EPO is required above and beyond intravenous iron in cases of pure iron deficiency. This is an important issue as EPO is associated with additional adverse reactions and many clinicians argue that it is not necessary in the case of iron deficiency. Review of the literature comparing EPO plus iron with iron alone shows increased efficacy by adding EPO to iron in patients undergoing cardiac surgery and in patients with other medical conditions.[8] This positive effect of EPO is supported by the current study.

In summary, this new study provides evidence that pragmatic approaches to treating anaemia and iron deficiency can reduce the use of allogeneic RBC transfusion and increase postoperative Hb concentration. Whether such approaches can reduce adverse effects associated with anaemia in patients undergoing cardiac surgery remains to be confirmed. In addition, with the development of additional novel treatments of anaemia, including small peptide prolyl hydroxylase inhibitors,[9] ongoing trials will be needed to assess the relative efficacy and safety of both new and older therapies.

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Emergency general surgery: can we do better?

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See **Articles** page 2213

In *The Lancet,* Carol Peden and colleagues[1] report a randomised trial of a quality improvement (QI) effort to enhance the outcomes of emergency abdominal surgery. The Enhanced Peri-Operative Care for High-risk patients (EPOCH) group attempted to implement a 37-element care bundle at 93 hospitals across the UK. National Health Service hospitals doing a substantial volume of emergency abdominal surgery and contributing to the National Emergency Laparotomy Audit were eligible for inclusion. The most frequently enrolled patients had intestinal obstruction or perforation. Institutional leaders in surgery, anaesthesia, and critical care worked with their QI teams with a primary objective to reduce 90-day mortality from 25% to 16%. Both the QI and usual care groups had a 90-day mortality of 16%. The QI group were more likely than the usual care group to have preoperative documentation of risk (66% *vs* 55%), to receive goal directed fluid therapy (59% *vs* 47%), and to have serum lactate measured at the end of surgery (60% *vs* 54%). However, secondary outcomes, including 180-day mortality, length of stay, and readmissions, also did not differ between the QI and usual care groups.

Foremost, the authors should be congratulated on accomplishing such a large-scale QI randomised

trial. This study was a pragmatic, real-world attempt at improving the quality of emergency abdominal surgery. Standardising the care of such a complex and heterogeneous patient cohort is highly challenging. These efforts require buy-in and support from multiple disciplines and many months of planning and preparation. Success has been achieved on a smaller scale. The ELPQuiC group[2] improved emergency abdominal surgery mortality in four hospitals. As noted in that previous study, and the current one, wide hospital-level variation was observed with respect to compliance with the process measures. Every hospital has its own culture and barriers to QI.

Implementation of a 37-element pathway in this QI project was very ambitious. These efforts included ten preoperative, 16 intraoperative, and 11 postoperative best practices. Some of these elements such as timely administration of antibiotics, normothermia, glucose control, and early postoperative physiotherapy should be routine for all emergency general surgery services. However, other practices such as goal-directed fluid management, measurement of serum lactate at the end of the operation, and early nutrition review might not have been routine and often take considerable time or resources to implement.

The authors acknowledge that their QI interventions were limited by time and resources, which were needed to improve patient care. The stepped-wedge cluster study design clearly limited the time for QI efforts to affect change. With this design, half of the hospitals had less than 45 weeks and some had as few as 10 weeks of observation after QI implementation. This time factor and limited QI personnel at some hospitals reduced the likelihood of observing improvements in mortality, length of stay, or readmissions. Another possibility to explain the negative results of this trial is that intraoperative decision making is key for optimal outcomes but difficult to measure.[3] In addition, data for individual complications, which vary in their effect on outcomes, were not available.[4]

The fact that the actual mortality in the QI and usual care groups (16%) was so much better than the study's estimate (25%) also influenced the results. One possible explanation is that usual care in the UK has improved in recent years. Implementation of many best practices through Enhanced Recovery After Surgery protocols might explain improved outcomes in the usual care group. Another possibility is that the EPOCH study patients were not as ill as the patients from whom the 25% mortality was derived. Only a small proportion of the study patients had intestinal ischaemia or other life-threatening conditions like toxic megacolon.

Dr Barry Slaven/Science Photo Library

The burden of emergency general surgery is only increasing as our populations age and have more comorbidities.[5] Rates of emergency general surgery are increasing in both the UK and the USA, and the cost to maintain these services is staggering.[6–9] Thus, all efforts to improve outcomes are welcome. However, improving the quality of care is difficult. The authors of the EPOCH trial clearly outlined the challenges they encountered in terms of implementing best practices. Although their work did not result in improved outcomes, this trial should not deter future efforts. Ongoing endeavours to reduce variation and implement best practices will lead to better outcomes for our patients requiring emergency general surgery.

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Peanut oral immunotherapy: balancing benefits and risks for individuals

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See **Articles** page 2222

Peanut allergy affects around 2% of the population.[1] Fatal anaphylactic reactions are rare but can occur.[2] It has a considerable negative impact on the quality of life of patients and their families,[3] and all patients need to avoid peanuts and carry self-injectable adrenaline. With many foods being labelled as "may contain nuts", complete avoidance is a challenge.[4] Until this decade, no treatment for food allergy was available;[5,6] hence considerable efforts were made to develop oral immunotherapy for food allergy.[7]

The systematic review and meta-analysis by Derek Chu and colleagues in *The Lancet* summarises the evidence for oral immunotherapy for peanut allergy.[8] Traditionally, the primary outcome for food allergy oral immunotherapy trials is passing a graded oral food challenge because this is an objective outcome that can be carefully controlled. In contrast, for their primary outcome, Chu and colleagues have used the more patient-centred endpoint of peanut-induced anaphylaxis, either as a result of unplanned exposure to peanuts or as a result of the daily doses of peanuts in the oral immunotherapy. This endpoint arguably provides a much better summary of a patient's experience in day-to-day living than one oral peanut challenge.

Tim Grist Photography/Getty Images

Their systematic review[8] included 1041 participants (median age 8·7 years [IQR 5·9–11·2]; 39% female participants) across 12 randomised controlled trials of peanut oral immunotherapy. Participants in the oral immunotherapy groups in these trials were given increasing doses of peanuts on a daily basis until they reached a maintenance dose. The median starting dose of peanut protein was 0·5 mg and the median maintenance dose was 2000 mg (about four peanuts). The meta-analysis found that oral immunotherapy actually increased the risk of anaphylaxis (relative risk 3·12 [95% CI 1·76–5·55]; no important heterogeneity).[8] This outcome contrasts with passing an oral peanut challenge, which was much more probable with oral immunotherapy (12·4 [6·82–22·61]). Oral immunotherapy also did not improve quality of life in the small number of studies that assessed it (1·21 [0·87–1·69]).

The key criticism of this systematic review[8] is inherent in its method because studies with different designs were grouped together. Although most of the trials compared immunotherapy with placebo, avoidance was the comparator in three studies and

Effectiveness of a national quality improvement programme to improve survival after emergency abdominal surgery (EPOCH): a stepped-wedge cluster-randomised trial

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Summary

Background Emergency abdominal surgery is associated with poor patient outcomes. We studied the effectiveness of a national quality improvement (QI) programme to implement a care pathway to improve survival for these patients.

Methods We did a stepped-wedge cluster-randomised trial of patients aged 40 years or older undergoing emergency open major abdominal surgery. Eligible UK National Health Service (NHS) hospitals (those that had an emergency general surgical service, a substantial volume of emergency abdominal surgery cases, and contributed data to the National Emergency Laparotomy Audit) were organised into 15 geographical clusters and commenced the QI programme in a random order, based on a computer-generated random sequence, over an 85-week period with one geographical cluster commencing the intervention every 5 weeks from the second to the 16th time period. Patients were masked to the study group, but it was not possible to mask hospital staff or investigators. The primary outcome measure was mortality within 90 days of surgery. Analyses were done on an intention-to-treat basis. This study is registered with the ISRCTN registry, number ISRCTN80682973.

Findings Treatment took place between March 3, 2014, and Oct 19, 2015. 22 754 patients were assessed for elegibility. Of 15 873 eligible patients from 93 NHS hospitals, primary outcome data were analysed for 8482 patients in the usual care group and 7374 in the QI group. Eight patients in the usual care group and nine patients in the QI group were not included in the analysis because of missing primary outcome data. The primary outcome of 90-day mortality occurred in 1210 (16%) patients in the QI group compared with 1393 (16%) patients in the usual care group (HR 1·11, 0·96–1·28).

Interpretation No survival benefit was observed from this QI programme to implement a care pathway for patients undergoing emergency abdominal surgery. Future QI programmes should ensure that teams have both the time and resources needed to improve patient care.

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See Comment page 2179

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See Online for appendix

Introduction

More than 1·53 million adults undergo inpatient surgery in the UK National Health Service (NHS) each year, with a 30-day mortality of 1·5%.[1] However, patients undergoing emergency abdominal surgery have a much greater risk of death.[2,3] Around 30 000 patients undergo emergency abdominal surgery in NHS hospitals each year, with a 30-day mortality in excess of 10%.[2] Widespread variations exist in standards of care between hospitals,[2,3] including the involvement of senior surgeons and anaesthetists and postoperative admission to critical care. These variations have been associated with differences in mortality.[2,3]

In small studies, quality improvement (QI) initiatives to implement either individual interventions or so-called bundles including several treatments, have been associated with improved survival after emergency abdominal surgery.[4–7] In a report commissioned by the UK Department of Health,[8] the Royal College of Surgeons of England proposed more extensive improvements to quality of care for this patient group. Recommendations included consultant-led decision making, cardiac output-guided fluid therapy, and early admission to critical care. However, the feasibility of implementing such an extensive acute care pathway on a national scale, and the benefits of doing so, remain uncertain. Good examples exist in which discrete QI interventions have been associated with improved patient outcomes,[9,10] but others have yielded disappointing results.[11,12] This variability is especially true for complex interventions requiring coordinated change across a health-care system.[13,14] The benefits of QI initiatives are clear to some,[15] but others question the value of these projects, citing high costs, failure to engage clinicians, and low scientific rigour.[16,17] Despite this disagreement, the direction in health-care policy is towards ever more widespread use of QI to drive large-scale change.[18]

The launch of the National Emergency Laparotomy Audit (NELA) in December, 2013,[2] provided a unique opportunity to study a QI programme to implement a

Research in context

Evidence before this study

Emergency abdominal surgery is associated with poor postoperative outcomes. Around 30 000 patients undergo emergency abdominal surgery each year in the UK National Health Service (NHS), with 30-day mortality in excess of 10% and wide variation in standards of care between hospitals. We searched MEDLINE, The Cochrane Library, Embase, and CINAHL for peer-reviewed publications describing the effects of quality improvement (QI) programmes on survival for adult patients published between Jan 1, 2000, and April 30, 2018. We searched for English language publications only using the search terms "emergency abdominal surgery" and "emergency laparotomy". Several groups have studied the effect of QI initiatives to implement individual interventions or care bundles of several treatments, and to improve care for these patients. Overall, the findings of these small studies suggest survival benefit, but most used weak, uncontrolled before-and-after study designs associated with a high risk of bias. The feasibility and benefit of a national QI programme to implement a more extensive acute care pathway for this patient group remains uncertain.

Added value of this study

We implemented a large, national QI programme to implement a care pathway for patients undergoing emergency abdominal surgery. In a stepped-wedge cluster-randomised trial of 15 873 patients aged 40 years or older, in 93 NHS hospitals organised into 15 geographical clusters, we did not identify any survival benefit at 90 or 180 days after surgery. There was good engagement with the QI programme but staff had limited time and resources to implement change. Consequently, there were only modest overall changes in the processes of patient care from before to after QI implementation. There were wide variations in intervention fidelity between hospitals, with differences in the processes that teams tried to change, the rate of change, and eventual success. These findings show that the context of quality improvement is far more complex than previously thought, especially in large national programmes. The context can be a crucial factor in the success or failure of quality improvement programmes.

Implications of all the available evidence

Despite the success of some smaller projects, there was no survival benefit from a national QI programme to implement a care pathway for patients undergoing emergency abdominal surgery. To succeed, large national QI programmes need to allow for differences between hospitals and ensure teams have both the time and resources needed to improve patient care.

complex care pathway at a national level. We aimed to evaluate the hypothesis that implementing this pathway would improve survival following emergency abdominal surgery in NHS hospitals in the UK using a stepped-wedge cluster-randomised controlled trial. We chose a stepped-wedge design to allow the delivery of the intervention at an organisational level with assessment of outcome measures at a patient level. This design allowed us to control adoption bias and adjust for time-based changes in the background level of patient care in the statistical analysis, and made it possible to offer the QI intervention to every site that took part.

Methods

Study design and participants

EPOCH was a multicentre, stepped-wedge cluster-randomised trial of a QI intervention to promote the implementation of a perioperative care pathway for patients undergoing emergency abdominal surgery in NHS hospitals in the UK.

Clusters consisted of NHS hospitals within defined geographical areas. The geographical areas were defined by the investigators and developed according to regional health-care systems, in particular junior doctor training rotations. The only part of the UK not included was Northern Ireland. We planned to include 15 geographical clusters of five to seven hospitals (appendix). Clusters were randomly assigned to one of 15 start dates for the QI intervention. Hospitals in every cluster (geographical area) started in the usual care group and ended in the QI group, resulting in 17 time periods in total. The QI intervention lasted 80 weeks (the first cluster began the intervention 5 weeks after study start), with one geographical cluster commencing the intervention every 5-week step from the second to the 16th time period. Local investigators in each geographical area were notified 12 weeks in advance of activation of the QI programme at their hospital. The organisation of hospitals into geographical clusters minimised any contamination between sites due to natural workforce movements between hospitals. NHS hospitals delivering an emergency general surgical service were eligible for inclusion in a cluster provided they undertook a substantial volume of emergency abdominal surgery cases and contributed data to NELA. Hospitals were required to nominate specialty leads from surgery, anaesthesia, and critical care, and to secure support from their NHS Trust Board or equivalent. Hospitals that were already implementing a care pathway to improve treatment for this patient group were excluded.

Patients were eligible for inclusion in the data analysis if they were aged 40 years or older and undergoing emergency open abdominal surgery in a participating hospital during the 85-week trial period from March 3, 2014, to Oct 19, 2015. Patients were excluded from the analysis if they were undergoing a simple appendicectomy, surgery related to organ transplant, bowel resection at the same

time as emergency abdominal aortic aneurysm repair, gynaecological surgery, laparotomy for traumatic injury, treatment of complications of recent elective surgery, or if they had previously been included in the EPOCH trial.

The trial was approved by the East Midlands (Nottingham 1) Research Ethics Committee (Ref: 13/EM/0415). Data were analysed without individual patient consent in accordance with section 251 of the National Health Services Act 2006. The trial protocol was published prospectively by *The Lancet* (Protocol 13PRT/7655)[19] and on the trial website.

Randomisation and masking

The chief investigator (RP) recruited hospitals and allocated them to clusters based on geography and regional health-care systems. Clusters were randomly assigned to one of 15 start dates for the QI intervention using a computer-generated random allocation sequence. An independent statistician at the Pragmatic Clinical Trials Unit generated the randomisation schedule and assigned clusters to sequences. Because local investigators were engaged in delivery of the intervention, it was not possible to mask hospital staff. Participating patients were identified and enrolled by clinical staff in participating hospitals. Patients were masked to study group allocation.

Procedures

The EPOCH trial care pathway was developed through an evidence-based Delphi consensus process to update existing guidelines published by the Royal College of Surgeons of England.[8] A list of the 37 component interventions is provided in the appendix, and a full summary of evidence grading is available on the trial website. Because of the stepped-wedge trial design, the duration of the QI intervention varied between clusters from 5 to 80 weeks. We developed an evidence-based QI programme to change the practice and culture of care for patients undergoing emergency abdominal surgery. QI leads from each stakeholder discipline (ie, surgery, anaesthesia, and critical care) were tasked with leading a hospital-wide improvement programme to implement the care pathway with the support and guidance of the national EPOCH QI team. The key features of the QI methodology were: (1) reframing the high mortality for such patients as a social problem requiring re-organisation of existing care processes rather than technical innovation; (2) supporting QI leads to engage their frontline staff and executive leaders in the change process; (3) training local QI leads in basic improvement skills based around the Model for Improvement;[20] and (4) supporting teams to analyse and feed back key process measure data to their colleagues to drive change. The EPOCH QI team provided a 1-day activation and education meeting for each geographical cluster shortly before or during the first week of activation. The purpose of this meeting was to develop the knowledge, skills, and attitudes that the QI leaders required to achieve change. Nominated QI leads were informed 12 weeks before the date of activation to the intervention. Five weeks before activation, QI leads were sent a pre-activation checklist, which included planning a local stakeholder meeting, recruiting colleagues to their change teams, and developing a presentation entitled "where we are now", including baseline data, local challenges, and ideas for improvement to share at the cluster activation meeting. The EPOCH QI team provided further advice and support by telephone and email. All QI resources, including data analysis tools, training materials, and promotional documents were available online through a virtual learning environment. Clusters were offered a half-day follow-up meeting 16 weeks after activation so that QI leads and their teams could meet and share experiences. There were also two national meetings to facilitate shared learning during the trial period. QI leads were only eligible to attend these meetings if their hospital had been assigned to the trial intervention.

For the **trial protocol** see http://www.epochtrial.org/protocol

Trial data were collected through the NELA database, and then linked using unique patient identifiers to Hospital Episode Statistics and Office for National Statistics in England and Wales, and the Information Services Division of NHS Scotland, to provide data describing mortality and hospital re-admissions.

For the **NELA database** see https://www.nela.org.uk/

Outcomes

The primary outcome measure was all-cause mortality within 90 days following surgery. Secondary outcomes were all-cause mortality within 180 days following surgery, duration of hospital stay after surgery, and hospital re-admission within 180 days of surgery. We selected ten predefined process measures (key components of the care pathway) for inclusion in the main report: (1) consultant led decision to operate; (2) consultant review of patient before surgery; (3) pre-operative documentation of risk; (4) time from decision to operate to entry into operating theatre; (5) patient entered operating theatre within time-frame specified by their urgency (<2 h, 2–6 h, 6–18 h, or >18 h); (6) consultant surgeon present in operating theatre; (7) consultant anaesthetist present in operating theatre; (8) cardiac output-guided fluid therapy used during surgery; (9) serum lactate measured at end of surgery; and (10) critical care admission immediately after surgery.

For **trial website** see http://www.epochtrial.org/epoch.php

Statistical analysis

A stepped-wedge design was chosen to improve statistical power by facilitating within-cluster comparison. Sample size calculations were based on the Hussey and Hughes approach,[21] for an analysis with fixed time effects and random cluster effects, modified to exclude data collected during the 5-week period in which the intervention commenced in individual clusters. Using Hospital Episodes Statistics data provided in the trial protocol, we estimated that 27 540 eligible patients would be registered across 90 NHS hospitals over 85 weeks, with a 90-day mortality of 25% in the usual care group, and a between-hospital coefficient of variation of 0·15. Assuming a

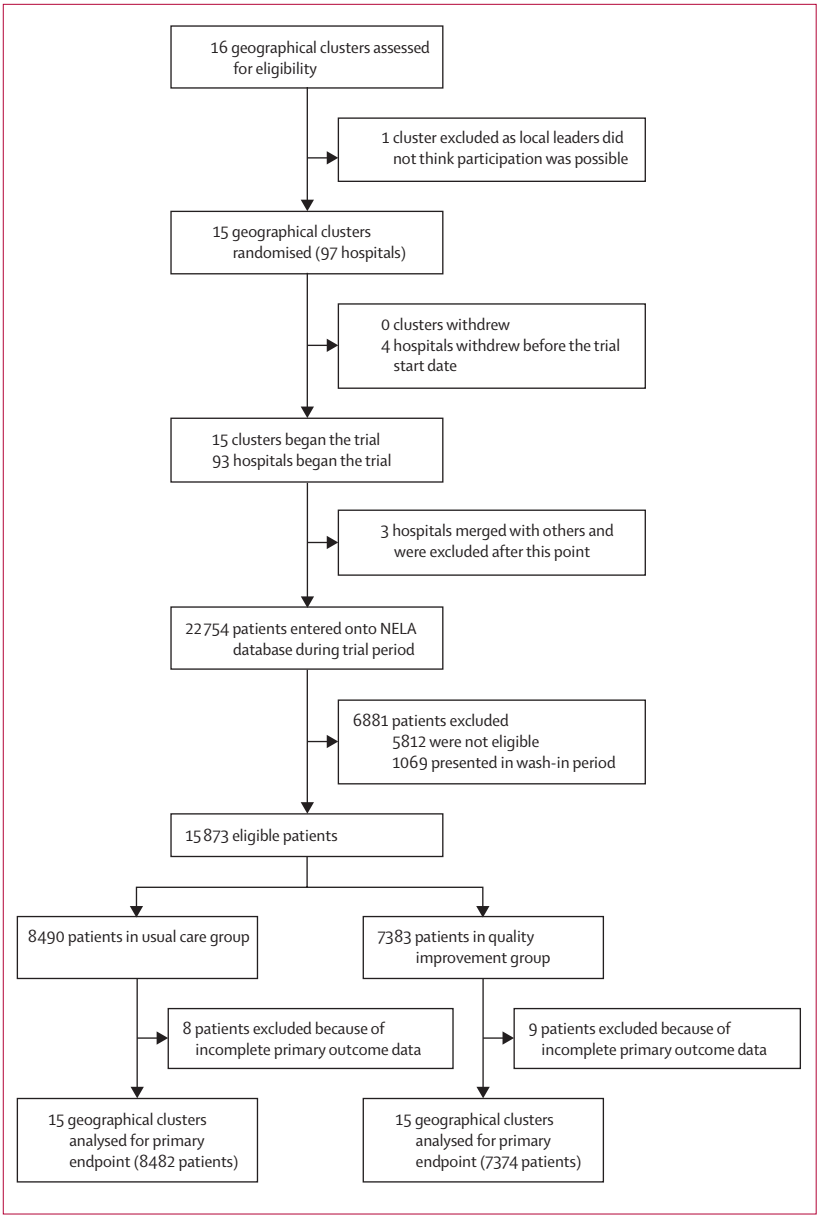

Figure 1: **Trial profile**
NELA=National Emergency Laparotomy Audit.

constant case-load (18 patients per 5 weeks per hospital), independent hospital effects, and a 5% significance level, the trial would have 92% power to detect a reduction in 90-day mortality from 25% to 22%. If the assumption of independent hospital effects was not met, and the 15 geographical clusters functioned effectively as 15 large hospitals, power would be reduced to 83%.

All analyses were done according to intention-to-treat principles. All eligible patients with available outcome data (ie, recorded in the EPOCH database) were included in the analysis, and analysed according to the randomisation schedule.[22] Patients who presented during the 5-week time period immediately after QI activation were excluded from the analysis. Hospitals that initially agreed to participate but subsequently withdrew before the trial start date were excluded; however, hospitals that withdrew after the trial start date, or did not implement the intervention, were included in the analysis. Hospitals that merged with other hospitals during the trial period were included in the analysis up to the point of the merger.

We were unable to procure data describing survival status after hospital discharge for patients in Wales. We therefore changed our primary analysis on April 4, 2018, from a binary to a time-to-event approach allowing inclusion of mortality events censored at hospital discharge. All analyses included time period as a fixed effect using indicator variables, and adjusted for age, sex, and indication for surgery using fixed factors.[23] Age was included as a continuous covariate, assuming a linear association with outcome.[24] Missing baseline data for indication for surgery were handled using a missing indicator approach.[25] All-cause mortality within 90 days of surgery was analysed using a mixed-effects parametric survival model with a Weibull survival distribution. The model included random intercepts for geographical area, hospital, and hospital period (ie, the time period within hospital). This method allowed additional correlation between patients in the same hospital and the same period, compared with patients in other periods, as is recommended.[26] All-cause mortality within 180 days was analysed using the same approach. Duration of hospital stay was analysed using competing risk time-to-event models, with mortality before the outcome event acting as the competing risk, and robust SEs to account for clustering by geographical area. The hazard ratio (HR) from this analysis measures the relative probability of hospital discharge between treatment groups, with an HR less than 1 indicating a lower probability of discharge in the QI group (and therefore longer hospital stay). Hospital re-admission within 180 days was analysed using the same approach (with an HR <1 indicating a lower probability of re-admission). All analyses were done using Stata 14.

As part of the wider EPOCH project, a prospective ethnographic evaluation was undertaken in six trial sites by researchers outside the main trial team. Ethnography draws on anthropological methods, including observation and interview, to provide a rich description of events that occur within a specific context. A maximum variation sample of sites was chosen with criteria focused on size, surgical volume, and discipline of the primary QI lead. A process evaluation was done to describe the delivery of the QI intervention. Data were collected describing the activity of QI teams and an exit questionnaire was completed by local QI leads to report their experience of the QI process. All data were collected and analysed before the main trial analysis. Detailed methods are presented in the full reports.[27,28] In this Article, we summarise key themes to provide the perspective needed to interpret our main findings. This study was registered retrospectively with the ISRCTN registry, number ISRCTN80682973.

Role of the funding source
The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of this report. RMP and BCK had full access to all the data in the study and all authors had final responsibility for the decision to submit for publication.

Results
Of 16 potentially eligible geographical clusters, 15 geographical clusters were randomly assigned to a date at which they would begin to implement the QI intervention, comprising 97 NHS hospitals. Four hospitals withdrew before the start of the trial, leaving 93 participating. Western Infirmary Glasgow merged with two non-EPOCH hospitals on June 1, 2015. This hospital merged before switching to QI, and thus enrolled only usual care patients. North Tyneside Hospital and Wansbeck Hospital merged together on June 16, 2015. These two hospitals merged after switching to QI, and thus enrolled both usual care and QI patients. Between March 3, 2014, and Oct 19, 2015, of 22 754 patients in the NELA database, 15 873 eligible patients underwent emergency abdominal surgery in participating hospitals (8490 patients were treated while their hospital was following a usual care programme [usual care group], and 7383 patients were treated while their hospital was following the QI intervention [QI group]; figure 1). Eight patients in the usual care group and nine patients in the QI group were excluded because of incomplete primary outcome data 8482 individuals in the usual care group and 7374 individuals in the QI group were included in the analysis of the primary endpoint. The mean number of analysed patients across clusters was 1057·1 (range 501–1541). Baseline characteristics were similar between groups (table 1).

Patient-level process measures are described in table 2. 91 (98%) of 93 hospitals were represented at the initial QI meeting for the relevant geographical cluster and 53 (57%) hospitals were represented at the follow-up QI meeting. This representation included a named hospital QI lead for 89 (96%) of 93 hospitals at the first meeting and 47 (51%) hospitals at the second meeting. 13 of 15 meetings occurred within 2 weeks of the activation date. In accordance with our analysis plan, we did not test the patient level process measures for statistical significance.

Complete primary outcome data were available for 8482 (>99%) patients in the usual care group and 7374 (>99%) patients in the QI group (figure 1, appendix). The primary outcome of 90-day mortality occurred in 1393 (16%) of 8482 patients in the usual care group compared with 1210 (16%) of 7374 patients in the QI group (HR 1·11, 95% CI 0·96–1·28; figure 2, table 3).

Results were similar to the 90-day data for mortality within 180 days (HR 1·12, 95% CI 0·98–1·28; appendix p 5). Patients in the QI group had a lower probability of hospital discharge (HR 0·90, 95% CI 0·83–0·97), leading to a marginally longer hospital stay (median 8 days, IQR 13–23 in the usual care group *vs* 8 days, 13–24 in the QI group), although this difference was not clinically meaningful (figure 3). No significant difference was observed between groups in hospital re-admission within 180 days (1618 [20%] of 7969 with usual care *vs* 1242 [18%] of 6723 with QI intervention; HR for re-admission 0·87 [0·73–1·04]; appendix p 6). In a secondary analysis, we found no evidence that the QI strategy became more effective the longer it had been adopted (appendix p 4). To assess the effect of missing mortality data following hospital discharge from patients in Wales, we assessed the number of mortality events that occurred after hospital discharge but before 90 days in English and Scottish hospitals. Only 631 (4·8%) of 13 034 patients died between hospital discharge and 90 days, suggesting few outcome events in Wales were missed.

	Number of patients with available data		Summary measure	
	Usual care (n=8490)	Quality improvement (n=7383)	Usual care	Quality improvement
Sex	8490 (100%)	7383 (100%)		
Female	..	..	4550 (54%)	3938 (53%)
Male	..	..	3940 (46%)	3445 (47%)
Age (years)	8490 (100%)	7383 (100%)	68 (13)	68 (13)
Indication for surgery	8477 (>99%)	7378 (>99%)		
Peritonitis	..	..	352 (4%)	251 (3%)
Perforation	..	..	765 (9%)	693 (9%)
Intestinal obstruction	..	..	3840 (45%)	3379 (46%)
Haemorrhage	..	..	213 (3%)	149 (2%)
Ischaemia	..	..	366 (4%)	332 (5%)
Abdominal infection	..	..	296 (3%)	239 (3%)
Other	..	..	523 (6%)	472 (6%)
Multiple indications	..	..	2122 (25%)	1863 (25%)
Estimated risk of death	8332 (98%)	7361 (>99%)		
Not documented	..	..	3762 (45%)	2468 (34%)
Low (<5%)	..	..	1354 (16%)	1646 (22%)
Medium (5–10%)	..	..	1019 (12%)	1102 (15%)
High (>10%)	..	..	2197 (26%)	2145 (29%)
ASA grade	8334 (98%)	7360 (>99%)		
1 (no systemic disease)	..	..	615 (7%)	533 (7%)
2 (mild systemic disease)	..	..	2815 (34%)	2461 (33%)
3 (severe systemic disease, not life threatening)	..	..	3112 (37%)	2745 (37%)
4 (severe systemic disease, life threatening)	..	..	1605 (19%)	1465 (20%)
5 (moribund patient)	..	..	187 (2%)	156 (2%)
P-POSSUM score	8338 (98%)	7370 (>99%)	7·6 (2·9–22·7)	7·4 (2·8–22·9)
Systolic blood pressure	8235 (97%)	7236 (98%)	128 (24)	128 (25)
Glasgow coma score	8269 (97%)	7311 (99%)	14·8 (1·4)	14·7 (1·5)
Blood lactate	4387 (52%)	4513 (61%)	1·6 (1·1–2·8)	1·5 (1·0–2·6)

Data are n (%), mean (SD), or median (IQR). ASA=American Society of Anesthesiologists physical status score. P-POSSUM=Portsmouth Physiological and Operative Severity Score for the enumeration of Mortality and morbidity score.

Table 1: **Baseline and pre-operative patient characteristics**

	Number of patients with missing data		Summary measure	
	Usual care (n=8490)	Quality improvement (n=7383)	Usual care (n=8490)	Quality improvement (n=7383)
Consultant decision to operate	184 (2%)	72 (1%)	7472/8306 (90%)	6589/7311 (90%)
Consultant reviewed patient at time of decision	448 (6%)	334 (5%)	5961/7024 (85%)	5271/6255 (84%)
Pre-operative documentation of risk	158 (2%)	22 (<1%)	4570/8332 (55%)	4893/7361 (66%)
Patient entered operating theatre within specified urgency time frame	1012 (12%)	430 (6%)	5636/7478 (75%)	5515/6953 (79%)
Consultant surgeon present in operating theatre	155 (2%)	17 (<1%)	7117/8335 (85%)	6472/7366 (88%)
Consultant anaesthetist present in operating theatre	160 (2%)	14 (<1%)	6313/8330 (76%)	5832/7369 (79%)
Goal directed fluid therapy used during surgery	180 (2%)	24 (<1%)	3942/8310 (47%)	4329/7359 (59%)
Serum lactate measured at end of surgery	171 (2%)	24 (<1%)	4474/8319 (54%)	4431/7359 (60%)
Time from decision to operate to entry into operating theatre (hours)	630 (7%)	417 (6%)	5·0 (2·1–16·8)	4·3 (2·0–15·3)
Critical care admission immediately after surgery*	163 (2%)	22 (<1%)	5395/8298 (65%)	5050/7334 (69%)

Data are n (%), n/N (X), or median (IQR). *29 patients in the usual care group and 27 patients in the quality improvement group died during surgery.

Table 2: Patient level process measures

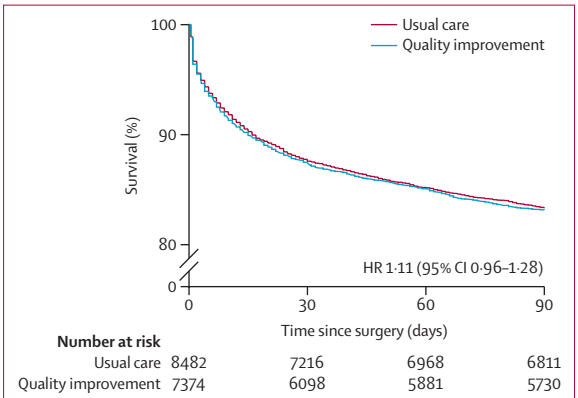

Figure 2: All-cause mortality within 90 days of emergency abdominal surgery

Our prospective ethnographic study and process evaluation are reported in full elsewhere.[27,28] The findings showed that teams reflected positively on the QI programme, in particular the practical nature of the activation and education meetings, and the opportunity to share ideas and learn from others, and the utility of the online resources. However, staff in each of the six sites studied encountered multiple challenges as they attempted to improve patient care during the intervention period and often had little or no additional time in their job plans to accommodate this change. In particular, the task of collecting and entering data into the NELA database was more time consuming than expected. In addition, we observed differences in the fidelity with which teams used our recommended QI methods, differences in the clinical processes teams chose to attempt to change, the rate of this change, and the eventual degree of success. Even among the sites that adhered to the QI intervention more closely, local adaptations to the care pathway were required to make this change fit with the prevailing conditions of the hospital. The ethnographic evaluation supported the primarily social nature of the trial intervention. To a large extent, more successful QI teams drew on existing relationships within their hospital to influence colleagues and make change happen. Successful change seemed to be linked to the strength and number of these relationships; for QI teams in which these relationships were absent, additional effort was required to garner support for change. These findings suggest that although the QI programme might have provided QI leads and their teams with additional capabilities to lead change, the capacity to make change happen, especially in terms of protected time, was absent. The extent to which the QI programme was delivered as intended, and enablers and barriers to change are described in full in the report of the EPOCH trial process evaluation.[28]

Discussion

The principal finding of this trial was that there was no survival benefit associated with a national QI programme to implement an evidence-based care pathway for patients undergoing emergency abdominal surgery. Furthermore, no beneficial effects were observed for 180-day mortality, length of hospital stay, or frequency of hospital re-admission. At a national level, there were only modest improvements among the ten measures selected to reflect key processes of care within the pathway. In some hospitals, the baseline rate of adherence to process measures was higher than anticipated. Experience from individual hospitals suggested wide variations in which of the 37 pathway elements local QI teams chose to tackle, the rate of change they achieved, and their eventual success. The baseline contexts of participating hospitals also differed. Implementation of change was slower when existing relationships within and beyond the perioperative team were weaker, and so QI leads had to spend time developing relationships with stakeholders. At the time of trial design, the EPOCH care pathway was widely agreed

	Number of patients included in analysis		Summary outcome measure		
	Usual care (n=8490)	Quality improvement (n=7383)	Usual care	Quality improvement	HR (quality improvement *vs* usual care)
All-cause mortality within 90 days of surgery	8482 (>99%)	7374 (>99%)	1393/8482 (16%)	1210/7374 (16%)	1·11 (0·96–1·28)
All-cause mortality within 180 days of surgery	8482 (>99%)	7374 (>99%)	1698/8482 (20%)	1440/7374 (20%)	1·12 (0·98–1·28)
Duration of hospital stay (days)	8320 (98%)	7353 (>99%)	8 (IQR 13–23)	8 (IQR 13–24)	0·90 (0·83–0·97)
Hospital re-admission within 180 days of surgery	7969 (94%)	6723 (91%)	1618/7969 (20%)	1242/6723 (18%)	0·87 (0·73–1·04)

Data are median (IQR), n (%), n/N (%), or HR with 95% CI. HR=hazard ratio.

Table 3: **Patient outcomes**

to represent an achievable standard of care that informed clinicians would wish to deliver for their patients, but commonly did not provide because of poor awareness among the perioperative team. Our findings reveal that implementation of such an extensive care pathway was a more complex challenge than expected by our clinical community. It is important to interpret the results of this trial alongside those of the ethnographic study and process evaluation,[27,28] which together suggest that QI programmes designed to implement complex care pathways require more resources than that allotted in the present trial, with dedicated time for clinical teams to focus on implementing change.

Several reports have been published on the effects of small-scale QI projects to improve outcomes for patients undergoing emergency abdominal surgery. In the UK, the ELPQuiC group[4] examined the implementation of a care bundle of five interventions in four NHS hospitals in an uncontrolled before-and-after study. They reported a reduction in mortality (risk ratio 0·61, 95% CI 0·45–0·84) among 726 patients. This study design is more prone to bias than a stepped-wedge cluster-randomised trial.[29] The difference in findings might also relate to the simpler intervention, and stronger pre-existing relationships between staff leading implementation in these early adopter hospitals. The simpler objective was more readily achieved than that of the national EPOCH trial, which set more ambitious targets in hospitals in which there might have been a less favourable context for change than hospitals in the ELPQuiC study. Researchers from Denmark[5–7] reported differing results from three separate studies of perioperative QI interventions for patients undergoing emergency abdominal surgery. The PULP study group[6] used an uncontrolled before-and-after design with historical controls to study the effect of a multidisciplinary perioperative care protocol in seven hospitals and reported a considerable reduction in 30-day mortality. However, 56 of the 173 patients allocated to the study intervention were excluded from the analysis because they did not receive the full intervention, making it harder to interpret these findings. The InCare group[5] did not identify any beneficial effect on 30-day survival from

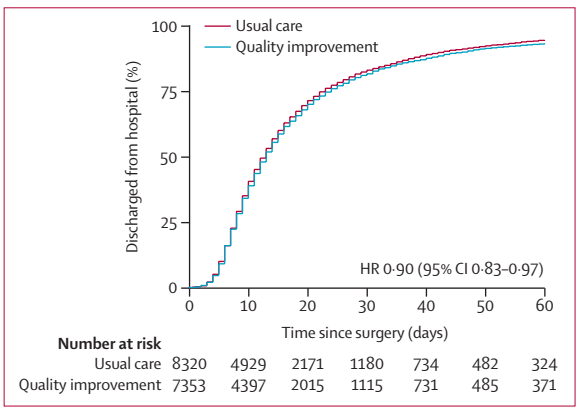

Figure 3: **Duration of hospital stay after emergency abdominal surgery**

admission to an intermediate unit (critical care) among 286 patients undergoing emergency abdominal surgery in seven hospitals. This intervention appeared to change the process of patient care in the 48 h following surgery, but the study was stopped for futility partly because of a lower than expected mortality in both treatment groups. Finally, the AHA group[7] again studied the effect of a multidisciplinary protocol in a single-centre uncontrolled before-and-after study with historical controls, finding a more modest reduction in 30-day mortality from 22% in 600 control patients to 16% in 600 intervention patients. It is possible that a background trend to improved survival might explain the findings of these previous studies, especially given the growing international focus on poor patient outcomes following emergency abdominal surgery. Although our analysis accounts for temporal trends during the EPOCH trial, it is possible that a general trend for decreasing mortality beforehand might explain why the mortality was lower than that predicted from NHS registry data. Since the completion of EPOCH, a further quality improvement project in 28 NHS hospitals was more successful in achieving change in processes of care for patients having emergency abdominal surgery.[30] This project involved the implementation of a more discrete bundle of six interventions over a longer time period than the EPOCH intervention. This approach was associated with

decreasing mortality over time although the causal relationship to the intervention is unconfirmed. Meanwhile, studies of QI in other clinical areas have delivered mixed results.[31–34] These findings suggest that more focused, discrete clinical interventions might be more successfully implemented than interventions that include larger numbers of care processes. The evidence is less clear in defining the optimal improvement methods. Several theoretical models of implementation exist, including the Consolidated Framework for Implementation Research and the COM-B model.[35,36] These models provide frameworks for designing and evaluating effective implementation, clinical processes, and behaviour change. However, none of the models gives emphasis to institutional support or protected leadership time. Our findings suggest that these more practical considerations are essential for clinicians to successfully lead QI projects. In the EPOCH trial, teams were encouraged to begin with easier interventions, before building towards full pathway implementation. However, our process evaluation reveals that many teams did not have the time or capacity to progress beyond simpler interventions (eg, documentation of patient risk) to implementation of more important but challenging interventions such as admission to critical care. It is also important to note that NELA was launched only 3 months before the EPOCH trial commenced. Our ethnographic findings[27] suggest that the task of collecting and entering data into the NELA database was more time consuming than expected, leaving some QI leads with little time to focus on change. We allowed a 5-week period for the transition between usual care and the launch of the QI programme in each cluster. Longer transition and intervention periods with dedicated time for QI leads to plan, negotiate, and implement change might have led to more successful implementation. However, we also note that there was no evidence of survival benefit among hospitals using the QI programme for longer than 10 weeks, which included hospitals that were using the programme for up to 80 weeks.

The strengths of this trial include wide generalisability (ie, large number of consecutive patients enrolled by many hospitals), robust trial design, and the devolved leadership to local clinical QI teams. The EPOCH care pathway was developed through a Delphi consensus process to update national professional guidelines.[8] As with many evidence-based treatment guidelines, some recommendations were graded as strong although the available evidence was weak. The choice of component interventions such as critical care admission and consultant-led care was primarily based on expert opinion; it is unclear how this evidence base could be improved. Partnership with NELA allowed an efficient trial design with no additional data collection for participating staff. However, our final dataset required linkage to four national registries in the devolved nations of the UK, and despite completing the trial on time, some organisations involved imposed substantial delays in access to these datasets. On several occasions, organisations changed their position on information governance regulations, requiring revision of previous agreements between each of the parties involved. In hindsight, we would have encountered fewer problems had we confined the trial to the jurisdictions of fewer organisations with information governance oversight. Despite the large sample, fewer patients than expected underwent emergency abdominal surgery, and 90-day mortality was lower than anticipated. The sample size calculation was based on Hospital Episodes Statistics data, which do not provide a specific diagnostic code for emergency abdominal surgery. Instead we identified a series of codes for relevant procedures. We chose to power the trial to detect a very modest treatment effect, partly to accommodate the possibility that these data were poorly representative of the EPOCH trial population. However, the 95% CI for our primary effect estimate was narrow, with a lower limit that indicates a maximum potential relative mortality reduction of 4%. Our findings are unlikely to change with a larger sample size. Because of difficulty in obtaining post-discharge survival data in Wales, we changed our primary analysis from a binary to a time-to-event approach, allowing inclusion of mortality events censored at hospital discharge. However, post-discharge data from England and Scotland suggest few events were missed through this approach. The additional application required to obtain post-discharge mortality data for Wales would have further delayed the trial results by many months.

In this stepped-wedge cluster-randomised trial, we did not identify any survival benefit from a national QI programme to implement an enhanced pathway of care for patients undergoing emergency abdominal surgery. This finding is likely to be due to variation between hospitals in fidelity of implementation, prioritisation of pathway components, and the time required to achieve effective change. These findings suggest future QI programmes should implement fewer, more discrete changes and ensure leadership teams have adequate time to achieve sustained improvements in patient care. Undue emphasis on success stories from small early studies might lead us to under-estimate the requirements for successful QI interventions.

Contributors

CJP, TS, GM, BCK, AT, KR, DW, GR, SK, JB, and RMP contributed to protocol development and design of the EPOCH trial. CJP and TS designed and delivered the EPOCH QI Programme. TS, RMP, and CJP led the process evaluation with input from GM. GM led the ethnographic study with input from TS, CJP, and RMP. RMP, AT, TS, BCK, and SK were responsible for conduct of the trial. All authors read and approved the final manuscript.

Declaration of interests

CJP reports personal fees from Merck, the Institute for Healthcare Improvement, and Fidelity Health outside the submitted work. RMP reports personal fees from GlaxoSmithkline, grants and personal fees from Edwards Lifesciences, grants from Intersurgical, grants from

B Braun, and personal fees from Medtronic outside the submitted work. CJP, RMP, SK, KR, and GM report grants from National Institute for Health Research during the conduct of this trial. All other authors declare no competing interests.

Data sharing

Due to information governance restrictions imposed by organisations governing data access, we are unable to share the trial data unless applicants secure the relevant permissions. All trial materials are freely available on the trial website (https://www.epochtrial.org).

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