Randomized clinical trial

Laparoscopic *versus* open colorectal surgery in the acute setting (LaCeS trial): a multicentre randomized feasibility trial

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Background: **Approximately 30 000 people undergo major emergency abdominal gastrointestinal surgery annually, and 36 per cent of these procedures (around 10 800) are carried out for emergency colorectal pathology. Some 14 per cent of all patients requiring emergency surgery have a laparoscopic procedure. The aims of the LaCeS (laparoscopic *versus* open colorectal surgery in the acute setting) feasibility trial were to assess the feasibility, safety and acceptability of performing a large-scale definitive phase III RCT, with a comparison of emergency laparoscopic *versus* open surgery for acute colorectal pathology.**

Methods: **LaCeS was designed as a prospective, multicentre, single-blind, parallel-group, pragmatic feasibility RCT with an integrated qualitative study. Randomization was undertaken centrally, with patients randomized on a 1 : 1 basis between laparoscopic or open surgery.**

Results: **A total of 64 patients were recruited across five centres. The overall mean steady-state recruitment rate was 1·2 patients per month per site. Baseline compliance for clinical and health-related quality-of-life data was 99·8 and 93·8 per cent respectively. The conversion rate from laparoscopic to open surgery was 39 (95 per cent c.i. 23 to 58) per cent. The 30-day postoperative complication rate was 27 (13 to 46) per cent in the laparoscopic arm and 42 (25 to 61) per cent in the open arm.**

Conclusion: **Laparoscopic emergency colorectal surgery may have an acceptable safety profile. Registration number: ISRCTN15681041 (http://www.controlled-trials.com).**

*The LaCeS Collaborators are co-authors of this study and can be found under the heading Collaborators

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Background

The UK National Emergency Laparotomy Audit (NELA)[1] has reported that approximately 30 000 people per annum undergo major abdominal gastrointestinal surgery, and that 36 per cent of these operations (around 10 800) are carried out for emergency colorectal pathology. The management of emergency colorectal pathology can be challenging owing to the range of presenting pathology, including colorectal cancer, inflammatory bowel disease and diverticular disease, combined with variable patient physiology, associated sepsis and potentially advanced disease. Emergency colorectal surgery is associated with significant morbidity, with reported rates of postoperative morbidity and mortality of 33–71 and 14–17 per cent respectively[2,3].

A number of initiatives have been launched to improve outcomes in patients undergoing emergency laparotomy, including the use of perioperative bundles to identify high-risk patients[4,5], timely management of sepsis and delivery of consultant-led services. Surgeons have explored the possibility of adopting a laparoscopic approach in the emergency setting[6–9]. The current evidence base informing the use of laparoscopic surgical resection in the emergency colorectal setting is weak, being limited to a small number of population-based registries and retrospective cohort studies[10–12]. However, there are a number of emerging trials[13–15] successfully investigating the role

of laparoscopic lavage for perforated diverticulitis. Initial reports for colorectal resection in the emergency setting indicate benefits of laparoscopic surgery, but the findings have not been uniform across a highly selected patient population consisting of younger and physiologically fitter patients[10]. There is a lack of transparent outcome reporting, with missing data on complications, reoperation rates and mortality. In a systematic review of 39 studies, Agresta and colleagues[12] concluded that the current evidence for emergency laparoscopic colorectal surgery was 'early, controversial and focused on short term outcomes'. The lack of confirmatory data regarding the benefits of emergency laparoscopic colorectal surgery has in part led to the lack of adoption in clinical practice, with NELA[1] reporting static rates of emergency laparoscopic surgery of approximately 14 per cent over the past 3 years.

Surgical trials are associated with a number of practical and methodological challenges, which include difficulties in randomization, lack of equipoise[16], and variability in experience and delivery of surgical interventions. Surgical trials in the emergency setting add an additional layer of complexity given the time constraints associated with delivering definitive treatment, and balancing these against trial-related processes including consent and recruitment. A number of surgical trials have closed early in the emergency colorectal setting either because of poor recruitment rates[17,18] or a higher rate of adverse events than anticipated[13]. Given these recognized difficulties, a feasibility trial investigating emergency laparoscopic colorectal surgery was designed. The LaCeS feasibility trial aimed to assess the safety and acceptability of performing a phase III RCT comparing laparoscopic with open surgery for emergency colorectal pathology.

Methods

LaCeS was designed as a prospective, multicentre, single-blind, parallel-group, pragmatic feasibility RCT with an integrated qualitative study. The LaCeS feasibility trial protocol has been published previously[19]. The LaCeS feasibility trial was approved by Yorkshire and the Humber Research Ethics Committee (REC reference: 15/YH/0542).

Patients were recruited from five National Health Service (NHS) Trusts across the UK. All participating sites had dedicated emergency surgery services, with appropriate provisions and expertise to conduct laparoscopic surgery. Randomization was performed centrally, with patients randomized on a 1 : 1 basis between laparoscopic or open surgery using minimization incorporating a random element, stratified by intended consultant surgeon, patient age, BMI, ASA fitness grade, nature of the underlying pathology and intended surgical procedure. Patients were blinded to the treatment allocation for up to 7 days after surgery, or until the day of discharge if earlier.

Eligibility

Patient inclusion criteria were: age at least 18 years; acute colorectal pathology requiring resectional surgery; a National Confidential Enquiry into Patient Outcome and Death classification[20] of urgent, requiring surgery within between 2 and 6 h (classification 2A) or 6–18 h (classification 2B); suitability for both laparoscopic and open surgery; and ability to either provide written informed consent, or use of a personal consultee to provide advice on participation in the event of temporary impairment in capacity. Exclusion criteria were: haemodynamic instability requiring inotropic support; acute non-colorectal pathology; hand-assisted laparoscopic surgery; laparoscopy and peritoneal lavage alone for colorectal pathology; insertion of an endoscopic stent as a bridge to surgery; pregnancy; pre-existing cognitive impairment; and participation in another surgical trial. Surgeon eligibility criteria included: a minimum of 50 previously performed laparoscopic colorectal resections, with an annual rate of at least 20 elective laparoscopic resections, and with equivalent experience in the open setting.

Treatment

Patients received perioperative treatment according to the institutional protocol. Laparoscopic surgery included the use of multiport and single-port incisions to establish pneumoperitoneum and facilitate surgical resection. Conversion to open surgery was defined as the use of a midline laparotomy wound for any part of the colorectal dissection. The use of a midline wound to facilitate specimen extraction was permissible. Open surgery was performed through a standard midline laparotomy.

Outcome assessment

A mixed-methods approach was employed to assess recruitment, feasibility and acceptability of the trial, and also the safety profile of laparoscopic surgery in the acute setting.

Recruitment

The primary outcome measure of the LaCeS trial was the overall recruitment rate, with an anticipated recruitment rate of one patient per centre per month. Total numbers of screened, eligible and randomized patients were examined

to identify the total available population pool for inclusion in a future phase III trial. Qualitative data were gathered to assess both the practicalities of recruitment and randomization in the emergency setting.

Feasibility and acceptability of trial processes

The feasibility of data collection was examined, including the collection of data on patient and disease characteristics, operative factors, pain, health-related quality of life (HRQoL), healthcare resource use, postoperative morbidity and mortality, reoperation and readmission data. Patient-reported generic HRQoL was measured using the Short Form 12 (SF-12®; Optum, Eden Prairie, Minnesota, USA)[21] and EuroQol Five Dimensions 5 L (EQ-5D-5 L™; EuroQol Group, Rotterdam, the Netherlands)[22] questionnaires, whereas disease-specific HRQoL was assessed using the Gastrointestinal Quality of Life Index[23]. Patient-reported pain was measured using an adapted version of the Brief Pain Inventory[24]. Healthcare resource use was recorded using clinician-completed procedure and discharge forms, which documented procedure staffing, assessments conducted, imaging, medications and duration of hospital stay. Patient-completed forms captured use of primary and secondary care. Data were collected on paper by clinicians, trainees and research nurses, and uploaded centrally to the clinical trials research unit (CTRU).

The feasibility of longitudinal clinical and patient-reported data collection was assessed at baseline, 3, 7 and 30 days, and 3, 6 and 12 months (the latter using a subset of patients) after surgery. Patient questionnaires were completed in hospital; baseline questionnaires were completed before randomization. Data compliance was calculated for each of these time points as the proportion of completed case report forms or HRQoL questionnaires returned to the CTRU.

The Bang Blinding Index[25] was used to assess the success of blinding, on a scale ranging from −1 to 1; 1 indicates a complete lack of blinding, 0 is consistent with perfect blinding, and −1 indicates opposite guessing which may be related to unblinding.

The acceptability of trial processes and follow-up were assessed using in-depth qualitative interviews with clinicians and patients[19]. All interviews were informed by a topic guide, and were audio recorded and transcribed verbatim. Qualitative data were analysed using the principles of thematic analysis[26] in Nvivo[27]. Data were coded independently by two qualitative researchers for emerging themes. Codes and themes were compared and contrasted between the two researchers, and any discrepancies resolved by consensus.

Safety

The safety of laparoscopic emergency colorectal surgery was assessed by measuring intraoperative and postoperative complication and mortality rates. Patient safety indicators (PSIs), as defined by the Agency for Healthcare Research and Quality, were also collected. PSIs are a measure of adverse events that patients experience as a result of exposure to the healthcare system. Intraoperative conversion rates were also calculated.

Endpoint evaluation

Endpoint evaluation was carried out to establish optimal outcome measures and their timings to inform the design of a large-scale definitive trial. Qualitative interviews explored a range of clinical and patient-reported outcomes to identify which endpoint will have most meaning and value to clinicians and patients as a primary endpoint for a definitive trial. Candidate endpoints were analysed quantitatively for completion rates and estimation of variability to help inform future power calculations.

Sample size

The target sample size of at least 66 participants was determined to allow precise estimation of parameters of interest according to published recommendations[28] and accounting for a 10 per cent attrition rate. In addition, this sample size allowed estimation of morbidity and mortality rates in the laparoscopic arm, with 95 per cent two-sided confidence intervals of at most ±17 per cent, allowing the safety profile of laparoscopic emergency surgery to be demonstrated. Achieving this recruitment target from five centres over 15 months also allowed pragmatic estimation of the recruitment rate for a definitive phase III trial.

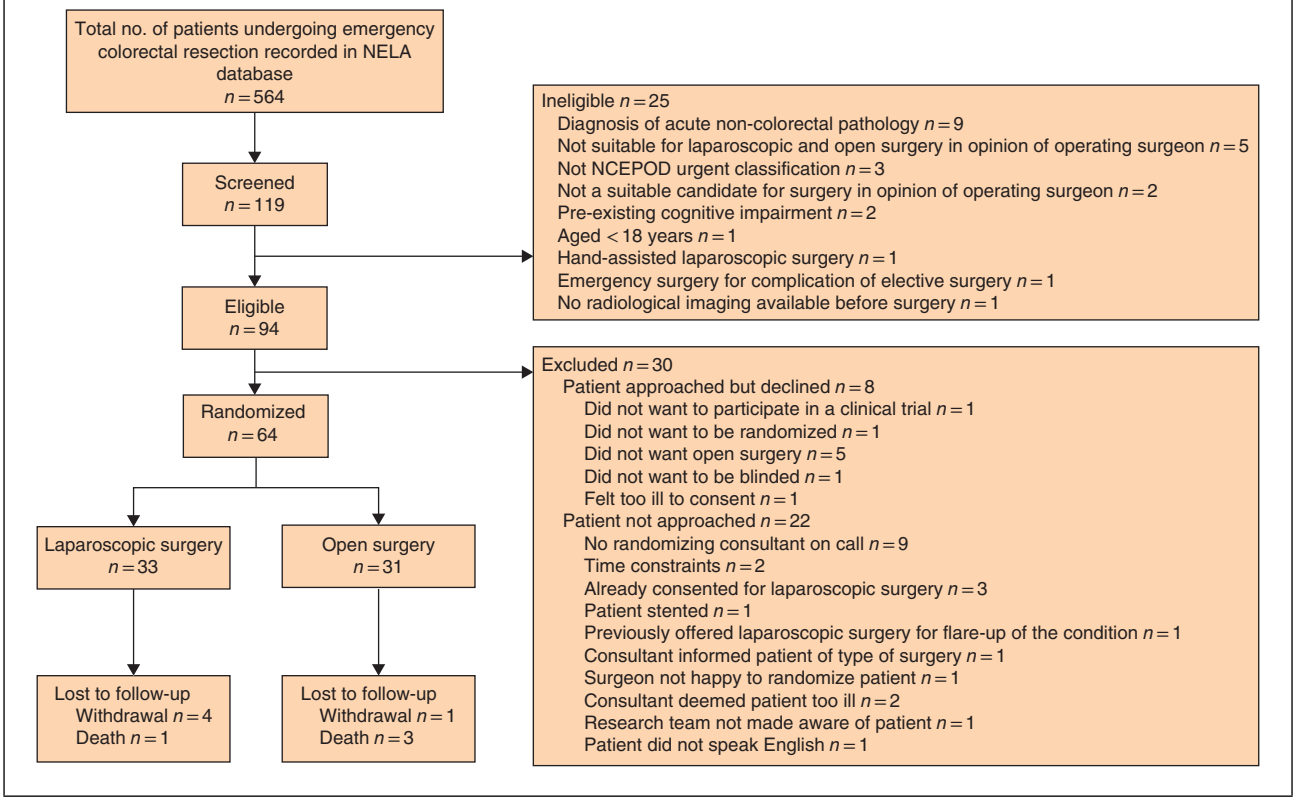
Statistical analysis

No endpoints were subjected to formal statistical testing as no statistical hypotheses were proposed or powered. Data were summarized descriptively using appropriate frequencies and summary statistics, estimating levels of variability using SAS® version 9.4 (SAS Institute, Cary, North Carolina, USA). Data summaries included all randomized patients according to the intervention received.

Results

Patients were recruited from two teaching hospitals and three district general hospitals across the UK; four sites provide emergency general surgery services and one site a

Fig 1 CONSORT diagram for the trial



NELA, National Emergency Laparotomy Audit; NCEPOD, National Confidential Enquiry into Patient Outcome and Death.

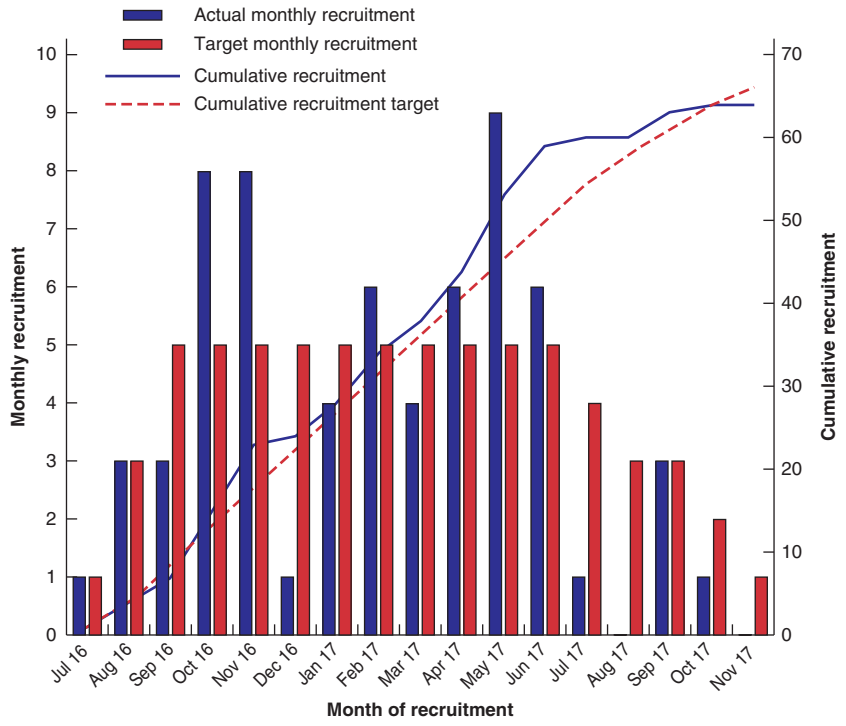
dedicated colorectal emergency surgery service. Thirteen surgeons recruited patients across all sites between July 2016 and November 2017. According to the NELA data set, 564 patients were identified as undergoing emergency colorectal resection across the five trial sites during the recruitment period. A total of 119 patients were screened and assessed for eligibility, of whom 94 (79·0 per cent) were considered eligible and 72 (77 per cent of those considered eligible) were approached to participate in the trial. A total of 64 patients were randomized (53·8 per cent of 119 screened; 89 per cent of 72 approached): 33 to laparoscopic and 31 to open surgery (*Fig. 1*). All patients received the allocated treatment. Twenty-five patients were not eligible for inclusion in the trial and eight patients declined to participate. Twenty-two screened patients were not approached by the research teams; the most common reason for this was the lack of a randomizing consultant on call.

The overall mean steady-state recruitment rate was 1·2 patients per month per site. The steady-state recruitment rate per site varied between 0·57 and 2·78 patients per month (*Fig. 2*). The overall mean steady-state recruitment rate was 0·9 patients per month per site when the lead site assumed the rate of the next highest recruiting site.

Baseline characteristics of all randomized patients are shown in *Table 1*. The recruited patient population demonstrated good representation of ages, physiological status and disease types.

Qualitative interviews were conducted with 16 trial patients (laparoscopic surgery, 6; laparoscopic procedure converted to open surgery, 3; open surgery, 7) and 14 healthcare professionals (8 consultant surgeons, 3 research nurses and 3 surgical trainees). Qualitative data indicated that the recruitment and randomization processes were acceptable. Patients were accepting of the trial design and treatment arms, and were willing to be recruited and randomized appropriately. A small proportion of patients expressed a treatment preference, but this was not considered to be a barrier to participating in the trial. Barriers to recruitment from a clinical perspective included: lack of complete equipoise, this being most relevant in younger patients and patients with inflammatory bowel disease; difficulty in addressing and challenging patient treatment preferences; and reluctance to approach acutely unwell

Fig 2 Overall and monthly recruitment to LaCeS feasibility trial



patients or patients with a complex clinical diagnosis. Organizational barriers to recruitment were lack of available colorectal surgeons on call, lack of research nurse support and lack of previous experience in recruiting into trials.

Feasibility and acceptability of trial processes

Data compliance

Overall, compliance with collection of clinical and patient-reported HRQoL data at baseline and follow-up was good (*Table 2*). Baseline compliance for clinical and HRQoL data was 99·8 and 93·8 per cent respectively. Data compliance rates related to important clinical endpoints, including conversion rates, reoperation rates, readmission rates, PSIs, duration of hospital stay, postoperative morbidity and mortality rates, and restoration of gastrointestinal function, were all above 95 per cent. Compliance rates for clinical data remained above 90 per cent throughout follow-up (*Table 2*). Compliance rates for the patient-reported HRQoL questionnaires declined during the trial follow-up period to 58·3 per cent at 12 months (*Table 2*; *Table S1*, supporting information). Healthcare resource use data provided by healthcare professionals were of high quality and in most instances achieved 100 per cent completion. Patient-completed resource use form returns declined over time but were at least 50 per cent at 6 months (*Table S2*, supporting information).

Blinding

Eight patients were unblinded during the trial: one by the anaesthetic team before surgery, two after operation, three during dressing changes, and two before filling out the Bang Blinding Index form. The Bang Blinding Index was 0·21 (95 per cent c.i. 0·14 to 0·27) in the laparoscopic and 0·53 (0·48 to 0·59) in the open arm. These results suggest that there was a failure to adequately blind patients in both treatment arms.

Acceptability of trial processes

Qualitative interviews conducted with patients identified the trial processes to be acceptable; however, patients felt that the number of questionnaires required to be completed was high. Patients thought the pain questionnaire (Brief Pain Inventory) was irrelevant and not an appropriate assessment measure in the emergency setting. They would have liked online and paper access to questionnaires. Patients found the process of blinding unnecessary, and often guessed their treatment allocation correctly. They

Table 1 Baseline characteristics

	Laparoscopic ($n = 33$)	Open ($n = 31$)	Total ($n = 64$)
Age (years)			
18–49	7	9	16
50–59	4	4	8
60–69	11	6	17
70–79	6	5	11
≥ 80	5	7	12
BMI (kg/m^2)			
< 25·0	14	14	28
25·0–29·9	12	12	24
≥ 30·0	7	5	12
ASA fitness grade			
I	6	10	16
II	22	14	36
III	5	7	12
Preoperative diagnosis			
Colorectal cancer	14	9	23
Diverticular disease	7	6	13
Inflammatory bowel disease	4	6	10
Other	8	10	18
Intended surgical procedure			
Segmental colectomy	0	1	1
Right hemicolectomy	14	10	24
Left hemicolectomy	0	1	1
Sigmoid colectomy	1	5	6
Hartmann's procedure	10	9	19
Subtotal colectomy	6	4	10
Other	2	1	3

Table 2 Data compliance at candidate time points during trial

	Clinical data compliance (%)	Overall patient-reported HRQoL questionnaire compliance (%)	Visit attendance compliance (%)		
			Attended, in hospital	Attended, via telephone follow-up	Attended, method of attendance unknown*
Baseline	99·8	93·8	n.a.	n.a.	n.a.
3 days after surgery	100	98·4	98	n.a.	n.a.
7 days after surgery	100	98·4	84	9	n.a.
30 days after surgery	95·0	76·7	28	31	22
3 months after surgery	94·8	70·7	28	38	9
6 months after surgery	98·2	64·9	31	33	6
12 months after surgery	95·5	58·3	16	47	5
Overall compliance	98·2	82·0			

Candidate time points are time points that are likely to be included in a definitive phase III trial. *Method of attendance was not collected on earlier versions of case report forms. HRQoL, health-related quality of life; n.a., not applicable.

expressed a preference to be told of their treatment allocation immediately after surgery, as opposed to being blinded for up to 7 days.

Overall, healthcare professionals were accepting of the trial design and trial-related processes. Despite appropriate measures being in place to maintain blinding, including appropriate ward notes, team briefings across all medical and nursing staff, and appropriate signage and documentation, surgeons felt that blinding was impractical in the emergency setting. The follow-up processes were deemed

Table 3 Safety data

	Laparoscopic	Open	Overall
Intraoperative complications (%)	3 (0, 16)	3 (0, 17)	3 (0, 11)
30-day postoperative complications (%)	27 (13, 46)	42 (25, 61)	34 (23, 47)
90-day postoperative complications (%)	36 (20, 55)	42 (25, 61)	39 (27, 52)
Patient safety indicators (%)	12 (3, 28)	16 (6, 34)	14 (7, 25)
30-day postoperative mortality (%)	0 (0, 11)	3 (0, 17)	2 (0, 8)
90-day postoperative mortality (%)	0 (0, 11)	3 (0, 17)	2 (0, 8)

Values in parentheses are 95 per cent confidence intervals.

to be challenging by the research nurses, as the time points did not always coincide with a natural clinical visit. However, surgeons regarded the time points as important and agreed that the proposed time points were appropriate to ensure that all relevant differences between the two treatment arms were captured appropriately. Surgeons agreed that a minimum follow-up of 12 months was necessary for appropriate evaluation of the short- and medium-term outcomes of emergency laparoscopic colorectal surgery.

Safety

Overall, the safety data obtained for laparoscopic emergency colorectal surgery indicated an acceptable safety profile. A total of 22 patients experienced a postoperative complication within 30 days; this extended to 25 patients within 90 days (*Table 3*). There were a total of four deaths during the trial period, one within 90 days of surgery.

There were 13 conversions from laparoscopic to open surgery, a rate of 39 (95 per cent c.i. 23 to 58) per cent. The decision to convert was made on establishment of pneumoperitoneum in one patient, following a period of trial dissection in 11 and because of an intraoperative complication in one patient.

Endpoint evaluation

Qualitative interviews with patients identified postoperative complications as an important outcome after emergency surgery. Other important outcomes to patients were HRQoL and postoperative recovery. Surgeons participating in the LaCeS feasibility trial shared this perspective, and considered a reduction in postoperative complications to be an important key outcome in the evaluation of laparoscopic emergency colorectal surgery.

Discussion

LaCeS has demonstrated that it is possible to recruit to a surgical trial in the emergency setting, with good compliance with trial procedures and processes, and overall acceptability by patients and clinicians. The safety data suggest that emergency colorectal laparoscopic surgery has an acceptable profile, with the morbidity rate as expected. The observed conversion rate is close to current practice; NELA[1] reported a rate of 47 per cent.

The LaCeS trial is relevant to a significant proportion of patients undergoing emergency surgery; a population of 564 patients who underwent emergency colorectal surgery across the five participating centres was identified from the NELA data set during recruitment. The steady-state rates of recruitment suggest that it is feasible to recruit across a range of hospital types and emergency surgery services, including split subspecialty (upper and lower gastrointestinal surgery) and general surgery on-call rotas. The ability to recruit across a range of hospitals is important to ensure appropriate upscaling to a definitive phase III trial, to ensure the generalizability of results, and to facilitate implementation.

Challenges to recruitment in surgical trials are well recognized, and include lack of equipoise, the complexity of combining clinical and research activities, lack of training and inability to explore patient treatment preferences[29–31]. There is a paucity of research into recruitment strategies in the emergency setting[32]. The use of qualitative methods to explore recruitment within elective clinical trials is effective in identifying challenges, proposing appropriate strategies and driving training pathways[33,34]. Qualitative initiatives such as QuinteT (qualitative research integrated in trials)[35] and Granule (generating recruiters for randomized trials in surgery) have improved how surgeons are trained to approach, recruit and randomize patients.

The routine collection of patient-reported outcome data in the emergency setting was previously documented to be of low quality, with poor reporting of baseline data[36]. This is coupled with high rates of attrition, with Mason and colleagues[37] reporting 6-week response rates of 48·4 per cent, despite an initial baseline compliance rate of 93 per cent among 156 patients presenting to emergency general surgery services. LaCeS has demonstrated that it is possible to collect high-volume, good-quality clinical and

patient-reported outcome data in the emergency setting both at baseline and during follow-up. Although attrition was noted during follow-up with regard to HRQoL data, response rates in this study were much higher than previously reported at all candidate follow-up time points[37]; the lowest response rate of 58·3 per cent was observed at 12 months. Data from qualitative patient interviews suggested that the burden of questionnaire completion was high and some questionnaires were deemed irrelevant to the patients' clinical status. It is possible that as patients improved clinically and recovered from surgery, they were less inclined to complete HRQoL questionnaires owing to the lack of relevance. The mode of follow-up visits also changed as the trial progressed, with a greater proportion of the later visits being done by telephone. Research nurses stated this made it more difficult to complete and collect HRQoL data, which may have contributed to the reduced response rates at 6 and 12 months after surgery. The collection of HRQoL data in the emergency setting therefore requires the use of appropriate, accessible and user-friendly patient-reported outcome measures, coupled with a follow-up strategy that is relevant and acceptable to patients and clinicians.

Feasibility trials are important in providing sufficient methodological evidence regarding trial design, delivery and justification. The successful delivery of the LaCeS feasibility trial has shown that it is possible to recruit in the emergency setting and to initiate trial-related processes while delivering definitive emergency care in a timely manner. This trial has enabled the authors to pilot data collection, blinding and follow-up processes, and assess their efficacy appropriately. Employing this approach before conducting a large-scale definitive trial ensures the feasibility of delivery of that trial, the acceptability and appropriate modification of the proposed trial processes. To evaluate the role, efficacy and safety of laparoscopic surgery in the emergency colorectal setting, a further large-scale, definitive phase III multicentre RCT is required. Data from the LaCeS feasibility trial have demonstrated that it is feasible to deliver such a trial of laparoscopic *versus* open emergency colorectal resection within the NHS.

Collaborators

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References

1 National Emergency Laparotomy Audit. *National Emergency Laparotomy Audit Report* 2018. https://www.nela.org.uk/reports [accessed 17 November 2018].
2 Tengberg LT, Cihoric M, Foss NB, Bay-Nielsen M, Gogenur I, Henriksen R *et al.* Complications after emergency laparotomy beyond the immediate postoperative period – a retrospective, observational cohort study of 1139 patients. *Anaesthesia* 2017; **72**: 309–316.
3 Tolstrup MB, Watt SK, Gogenur I. Morbidity and mortality rates after emergency abdominal surgery: an analysis of 4346 patients scheduled for emergency laparotomy or laparoscopy. *Langenbecks Arch Surg* 2017; **402**: 615–623.
4 Huddart S, Peden CJ, Swart M, McCormick B, Dickinson M, Mohammed MA *et al.*; ELPQuiC Collaborator Group. Use of a pathway quality improvement care bundle to reduce mortality after emergency laparotomy. *Br J Surg* 2015; **102**: 57–66.
5 Ebm C, Aggarwal G, Huddart S, Cecconi M, Quiney N. Cost-effectiveness of a quality improvement bundle for emergency laparotomy. *BJS Open* 2018; **2**: 262–269.
6 Agresta F, Ansaloni L, Baiocchi GL, Bergamini C, Campanile FC, Carlucci M *et al.* Laparoscopic approach to acute abdomen from the Consensus Development Conference of the Societa Italiana di Chirurgia Endoscopica e nuove tecnologie (SICE), Associazione Chirurghi

Ospedalieri Italiani (ACOI), Societa Italiana di Chirurgia (SIC), Societa Italiana di Chirurgia d'Urgenza e del Trauma (SICUT), Societa Italiana di Chirurgia nell'Ospedalita Privata (SICOP), and the European Association for Endoscopic Surgery (EAES). *Surg Endosc* 2012; **26**: 2134–2164.

7 Binda GA, Bonino MA, Siri G, Di Saverio S, Rossi G, Nascimbeni R *et al.*; LLO Study Group. Multicentre international trial of laparoscopic lavage for Hinchey III acute diverticulitis (LLO Study). *Br J Surg* 2018; **105**: 1835–1843.

8 Schultz JK, Wallon C, Blecic L, Forsmo HM, Folkesson J, Buchwald P *et al.*; SCANDIV Study Group. One-year results of the SCANDIV randomized clinical trial of laparoscopic lavage *versus* primary resection for acute perforated diverticulitis. *Br J Surg* 2017; **104**: 1382–1392.

9 Wright DB, Koh CE, Solomon MJ. Systematic review of the feasibility of laparoscopic reoperation for early postoperative complications following colorectal surgery. *Br J Surg* 2017; **104**: 337–346.

10 Harji DP, Griffiths B, Burke D, Sagar PM. Systematic review of emergency laparoscopic colorectal resection. *Br J Surg* 2014; **101**: e126–e133.

11 Chand M, Siddiqui MR, Gupta A, Rasheed S, Tekkis P, Parvaiz A *et al.* Systematic review of emergent laparoscopic colorectal surgery for benign and malignant disease. *World J Gastroenterol* 2014; **20**: 16 956–16 963.

12 Agresta F, Arezzo A, Allaix ME, Arolfo S, Anania G. Current status of laparoscopic colorectal surgery in the emergency setting. *Updates Surg* 2016; **68**: 47–52.

13 Vennix S, Musters GD, Mulder IM, Swank HA, Consten EC, Belgers EH *et al.*; Ladies trial colloborators. Laparoscopic peritoneal lavage or sigmoidectomy for perforated diverticulitis with purulent peritonitis: a multicentre, parallel-group, randomised, open-label trial. *Lancet* 2015; **386**: 1269–1277.

14 Angenete E, Thornell A, Burcharth J, Pommergaard HC, Skullman S, Bisgaard T *et al.* Laparoscopic lavage is feasible and safe for the treatment of perforated diverticulitis with purulent peritonitis: the first results from the randomized controlled trial DILALA. *Ann Surg* 2016; **263**: 117–122.

15 Kohl A, Rosenberg J, Bock D, Bisgaard T, Skullman S, Thornell A *et al.* Two-year results of the randomized clinical trial DILALA comparing laparoscopic lavage with resection as treatment for perforated diverticulitis. *Br J Surg* 2018; **105**: 1128–1134.

16 Kaur G, Hutchison I, Mehanna H, Williamson P, Shaw R, Tudur SC. Barriers to recruitment for surgical trials in head and neck oncology: a survey of trial investigators. *BMJ Open* 2013; **3**: e002625.

17 Oberkofler CE, Rickenbacher A, Raptis DA, Lehmann K, Villiger P, Buchli C *et al.* A multicenter randomized clinical trial of primary anastomosis or Hartmann's procedure for perforated left colonic diverticulitis with purulent or fecal peritonitis. *Ann Surg* 2012; **256**: 819–827.

18 Binda GA, Karas JR, Serventi A, Sokmen S, Amato A, Hydo L *et al.*; Study Group on Diverticulitis. Primary anastomosis *vs* nonrestorative resection for perforated diverticulitis with peritonitis: a prematurely terminated randomized controlled trial. *Colorectal Dis* 2012; **14**: 1403–1410.

19 Harji D, Marshall H, Gordon K, Crow H, Hiley V, Burke D *et al.* Feasibility of a multicentre, randomised controlled trial of laparoscopic *versus* open colorectal surgery in the acute setting: the LaCeS feasibility trial protocol. *BMJ Open* 2018; **8**: e018618.

20 National Confidential Enquiry into Patient Outcome and Death. *The NCEPOD Classification of Intervention*; 2004. https://www.ncepod.org.uk/classification.html [accessed 17 November 2018].

21 Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; **34**: 220–233.

22 EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990; **16**: 199–208.

23 Eypasch E, Williams JI, Wood-Dauphinee S, Ure BM, Schmulling C, Neugebauer E *et al.* Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. *Br J Surg* 1995; **82**: 216–222.

24 Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med* 1994; **23**: 129–138.

25 Bang H, Ni L, Davis CE. Assessment of blinding in clinical trials. *Control Clin Trials* 2004; **25**: 143–156.

26 Elo S, Kyngas H. The qualitative content analysis process. *J Adv Nurs* 2008; **62**: 107–115.

27 Silecchia G, Cavallaro G, Raparelli L, Olmi S, Baldazzi G, Campanile FC. Titanium *versus* absorbable tacks comparative study (TACS): a multicenter, non-inferiority prospective evaluation during laparoscopic repair of ventral and incisional hernia: study protocol for randomized controlled trial. *Trials* 2015; **16**: 249.

28 Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract* 2004; **10**: 307–312.

29 Blazeby J. Recruiting patients into randomized clinical trials in surgery. *Br J Surg* 2012; **99**: 307–308.

30 Blencowe NS, Brown JM, Cook JA, Metcalfe C, Morton DG, Nicholl J *et al.*; Members of the MRC Hub for Trials Methodology Research Network Workshop. Interventions in randomised controlled trials in surgery: issues to consider during trial design. *Trials* 2015; **16**: 392.

31 Cook JA. The challenges faced in the design, conduct and analysis of surgical randomised controlled trials. *Trials* 2009; **10**: 9.

32 Rowlands C, Rooshenas L, Fairhurst K, Rees J, Gamble C, Blazeby JM. Detailed systematic analysis of recruitment strategies in randomised controlled trials in patients with an unscheduled admission to hospital. *BMJ Open* 2018; **8**: e018581.

33 Elliott D, Husbands S, Hamdy FC, Holmberg L, Donovan JL. Understanding and improving recruitment to randomised controlled trials: qualitative research approaches. *Eur Urol* 2017; **72**: 789–798.
34 Rooshenas L, Scott LJ, Blazeby JM, Rogers CA, Tilling KM, Husbands S *et al.*; CSAW study group; HAND-1 study group; Optima prelim study group; Romio feasibility study group. The QuinteT Recruitment Intervention supported five randomized trials to recruit to target: a mixed-methods evaluation. *J Clin Epidemiol* 2019; **106**: 108–120.
35 Paramasivan S, Rogers CA, Welbourn R, Byrne JP, Salter N, Mahon D *et al.* Enabling recruitment success in bariatric surgical trials: pilot phase of the By-Band-Sleeve study. *Int J Obes (Lond)* 2017; **41**: 1654–1661.
36 Stevens DJ, Blencowe NS, McElnay PJ, Macefield RC, Savovic J, Avery KN *et al.* A systematic review of patient-reported outcomes in randomized controlled trials of unplanned general surgery. *World J Surg* 2016; **40**: 267–276.
37 Mason JD, Blencowe NS, McNair AG, Stevens DJ, Avery KN, Pullyblank AM *et al.* Investigating the collection and assessment of patient-reported outcome data amongst unplanned surgical hospital admissions: a feasibility study. *Pilot Feasibility Stud* 2015; **1**: 16.

Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.