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Abstract: Background

With rapid advancement in the genomics of oesophagogastric (OG) cancer and raised expectations in clinical outcomes from patients and clinicians alike there is a clear need to determine the current research priorities in OG cancer surgery. The aim of our study was to use a modified Delphi process to determine the research priorities among OG cancer surgeons in the United Kingdom.

Methods

Delphi methodology may be utilised to develop consensus opinion amongst a group of experts. Members of the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland were invited to submit individual research questions via an online survey (phase I). Two rounds of prioritisation by multidisciplinary expert healthcare professionals (phase II and III) were completed to determine a final list of high priority research questions. All questions submitted and subsequently ranked were analysed on an anonymised basis.

Results

In total, 427 questions were submitted in phase I and 75 with an OG cancer focus were taken forward for prioritisation in phase II. Phase III produced a final list of 12 high priority questions with an emphasis on tailored or personalised treatment strategies in OG cancer surgery.

Conclusion

A modified Delphi process produced a list of 12 high priority research questions in OG cancer surgery. Future studies and awards from funding bodies should reflect this consensus list of prioritised questions in the

interest of improving patient care and encouraging collaborative research across multiple centres.

12 Nov 2019

Dear Editor of The Surgeon,

As the corresponding author for this manuscript we would be grateful if you would consider this revised manuscript for publication in your respected journal.

We believe that we have undertaken a valuable piece of work that has produced a validated list of future research priorities in the surgical subspecialty of oesophagogastric cancer. This has been achieved by utilising a modified Delphi process.

If ultimately successful we would also request a deviation from the standard authorship format. In addition to the authorship provided we would appreciate that the following is added: *on behalf of AUGIS*.

As requested, I can also confirm the following:

- * The manuscript is not under consideration elsewhere
- * The work is original
- * All authors have agreed to submission to The Surgeon

Yours sincerely,

Michael Wilson
Corresponding author

Reviewer 1:

This study addresses research priorities by a modified Delphi technique in oesophagogastric surgery. A total of 427 questions were submitted by 140 AUGIS members. This selection was prioritized firstly by 52 stakeholders then by an expert steering committee of 6 individuals. A final list of 12 questions was generated. A rationale has been provided for questions that were NOT prioritized. The participants were predominantly surgeons.

Main points:

1. A key feature of the Delphi process of forecasting by structured communication, is that all participants should remain anonymous. This step prevents a bandwagon or halo effect, whereby one or two influential members dominate the outcomes. It is not clear whether participants were in fact anonymous at all stages. The authors should clarify this step. If anonymization was not carried out, the authors should justify this and consider removal of the reference to the Delphi process from the title.

Response: Thank you. This is a valid point. We can confirm that responses were assessed on an anonymised basis at all stages of our modified Delphi process. Only one member of the steering committee (MW) had sight of the names who submitted/ranked questions. We have amended our manuscript (methods – abstract and main body) to emphasise this point.

2. The details of the participants in terms of Augis membership and steering committee have been provided. Details of the 52 stakeholders are sparse. Why were they selected from the Augis membership and what is their specialty/seniority/gender distribution.

Response: Thank you. To clarify this uncertainly, stakeholders were not chosen to take part in this Delphi process. Those who submitted or ranked questions did so on an entirely voluntary basis after email invitation using the AUGIS membership database. We have amended the methods and results section of our manuscript to further emphasise this point.

In terms of specialty/seniority/gender distribution we have amended our results to provide this data for phase II and phase III of the Delphi process.

A modified Delphi process to establish future research priorities in malignant oesophagogastric surgery

Authors

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Competing Interests: All authors declare no competing interests

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Highlights

- We have produced a list of future research priorities for malignant OG surgery by undertaking a Delphi process incorporating members of the OG MDT
- There is a particular emphasis on the future development of personalised therapies in OG cancer surgery
- Other research priorities identified include; prehabilitation, early detection, optimal palliation and identifying those who would receive no benefit from adjuvant therapies

A modified Delphi process to establish future research priorities in malignant oesophagogastric surgery

Abstract

Background

With rapid advancement in the genomics of oesophagogastric (OG) cancer and raised expectations in clinical outcomes from patients and clinicians alike there is a clear need to determine the current research priorities in OG cancer surgery. The aim of our study was to use a modified Delphi process to determine the research priorities among OG cancer surgeons in the United Kingdom.

Methods

Delphi methodology may be utilised to develop consensus opinion amongst a group of experts. Members of the Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland were invited to submit individual research questions *via* an online survey (phase I). Two rounds of prioritisation by multidisciplinary expert healthcare professionals (phase II and III) were completed to determine a final list of high priority research questions. [All questions submitted and subsequently ranked were analysed on an anonymised basis.](#)

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In total, 427 questions were submitted in phase I and 75 with an OG cancer focus were taken forward for prioritisation in phase II. Phase III produced a final list of 12 high priority questions with an emphasis on tailored or personalised treatment strategies in OG cancer surgery.

Conclusion

A modified Delphi process produced a list of 12 high priority research questions in OG cancer surgery. Future studies and awards from funding bodies should reflect this consensus list of prioritised questions in the interest of improving patient care and encouraging collaborative research across multiple centres.

Keywords

Delphi process, oesophagogastric cancer, surgery, research priorities

Introduction

Oesophagogastric (OG) cancer is a collective term used to describe cancers of the oesophagus and stomach. Worldwide, oesophageal cancer is the 8th most common cancer and was responsible for 5% of all cancer deaths in 2012. Gastric cancer was responsible for 9% of worldwide cancer deaths in 2012 (1). Overall 5-year survival for OG cancer is in the region of 15% and is dependent upon tumour stage, subtype, comorbidities and patient performance status (2, 3). In those who undergo either surgery or endoscopic treatment for early stage oesophageal adenocarcinoma the anticipated 5-year survival is 65% (4). The management of OG cancer patients encompasses a multidisciplinary approach to patient care. Treatment modalities may be curative or palliative, with chemotherapy, radiotherapy and surgery used in combination or independently in the majority of fit patients. However, the evidence base for treatment decisions is limited and often conflicting. For example, in the curative setting neoadjuvant treatment demonstrates a survival advantage (5-8), but the choice between chemotherapy and chemoradiotherapy is determined largely by local provision and clinician choice. Unfortunately, less than 20% of patients will derive benefit from any form of pre-operative treatment, possibly at the expense of harm to those whose surgery is delayed (9). Similar unanswered questions exist in the setting of advanced disease and cancer recurrence. Recent international efforts to determine the genomic and molecular landscape of OG cancer are leading to potential new patient stratification and treatment options that need to be applied and evaluated in a responsible and scientifically robust manner for patient benefit (10-14). In this context a clear consensus about the research priorities for OG cancer is required.

A modified Delphi process can be used to develop a list of priorities by consensus from a group of experts. This has been successfully used in colorectal surgery (15), orthopaedics (16) plastic surgery (17) ~~and~~ hepato-pancreato-biliary surgery (18) and bariatric surgery (19).

This approach in determining research priorities improves efficiency and adds greater value to those who fund OG cancer research (20). To our knowledge no attempt has previously been made to determine the future research priorities in OG cancer surgery. However, Delphi methods have been used to produce core information and outcome sets for patients undergoing oesophageal cancer surgery (21), the management of Barrett's dysplasia (22) and gastric cancer prevention (23). The aim of our study, was to undertake a modified Delphi process to determine the research priorities in OG cancer surgery.

Methods and Materials

A three-phased modified Delphi process was undertaken (Figure 1). This included two distinct phases of prioritisation by expert multidisciplinary stakeholders utilising established methodology previously described for a number of clinical projects (15, 24, 25).

Stakeholders were asked to submit questions and, thereafter, prioritise their responses based upon their own perceived clinical need. During the prioritisation phases (II and III), only complete submissions where all questions were ranked were included in the analysis.

Phase I

Experts were recruited from the Association of Upper GI Surgeons of Great Britain and Ireland (AUGIS) membership, which includes medical professionals and members of the wider multidisciplinary team such as research nurses, dieticians and cancer specialist nurses. Members were invited by email to submit research questions across the entire spectrum of upper gastrointestinal (Upper GI) and hepato-pancreato-biliary (HPB) surgery (including both benign and malignant conditions) via an online survey (<http://surveyMonkey.com>). The social media platform Twitter was also used to broaden the awareness of the Delphi process amongst interested stakeholders. There was no limit on the number of research questions that an individual could submit. The survey was open submissions for 3 months with three email reminders sent to the AUGIS membership during this period.

Submitted questions were collated, anonymised and then grouped into four categories: 1) Hepato-Pancreatic and B 2) Benign upper GI 3) Malignant OG and 4) Bariatric and metabolic surgery. Any disagreements regarding categorisation were resolved by consensus.

For category (3), an OG cancer surgery steering committee was then formed. Duplicate questions were removed. Questions with a similar theme were altered by consensus agreement of the steering committee. Care was taken not to alter the meaning of the reviewed questions.

Phase II

OG cancer surgery research questions were prioritised by AUGIS members by email invitation with a link to an online survey (Google forms). Twitter was again used to highlight the prioritisation process amongst interested stakeholders. The survey contained all of the OG cancer surgery research questions and respondents were asked to prioritise each question using a Likert scale (1 – lowest priority to 5 – highest priority). The survey remained open to submissions for 16 weeks with three email reminders sent to AUGIS members. The results were anonymised and reviewed by the steering committee and a 'cut-off' point agreed by consensus based on a mean score ≥ 3.7 following prioritisation for inclusion in the final round of prioritisation.

Phase III

A final round of prioritisation was performed after AUGIS members were again invited by email and Twitter to follow a link to a Google forms survey and prioritise the questions using the same Likert scale as in Phase II. The survey remained open for 8 weeks and three email reminders were sent. Results were anonymised and reviewed by the steering committee to identify the final list of prioritised questions. The criteria for inclusion in the final list of research priorities was a mean score of ≥ 3.5 , a Likert score of 4-5 by $>65.0\%$ respondents and a Likert score of 1-2 by $<15.0\%$ respondents.

Steering committee

The OG cancer surgery steering committee consisted of two Upper GI surgical senior trainees (NB, MW), two consultant OG cancer surgeons (RV and TU), a consultant oncologist (RP) and a lay representative (CB). The overall role of the steering committee was to ensure relevance of the submitted questions from both a clinical and patient perspective and to provide consensus agreement.

Results

In total, 427 research questions were submitted by 140 AUGIS members in Phase I, representing 47.6% of the membership (Figure 2). Of those responding, a sub-specialisation OG cancer surgery interest was declared by 57 (40.7%).

Once duplicated and similar questions were reviewed and amended or removed by consensus agreement, 75 questions were moved forward for prioritisation in phase II. Fifty-two stakeholders voluntarily prioritised the questions in phase II. Responses were received from 34 consultant surgeons, 12 trainee grade surgeons, 3 dietitians, 1 consultant oncologist, 1 UGI nurse specialist and 1 public health research fellow. An analysis of the prioritisation was performed by the steering committee and consensus reached regarding a cut-off for inclusion (mean ≥ 3.7) in phase III.

Twenty-one questions were included in the final phase of prioritisation and 46 stakeholders took part. Responses were received from 36 consultant surgeons, 7 trainee grade surgeons, 2 dietitians and 1 consultant anaesthetist. Following review by the steering committee with consensus agreement on the criteria for inclusion on the final list of clinical priorities, 12 questions were included on the final list of OG cancer surgery questions with high research priority (Figure 3). Our list of prioritised questions focuses on questions with the following themes

- 1) **Personalised treatment regimens** – molecular characterisation with personalised or tailored immunotherapies
- 2) **Identifying those who will not benefit from adjuvant therapies**
- 3) **Optimal palliation** – chemotherapy, surgery or best supportive care
- 4) **Earlier detection of OG cancer**

5) **Prehabilitation prior to OG resectional surgery** – is it beneficial and what is the optimal programme?

The questions which failed to make the final list of research priorities from phase III can be seen in Appendix 1.

Discussion

This study has produced a list of 12 high priority research questions in the field of OG cancer surgery using a modified Delphi process. To our knowledge this is the first time that such a project has been undertaken in the field of OG cancer surgery. Previous studies have used a Delphi process to develop consensus statements for the management of Barrett's dysplasia and early stage gastric cancer (22), gastric cancer prevention (23) and a core information set for oesophageal cancer surgery (21). This study was undertaken as part of a wider project to develop the research priorities in the field of Upper GI surgery (also incorporating the subspecialty interests of bariatric and metabolic surgery, HPB and benign upper GI surgery).

From our list of prioritised questions there is a significant emphasis on focusing future research on tailored or personalised treatments in OG cancer. These include personalised chemo/radiotherapy treatments, randomised trials of tailored therapy following the molecular characterisation of OG cancers and identifying patients who are the most likely to benefit from adjuvant treatments. Looking to the future a need to further define the role of immunotherapy in the management of OG cancer was also identified.

From phase II of the study a number of questions failed to make the final list of prioritised questions. The reasons for failing to make the final list will be multifactorial. However, one explanation could be that ongoing research projects will hopefully answer some of the proposed questions. An example of this relates to the prevention of anastomotic leaks in OG cancer surgery. This question is being addressed in the Oesophagogastric anastomosis audit (OGAA) study (26). The outcome of the ROMIO (27) study should also help to determine the best predictors of long term survival following oesophagectomy. Some questions may have failed to be prioritised sufficiently because they were addressing oesophageal or gastric

cancer separately. It may have been better to use the term OG cancer consistently (e.g. What are the best predictors of long term survival for OG cancer?). This may also explain why the optimal palliation question pertaining to oesophageal cancer failed to be prioritised but the same question for gastric cancer was sufficiently prioritised.

In the final round of prioritisation, 93.6% respondents were surgeons. This is a limitation of our study. A broader range of contributions from across the OG cancer multidisciplinary team (oncologists, dietitians, radiologists, specialist nurses, pathologists) may have altered the list of highly prioritised questions. Nevertheless, a number of the prioritised questions do not specifically relate to the surgical management or outcomes following OG cancer. The topics in the final prioritised list range from improving earlier detection of OG cancer to the optimal palliative treatment options. Twitter was used to publicise the existence of the survey, and therefore the survey was in the public domain and open to submissions from lay individuals, patients and family members. Unfortunately, no submissions were received from non-healthcare professionals. We did however have lay representation on the steering committee (CB). CB was involved in the discussion and agreement upon methodology in phase II and III of the study. Reassuringly, the final list of priorities mirrors those in the OCCAMS consortium and Oelixir projects (personal communication, TU). Both are UK-wide research initiatives in oesophageal cancer where extensive patient and public engagement has been at the core of agenda-setting.

Previous Delphi processes in other specialties reported response rates ranging from 11 to 25% (15, 17). Our response rate in phase I across all specialties was 47.6% and this should therefore be considered as sufficient engagement from the AUGIS membership. The list of

prioritised research questions will be shared with funding bodies. The expectation is that our list of research questions will provide a focus of future research topics and be a useful resource for research grant and clinical trial applications. Further, AUGIS members who contributed to this study at any point from phase I to II may become motivated to undertake future research in to some of the questions identified by this consensus agreed Delphi process. Indeed, this is already being taken forward by the AUGIS/Heartburn Cancer UK, Royal College of Surgeons of England Surgical Specialty Lead for Oesophageal Cancer as part of the Surgical Trials Initiative.

Conclusion

In summary, our modified Delphi process has produced a list of questions that have been deemed by consensus amongst UK OG cancer specialists to have the highest research priority in the field of OG cancer surgery. There is an emphasis on tailored or personalised treatment options particularly in relation to the role of immunotherapy in the management of OG cancer. Future research projects should seek to address these questions as well as to engage improved patient and public involvement.

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Figure 1. The modified Delphi process used to prioritise research questions in oesophagogastric cancer surgery

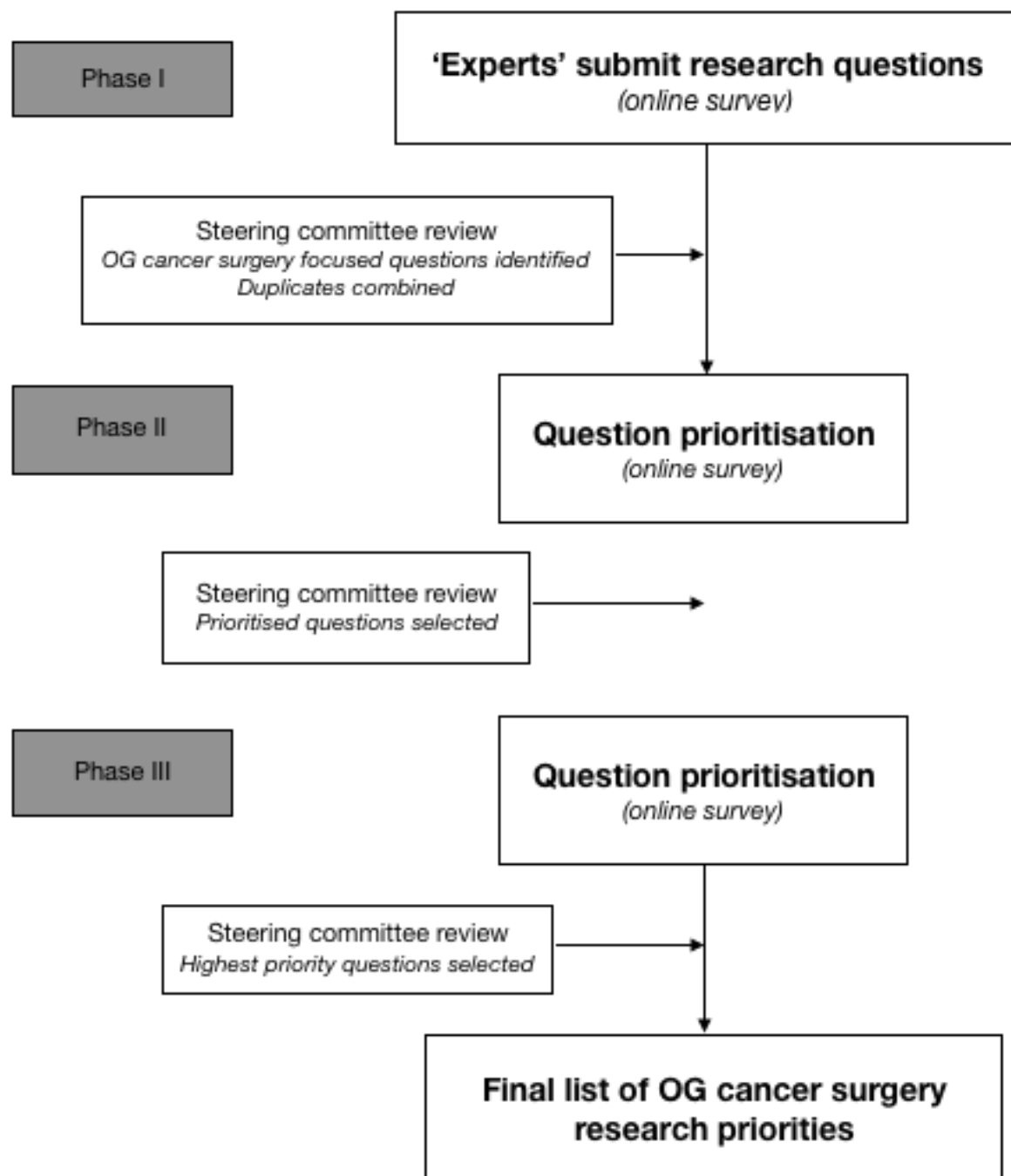


Figure 2. Overview of responses during modified Delphi process

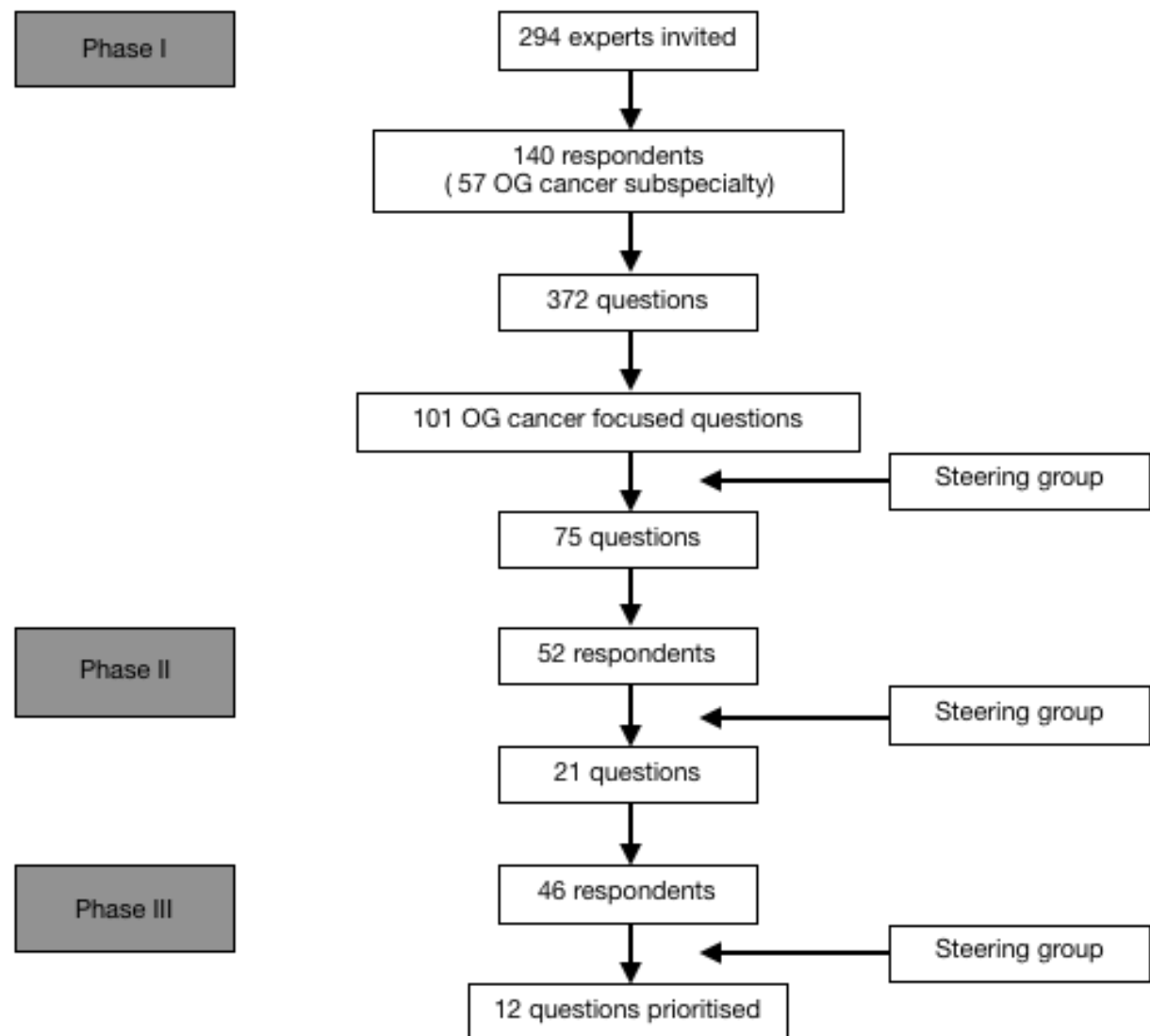


Figure 3 Research priorities for oesophagogastric cancer surgery

INCLUDED Questions
Is neoadjuvant chemoradiotherapy better than chemotherapy alone for oesophageal adenocarcinoma?
Is surgery (with neoadjuvant treatment) more effective than optimal non-surgical oncological treatment in patients with advanced but non metastatic OG cancer?
Are personalised chemotherapy treatments possible for OG cancer?
Is there a role for tailored chemo/radiotherapy for OG cancer?
Why do some patients fail to respond to chemotherapy for OG cancer?
What is the best way to identify patients with OG cancer who will not benefit from peri-operative chemotherapy?
Should we support the molecular characterisation of OG cancers and randomised trials of tailored therapy?
How can we improve the identification of patients who are most likely to benefit from adjuvant treatment for resectable OG cancer?
What is the role of immunotherapy or other novel therapies in the treatment of OG cancer?
What palliative treatment provides the best quality of life in irresectable gastric cancer; chemotherapy, surgery or best supportive care?
How can we detect OG cancer earlier?
Is there a role for prehabilitation in OG cancer and what would be the optimal programme?

Appendix 1

[Click here to download Supplementary Material: Appendix 1 OG cancer.docx](#)