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A Protocol to Develop a Core Outcome Set in Incisional Hernia Surgery – The HarMoNY Project

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NoSTRA HarMoNY

(Northern Surgical Trainees Research Association Hernia & Abdominal Reconstruction - Measuring Outcomes, Nociception & qualitY of life) collaborative research group.

All authors including the corresponding author will come under the collaborative authorship of NoSTRA HarMoNY.

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Abstract

Introduction

Incisional hernia has an incidence of up to 20% following laparotomy and is associated with significant morbidity and impairment of quality of life. A variety of surgical strategies including techniques and mesh types are available to manage patients with incisional hernia. Previous works have reported significant heterogeneity in outcome reporting for abdominal wall herniae, including ventral and inguinal hernia. This is coupled with under-reporting of important clinical and patient-reported outcomes. The lack of standardisation in outcome reporting contributes to reporting bias, hinders evidence synthesis and adequate data comparison between studies. This project aims to develop a core outcome set (COS) of clinically important, patient-oriented outcomes to be used to guide reporting of future research in incisional hernia.

Methods

This project has been designed as an international, multi-centre, mixed-methods project. Phase I will be a systematic review of current literature to examine the current clinical and patient-reported outcomes

for incisional hernia and abdominal wall reconstruction. Phase II will identify the outcomes of importance to all key stakeholders through in depth qualitative interviews. Phase III will achieve consensus on outcomes of most importance and for inclusion into a COS through a Delphi process. Phase IV will achieve consensus on the outcomes that should be included in a final COS.

Ethics and Dissemination

Ethical approval for this study has been granted by the Health Research Authority. The results of this study will be disseminated through publication in peer-reviewed journals and presentations.

The adoption of this COS into clinical and academic practice will be endorsed by the American, British and European Hernia Societies. Its utilisation in future clinical research will enable appropriate data synthesis and comparison and will enable better clinical interpretation and application of the current evidence base. This study has been registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative.

Trial Registration: PROSPERO registration CRD42018090084.

Strengths and Limitations

- This project will ensure the development of an international, clinically relevant, patient-oriented core outcome set to be used to guide outcome reporting in future clinical research.
- A robust systematic review will identify current outcomes in randomised and non-randomised studies reporting outcomes in incisional hernia.
- In-depth qualitative interviews with key stakeholders including patients, nurses, radiologists, physiotherapists, members of international hernia societies and industry partners will identify outcomes of importance to all these groups.
- This project will determine which outcomes to measure, however, further work will be necessary to agree and recommend a definition or measurement instrument for each of the outcomes in the COS.

Background

Incisional hernia following laparotomy has an incidence of up to 20% and is associated with significant morbidity and impairment of quality of life [1]. The management of incisional hernia has evolved over recent years, with a variety of techniques, meshes and operative strategies available to manage this challenging cohort of patients. Given the range of options available there is significant complexity involved in the management of patients with incisional hernia. Alongside this there is considerable variation in management and outcome reporting. Despite an exponential increase in the number of peer-reviewed publications on the management of incisional hernia over the last decade [2], the methodological quality of the majority of these studies is poor, with the majority of studies reporting outcomes on incisional hernia being of Level 4 quality according to the Oxford Centre for Evidence Based Medicine [3]. A recent systematic review reported over 75% of randomised controlled trials and meta-analyses reporting outcomes on ventral hernias were methodologically flawed, with variable adherence to standardised reporting frameworks such as Consolidated Standards of Reporting Trials (CONSORT) checklist or Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist PRISMA [3].

There is little known about standardised outcome reporting in patients with incisional hernia. Previous work examining outcome reporting for inguinal hernia identified significant variation in outcomes employed to report clinical outcomes in this group. Significant heterogeneity in outcome definitions and assessment instruments exist in inguinal hernia outcome reporting, alongside under-reporting of a number of important clinical and patient-reported outcomes [4]. More recently, work examining outcome reporting in randomised controlled trials of ventral hernia revealed marked heterogeneity in outcome reporting of clinical endpoints related to hernia recurrence [5]. Subsequently, it may be hypothesised that similar variation and under-reporting of relevant outcomes exists within the current literature for incisional hernia repair.

Core outcome sets (COS) have been developed to overcome heterogeneity in outcome reporting, reduce reporting bias and enable adequate evidence synthesis, comparison of data between studies and meaningful clinical interpretation and application of current evidence [6]. COS are an agreed set of outcomes, which should be measured and reported, as a minimum in all studies and trials for a specific clinical area. This work was initiated and developed by the COMET (Core Outcome Measures in

Effectiveness Trials) initiative, which aims to facilitate and guide the development of a number of COS [7]. Currently, there is no COS for incisional hernia. However, there are guidelines available to guide reporting outcomes with regards to mesh properties [8] and clinical outcomes [9] associated with abdominal wall repair. Although, these guidelines are useful in trying to standardise reporting outcomes, they do not reflect the opinion of all stakeholders, in particular patients, when considering which outcomes are of the most importance when reporting outcomes related to incisional hernia repair. To improve the quality of the current evidence base and to improve outcome reporting a COS in incisional hernia is highly desirable.

Aims

The aim of this project is to develop a COS of clinically important, patient-oriented outcomes to be used to guide reporting of future research in incisional hernia.

Methods

An international, mixed-methods study will be conducted in accordance with Core Outcome Measures in Effectiveness Trials (COMET) guidelines to develop a COS for use in incisional hernia. Phase I will examine the current clinical and patient-reported outcomes for incisional hernia and abdominal wall reconstruction within the literature. Phase II will identify the outcomes of importance to all key stakeholders through in depth qualitative interviews. Phase III will achieve consensus on outcomes of most importance and for inclusion into a COS through a Delphi process. Phase IV will achieve consensus on the outcomes that should be included in a final COS.

Phase I: Systematic review of clinical and patient-reported outcomes

A number of detailed systematic reviews of currently reported clinical and patient reported outcomes in incisional hernia and complex abdominal wall reconstruction will be conducted. The full protocol including eligibility criteria and search strategy is available online via the PROSPERO database (CRD42018090084).

Phase II: Stakeholder Qualitative Interviews

To ensure all key stakeholders are appropriately represented and all outcomes are captured within the COS we will conduct in-depth qualitative interviews with patients and other stakeholders that are not adequately represented within the current literature i.e. nurses, radiologists, physiotherapists. We will also interview key members of the international hernia societies including the American Hernia Society, British Hernia Society and the European Hernia Society and industry partners in a bid to gauge a wider perspective.

Recruitment

Healthcare professionals

All members of the American Hernia Society, the British Hernia Society and the European Hernia Society will be contacted and invited to participate.

Industry Partners

Industry partners will be identified through key hernia organisations including the American Hernia Society, the British Hernia Society and the European Hernia Society. Industry stakeholders will be contacted and invited to participate.

Patients

Members of the American Hernia Society, British Hernia Society and the European Hernia Society will be asked to identify potential patient participants from clinic lists, theatre lists and patient records. Recruitment letters will be sent to the identified patients, either in person during routine follow up visits or by post. The recruitment letter will give a full explanation of the qualitative interviews, instructions to participate and the contact details of the research team.

Methodology

In-depth face-to-face or telephone cognitive interviews will be undertaken with eligible patients and stakeholders. Interviews will explore patients' perceptions and experiences regarding living with an incisional hernia and will identify the thoughts and opinions of stakeholders who are not adequately represented within the current literature. A standardised, semi-structured interview guide will inform the cognitive interviews. All interviews will be recorded. Open-ended questions will be used at the start of

the cognitive interview followed by close-ended questions to further explore any relevant themes. To ensure appropriate representation of all stakeholders, we will conduct interviews with patients and other key stakeholders from all participating countries. We will aim to conduct between 5-10 interviews per country.

Patient Eligibility Criteria

Inclusion criteria:

- Aged >18 years old.
- With an existing incisional hernia **or**
- A surgically treated incisional hernia in the last 12 months **and**
- Able to provide written informed consent

Exclusion criteria:

- An existing other ventral hernia i.e. epigastric, umbilical, paraumbilical, inguinal, port-site hernia **or**
- A surgically treated ventral hernia i.e. epigastric, umbilical, paraumbilical, inguinal, port-site hernia **or**

To ensure our COS is representative of all stakeholders, with particular reference to patients with incisional hernia a purposive sampling strategy has been designed to aid recruitment (Table 1). Our sampling strategy will target a number of key factors to reflect the range and diversity of the target population. There is no minimal sample size for cognitive interviews.

Table 1: Purposive Sampling Strategy

Patient Factors	**Number of Patients**
Age 18-30	4

31 – 60	4
>60	4
Gender	
Male	8-10
Female	8-10
Presentation	
Elective	6-8
Emergency	6-8
Repair	
Primary	6-8
Mesh	6-8
No of repairs	
1st repair	4
Recurrent incisional hernia repair	4
Hernia size	
<10cm in width	8 – 10
>10cm in width	8 – 10
Use of adjuncts	
Yes	4
No	4
Stakeholder Factors	Number of Participants
Speciality	
General Surgery	4-6
Plastic Surgery	4-6
Radiology	4-6
Specialist nurses/physiotherapists	4-6
Industry partner	4-6
Country	
UK	4
	4

Europe USA Australia	4 4

Data Analysis

All interviews will be audio recorded and transcribed verbatim and transcripts will be imported into NVivo. All transcripts will be anonymised. Interviews will be coded using the principles of thematic content analysis [10]. Relevant outcomes will be identified and appropriately coded from the transcripts using a provisional coding framework based on the outcomes extracted from the systematic review. Coded outcomes that are sufficiently similar will be grouped into similar categories and then themes. Analysis will be an iterative process, with data being analysed after rounds of three consecutive interviews. Data analysis will be continued up until the point of data saturation. This is the point on the data analysis process where no further information is elicited.

Phase III: Delphi Study

Consolidation of Outcomes

The outcomes identified in Phase I and II will be combined, developed into a long-list of items and categorised into broad domains using the principles of thematic content analysis. Appropriate questions will be mapped to these domains and will form the basis of the Delphi study. Questions will have a lay translation available. We will pilot the Delphi study with our steering committee to ensure it is accessible, comprehensible and content valid.

Forward-Backward Translation

Given the international nature of this study, we will translate the Delphi study using forward-backward translation to ensure accessibility of the study by all international participants. The aim of translation is to achieve different language versions of the original Delphi questionnaire. The linguistic and translation process should ensure that the translated version of the Delphi are conceptual, semantic and pragmatic equivalents of the original questionnaire, whilst ensuring it is culturally appropriate, relevant and

meaningful to the target countries. The original Delphi questionnaire (English) will be used as the standard from which all other translations are made.

Forward translation will be undertaken by two healthcare professionals with an understanding of incisional hernia. The translators will be bilingual with their primary language being that of the target country. They will perform a detailed review of the Delphi questionnaire and translate the questionnaire appropriately. Two independent translations will be prepared; these will be reviewed and compared to achieve a consensus version. Any discrepancies between the translated version and the original Delphi questionnaire will be discussed with the steering committee.

The final translated version will be translated back into English (backward translation). This will be done by a native English speaker who is also proficient in the target language. The original Delphi questionnaire will be compared to the backward translation version and reviewed to ensure consistency. The aim is to ensure linguistic and conceptual equivalence between the original and translated versions of the Delphi. Any discrepancies will be discussed and resolved with the steering committee and the bilingual translators who undertook the forward translation. If equivalent versions have not been created further translational work may be required. This may include additional forward translations and/or the addition of further items/questions and will be repeated as many times as necessary to achieve a satisfactory translated version.

Recruitment

Method of recruitment will be the same as Phase II. Healthcare professionals, patients and industry stakeholders will be invited to participate through online web and social media platforms of the participating hernia societies (American, British and European) and through the Northern Surgical Trainees Research Association. Snowball sampling will be allowed to increase the sample size and reach of the study.

Sample Size

There are no pre-requisite criteria for sample size for participation in Delphi studies. We hope by engagement with the American, British and European hernia societies we will capture the majority of individuals interested in incisional hernia.

Consent

No explicit consent will be obtained for participation in the Delphi study. Consent will be implied through the process of participation. The registration page of the website hosting the Delphi study will outline that registration to participate in the Delphi process through submission of name and email address will indicate agreement to participate.

Delphi Process

The aim of the Delphi study is to achieve consensus amongst all key stakeholders including patients, surgeons, radiologists and specialist nurses on the importance of different outcomes in sequential questionnaires. The Delphi questionnaires will be developed using the DelphiManager software developed by the COMET initiative. Relevant demographics will be collected for each stakeholder group.

Two sequential rounds of Delphi voting will be held with a feedback round in between. The first Delphi round will enable participants to suggest outcomes that may not have been included or overlooked. The spread of scores for each question item should reduced in between rounds as consensus is reached. Following the first Delphi round participants will be provided with feedback. Participants will have access to their individual scores from the first round and scores from key stakeholder group.

All included outcomes will be scored on a 9 point Likert scale, with 1 being ‘not essential’ to 9 being ‘absolutely essential’ for inclusion into a COS. The 9 point Likert scale will be grouped into three categories; 1-3 (limited importance), 4-6 (important but not critical), 7-9 (of critical importance).

Consensus will be defined as the following:

For inclusion: more than 75% of respondents within a stakeholder group rate the outcome as critically important and less than 15% of respondents rate the outcome as of limited importance.

For exclusion: more than 75% of respondents within a stakeholder group the outcome as of limited importance and less than 15% of respondents rate the outcome as of critical importance.

No consensus

Phase IV: Consensus Meeting

A consensus meeting of all key stakeholders will be held in conjunction with a European Hernia Society meeting to discuss the results from the Delphi study. All participants registering to complete the Delphi study will be invited to participate in the consensus meeting. The aim of this consensus meeting is to agree on the final COS for incisional hernia. All outcomes will be discussed; a proposal will be made to include all outcomes in the final COS that have been categorised as 'for inclusion' by all stakeholders and to exclude all outcomes that have been categorised as 'for exclusion' by all stakeholders. Participants will vote electronically to accept or reject these proposals. All other outcomes categories as 'for inclusion', 'for exclusion' or 'no consensus' by one or two stakeholders will be discussed and further rounds of voting will be used to agree the final COS. If no consensus is achieved a further consensus meeting will be held.

Patient and Public Involvement

The HarMoNY project has been discussed with patients at national hernia meetings and has been well received. A dedicated, international patient and public (PPI) steering group will be appointed to inform the processes of Phases II-IV of this project. Patients will be approached by key members of the project team to participate in this steering group. This PPI steering group will help inform recruitment processes, help design and evaluate all patient information sheets to ensure all information is applicable and understandable and advise on the content and format of dissemination of the final COS.

Ethics

Ethical approval has been obtained from the Health Research Authority and Health and Care Research Wales (REC 21/WA/0278). Appropriate ethical approval will be sought from all participating countries in accordance with local and national guidelines. This study will be conducted in keeping with the Declaration of Helsinki.

Discussion

Defining important outcomes and standardising their reporting has been recognised to be of key importance in clinical research, which has subsequently led to the development of a number of COS. There has been a steady rise in the adoption and utilisation of COS [11], with a number of key stakeholders, including commissioners and funding bodies recognising the importance and benefits of COS for improving reporting outcomes [12]. Incisional hernia repair can be complex with significant variation in clinical management due to the great diversity of available surgical techniques [13, 14]. To ensure clinical heterogeneity is not reflected in outcome reporting the development of COS in this cohort of patients is essential. Ensuring consistent outcome reporting will reduce reporting bias, improve data synthesis and comparison, and will enable better clinical interpretation and application of the current evidence base. It is hoped through the development of a COS for incisional hernia, internationally agreed by patients, clinicians and key stakeholders, including the American, British and European Hernia Society, a minimum number of key outcomes will be reported in future clinical studies. This will help strengthen the current evidence base informing incisional hernia repair through standardised reporting.

Contributorship:

Study design: DH/CT/NS/BG/LH

Protocol writing: DH/CT/NS/BG

Methodological input: AM/FM/MM/TH/BP/AA/FK/WR

Manuscript review: MLC/LM/MM/HG/HC

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References

1. van Ramshorst, G.H., et al., *Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study.* Am J Surg, 2012. **204**(2): p. 144-50.
2. Kulacoglu, H. and D. Oztuna, *Growth and trends in publications about abdominal wall hernias and the impact of a specific journal on herniology: a bibliometric analysis.* Hernia, 2011. **15**(6): p. 615-28.
3. Holihan, J.L., et al., *A systematic review of randomized controlled trials and reviews in the management of ventral hernias.* J Surg Res, 2016. **204**(2): p. 311-318.
4. Bhangu, A., et al., *A detailed analysis of outcome reporting from randomised controlled trials and meta-analyses of inguinal hernia repair.* Hernia, 2015. **19**(1): p. 65-75.
5. Parker, S.G., et al., *A systematic methodological review of reported perioperative variables, postoperative outcomes and hernia recurrence from randomised controlled trials of elective ventral hernia repair: clear definitions and standardised datasets are needed.* Hernia, 2018. **22**(2): p. 215-226.
6. Williamson, P. and M. Clarke, *The COMET (Core Outcome Measures in Effectiveness Trials) Initiative: Its Role in Improving Cochrane Reviews.* Cochrane Database Syst Rev, 2012(5): p. ED000041.
7. http://www.comet-initiative.org.
8. Bringman, S., et al., *Hernia repair: the search for ideal meshes.* Hernia, 2010. **14**(1): p. 81-7.
9. Muysoms, F.E., et al., *Recommendations for reporting outcome results in abdominal wall repair: results of a Consensus meeting in Palermo, Italy, 28-30 June 2012.* Hernia, 2013. **17**(4): p. 423-33.
10. Braun V, C.V., *Using thematic analysis in psychology. Qualitative Research in Psychology. 2006.*

. 2006.

11. Bautista-Molano, W., et al., *How well are the ASAS/OMERACT Core Outcome Sets for Ankylosing Spondylitis implemented in randomized clinical trials? A systematic literature review.* Clin Rheumatol, 2014. **33**(9): p. 1313-22.
12. Clarke, M. and P. Williamson, *Core outcome sets and trial registries.* Trials, 2015. **16**: p. 216.
13. Kokotovic, D., I. Gogenur, and F. Helgstrand, *Substantial variation among hernia experts in the decision for treatment of patients with incisional hernia: a descriptive study on agreement.* Hernia, 2017. **21**(2): p. 271-278.
14. Pawlak, M., K. Bury, and M. Smietanski, *The management of abdominal wall hernias - in search of consensus.* Wideochir Inne Tech Maloinwazyjne, 2015. **10**(1): p. 49-56.

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Abstract

Introduction

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- A robust systematic review will identify current outcomes in randomised and non-randomised studies reporting outcomes in incisional hernia.
- In-depth qualitative interviews with key stakeholders including patients, nurses, radiologists, physiotherapists, members of international hernia societies and industry partners will identify outcomes of importance to all these groups.
- This project will determine which outcomes to measure, however, further work will be necessary to agree and recommend a definition or measurement instrument for each of the outcomes in the COS.

Background

Incisional hernia following laparotomy has an incidence of up to 20% and is associated with significant morbidity and impairment of quality of life [1]. The management of incisional hernia has evolved over recent years, with a variety of techniques, meshes and operative strategies available to manage this

challenging cohort of patients. Given the range of options available there is significant complexity involved in the management of patients with incisional hernia. Alongside this there is considerable variation in management and outcome reporting. Despite an exponential increase in the number of peer-reviewed publications on the management of incisional hernia over the last decade [2], the methodological quality of the majority of these studies is poor, with the majority of studies reporting outcomes on incisional hernia being of Level 4 quality according to the Oxford Centre for Evidence Based Medicine [3]. A recent systematic review reported over 75% of randomised controlled trials and meta-analyses reporting outcomes on ventral hernias were methodologically flawed, with variable adherence to standardised reporting frameworks such as Consolidated Standards of Reporting Trials (CONSORT) checklist or Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Checklist PRISMA [3].

There is little known about standardised outcome reporting in patients with incisional hernia. Previous work examining outcome reporting for inguinal hernia identified significant variation in outcomes employed to report clinical outcomes in this group. Significant heterogeneity in outcome definitions and assessment instruments exist in inguinal hernia outcome reporting, alongside under-reporting of a number of important clinical and patient-reported outcomes [4]. More recently, work examining outcome reporting in randomised controlled trials of ventral hernia revealed marked heterogeneity in outcome reporting of clinical endpoints related to hernia recurrence [5]. Subsequently, it may be hypothesised that similar variation and under-reporting of relevant outcomes exists within the current literature for incisional hernia repair.

Core outcome sets (COS) have been developed to overcome heterogeneity in outcome reporting, reduce reporting bias and enable adequate evidence synthesis, comparison of data between studies and meaningful clinical interpretation and application of current evidence [6]. COS are an agreed set of outcomes, which should be measured and reported, as a minimum in all studies and trials for a specific clinical area. This work was initiated and developed by the COMET (Core Outcome Measures in Effectiveness Trials) initiative, which aims to facilitate and guide the development of a number of COS [7]. Currently, there is no COS for incisional hernia. However, there are guidelines available to guide reporting outcomes with regards to mesh properties [8] and clinical outcomes [9] associated with

abdominal wall repair. Although, these guidelines are useful in trying to standardise reporting outcomes, they do not reflect the opinion of all stakeholders, in particular patients, when considering which outcomes are of the most importance when reporting outcomes related to incisional hernia repair. To improve the quality of the current evidence base and to improve outcome reporting a COS in incisional hernia is highly desirable.

Aims

The aim of this project is to develop a COS of clinically important, patient-oriented outcomes to be used to guide reporting of future research in incisional hernia.

Methods

An international, mixed-methods study will be conducted in accordance with Core Outcome Measures in Effectiveness Trials (COMET) guidelines to develop a COS for use in incisional hernia. Phase I will examine the current clinical and patient-reported outcomes for incisional hernia and abdominal wall reconstruction within the literature. Phase II will identify the outcomes of importance to all key stakeholders through in depth qualitative interviews. Phase III will achieve consensus on outcomes of most importance and for inclusion into a COS through a Delphi process. Phase IV will achieve consensus on the outcomes that should be included in a final COS.

Phase I: Systematic review of clinical and patient-reported outcomes

A number of detailed systematic reviews of currently reported clinical and patient reported outcomes in incisional hernia and complex abdominal wall reconstruction will be conducted. The full protocol including eligibility criteria and search strategy is available online via the PROSPERO database (CRD42018090084).

Phase II: Stakeholder Qualitative Interviews

To ensure all key stakeholders are appropriately represented and all outcomes are captured within the COS we will conduct in-depth qualitative interviews with patients and other stakeholders that are not adequately represented within the current literature i.e. nurses, radiologists, physiotherapists. We will

also interview key members of the international hernia societies including the American Hernia Society, British Hernia Society and the European Hernia Society and industry partners in a bid to gauge a wider perspective.

Recruitment

Healthcare professionals

All members of the American Hernia Society, the British Hernia Society and the European Hernia Society will be contacted and invited to participate.

Industry Partners

Industry partners will be identified through key hernia organisations including the American Hernia Society, the British Hernia Society and the European Hernia Society. Industry stakeholders will be contacted and invited to participate.

Patients

Members of the American Hernia Society, British Hernia Society and the European Hernia Society will be asked to identify potential patient participants from clinic lists, theatre lists and patient records. Recruitment letters will be sent to the identified patients, either in person during routine follow up visits or by post. The recruitment letter will give a full explanation of the qualitative interviews, instructions to participate and the contact details of the research team.

Methodology

In-depth face-to-face or telephone cognitive interviews will be undertaken with eligible patients and stakeholders. Interviews will explore patients' perceptions and experiences regarding living with an incisional hernia and will identify the thoughts and opinions of stakeholders who are not adequately represented within the current literature. A standardised, semi-structured interview guide will inform the cognitive interviews. All interviews will be recorded. Open-ended questions will be used at the start of the cognitive interview followed by close-ended questions to further explore any relevant themes. To ensure appropriate representation of all stakeholders, we will conduct interviews with patients and other

key stakeholders from all participating countries. We will aim to conduct between 5-10 interviews per country.

Patient Eligibility Criteria

Inclusion criteria:

- Aged >18 years old.
- With an existing incisional hernia **or**
- A surgically treated incisional hernia in the last 12 months **and**
- Able to provide written informed consent

Exclusion criteria:

- An existing other ventral hernia i.e. epigastric, umbilical, paraumbilical, inguinal, port-site hernia **or**
- A surgically treated ventral hernia i.e. epigastric, umbilical, paraumbilical, inguinal, port-site hernia **or**

To ensure our COS is representative of all stakeholders, with particular reference to patients with incisional hernia a purposive sampling strategy has been designed to aid recruitment (Table 1). Our sampling strategy will target a number of key factors to reflect the range and diversity of the target population. There is no minimal sample size for cognitive interviews.

Table 1: Purposive Sampling Strategy

Patient Factors	**Number of Patients**
Age	
18-30	4
31 – 60	4
>60	4

Gender	
Male	8-10
Female	8-10
Presentation	
Elective	6-8
Emergency	6-8
Repair	
Primary	6-8
Mesh	6-8
No of repairs	
1st repair	4
Recurrent incisional hernia repair	4
Hernia size	
<10cm in width	8 – 10
>10cm in width	8 – 10
Use of adjuncts	
Yes	4
No	4
Stakeholder Factors	Number of Participants
Speciality	
General Surgery	4-6
Plastic Surgery	4-6
Radiology	4-6
Specialist nurses/physiotherapists	4-6
Industry partner	4-6
Country	
UK	4
Europe	4
USA	4
Australia	4

Data Analysis

All interviews will be audio recorded and transcribed verbatim and transcripts will be imported into NVivo. All transcripts will be anonymised. Interviews will be coded using the principles of thematic content analysis [10]. Relevant outcomes will be identified and appropriately coded from the transcripts using a provisional coding framework based on the outcomes extracted from the systematic review. Coded outcomes that are sufficiently similar will be grouped into similar categories and then themes. Analysis will be an iterative process, with data being analysed after rounds of three consecutive interviews. Data analysis will be continued up until the point of data saturation. This is the point on the data analysis process where no further information is elicited.

Phase III: Delphi Study

Consolidation of Outcomes

The outcomes identified in Phase I and II will be combined, developed into a long-list of items and categorised into broad domains using the principles of thematic content analysis. Appropriate questions will be mapped to these domains and will form the basis of the Delphi study. Questions will have a lay translation available. We will pilot the Delphi study with our steering committee to ensure it is accessible, comprehensible and content valid.

Forward-Backward Translation

Given the international nature of this study, we will translate the Delphi study using forward-backward translation to ensure accessibility of the study by all international participants. The aim of translation is to achieve different language versions of the original Delphi questionnaire. The linguistic and translation process should ensure that the translated version of the Delphi are conceptual, semantic and pragmatic equivalents of the original questionnaire, whilst ensuring it is culturally appropriate, relevant and meaningful to the target countries. The original Delphi questionnaire (English) will be used as the standard from which all other translations are made.

Forward translation will be undertaken by two healthcare professionals with an understanding of incisional hernia. The translators will be bilingual with their primary language being that of the target country. They will perform a detailed review of the Delphi questionnaire and translate the questionnaire appropriately. Two independent translations will be prepared; these will be reviewed and compared to achieve a consensus version. Any discrepancies between the translated version and the original Delphi questionnaire will be discussed with the steering committee.

The final translated version will be translated back into English (backward translation). This will be done by a native English speaker who is also proficient in the target language. The original Delphi questionnaire will be compared to the backward translation version and reviewed to ensure consistency. The aim is to ensure linguistic and conceptual equivalence between the original and translated versions of the Delphi. Any discrepancies will be discussed and resolved with the steering committee and the bilingual translators who undertook the forward translation. If equivalent versions have not been created further translational work may be required. This may include additional forward translations and/or the addition of further items/questions and will be repeated as many times as necessary to achieve a satisfactory translated version.

Recruitment

Method of recruitment will be the same as Phase II. Healthcare professionals, patients and industry stakeholders will be invited to participate through online web and social media platforms of the participating hernia societies (American, British and European) and through the Northern Surgical Trainees Research Association. Snowball sampling will be allowed to increase the sample size and reach of the study.

Sample Size

There are no pre-requisite criteria for sample size for participation in Delphi studies. We hope by engagement with the American, British and European hernia societies we will capture the majority of individuals interested in incisional hernia.

Consent

No explicit consent will be obtained for participation in the Delphi study. Consent will be implied through the process of participation. The registration page of the website hosting the Delphi study will outline that registration to participate in the Delphi process through submission of name and email address will indicate agreement to participate.

Delphi Process

The aim of the Delphi study is to achieve consensus amongst all key stakeholders including patients, surgeons, radiologists and specialist nurses on the importance of different outcomes in sequential questionnaires. The Delphi questionnaires will be developed using the DelphiManager software developed by the COMET initiative. Relevant demographics will be collected for each stakeholder group.

Two sequential rounds of Delphi voting will be held with a feedback round in between. The first Delphi round will enable participants to suggest outcomes that may not have been included or overlooked. The spread of scores for each question item should reduced in between rounds as consensus is reached. Following the first Delphi round participants will be provided with feedback. Participants will have access to their individual scores from the first round and scores from key stakeholder group.

All included outcomes will be scored on a 9 point Likert scale, with 1 being 'not essential' to 9 being 'absolutely essential' for inclusion into a COS. The 9 point Likert scale will be grouped into three categories; 1-3 (limited importance), 4-6 (important but not critical), 7-9 (of critical importance).

Consensus will be defined as the following:

For inclusion: more than 75% of respondents within a stakeholder group rate the outcome as critically important and less than 15% of respondents rate the outcome as of limited importance.

For exclusion: more than 75% of respondents within a stakeholder group the outcome as of limited importance and less than 15% of respondents rate the outcome as of critical importance.

No consensus

Phase IV: Consensus Meeting

A consensus meeting of all key stakeholders will be held in conjunction with a European Hernia Society meeting to discuss the results from the Delphi study. All participants registering to complete the Delphi study will be invited to participate in the consensus meeting. The aim of this consensus meeting is to agree on the final COS for incisional hernia. All outcomes will be discussed; a proposal will be made to include all outcomes in the final COS that have been categorised as 'for inclusion' by all stakeholders and to exclude all outcomes that have been categorised as 'for exclusion' by all stakeholders. Participants will vote electronically to accept or reject these proposals. All other outcomes categories as 'for inclusion', 'for exclusion' or 'no consensus' by one or two stakeholders will be discussed and further rounds of voting will be used to agree the final COS. If no consensus is achieved a further consensus meeting will be held.

Patient and Public Involvement

The HarMoNY project has been discussed with patients at national hernia meetings and has been well received. A dedicated, international patient and public (PPI) steering group will be appointed to inform the processes of Phases II-IV of this project. Patients will be approached by key members of the project team to participate in this steering group. This PPI steering group will help inform recruitment processes, help design and evaluate all patient information sheets to ensure all information is applicable and understandable and advise on the content and format of dissemination of the final COS.

Ethics

Ethical approval has been obtained from the Health Research Authority and Health and Care Research Wales (REC 21/WA/0278). Appropriate ethical approval will be sought from all participating countries in accordance with local and national guidelines. This study will be conducted in keeping with the Declaration of Helsinki.

Discussion

Defining important outcomes and standardising their reporting has been recognised to be of key importance in clinical research, which has subsequently led to the development of a number of COS. There has been a steady rise in the adoption and utilisation of COS [11], with a number of key stakeholders, including commissioners and funding bodies recognising the importance and benefits of COS for improving reporting outcomes [12]. Incisional hernia repair can be complex with significant variation in clinical management due to the great diversity of available surgical techniques [13, 14]. To ensure clinical heterogeneity is not reflected in outcome reporting the development of COS in this cohort of patients is essential. Ensuring consistent outcome reporting will reduce reporting bias, improve data synthesis and comparison, and will enable better clinical interpretation and application of the current evidence base. It is hoped through the development of a COS for incisional hernia, internationally agreed by patients, clinicians and key stakeholders, including the American, British and European Hernia Society, a minimum number of key outcomes will be reported in future clinical studies. This will help strengthen the current evidence base informing incisional hernia repair through standardised reporting.

Contributorship:

Study design: DH/CT/NS/BG/LH

Protocol writing: DH/CT/NS/BG

Methodological input: AM/FM/MM/TH/BP/AA/FK/WR

Manuscript review: MLC/LM/MM/HG/HC

Competing Interests: None

Data Sharing: None available at present

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References

1. van Ramshorst, G.H., et al., *Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study.* Am J Surg, 2012. **204**(2): p. 144-50.
2. Kulacoglu, H. and D. Oztuna, *Growth and trends in publications about abdominal wall hernias and the impact of a specific journal on herniology: a bibliometric analysis.* Hernia, 2011. **15**(6): p. 615-28.
3. Holihan, J.L., et al., *A systematic review of randomized controlled trials and reviews in the management of ventral hernias.* J Surg Res, 2016. **204**(2): p. 311-318.
4. Bhangu, A., et al., *A detailed analysis of outcome reporting from randomised controlled trials and meta-analyses of inguinal hernia repair.* Hernia, 2015. **19**(1): p. 65-75.
5. Parker, S.G., et al., *A systematic methodological review of reported perioperative variables, postoperative outcomes and hernia recurrence from randomised controlled trials of elective ventral hernia repair: clear definitions and standardised datasets are needed.* Hernia, 2018. **22**(2): p. 215-226.
6. Williamson, P. and M. Clarke, *The COMET (Core Outcome Measures in Effectiveness Trials) Initiative: Its Role in Improving Cochrane Reviews.* Cochrane Database Syst Rev, 2012(5): p. ED000041.
7. http://www.comet-initiative.org.
8. Bringman, S., et al., *Hernia repair: the search for ideal meshes.* Hernia, 2010. **14**(1): p. 81-7.
9. Muysoms, F.E., et al., *Recommendations for reporting outcome results in abdominal wall repair: results of a Consensus meeting in Palermo, Italy, 28-30 June 2012.* Hernia, 2013. **17**(4): p. 423-33.
10. Braun V, C.V., *Using thematic analysis in psychology. Qualitative Research in Psychology. 2006.*

. 2006.

11. Bautista-Molano, W., et al., *How well are the ASAS/OMERACT Core Outcome Sets for Ankylosing Spondylitis implemented in randomized clinical trials? A systematic literature review.* Clin Rheumatol, 2014. **33**(9): p. 1313-22.
12. Clarke, M. and P. Williamson, *Core outcome sets and trial registries.* Trials, 2015. **16**: p. 216.
13. Kokotovic, D., I. Gogenur, and F. Helgstrand, *Substantial variation among hernia experts in the decision for treatment of patients with incisional hernia: a descriptive study on agreement.* Hernia, 2017. **21**(2): p. 271-278.
14. Pawlak, M., K. Bury, and M. Smietanski, *The management of abdominal wall hernias - in search of consensus.* Wideochir Inne Tech Maloinwazyjne, 2015. **10**(1): p. 49-56.