- Intervention 1: completely open abdominothoracic oesophagectomy.
- Intervention 2: hybrid abdominothoracic oesophagectomy (laparoscopy and thoracotomy).
- Intervention 3: hybrid abdominothoracic oesophagectomy (laparotomy and thoracoscopy).
- Intervention 4: completely minimally invasive abdominothoracic oesophagectomy (laparoscopy and thoracoscopy).
- Intervention 5: hybrid abdominothoracic oesophagectomy (robotic laparoscopy and thoracotomy).
- Intervention 6: hybrid abdominothoracic oesophagectomy (laparotomy and robotic thoracoscopy).
- Intervention 7: completely robot-assisted abdominothoracic oesophagectomy (robotic laparoscopy and robotic thoracoscopy).

Since a combination of minimally invasive and robot-assisted techniques is not practised, seven nodes, one for each intervention, can be defined.

Types of outcome measures

We will define both main and additional outcomes in our analysis

Main outcomes

- Overall survival, defined as the time to death of any cause, measured from the date of randomisation until death from any cause. If the time after randomisation is not reported, the time after surgery will be analysed instead.
- Postoperative mortality (defined as death of any cause until 90 days after surgery). If 90-day mortality is not defined, 30-day mortality will be analysed. If 30-day mortality is not defined, in-hospital mortality will be analysed instead.
- Postoperative morbidity (any complication that would be classified as Clavien-Dindo grade I to IV). Postoperative complications will be categorised according to the Esophagectomy Complications Consensus Group definitions.[18]

Additional outcomes

- Disease-free survival, defined as the time from randomisation until recurrence or death from any cause. If the time after randomisation is not reported, the time after surgery will be analysed instead.
- Local-recurrence-free survival, defined as the time from randomisation until local recurrence. If the time after randomisation is not reported, the time after surgery will be analysed instead.
- Distant-recurrence-free survival, defined as the time from randomisation until distant recurrence. If the time after randomisation is not reported, the time after surgery will be analysed instead.
- Achievement of tumour-free resection margins (R0 resectability).
- Number of lymph nodes resected.
- Length of hospital stay.
- Pathological tumour stage at resection, according to the International Union against Cancer Tumour Node Metastasis (UICC TNM) classification.
- Quality of life, as measured in the single trials. Quality-of-life outcomes will be assessed using both generic and disease-specific instruments. Generic measures will include the 36-Item Short Form Health Survey (SF-36) and EuroQol-5 Dimensionen (EQ-5D), while disease-specific assessments will incorporate the European Organisation for Research and Treatment of Cancer Oesophageal Cancer Module (EORTC QLQ-OES18) and European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) to evaluate the impact of oesophagectomy on patient-reported outcomes.

Search methods for identification of studies

We will conduct a literature search to identify all published and unpublished RCTs in all languages (online supplemental material 1).

Electronic searches

We will search the following electronic databases (online supplemental material 1)

- PubMed/Medline (1966–present)
- Cochrane Library (inception–present)
- Embase (inception–present)
- Cumulative Index to Nursing and Allied Health Literature (1982–present)
- ClinicalTrials.gov (inception–present)
- International Clinical Trials Registry Platform (inception–present)

Searching other resources

We will examine the reference lists of both primary studies and review articles to discover additional hits.

We will contact the authors of identified trials via their institutional email addresses and request their assistance in identifying other published and unpublished studies.

Additionally, we will contact medical device manufacturers and experts in the field. Experts will be identified from academic institutions, surgical societies and medical device manufacturers specialising in oesophageal surgery. Selection criteria will include publication records, clinical expertise and contributions to guideline development. In addition, medical device manufacturers focusing on minimally invasive and robotic-assisted surgical technologies will be contacted. To ensure a diverse perspective, experts from North America, Europe and Asia will be included. The primary points of contact within each industry will consist of representatives from clinical research departments, medical affairs divisions and product development teams.

Data collection and analysis

Selection of studies

Two review authors (AR and JF) will individually assess the titles and abstracts of the identified studies to determine their suitability for inclusion. Based on this assessment, each study will be categorised as either 'retrieve' (eligible, potentially eligible or unclear) or 'do not retrieve'. The full texts of potentially eligible studies will be obtained, and, again, both AR and JF will independently review the full texts to determine their inclusion in the review. Reasons for excluding ineligible studies will be identified and documented. In case of any disagreements, a discussion will be held to reach a consensus, and, if necessary, a third author (UR) will be consulted. Duplicate studies will be identified and removed, and multiple reports of the same study will be consolidated, ensuring that each study is considered as the primary unit of interest in the review. A detailed account of the selection

process will be recorded to facilitate the creation of a Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram and a 'Characteristics of excluded studies' table.

Data extraction and management

Published aggregate data

To collect study characteristics and outcome data, we will use a standardised data collection form. The extraction of study characteristics from the included studies will be performed independently by two of the review authors, AR and JF. The following study characteristics and results will be extracted:

- General study information: title, authors, contact address, funding source, language, publication status, year of publication and place(s) and year(s) of study conduction.
- Study design issues: inclusion/exclusion criteria, randomisation, risk of bias and length of study/follow-up period.
- Baseline characteristics of participants: size of intervention and comparison groups and, for each group, the distribution of age, sex, co-morbidity (measured, if given as WHO performance status or American Society of Anesthesiologists classification), histology (adenocarcinoma/squamous cell carcinoma), tumour location (oesophagus or gastro-oesophageal junction, using the Siewert classification), tumour stage (TNM stage and UICC stage) and administration of preoperative and adjuvant therapies.
- Characteristics of the intervention: Intervention 1: completely open abdominothoracic oesophagectomy, intervention 2: hybrid abdominothoracic oesophagectomy (laparoscopy and thoracotomy), intervention 3: hybrid abdominothoracic oesophagectomy (laparotomy and thoracoscopy), intervention 4: completely minimally invasive abdominothoracic oesophagectomy (laparoscopy and thoracoscopy), intervention 5: hybrid abdominothoracic oesophagectomy (robotic laparoscopy and thoracotomy), intervention 6: hybrid abdominothoracic oesophagectomy (laparotomy and robotic thoracoscopy) and intervention 7: completely robot-assisted abdominothoracic oesophagectomy (robotic laparoscopy and robotic thoracoscopy).
- Loss to follow-up.
- HR and its 95% CI both for overall survival and, if available, disease-free survival, local-recurrence-free survival and distant-recurrence-free survival.
- Postoperative mortality (in-hospital mortality, 30-day mortality or 90-day mortality).
- Postoperative morbidity (any complication that would be classified as Clavien-Dindo grade I–IV).
- Completeness of resection margins (R0/R1/R2).
- Pathological tumour stage at resection, as assessed from the surgical specimen according to the UICC TNM classification.
- Quality of life, as measured within the single trial.
- Notes: funding for the trial and notable conflicts of interest of trial authors.

To ensure accuracy and completeness, we will reach out to investigators or study sponsors to verify important study characteristics and gather any missing data.

Assessment of risk of bias in included studies

The risk of bias for each included study will be evaluated independently by two review authors, AR and JF. We will follow the criteria provided in the Cochrane Handbook for Systematic Reviews of Interventions to conduct this assessment from Higgins *et al*[19] and the Cochrane 'Risk of bias' (RoB 2) tool V.2.[20] Disagreements, if any, will be resolved through discussions or by seeking input from a third review author (UR).

The effect of interest will be the effect of the assignment on the interventions at baseline, regardless of whether the interventions were actually received and adhered to as intended. The following results for all outcomes will be assessed using RoB 2.

Each potential source of bias will be evaluated and assigned a grading of 'high,' 'some concerns' or 'low.' The 'Risk of bias' table will include a quotation from the study report along with a justification for our assessment. The judgements on 'Risk of bias' for each domain across studies will be summarised.

To determine the overall risk of bias, we will use the signalling questions and algorithm provided by the RoB 2 tool. The RoB 2 Excel tool will be employed to manage the bias assessment process. In the evaluation of treatment effects, the overall RoB 2 judgement will guide the Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment. Given the anticipated large volume of data, the consensus decisions for the signalling questions will be presented in the full review, while the complete dataset will be provided in a supplementary section.

Data synthesis

To address the question of the most effective surgical approach, an NMA will be performed for each of the outcomes mentioned above. A closed network of interventions, as shown in figure 1, is expected at least for the main outcomes. If it is not feasible to perform a NMA, a pairwise meta-analysis will be conducted. We will only perform meta-analysis if the studies are sufficiently similar in terms of the definition of the outcomes, conducted treatments, characteristics of the participants and effect modifiers.

The standardised mean difference with its 95% CI will be used as the effect measure for the continuous outcomes. If the mean is not available, it will be estimated out of other measures as proposed by Wan *et al*.[21]

The OR with 95% CI will be calculated for the binary outcomes.

The HR with 95% CI will be calculated for time-to-event (TTE) outcomes. If the HR is not available, it will be derived from other summary data or Kaplan-Meier plots

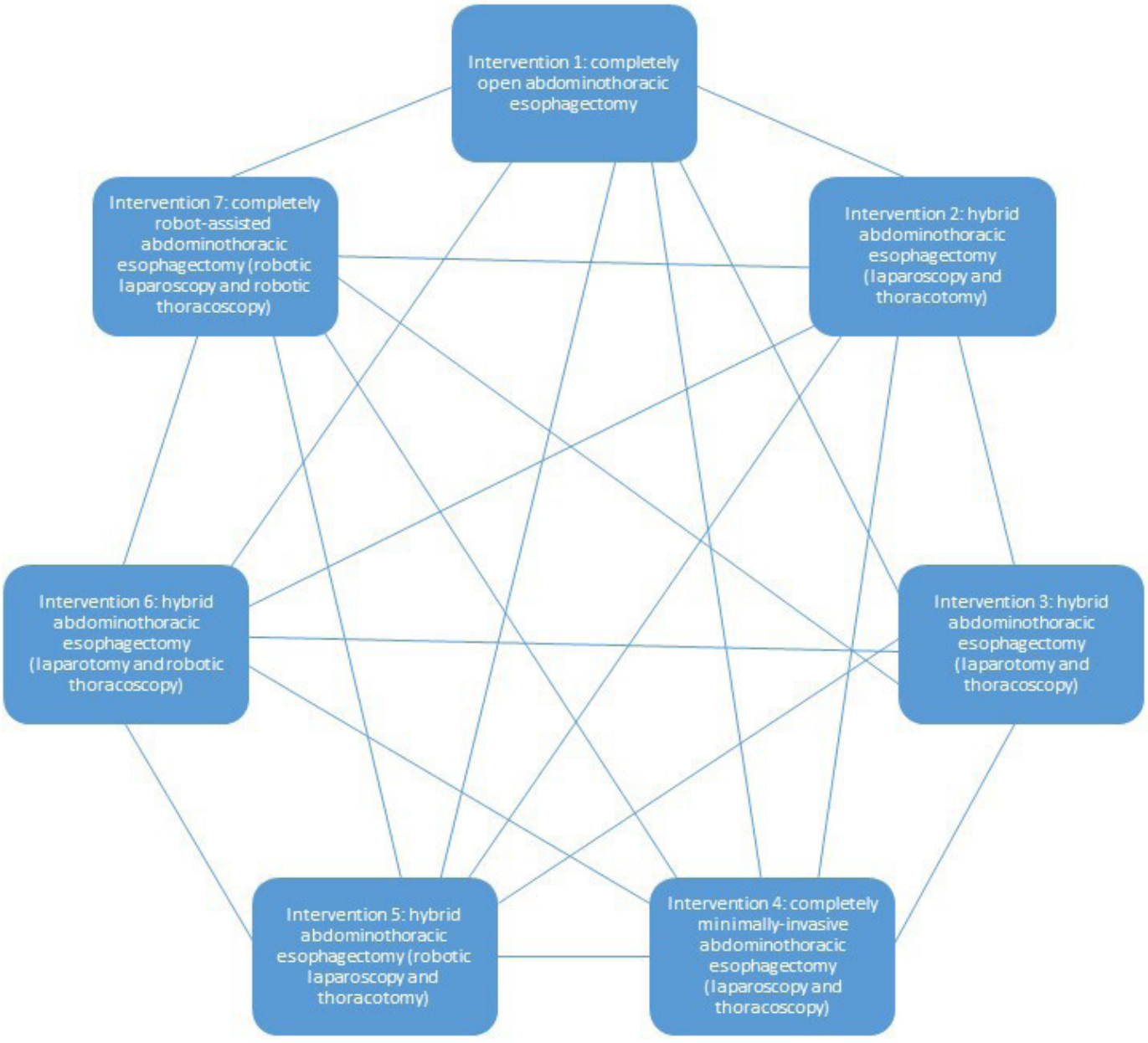

Figure 1 Network graph.

according to the methods described by Parmar *et al*[22] and Tierney *et al*.[23] If TTE results are only reported graphically, then we will estimate the values from these figures with reliable software.

If there is more than one publication of the same study at different points in time, the publication with the longest observation period for Overall survival (OS) will be selected for inclusion in the NMA. The other publications of the same study will be excluded from the analysis. If a trial includes further treatment arms, we will include only the relevant arms in our analysis, while indicating the availability of additional arms in the 'Characteristics of included studies' table.

Frequentist NMA using random effects models as proposed by Rücker[24] or generalised linear mixed models (in case of binary outcomes) will be calculated to synthesise the available evidence. Studies with more than two arms will be included in the NMA considering the within-study correlation.[25]

To assess heterogeneity between studies, the prediction interval, the p value of the Q-test, the between-study variance τ^2 and the I^2 statistics will be estimated and considered. By performing subgroup analyses for the subgroups mentioned below, we will investigate reasons for the heterogeneity that may be present.[19] We will use the formal Q-test to investigate differences between the subgroups. Additionally, we will consider any statistical heterogeneity that may be present when interpreting the results.

The consistency, that is the statistical magnification of the assumption of transitivity, will be statistically assessed by comparing the direct and indirect evidence.[17 26]

Treatment approaches will be ranked in terms of efficacy using the p value, allowing an indication of the most effective treatment.[27]

Results will be presented using forest plots

If more than 10 trials can be pooled, possible publication bias will be investigated using a funnel plot for pairwise meta-analyses and comparison-adjusted funnel plots for NMA.[25]

If sufficient data are available, we plan to perform the following subgroup analyses:

- Tumour location (upper third, middle third, lower third and gastro-oesophageal junction)
- Histology (adenocarcinoma vs squamous cell carcinoma)
- Neoadjuvant therapy versus direct surgery

When possible, all outcomes will be used in subgroup analyses.

We will include all eligible studies in our analysis, and sensitivity analyses will be carried out based on the assigned risk of bias for each study, as previously described (low, some concerns or high). Sensitivity analyses based on the risk of bias will be performed for all outcomes, following the same categorisation (low, some concerns and high).

All statistical analyses will be performed using the latest version of the software R and the extensions meta, netmeta and metafor.

The literature search on the databases will start in September 2024. The NMA will be completed in September 2025.

A 'summary of findings' table will be prepared for the NMA, which will include both relative and absolute effect measures. Here, the GRADE criteria (study limitations, consistency of effect, imprecision, indirectness and publication bias) will be used to determine the quality of the evidence. In regard to this, a classification will distinguish between high, moderate, low and very low. The methods and recommendations described in the Cochrane handbook will be applied.

By performing this analysis, we can obtain a comprehensive assessment of the different surgical approaches for oesophagectomy and better understand their effectiveness in comparison to each other. This approach will allow us to integrate data from different studies and make direct as well as indirect comparisons between the different treatment modalities to draw informed conclusions. The results of this study could help to inform clinical practice and improve the treatment of patients with oesophageal cancer.

Contributors Guarantor: AR. Conceiving the protocol: AR. Designing the protocol: AR and UR. Coordinating the protocol: AR. Designing search strategies: MG. Writing the protocol: AR, UR, JF, JV and MM. Providing general advice on the protocol: JKlo and JKle. Securing funding for the protocol: AR. Data analysis: JV and MM.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Artur Rebelo http://orcid.org/0000-0002-5267-079X
Juliane Friedrichs http://orcid.org/0000-0001-8653-3948
Ulrich Ronellenfitsch http://orcid.org/0000-0003-1107-813X

REFERENCES

1 Bray F, Ferlay J, Soerjomataram I, *et al*. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394–424.
2 Gavin AT, Francisci S, Foschi R, *et al*. Oesophageal cancer survival in Europe: a EUROCARE-4 study. *Cancer Epidemiol* 2012;36:505–12.
3 Lagergren J, Smyth E, Cunningham D, *et al*. Oesophageal cancer. *The Lancet* 2017;390:2383–96.
4 Smyth EC, Lagergren J, Fitzgerald RC, *et al*. Oesophageal cancer. *Nat Rev Dis Primers* 2017;3:17048.
5 Torre LA, Siegel RL, Ward EM, *et al*. Global Cancer Incidence and Mortality Rates and Trends—An Update. *Cancer Epidemiol Biomarkers Prev* 2016;25:16–27.
6 NCCN. NCCN guidelines: esophageal and esophagogastric junction cancers. 2023. Available: www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf
7 Szakó L, Németh D, Farkas N, *et al*. Network meta-analysis of randomized controlled trials on esophagectomies in esophageal cancer: The superiority of minimally invasive surgery. *World J Gastroenterol* 2022;28:4201–10.
8 Bras Harriott C, Angeramo CA, Casas MA, *et al*. Open versus hybrid versus totally minimally invasive Ivor Lewis esophagectomy: Systematic review and meta-analysis. *J Thorac Cardiovasc Surg* 2022;164:e233–54.
9 Casas MA, Angeramo CA, Bras Harriott C, *et al*. Surgical outcomes after totally minimally invasive Ivor Lewis esophagectomy. A systematic review and meta-analysis. *Eur J Surg Oncol* 2022;48:473–81.
10 Wang B, Zuo Z, Chen H, *et al*. The comparison of thoracoscopic-laparoscopic esophagectomy and open esophagectomy: A meta-analysis. *Indian J Cancer* 2017;54:115–9.
11 Guo W, Ma X, Yang S, *et al*. Combined thoracoscopic-laparoscopic esophagectomy versus open esophagectomy: a meta-analysis of outcomes. *Surg Endosc* 2016;30:3873–81.
12 Magouliotis DE, Zotos P-A, Fergadi MP, *et al*. Meta-analysis of robot-assisted versus video-assisted McKeown esophagectomy for esophageal cancer. *Updates Surg* 2022;74:1501–10.
13 Mederos MA, de Virgilio MJ, Shenoy R, *et al*. Comparison of Clinical Outcomes of Robot-Assisted, Video-Assisted, and Open Esophagectomy for Esophageal Cancer: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2021;4:e2129228.
14 Wei Z-D, Zhang H-L, Yang Y-S, *et al*. Effectiveness of Transthoracic Hybrid Minimally Invasive Esophagectomy: A Meta-Analysis. *J Invest Surg* 2021;34:963–73.
15 Yibulayin W, Abulizi S, Lv H, *et al*. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. *World J Surg Oncol* 2016;14:304.

16 Salanti G, Marinho V, Higgins JPT. A case study of multiple-treatments meta-analysis demonstrates that covariates should be considered. *J Clin Epidemiol* 2009;62:857–64.
17 Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Res Synth Methods* 2012;3:80–97.
18 Low DE, Alderson D, Cecconello I, *et al*. International Consensus on Standardization of Data Collection for Complications Associated With Esophagectomy: Esophagectomy Complications Consensus Group (ECCG). *Ann Surg* 2015;262:286–94.
19 Higgins JPT, Thomas J, Chandler J, *et al*. *Cochrane Handbook for Systematic Reviews of Interventions*. 6th edn. 2021.
20 Sterne JAC, Savović J, Page MJ, *et al*. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898.
21 Wan X, Wang W, Liu J, *et al*. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;14:135.
22 Parmar MKB, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. *Statist Med* 1998;17:2815–34.
23 Tierney JF, Stewart LA, Ghersi D, *et al*. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials* 2007;8:16.
24 Rücker G. Network meta-analysis, electrical networks and graph theory. *Res Synth Methods* 2012;3:312–24.
25 Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. *BMC Med Res Methodol* 2015;15:58.
26 Rücker G, Schwarzer G. Reduce dimension or reduce weights? Comparing two approaches to multi-arm studies in network meta-analysis. *Stat Med* 2014;33:25:4353–69:.
27 Dias S, Welton NJ, Caldwell DM, *et al*. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med* 2010;29:932–44.